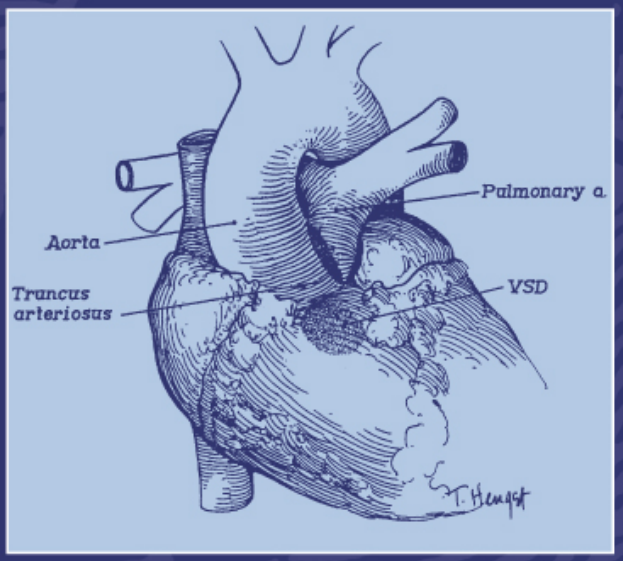
# Anesthesia for Congenital Heart Disease

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# Foreword by George A. Gregory

During the past 50 years, enormous progress has been made in the diagnosis and treatment of congenital cardiac lesions. Physicians and surgeons have gone from only being able to close a patent ductus arteriosus to performing cardiac surgery *in utero*. Between these two extremes is the ability to repair or palliate many life-threatening lesions with great success. Those of us who have lived through this development find it truly amazing. Much of the success of such surgical ventures is the result of the better understanding of cardiac disease, pathophysiology, and physiology that have come from the laboratories of many people, including Abe Rudolph and his associates at the University of California, San Francisco. As a result of the advances in echocardiography for rapid and accurate diagnosis of congenital heart lesions in the intensive care nursery and the extension of this technique into the operating room, neonates, infants and children can now have corrective surgery, and residual lesions can be detected before the operation is ended. The ability to perform the complicated and dangerous procedures now done routinely would not be possible without the pre and postoperative care infants and children receive in intensive care units. The use of positive end-expiratory pressure during mechanical ventilation or spontaneous breathing and the development of new techniques for mechanical ventilation has allowed many patients to survive and the routine rapid availability of ECMO now permits some patients to live who never could have done so in the past.

*Anesthesia for Congenital Heart Disease* brings together in one place the advances that have occurred in pediatric cardiac anesthesia over this time. It presents in a well thought out, organized way an approach to understanding this complex and exciting area of medicine. For those of us who pioneered the development of this field, this book is like seeing a child grow up and become mature. But in reality it provides a wonderful way for clinicians at all levels of knowledge to understand the complexities of the field and does so based on a thorough understanding of physiology, pharmacology, and clinical medicine. This information will lead to better care for and improve the lives of infants and children. In the end, this is what it is all about!

*George A. Gregory*, MD
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November 2003

# Foreword by Burdett S. Dunbar

This book represents what I consider to be the coming of age for pediatric cardiovascular anesthesiology. It represents the careful documentation of a rapidly growing, team-oriented approach to patient care. Up-to-date in every sense of the word, this volume sets out what the experience has been from a broad spectrum of experts in this special field of caring for children with congenital heart disease.

Recently, Arthur S. Keats, MD, who is arguably a father, if not the father, of the specialty, was honored by having his name attached to the pediatric cardiovascular anesthesiology section at Texas Children's Hospital and the Baylor College of Medicine, Houston, Texas. In his acknowledgement, he remarked that he had never, until then, used the words "pediatric cardiovascular anesthesiology" together in a sentence.

That statement crystallizes the enormous progress in cardiac surgical and anesthesia care for pediatric patients, who undergo surgery at increasingly younger ages. *In utero* correction has already been accomplished.

This book details the dramatic improvement in mortality; the broadening effort of anesthesiologists in perioperative care of children with heart disease; the essential requirements for team-based actions and the emphasis so necessary to details of pathology, physiology, pharmacology, and genetics among other disciplines and research areas. I congratulate the authors and especially the editors, two of whom are colleagues at Baylor College of Medicine and Texas Children's Hospital, for the production of this textbook.

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# Preface

Care of the patient with congenital heart disease has undergone a dramatic transformation over the past 20 years. Nearly every congenital cardiac lesion is amenable to some form of surgical or catheter therapy, and anesthesiologists are faced with a bewildering array of diagnoses and procedures. Treatment for congenital heart disease now literally begins *in utero*, does not exclude tiny premature newborns, and includes an ever-growing population of teenagers and adults, who are survivors of lesions that were fatal even a few years ago. Indeed, survival for congenital heart surgery, even in an increasingly complex patient population, is over 98% in the most successful centers around the world. Anesthesiologists have helped create and sustain several generations of patients with congenital heart disease, and we are obligated to continue to care for them with compassion and skill. New cardiac surgical procedures, invasive catheter therapies, and diagnostic modalities such as cardiac magnetic resonance imaging challenge us to be creative and resourceful. Larger numbers of patients with complex lesions, such as patients with a single ventricle, present for more frequent and invasive non-cardiac surgery, taxing the expertise of the anesthesiologist. There is a need for an up-to-date textbook authored and edited by experts in the field of anesthesia for congenital heart disease, who have extensive current experience in caring for these patients, and in performing the research and conducting the education and training that is moving the field forward.

*Anesthesia for Congenital Heart Disease* recognizes the life-long nature of these disorders and the improved survival and quality of life in our patient population. We have included an illustration depicting truncus arteriosus on the cover because it was the first complex lesion to undergo complete correction in the newborn period, beginning in the early 1970s, and today we treat patients with this diagnosis from the newborn period through adulthood. This textbook includes chapters on non-cardiac procedures, catheterization laboratory anesthetic care, and cardiac intensive care recognizing the crucial importance of anesthesiologists' involvement in these areas. Congenital heart disease is truly not only pediatric in nature, and we have devoted a significant portion of this text to the older patient. Neurologic monitoring and outcome is emerging as one of the most important areas of research and progress in improving outcomes in our patients, and is emphasized in this book. Every chapter is authored by anesthesiologists with outstanding expertise in caring for patients with congenital heart disease, and who also contribute significantly to the research, education, and training in our field. It is our hope that this volume will help to teach all who are interested in the anesthetic care of the patient with congenital heart disease, and that it may contribute to improved outcomes for our patients.

*Dean B. Andropoulos*, MD
*Stephen A. Stayer*, MD
*Isobel A. Russell*, MD, PhD
November 2003

# Acknowledgements

The editors would like to acknowledge the tireless efforts of their institutions' editorial staffs. At Texas Children's Hospital/Baylor College of Medicine: Barbara S. Skjonsby, RN, Pediatric Anesthesia Research Nurse (and former high school English teacher) for diligence in improving the language and grammar of the text, and for performing the final formatting; Deborah L. East, RN, Pediatric Cardiovascular Anesthesia Research Nurse, for many hours working on formatting, locating thousands of references, and perfecting the art and science of producing figures and obtaining permissions; and at the University of California, San Francisco: Deryck Lodrick, PhD, for editorial advice. Their efforts have truly made this textbook a reality.

We would like to thank the extraordinary group of anesthesiologists and their associates, for their labors in writing the chapters of this book. They have all taken the time from their incredibly stressful, busy and typically overextended schedules to share their immense expertise in these pages. Their efforts will serve well all who provide anesthesia care to patients with congenital heart disease.

We would also each like to acknowledge the encouragement of our families, and in particular our spouses: Julie Andropoulos, Marce Stayer, and John Russell. Each of them has supported us and our respective families through the countless hours of weekend and evening work so that we could complete this text.

## Dedication

This book is dedicated to Arthur S. Keats, MD, the first anesthesiologist for cardiovascular surgery at Texas Children's Hospital and the Baylor College of Medicine. In 1955 Dr Keats, with Dr Denton, A. Cooley, and Dr Dan McNamara, began a remarkable era, pioneering many techniques in diagnosis and treatment of congenital heart disease, particularly in infants. Dr Keats is an inspiring figure who faced the daunting task of caring for these critically ill patients without the technology available today; his skill and compassion in producing remarkable results attests to the fact that he is a true giant in our field. We are proud to call him the founder of our service at Texas Children's Hospital.

This book is also dedicated to Susheela Sangwan, MD, who dedicated her life to the care of patients with congenital heart disease. Her excellence in clinical care and teaching skills resulted in significant contributions to the development of pediatric cardiac anesthesia.

# 1 History, education, and science

# 1 History of anesthesia for congenital heart disease

Dolly D. Hansen
Paul R. Hickey

## Introduction

Over the last 60 years pediatric cardiac anesthesia has developed as a subspecialty of pediatric anesthesia or, a subspecialty of cardiac anesthesia, depending on one's perspective. It is impossible to describe the evolution of pediatric cardiac anesthesia without constantly referring to developments in the surgical treatment of congenital heart disease (CHD) because of the great interdependency of the two fields. As pediatric anesthesia developed over the years surgical treatments of children with CHD were invented, starting with simple surgical ligation of a patent ductus arteriosus (PDA) to sophisticated, staged repair of complex intracardiac lesions in low birthweight neonates requiring cardiopulmonary bypass (CPB) and circulatory arrest. Practically every advance in surgical treatment of CHD had to be accompanied by changes in anesthetic management to overcome challenges that impeded successful surgical treatment or mitigated morbidity associated with surgical treatment.

This history will mostly be organized around the theme of how anesthesiologists met these new challenges using the then-available anesthetic armamentarium. The second theme running through this story is the slow change of interest and focus from just events in the operating room (OR) to perioperative care in its broadest sense, including perioperative morbidity. The last theme is the progressive reduction in the age of patients routinely presenting for anesthesia and surgery from the 9-year-old child undergoing the first PDA ligation in 1938[1] to the fetus recently reported in *The New York Times* in 2002[2] who had aortic atresia repaired *in utero*. Interestingly, both patients had had their cardiac procedures at the same institution!

This story will be told working through the different time frames. The first years, 1938–54; CPB and early repair, 1954–70; deep hypothermic circulatory arrest (DHCA) and the introduction of prostaglandin $E_1$ ($PGE_1$), 1970–80; hypoplastic left heart syndrome (HLHS), 1980–90; refinement and improvement in mortality/morbidity, 1990–2000.

## The first years, 1938–54

These years began with the ligation of the PDA and continued with palliative operations. The first successful operation for a CHD occurred in August 1938 when Robert E. Gross ligated the PDA of a 9-year-old girl. The operation and the postoperative course were smooth, but because of the interest in the case the child was kept in the hospital until the 13th day. In the report of the case Gross mentions that the operation was done under cyclopropane anesthesia, and continues: "The chest was closed, the lung being re-expanded with positive pressure anesthesia just prior to placing the last stitch in the intercostal muscles."[1]

A nurse using a "tight fitting" mask gave the anesthetic. There was no intubation and of course no postoperative ventilation. The paper does not mention any particular pulmonary complications so it cannot have been much different from an ordinary postoperative course of the day.[1]

In 1952 Dr Gross published a review of 525 PDA ligations where many, if not all, of the anesthetics were administered by the same nurse anesthetist, under surgical direction.[2] Here he states, "formerly we employed cyclopropane anesthesia for these cases, but since about half of the fatalities seemed to have been attributable to cardiac arrest or irregularities under this anesthetic, we have now completely abandoned cyclopropane and employ ether and oxygen as a routine."[3] It is probably correct that cyclopropane under these circumstances with insufficient airway control were more likely to cause cardiac arrhythmias than ether. An intralaryngeal airway was used which also served "to facilitate suction removal of any secretions from the lower airway" (and we may add, the stomach). Dr Gross claimed that the use of this airway reduced the incidence of postoperative pulmonary complications. Without having a modern, rigorous review of this series, it is hard to know what particular anesthetic challenges other than these confronted the anesthetist, but we may assume that intraoperative desaturation from the collapsed left lung, postoperative pulmonary complications,

and occasional major blood loss from an uncontrolled, ruptured ductus arteriosus were high on the list.

The next operation to be introduced was billed as "corrective" for the child with cyanotic CHD and was the systemic to pulmonary artery shunt. The procedure was proposed by Helen Taussig as an "artificial ductus arteriosus" and first performed by Albert Blalock at Johns-Hopkins Hospital in 1944. In a very detailed paper, Drs Blalock and Taussig described the first three patients to undergo the Blalock–Taussig shunt operation. Dr Harmel anesthetized the first and third patients, using ether and oxygen in an open drop method for the first patient and cyclopropane through an endotracheal tube for the third patient. The second patient was given cyclopropane through an endotracheal tube by Dr Lamont. Whether patients 1 and 3 were intubated is unclear, but it is noted that in all three cases positive pressure ventilation was used to reinflate the lung.[4] Interestingly, in this early kinder and gentler time, the surgical and pediatric authors reporting the Blalock–Taussig operation acknowledged by name the pediatricians and house officers who took such good care of the children postoperatively but still did not acknowledge in their paper the contribution of the anesthesiologists Lamont and Harmel!

Although intubation of infants was described by Gillespie as early as 1939 it is difficult to say exactly at what time intubations became routine.[5]

Doctors Harmel and Lamont, who were anesthesiologists, reported in 1946 on their anesthetic experience with 100 operations for congenital malformations of the heart "in which there is pulmonary artery stenosis or atresia."[6] They reported 10 anesthetic-related deaths in the series, so it is certain that they encountered formidable anesthetic problems in these surgical procedures.[6] This is the first paper we know of published in the field of pediatric cardiac anesthesia.

In 1952 Damman and Muller reported a successful operation in which the main pulmonary artery was reduced in size and a band placed around the artery in a 6-month-old infant with single ventricle (SV). It is mentioned that morphine and atropine were given preoperatively but no further anesthetic agents are mentioned. At that time infants were assumed to be oblivious to pain so we can wonder what was used beyond oxygen and restraint.[7]

Over the next 20 years many palliative operations for CHD were added and a number of papers appeared describing the procedures and the anesthetic management. In 1948 McQuiston described the anesthetic technique used at Children's Memorial Hospital in Chicago.[8] This is an excellent paper for its time, but a number of the author's conclusions are erroneous, although they were the results of astute clinical observations and current knowledge at the time. The anesthetic technique for shunt operations (mostly Potts' anastomosis) is discussed in some detail, but is mostly of historical interest today. McQuiston explained that he had no experience with anesthetic management used in other centers such as the pentothal-$N_2O$-curare used at Minnesota or the ether technique used at the Mayo Clinic. McQuiston used heavy premedication with morphine, pentobarbital and atropine and/or scopolamine; this is emphasized because it was important "to render the child sleepy and not anxious."[8] The effect of sedation with regard to a decrease in cyanosis (resulting in making the child look pinker) is noted by the authors. They also noted that children with severe pulmonic stenosis or atresia do not decrease their cyanosis "because of very little blood flow," and these children have the highest mortality.

McQuiston pointed out that body temperature control was an important factor in predicting mortality and advocated the use of moderate hypothermia, i.e. "refrigeration" with icebags, because of a frequently seen syndrome of hyperthermia. McQuiston worked from the assumption that hyperthermia is a disease in itself, but did not explore the idea that the rise in central temperature might be a symptom of low cardiac output with peripheral vasoconstriction. Given what we now know of shunt physiology, it is interesting to speculate that this "disease" was caused by pulmonary hyperperfusion after the opening of what would now be considered as an excessively large shunt, stealing a large portion of systemic blood flow.

In 1950 Harris described the anesthetic technique used at Mount Zion Hospital in San Francisco. He emphasized the use of quite heavy premedication with morphine, atropine and scopolamine. The "basal anesthetic agent" was Avertin (tribromoethanol). It was given rectally and supplemented with $N_2O/O_2$ and very low doses of curare. Intubation was facilitated by cyclopropane. The $F_{IO_2}$ was changed according to cyanosis, and bucking or attempts at respiration were thought to be due to stimulation of the hilus of the lung. This was treated with "cocainization" of the hilus.[9]

In 1952 Dr Robert M. Smith discussed the circulatory factors involved in the anesthetic management of patients with CHD. He pointed out the necessity to understand the pathophysiology of the lesion and also "the expected effect of the operation upon this unnatural physiology."[10] That is, he recognized that the operations are not curative. The anesthetic agents recommended were mostly ether following premedication.

While most of these previous papers had been about tetralogy of Fallot (TOF), Dr Smith also described the anesthetic challenges of surgery for coarctation of the aorta. He emphasized the hypertension following clamping of the aorta and warned against excessive bleeding in children operated on at older ages using ganglionic blocking agents. This bleeding was far beyond what anesthesiologists now see in patients operated on at younger ages, before the development of substantial collateral arterial vessels.[10]

## The heart–lung machine, 1954–70

From 1954 to 1970 the development of what was then called the "heart–lung machine" opened the heart to surgical repair of complex intracardiac congenital heart defects. At the time, the initial high morbidity of early CPB technology seen in adults was even worse in children, particularly smaller children weighing less than 10 kg. Anesthetic challenges multiplied rapidly in association with CPB coupled with early attempts at complete intracardiac repair. The lung as well as the heart received a large share of the bypass-related injuries leading to increased postoperative pulmonary complications. Brain injury began to be seen and was occasionally reported, in conjunction with CPB operations, particularly when extreme levels of hypothermia were used in an attempt to mitigate the morbidity seen in various organ systems after CPB.

In Kirklin's initial groundbreaking report of intracardiac surgery with the aid of a mechanical pump–oxygenator system at the Mayo Clinic, the only reference to anesthetic management is a brief remark that ether and oxygen were given.[11] In Lillehei's description of direct vision intracardiac surgery in humans using a simple, disposable artificial oxygenator, there is no mention of anesthetic management.[12] What strikes a "modern" cardiac anesthesiologist in these two reports is the high mortality: 50% in Kirklin's series and 14% in Lillehei's series. All of these patients were children with CHD ranging in age from 1 month to 11 years. Clearly such mortality and the associated patient care expense would not be tolerated today.

At that time, pediatric anesthesia was performed with open drop ether administration and later with ether using different non-rebreathing systems. Most anesthetics were given by nurses under the supervision of the surgeon. The first physician anesthetist to be employed by a children's hospital was Robert M. Smith in Boston in 1946.

The anesthetic agent to come into widespread use after ether was cyclopropane; in most of the early textbooks it was the recommended drug for pediatric anesthesia. Quite apart from being explosive, cyclopropane was difficult to use. It was obvious that carbon dioxide absorption was necessary with cyclopropane to avoid hypercarbia and acidosis, which might precipitate ventricular arrhythmias. However administration with a Waters' absorber could be technically difficult especially as tracheal intubation was considered dangerous to the child's small, delicate airway.

In all the early reports it is noted or implied that the patients were awake (more or less) and extubated at the end of the operation. In the description of the postoperative course, respiratory complications were frequent, either in the form of pulmonary respiratory insufficiency or airway obstruction. This latter problem was probably due to the fact that the largest tube which would fit through the larynx was used. Another reason may have been that the red rubber tube was not tissue tested. The former problem was probably often related to the morbidity of early bypass technology on the lung.

Arthur S. Keats, working at the Texas Heart Institute and Texas Children's Hospital with Denton A. Cooley, had much experience with congenital heart surgery and anesthesia from 1955–60, and provided the most extensive description of the anesthetic techniques used in this era.[13,14] He described anesthesia for congenital heart surgery without bypass in 150 patients, the most common operations being PDA ligation, Potts' operation, atrial septectomy (Blalock–Hanlon operation), or pulmonary valvotomy. Premedication was with oral or rectal pentobarbital, chloral hydrate per rectum, intramuscular meperidine, and intramuscular scopolamine or atropine. Endotracheal intubation was utilized, and ventilation was assisted using an Ayre's T-piece, to-and-fro absorption system, or circle system. Cyclopropane was used for induction, and a venous cutdown provided vascular access. Succinlycholine bolus and infusion were used to maintain muscle relaxation. Light ether anesthesia was used for maintenance until the start of chest closure, and then 50% $N_2O$ used as needed during chest closure. Of note is that the electrocardiogram, ear oximeter, and intra-arterial blood pressure recordings were used for monitoring during this period, as well as arterial blood gases and measurements of electrolytes and hemoglobin. The next year he published his experiences with 200 patients undergoing surgery for CHD with CPB, almost all of whom were children. Ventricular septal defect (VSD), atrial septal defect (ASD), TOF, and aortic stenosis were the most common indications for surgery. The anesthetic techniques were the same as above, except that D-tubocurare was given to maintain apnea during bypass.

Perfusion rates of 40–50 mL/kg/minute were used in infants and children, and lactic acidemia after bypass (average 4 mmol/L) was described. No anesthetic agent was added during bypass, and "patients tended to awaken during the period of bypass," [14] but apparently without recall or awareness. Arrhythmias noted ranged from frequent bradycardia with cyclopropane and succinylcholine, to junctional or ventricular tachycardia, ventricular fibrillation (VF), heart block, and rapid atrial arrythmias. Treatments included defibrillation, procainamide, digitalis, phenylephrine, ephedrine, isoproterenol, and atopine. Eleven of 102 patients with VSD experienced atrioventricular block. Epicardial pacing was attempted in some of these patients but was never successful. Fresh citrated whole blood was used for small children throughout the case, and transfusion of large amounts of blood was frequently necessary in small infants. Mortality rate was 13% in the first series[13] (36% in the 42 patients < 1 year of age), and 22.5% in the second series[14] (47.5% in the 40 patients < 1 year of age). Causes of death included low cardiac output after ventriculotomy, irreversible VF, coronary air emboli, postoperative atrioventricular block, hemorrhage,

pulmonary hypertension, diffuse atelectasis, and aspiration of vomitus. No death was attributed to the anesthetic alone. Reading these reports provides an appreciation of the daunting task of providing anesthesia during these pioneering times.

Tracheostomy after cardiac operations was not unusual and in some centers it was done "prophylactically" a week before the scheduled operation. These practices were certainly related to primitive (in present terms) techniques and equipment used for both endotracheal intubation and CPB. Postoperative ventilatory support did not become a routine until later when neonatologists and other intensive care specialists had proven it could be done successfully. Successful management of prolonged respiratory support was first demonstrated in the great epidemics of poliomyelitis in Europe and the USA in 1952–54.[15]

Halothane was introduced in clinical practice in the mid-1950s and it became rapidly the most popular agent in pediatric anesthesia, mostly because of the smooth induction compared to the older agents. Halothane was also widely used for pediatric cardiac anesthesia in spite of its depressive effect on the myocardium and the significant risk of arrhythmias. Halothane continues to be used in some places as the anesthetic agent of choice for pediatric cardiac cases, although newer inhalational agents like isoflorane and sevoflurane are now more widely used. Sevoflurane is probably the inhalational agent most often used for induction of anesthesia in pediatric cardiac cases in US academic centers.

During this period, adult cardiac anesthesiologists following the practice reported by Edward Lowenstein in 1970[16] began to use intravenous anesthesia based on opiates. Initially morphine in doses up to as much as 1 mg/kg was given with 100% oxygen and this technique became the anesthetic of choice for adult cardiac patients, but vasodilation and hypotension associated with its use slowed the incorporation of this technique into pediatric cardiac anesthesia until the synthetic opiates became available.

Before CPB was yet developed, or when it still carried high morbidity and mortality, a number of modalities were used to improve the outcome for infants. One was inflow occlusion (IO), another was the hyperbaric chamber. Inflow occlusion was useful and, if well managed, an elegant technique. The secret was the organization of the efforts of the entire operative team, and the technique required the closest cooperation between surgeon and anesthesiologists. The technique was as follows.

The chest was opened in the midline. After pericardiotomy, a side-clamp was placed on the right atrium (RA) free wall and an incision made in the RA or proximal on the pulmonary artery prior to placing the vascular clamps used to occlude caval return. Prior to application of the clamps, patients were hyperventilated with 100% oxygen. During IO, the superior vena cava (SVC) and inferior vena cava (IVC) inflow were occluded, ventilation held, the RA or the pulmonary artery clamp released; the heart was allowed to empty, and the septum primum excised or the pulmonic valve dilated. After excision of the septum or valvotomy, one caval clamp was released initially to de-air the atrium. The RA side-clamp or the pulmonary artery clamp was then reapplied and the other caval clamp released. The heart was resuscitated with bolus calcium gluconate (range 30–150 mg/kg) and bicarbonate (range 0.3–3.0 mEq/kg). Occasionally inotropes were administered, most often dopamine. It was important to titrate the inotropes so as not to aggravate rebound hypertension caused by endogenous catecholamines. The duration of the IO was between 1 and 3 minutes—terrifying minutes for the anesthesiologist, but quickly over.

Another modality used to improve the survival after shunt operations, pulmonary artery banding (PAB) and atrial septectomy, was to operate in the hyperbaric chamber, thereby benefiting from the increased amount of physically dissolved oxygen. It was a cumbersome affair operating in crowded and closed quarters. There was room for only two surgeons, two nurses, one anesthesiologist, and one baby, as the number of emergency oxygen units limited access. Retired navy divers ran the chamber and kept track of how many minutes the personnel had been in the hyperbaric chamber in the previous week. Help was not readily available because the chamber was buried in a sub-basement and people had to be sluiced in through a side arm that could be pressurized. The chamber was pressurized to 2–3 atmospheres so it was unpleasantly hot while increasing the oxygen pressure and cold while decreasing the pressure; people with glasses were at a disadvantage. It did not seem to add to survival and was abandoned circa 1974.

Anesthesia was a challenge in the hyperbaric chamber. The infants were anesthetized with ketamine and nitrous oxide. As the pressure in the chamber increased, the concentrations of $N_2O$ had to be decreased to avoid the hypotension and bradycardia that occurred rapidly.

Also in this era, the first infant cardiac transplant was performed by Kantrowitz in 1967.[17] The recipient was an 18-day-old, 2.6 kg patient with severe Ebstein's anomaly, who had undergone a Potts' shunt on day 3 of life. The donor was an anencephalic newborn. The anesthetic technique is not described, and the infant died 7 hours postoperatively of pulmonary dysfunction.

## The era of deep hypothermic circulatory arrest and the introduction of prostaglandin $E_1$, 1970–80

About 1970 physiological repair of CHD or "correction" had begun to come of age. In the adult world, coronary bypass operations and valve replacement spurred interest in cardiac anesthesia, which centered increasingly on the use of high dose narcotics and other pharmacological interventions. As

synthetic opiates with fewer hypotensive side effects became available, their use spread into pediatric cardiac anesthesia late in the 1970s and 1980s.

Children were still treated as "small adults" because major physiologic differences were not yet well appreciated, particularly as they related to CPB morbidity. Cardiopulmonary bypass was rarely employed during surgery on children weighing less than 10 kg because of the very high mortality and morbidity that had been experienced in the early years. The notion of repairing complex CHD in infancy was getting attention but was hindered by technical limitations of surgical techniques, CPB techniques, and anesthetic challenges in infants. Theoretically physiological repair early in life provides a more normal development of the cardiovascular and pulmonary systems and might avoid palliation all together. The advantage of this was that the sequelae after palliation, for instance, distorted pulmonary arteries after shunts and PAB, might be avoided. Pulmonary artery hypertension following Waterston and Potts' shunts occurred as a result of increased pulmonary blood flow and resulted in pulmonary obstructive disease. This would not develop if the defect were physiologically repaired at an early age. Furthermore, parents could be spared the anxiety of repeated operations and the difficulties of trying to raise a child with a heart that continued to be impaired.

The perceived need for early repair, together with the high mortality of bypass procedures, in infants and small children led to the introduction of DHCA. It was first practiced in Kyoto, Japan, but spread rapidly to Russia, the West coast of the USA at Seattle, and from there to midwestern and other US pediatric centers. As an example of the difficulties this presented to anesthesiologists, the introduction of DHCA in practice at the Children's Hospital in Boston is useful. The newly appointed chief of cardiovascular surgery at the Children's Hospital in Boston was Aldo R. Castaneda, MD, PhD, one of the first supporters of early total correction of CHD, who quickly embraced DHCA as a tool to accomplish his goals for repair in infants. In 1972, he immediately introduced DHCA into practice at the Children's Hospital in Boston and the rather shocked anesthesia department had to devise an anesthetic technique to meet this challenge, aided only by a couple of surgical papers in Japanese which Dr Castaneda kindly supplied to the anesthesia department. These papers had, of course, little reference to anesthesia.

The first description of the techniques of DHCA from Japan in the English literature was Horiuchi's from 1963.[18] They used a simple technique with surface cooling and rewarming during CPB, using ether as the anesthetic agent, without intubation. In 1972 Mori reported details of their technique for cardiac surgery in neonates and infants using deep hypothermia, again in a surgical publication. Their anesthetic technique was halothane/$N_2O$ combined with muscle relaxant; carbon dioxide was added to the anesthetic gas during cooling and rewarming (pH stat) to improve brain blood flow. The infants were surface cooled with icebags and rewarmed on CPB.[19]

Surprisingly, given the enormity of the physiological disturbances and challenges presented by DHCA, very few articles describing an anesthetic technique for DHCA were published, perhaps because DHCA and early correction was not widely accepted. A paper from Toronto described an anesthetic regime with atropine premedication occasionally combined with morphine.[20] Halothane and 50% $N_2O$ were used, combined with D-tubocurare or pancuronium. Carbon dioxide was added to "improve tissue oxygenation by maintaining peripheral and cerebral perfusion." The infants were cooled with surface cooling (plastic bags with melting ice) and rewarmed on CPB. It was noted that six of the 25 infants had VF when cooled to below 30°C.

Given the lack of any scientific data or studies to guide anesthetic management of such cases, a very simple technique with ketamine-$O_2$-$N_2O$ and curare supplemented by small amounts of morphine (0.1–0.3 mg/kg) was used at the Children's Hospital in Boston. This was the way infants were anesthetized for palliative cardiac surgical procedures in the hyperbaric chamber at Boston Children's Hospital. The infants were surface cooled in a bathtub filled with ice water to a core temperature of approximately 30°C. The bathtub was a green plastic bucket (for dishwashing!) bought at a Sears–Roebuck surplus store, keeping things as simple as possible (Fig. 1.1). This method was used in hundreds of infants over the next couple of years and only one infant developed VF in the ice water bathtub. This was an infant with TOF who suffered a coronary air embolus either from a peripheral i.v. or during an attempted placement of a central venous line. In retrospect, it is amazing that so few papers were published about the anesthetic management of this procedure that rapidly was seen to be lifesaving. The little material that was published about these techniques was restricted to surgical journals and did not describe or make any attempt to study the anesthetic techniques used for DHCA. The published surgical articles were largely unknown to cardiac and pediatric anesthesiologists.

It was during these 10 years that the "team concept" developed with cardiologists, cardiac surgeons and anesthesiologists working together in the OR and the intensive care unit (ICU) in the larger centers. These teams were facilitated by the anesthesiologists' "invasion" of weekly cardiology–cardiac surgeon conferences where the scheduled operations for the week were discussed. Dr Aldo Castaneda, the chief surgeon at Boston's Children's Hospital, was a leader in the creation of a cardiac team concept for pediatric cardiac surgery.

During the first year of using DHCA in Boston, it was noticed that a number of the infants had "funny, jerky" movements of the face and tongue. A few also had transient seizures during the postoperative period, but as they had normal electroencephalographs (EEGs) at 1-year follow up, it was felt that significant cerebral complications were not a

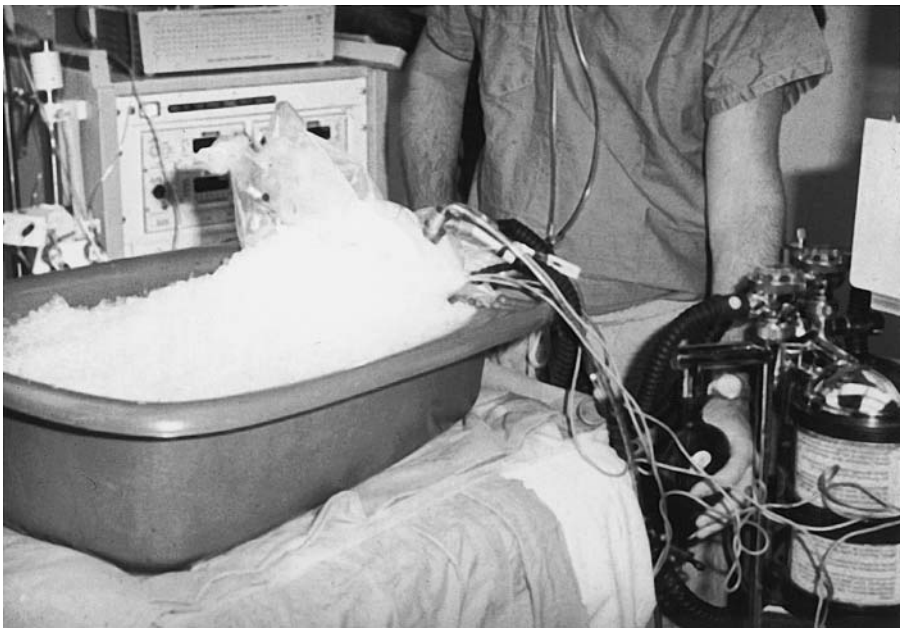

**Fig. 1.1** Infant submerged in ice water.

problem. In view of knowledge developed subsequently, these clues to neurologic damage occurring during and after pediatric cardiac surgery involving DHCA were overlooked. In hindsight maybe it will be more correct to say these clues were ignored, thus a great opportunity to study this problem was delayed for almost two decades. The issue of neurologic damage with DHCA was raised repeatedly by surgeons such as John Kirklin, but was not really studied until the group at Boston Children's Hospital led by Jane Newburger and Richard Jonas systematically followed a cohort of infants who had the arterial switch operation in the late 1980s using DHCA techniques.[21] In the late 1980s and early 1990s, Greeley and coworkers at Duke University performed a series of human studies delineating the neurophysiologic response to deep hypothermia and circulatory arrest.[22] These studies provided the crucial data in patients from which strategies for cooling and rewarming, length of safe DHCA, blood gas management, and perfusion were devised to maximize cerebral protection.

Those ongoing studies were followed by a number of studies comparing DHCA with hypothermic low flow perfusion, with different hematocrit in the perfusate and with different pH strategies during hypothermic CPB, pH-stat vs. α-stat.

During those years, the ketamine–morphine anesthetic technique had been supplanted by fentanyl-based high dose narcotic techniques. For the neurologic outcome studies the anesthetic technique was very tightly controlled, using fentanyl doses of 25 μg/kg at induction, incision, onset of bypass, and on rewarming, in addition to pancuronium. From the beginning of this period, surgical results as measured by mortality alone were excellent with steady increases in raw survival statistics. Because anesthetic techniques were evolving over this period of time, it was difficult to definitely ascribe any outcome differences to different anesthetic agents. A 1984 study of 500 consecutive cases of cardiac surgery in infants and children looked at anesthetic mortality and morbidity. Both were very low, so low in fact that they were probably not universally believed.[23]

As the new synthetic opioids such as fentanyl and sufentanil were developed, they replaced morphine to provide more hemodynamic stability in opiate-based anesthetic techniques for cardiac patients. In 1981, Gregory and his associates first described the use of "high dose" fentanyl, 30–50 μg/kg, combined with pancuronium in 10 infants undergoing PDA ligation. It is noteworthy that transcutaneous oxygen tension was measured as part of this study. This paper was in fact the introduction of high dose narcotics in pediatric cardiac anesthesia.[24]

The technique was a great success; one potential reason for that success was demonstrated 10 years later in Anand *et al.*'s paper showing attenuation of stress responses in infants undergoing PDA ligation who were given lesser doses of fentanyl in a randomized, controlled study.[25]

During this same period, synthetic opioids were replacing morphine in adult cardiac surgery. This technique slowly and somewhat reluctantly made its way into pediatric anesthesia,[26] replacing halothane and morphine, which had previously been the predominant choice of pediatric anesthesiologists dealing with patients with CHD. In the years from 1983 to 1995 a number of papers were published showing the effect of different anesthetic agents on the cardiovascular system in children with CHD. Ketamine, nitrous oxide, fentanyl, and sufentanil were systematically studied. Some

misconceptions stemming from studies of adult patients were corrected, like the notion that $N_2O$ combined with ketamine raises pulmonary artery pressure (*PAP*) and pulmonary vascular resistance (*PVR*).[27] On the other hand, the role of increased $P_{CO_2}$ or lower pH in causing higher *PVR* was also demonstrated and that subsequently became important in another connection.[28] A number of studies done at this time demonstrated in a controlled fashion the earlier clinical observation (Harmel and McQuiston in the late 1940s)[6,29] that in cyanotic patients the oxygen saturation would rise during induction of anesthesia, almost irrespective of the agent used.[30] These events only reinforce the value of acute clinical observation and provide an example of how the interpretation of such observations may well change as new knowledge is discovered.

## Patent ductus arteriosus and the introduction of prostaglandin $E_1$

In the mid-1970s several discoveries were made and introduced into clinical practice that turned out to be of great importance to the pediatric cardiac anesthesiologist and the rest of the cardiac team, the most important being the discovery that $PGE_1$ infused intravenously prevented normal ductal closure.[31] These developments revolved around the role of the PDA in the pathophysiology of both cyanotic and acyanotic CHD. The critical role of PDA closing and opening in allowing early neonatal survival of infants with critical CHD began to be appreciated and clinicians sought methods of either keeping the PDA open or closing it, depending on what type of critical CHD the neonate was born with and the role of patency of the ductus arteriosus in the CHD pathophysiology. In some cases, particularly in very small neonates, the importance of closing the PDA was increasingly appreciated and in other cases, the critical importance of maintaining the patency of a PDA was appreciated.

As the survival of very small premature infants began to improve, mostly because of technical improvements with the use of a warmed isolette and improved mechanical ventilation for very small newborns, it became apparent that in many of these infants the PDA would not undergo the normal closure over time. As the understanding of these infants' physiological problems improved and more infants survived, the role of continued patency of the PDA in neonates needing mechanical ventilation was appreciated. This led to medical therapy directed at promoting ductal closure using aspirin and indomethacin.

When such attempts failed, it was increasingly understood that necrotizing enterocolitis in the preemie was associated with decreased mesenteric blood flow secondary to the "steal" of systemic blood flow into the pulmonary circulation through a PDA. Thus, in cases when the PDA failed to close in premature infants, the need for operative treatment of the PDA in preemies arose as prophylaxis for necrotizing enterocolitis.

Pediatric and cardiac anesthesiologists were now faced with the task of anesthetizing these tiny preemies safely. This involved maintaining body temperature in infants of 1 kg or less with very large surface area/volume ratios. Intraoperative fluid restriction was important and low levels of $F_{IO_2}$ were used to decrease the risk of retinopathy of prematurity. As the decade progressed these issues emerged and were addressed. In 1980, Neuman and Hansen[32] described the anesthetic management of 70 such infants using an $O_2$/$N_2O$-muscle relaxant anesthesia technique with no mortality. Low $F_{IO_2}$ was used to reduce the risk of retrolental fibroplasia, and precautions were taken to prevent heat loss. In those days before acquired immunodeficiency syndrome (AIDS) became a wide concern, 40% of the infants received blood transfusion. Interestingly, the question of whether to operate in the neonatal intensive care unit (NICU) or the OR for closure of the PDA in the very small newborns was discussed at that time and remains unsettled today!

The PDA lesion presents an interesting story. In 1938 it was the first of the CHD lesions to be successfully treated surgically.[1] In the mid-1970s it was closed with medical therapy, first with aspirin and later with indomethacin. It was the first CHD lesion to be treated in the catheterization laboratory using different umbrella devices or coils.[33] Presently, if surgical closure is necessary, it is often done using a minimally invasive, thoracoscopic video-assisted technique.[34] This has the user-friendly, more benign effect of using four small incisions, avoiding an open thoracotomy, limiting dissection and trauma to the left lung. At the same time, this latest development of surgical technique required the anesthesiologist to again change the anesthetic approach to these patients. Unlike adult anesthesiologists who can use double-lumen endotracheal tubes for thoracoscopic procedures, pediatric anesthesiologists caring for 1–3 kg infants undergoing PDA ligation do not have the luxury of managing the left lung.[34] Another problem posed by thoracoscopic PDA ligation in the infant is the emerging need for neurophysiologic monitoring of the recurrent laryngeal nerve's innervation of the muscles of the larynx to avoid injury, a known complication of PDA surgery.[35] The last issue is tailoring the anesthetic so that the children are awake at the end of the operation, can be extubated and spend an hour or so in the post-anesthesia care unit, bypassing the cardiac intensive care unit (CICU). In fact, in 2001 a group led by Hammer at Stanford published the first description of true outpatient PDA ligation in two infants aged 17 days and 8 months.[36] These patients were managed with epidural analgesia, extubated in the OR, and discharged home 10 hours postoperatively. This report brings PDA closure full circle from a 13-day hospital stay following an ether mask anesthetic for an open thoracotomy to a day surgery procedure in an infant undergoing an endotracheal anesthetic for a thoracoscopic PDA ligation!

Maintaining patency of the PDA using $PGE_1$ is probably now of considerably greater importance than its closure, both

numerically and in terms of being life-sustaining in neonates with critical CHD. The introduction of $PGE_1$ suddenly improved the survival rate of a large number of neonates with CHD having lesions that require ductal patency to improve pulmonary blood flow, or to improve systemic blood flow distal to a critical coarctation of the aorta. The introduction of $PGE_1$ into clinical practice for therapy of neonatal CHD substantially changed the life of the pediatric cardiac surgeon and the pediatric cardiac anesthesiologist, as frequent middle-of-the-night shunt operations with extremely cyanotic infants almost immediately became a thing of the past. These operations were particularly daunting when one realizes that these procedures were most common before the availability of pulse oximetry; the only warning signs of impending cardiovascular collapse were the very dark color of the blood and preterminal bradycardia. To get an arterial blood gas with a $Pao_2$ in the low teens was not uncommon, and $Pao_2$ measurements in single digits in arterial blood samples from live neonates during such surgical procedures were recorded! Even more dramatic was the disappearance of the child with critical post-ductal coarctation. These infants were extremely acidotic with a pH of 7.0 or less at the start of the procedure (if it was possible to obtain an arterial puncture); they looked mottled and almost dead below the nipples. With the advent of $PGE_1$ therapy, they were resuscitated medically in the ICU and could be operated on the following day in substantially better condition than previously.

But the introduction of $PGE_1$ had an effect that was not clearly foreseen except maybe by some astute cardiologists. Survival of a number of these neonates presented pediatric cardiologists and cardiac surgeons (and then anesthesiologists) with rare and severe forms of CHD that had hitherto been considered a "rare" pathological diagnosis. Foremost among these were the infants with HLHS and some forms of interrupted aortic arch (IAA). As further experience was gained, it became obvious that these forms of disease were not so rare, but infants who had survived with those forms of CHD were very rare.

## The story of hypoplastic left heart syndrome, 1980–90

As mentioned above, the introduction of $PGE_1$ brought major changes to pediatric cardiac anesthesia, solving some problems and at the same time bringing new challenges for the cardiac team. New diagnoses of CHD presented for treatment and were recognized; some had been known previously but had until then presented insurmountable obstacles to any effective therapy.

One of these was HLHS. It had been accurately described in 1958 by Noonan and Nadas but only as a pathological diagnosis.[37] The syndrome is a ductus dependent lesion and had 100% mortality within a few days to weeks when the ductus underwent physiological closure. Hypoplastic left heart syndrome was therefore of no practical interest from a therapeutic standpoint until ductal patency could be maintained. When it became possible to keep the ductus arteriosus patent with $PGE_1$, these neonates rapidly became a problem that could not easily be ignored. In the beginning, most of the infants were misdiagnosed as having sepsis and being in septic shock—few babies reached the tertiary center without a telltale Band-Aid indicating a lumbar puncture to rule out sepsis.

But even with the ability to diagnose the defect in a live neonate temporarily kept alive with a $PGE_1$ infusion, the outlook was not much better. There was no operation devised, and in some centers such neonates were kept viable on a $PGE_1$ infusion for weeks and even months in the (usually) vain attempt to get them to grow large enough for some surgical procedure to be attempted.

In the next years several centers tried different approaches with ingenious conduits, trying to create an outlet from the right ventricle to the aorta and the systemic circulation.

Those were also the years where President Ronald Reagan's Baby Doe regulations were in effect. Anyone who thought an infant was being mistreated, i.e. not operated upon, could call a "Hot Line Number" which was posted in all neonatal ICUs to report the physicians "mistreatment" of the infant. Fortunately this rule died a quiet death after a few chaotic years.[38]

In the meantime the search for a palliative operation went on, also spurred by the increasing success of the Fontan operation, which had been introduced in 1970.[39] This meant that there now was a theoretical endpoint for HLHS as well as for other forms of single ventricle (SV) physiology. It was William Norwood at Boston Children's Hospital who was the first to devise not only a viable palliation but also to complete the repair with a Fontan operation the following year.[40] The publication of this landmark paper spurred considerable discussion. Many cardiologists and surgeons took the position that this operative procedure represented experimental and unethical surgery, and that these infants "were better off dead."

The current approach to these infants varies from multistage physiological repair with palliation followed by Fontan operation. Another alternative is neonatal transplantation as proposed by the group at Loma Linda in California.[41]

Some cardiologists are still advocates of conservative "comfort care" for neonates with HLHS.

With eventual survival of about 70% being achieved in many centers, these infants can no longer be written off as untreatable. Now the question is more about quality of survival, especially intellectual development. It is also recognized that many have both chromosomal and non-chromosomal anomalies both in the cerebral and gastrointestinal systems.[42]

As was the case from the beginnings of pediatric cardiac surgery, this new patient population presented a management dilemma for the anesthesiologists; they posed a new set of problems that required solution before acceptable operative results could be achieved. It was obvious that

patients with HLHS were hemodynamically unstable before CPB because of the large volume load on the heart coupled with coronary artery supply insufficiency. The coronary arteries in HLHS are supplied from the PDA retrograde through a hypoplastic ascending and transverse aorta that terminates as a single "main" coronary artery. A common event at sternotomy and exposure of the heart was VF secondary to mechanical stimulation. This fibrillation was sometimes intractable, necessitating emergent CPB during internal cardiac massage. This was not an auspicious beginning to a major experimental open heart procedure.

It was during these years that the transition from morphine–halothane–$N_2O$ to high dose narcotic technique with fentanyl or sufentanil combined with 100% oxygen took place. This technique seemed to provide some protection against the sudden VF events. Despite this modest progress in getting patients successfully onto CPB, it soon became painfully clear to us that we had not made much progress in treating this lesion when we tried to wean the patients from bypass. The infants were still unstable coming off bypass and severely hypoxemic, and it took some time before we discovered a way to deal with the problem.

A chance observation led us to a solution. We noticed that infants who came off bypass with low $PaO_2$ (around 30 mmHg) after the HLHS repair often did well, while the ones with immediate "excellent gases" ($PaO_2$ of 40–50 mmHg or better) became progressively unstable in the ICU a couple of hours later, developing severe metabolic acidosis and dying during the first 24 h.

This observation combined with discussions with the cardiologists about *PVR* and systemic vascular resistance (*SVR*) made us attempt to influence these resistances to assure adequate systemic flow. In retrospect, infants with low $PO_2$ after bypass had smaller pulmonary artery shunts and adequate systemic blood flow, while those with larger pulmonary shunts and higher initial $PO_2$ levels after weaning from bypass tended to "steal" systemic blood flow through the pulmonary artery shunt. This would occur in the postoperative period, as the *PVR* remained elevated as a result of CPB before returning to more normal levels. These observations led to the technique of lowering the $FIO_2$ sometimes as low as 0.21 and to allow hypoventilation to increase *PVR* in patients that had larger size shunts placed to supply adequate systemic blood flow as part of what became known as the Norwood operation.[43] A different technique used at other institutions to deal with this problem was to add carbon dioxide to the anesthetic gas flow, increasing *PVR* and continuing to use "normal ventilation" in children that had larger shunts placed and excessive pulmonary blood flow.[44] Both techniques represented different approaches to the same problem: finding ways of dealing with the need to carefully balance *PVR* and *SVR* after bypass in a fragile parallel circulation in the post-bypass period where dynamic changes were taking place in ventricular function.

These observations and the subsequent modifications in anesthetic and postoperative management improved the survival for the stage I palliation (Norwood procedure). It should be noted that the pediatric cardiac anesthesiologist was a full, contributing partner in the progressive improvement in outcome of this very complex and challenging lesion. More important, the techniques developed and the knowledge gained in this process also simplified the management of other patients with parallel circulation and SV physiology. The obvious example is truncus arteriosus where the "usual" ST depression and frequent VF that occurred intraoperatively almost always can be avoided. Any decrease in *PVR* during anesthesia in a child with unrepaired truncus arteriosus can lead to pulmonary "steal" of systemic blood flow and decreased diastolic pressure through the common trunk to the aorta and pulmonary artery, resulting in hypotension and insufficient systemic blood flow expressed initially as coronary insufficiency and ST depression (or elevation).

During the same decade the surgical treatment of transposition of the great arteries (TGA) underwent several changes. The Mustard operations (as one type of atrial switch procedure) were feared because of the risk of SVC obstruction as a complication of this surgical procedure. At the end of a Mustard procedure, it was not uncommon to see a child with a grotesquely swollen head who had to be taken back to the OR for immediate reoperation. Many of those children suffered brain damage, especially when reoperation was delayed. This resulted from low perfusion pressure during bypass because of venous hypertension in the internal jugular veins and SVC. The extent and prevalence of such damage was never systematically studied. The arterial pressure during bypass and in the immediate post-bypass period in the OR tended to be low and the pressure in SVC high. An article from Great Ormond Street Hospital for Children in London demonstrated arrested hydrocephalus in Mustard patients.[45] The Senning operation (another variant of the atrial switch approach to TGA) was better, but those children could develop pulmonary venous obstruction acutely in the OR, after the procedure, or progressively after hospital discharge. When the diagnosis was not promptly made and acted upon, these infants were often quite sick by the time they came to reoperation.

The successful application of the arterial switch procedure described by Jatene *et al*. then began to revolutionize operations for TGA.[46] It eliminated the risk of obstruction of the pulmonary and systemic venous return seen after the Mustard and Senning procedures. It also diminished the incidence of the subsequent sick sinus syndrome, a complication that might develop in the first 10 years postoperatively resulting from the extensive atrial suture lines and reconstructions required by these "atrial" switch procedures. The introduction of the arterial switch operation again involved anesthesiologists. The initial attempts at arterial switch operations in many institutions resulted in substantial numbers of

infants who had severe myocardial ischemia and even frank infarcts. This resulted from a variety of problems with the coronary artery transfer and reimplantation into the "switched" aorta that had been moved to the left ventricle outflow tract. Pediatric cardiac anesthesiologists gained extensive experience with intraoperative pressor and inotropic support, and nitroglycerine infusions. They were expected by surgeons to provide support to get infants through what later turned out to be iatrogenically caused myocardial ischemia. As surgeons learned to handle coronary artery transfers and reanastomoses well, these problems largely disappeared, along with the need for major pressor and inotropic support, and for nitroglycerine infusion inappropriately directed at major mechanical obstructions in the coronary arterial supply. The arterial switch operation has now been refined at most centers to the point where it is largely "routine" and presents, for the most part, no unique anesthetic challenges.

It was during the same time period that a randomized strictly controlled study of stress response in infants undergoing cardiac surgery while anesthetized with high dose sufentanil was performed. It showed that a high dose narcotic technique would suppress but not abolish stress responses. It also seemed to show a reduction in morbidity and possibly mortality.[47] However, when the study was repeated 10 years later, these results did not quite hold up. It must be pointed out that the patient population was older and refinement of the bypass technique had occurred.[48]

## Fontan and the catheterization laboratory, 1990–2000

After the anesthetic technique and preoperative management of the stage I palliation had been refined and we had been encouraged by the initial successes of stage II, problems arose. The Fontan operation became problematic as it was applied to younger patients with a great variety of SV types of CHD. Many of the patients had seemingly perfect Fontan operations but in the CICU they developed low cardiac output and massive pleural and pericardial effusions postoperatively. Many died in the postoperative period despite a variety of different support therapies; their course over the first 24–48 hours was relentlessly downward and could only be reversed by taking them back to the OR, reversing the Fontan operation, and reconstructing a systemic to pulmonary artery shunt. It was hard for the caretakers of those infants to accept such losses of children they had known from birth. They were our little friends and we knew the families too. All kinds of maneuvers were tried to avoid the above sequence of events, from early extubation to the use of a G-suit to improve venous return to the heart. In some centers a large balloon was placed tightly around the child's lower body and intermittently inflated by a Bird respirator asynchronous with ventilation.

After a couple of years two innovations changed the outlook. Both were linked to the understanding that a major limitation of the Fontan operation was the need for a normal or near normal *PVR* to allow survival through the postoperative period when CPB had caused, through release of a variety of inflammatory mediators and cytokines, a marked elevation of *PVR* in the early postoperative period. When this bypass-related increase in *PVR* was associated with younger age (< 2 years of age) at the time a Fontan was attempted, the higher baseline *PVR* of the infant made the bypass-related *PVR* worse and resulted in inadequate pulmonary blood flow and (single) ventricular filling in the early postoperative period, leading to a cycle of low cardiac output, pulmonary and systemic edema, further increases in *PVR*, acidosis and death.

One solution was to interpose a bidirectional cavopulmonary anastomosis (bidirectional Glenn procedure, BDG) 6–12 months before completion of the Fontan operation. This procedure, increasingly known as a "hemi-Fontan," directed only half of the systemic venous return through the lungs at a time when the infant's *PVR* had not fallen to normal levels, and preserved an alternative pathway for (single) ventricular filling through systemic venous return not routed through the lungs. This enabled the patients to maintain reasonable cardiac output, although a bit "blue", during the early postoperative period, when the *PVR* had been elevated by CPB. However this made a third operation, the completion of the Fontan, necessary.

The other innovation was the "fenestrated" Fontan where a small fenestration in the atrial baffle allowed systemic venous return to bypass the lungs as a right-to-left shunt thereby maintaining ventricular filling and systemic cardiac output during the early postoperative period of high *PVR*. Over time the fenestration closed as *PVR* fell and shunting decreased. Alternatively, a device delivered during an interventional cardiac catheterization could close the fenestrations.

This whole process of testing the applicability of the Fontan principle and various modifications of the Fontan operation to a wide variety of types of severe cyanotic CHD involved another set of challenges for the pediatric cardiac anesthesiologist and collaboration between anesthesiology, cardiology and surgery. The net result of a great deal of work and collaboration among these groups was that the outlook for the HLHS patients and indeed for all children with SV defects improved locally and, as these improvements spread and were amplified by work done in other centers, the improvement became national and international. In some institutions the preferred treatment was and is neonatal transplantation. Its limits are the long waiting time for a transplant, the unavoidable mortality during the waiting period and the ongoing morbidity of neonatal heart transplants, a lifetime of immunosuppression therapy, and the accelerated risk of coronary artery disease seen in heart transplants, even in young children.

The collaboration with pediatric cardiologists around postoperative care of HLHS, Fontan patients and others spread naturally to the cardiac catheterization laboratory. As pediatric cardiologists began to develop interventional procedures, the need for more control and support of vital functions became apparent. Previously, nurses operating under the supervision of the cardiologist performing the catheterizations had sedated the children for the procedures. In many institutions this involved high volumes of cases sedated by specially trained nurses while in others with smaller pediatric case loads the practice of using general anesthesia for children undergoing cardiac catheterizations had been routine.

The interventional cardiologists turned to pediatric cardiac anesthesiologists for help in managing these patients while the cardiologists themselves were dealing with the complex demands of doing interventional procedures in infants and children with CHD. As was the case with newly devised pediatric cardiac surgical procedures, the development of interventional procedures for CHD in the cardiac catheterization laboratory posed a whole new and different set of problems and challenges for pediatric cardiac anesthesia. Not the least of these was providing anesthesia and vital function support in the dark and difficult environment of the cardiac catheterization laboratory. The introduction of dilation techniques for pulmonary arteries and veins, mitral and aortic valves, and most recently, the dilation of fetal atretic aortic valves *in utero* along with device closure of the PDA, ASD, and VSD all placed progressively more demands on the anesthesiologists, who became more and more involved in these procedures.

The development of another set of interventional procedures, the use of radiofrequency ablation to deal with arrhythmias in the pediatric patient, illustrates the progressive complexity and difficulty of anesthesia care in these patients. Used initially only on healthy teenagers with structurally normal hearts but having paroxysmal atrial tachycardia (PAT), anesthesia care was quite straightforward. Now, in contrast, many of these radiofrequency ablation procedures are done in children with complex CHD, repaired or unrepaired, and frequently the children (or adults) may be quite cyanotic or have low cardiac output.[49] At present in Children's Hospital Boston the cardiac catheterization laboratory and the cardiac magnetic resonance imaging (MRI) unit present close to 1000 anesthesia cases per year over and above cardiac surgical cases.

But with all those developments the defects remain the same. If we look at the relative distribution of cases in 1982 and 2001 we see the same diagnosis and pretty much the same numerical relationship between the major groups. As Helen Taussig remarked in her paper about the global distribution of cardiac diagnosis, only surgical interventions change the numbers.[50] This we can see in the rise in numbers of Norwood and Fontan operations (Table 1.1).

**Table 1.1** Cardiovascular surgery at Children's Hospital Boston.

| | 1982 (%) | 2001 (%) |
|---|---|---|
| **Total cases** | **n = 538** | **n = 931** |
| Septal defects | 27.0 | 24.0 |
| VSD repair | 12.0 | 10.0 |
| ASD repair | 9.6 | 9.6 |
| CAVC repair | 5.9 | 4.6 |
| Cavopulmonary connection | 3.0 | 11.2 |
| Fontan procedure | 3.0 | 5.8 |
| Bidirectional Glenn | | 5.4 |
| Systemic outflow obstruction | 29.0 | 23.5 |
| Coarctation | 7.7 | 3.4 |
| Transposition of great arteries | | |
| Senning | 7.0 | |
| Arterial switch operation | | 4.2 |
| LVOT repair | 11.7 | 4.5 |
| Norwood procedure | 3.0 | 4.2 |
| Pulmonary outflow obstruction | 13.0 | 17.4 |
| TOF repair | 7.6 | 6.4 |
| Conduit placement/revision | 2.8 | 5.0 |
| Other RVOT reconstruction | 1.6 | 6.0 |
| Pacemaker, AICD placement | 5.0 | 4.3 |
| Patent ductus arteriosus | 8.0 | 5.1 |
| Miscellaneous | 15.0 | 14.1 |

AICD, automatic internal cardioverter-defibrillator; ASD, atrial septal defect; CAVC, complete atrioventricular canal; LVOT, left ventricular outflow tract; RVOT, right ventricular outflow tract; TOF, tetralogy of Fallot; VSD, ventricular septal defect.

## The future and finances

*Tempora mutantur et nos in illis* (time changes and we develop with time). It is 63 years since Robert Gross first ligated a PDA and we have seen amazing developments in the treatment of CHD. Concomitantly, anesthesiology has evolved and slowly defined pediatric anesthesia, then cardiac anesthesia, and now in the past two decades, pediatric cardiac anesthesia has developed as a distinct and separate area of subspecialization. There is no doubt that the current, "older" generation of pediatric cardiac anesthesiologists has played a major role in moving forward the whole field of treatment of CHD. Their contributions in adding to the knowledge of the physiology of CHD, the effects of anesthetic agents, and in enabling surgeons and cardiologists to develop new treatments are not always obvious or dramatic, but they are nonetheless important and essential parts of the progress made.

The last decade has seen many changes driven by the availability of new technology; these too provide new challenges

for the pediatric cardiac anesthesiologist to solve. Two-dimensional echocardiography has improved diagnosis both within and outside the OR and provided more challenges and opportunities for the pediatric cardiac anesthesiologist. Transesophageal echocardiography (TEE) is of special concern for the pediatric cardiac anesthesiologist. Its utility in congenital heart surgery was demonstrated in the late 1980s by the studies of several groups in Japan and the USA, including Russell and Cahalan at the University of California, San Francisco. The TEE interpretation of complex CHD and judgment of the adequacy of intraoperative repairs is considerably more challenging in CHD than in adult acquired heart disease. Many centers have called upon pediatric echocardiographers to make such judgments rather than have the pediatric cardiac anesthesiologist be responsible for that as well as for managing the patient in the post-bypass period. Also in contrast to adults, the TEE transducer may cause airway obstruction, alter left atrial pressure, or even extubate the child in the middle of an operation "under the drapes."

Similarly, the emerging availability of cardiac MRI for diagnosis and follow-up of CHD patients has compounded the difficulties of providing anesthesia and monitoring in an intense magnetic field with limited patient access, but requiring anesthesia to be delivered to patients with severe, complex CHD under difficult conditions. Such technological advances come at a high price and it is hard to see how innovations like the long and expensive search for a method of treatment of HLHS would be justified today.

Another technical innovation of great importance driving pediatric cardiac anesthesia is extracorporeal membrane oxygenation (ECMO) (Fig. 1.2). Use of rapid response ECMO for children with CHD who suffer cardiopulmonary collapse postoperatively, cannot be weaned from CPB, or need to be supported as a bridge to heart transplantation has proven very effective in reducing mortality rates to significantly lower levels.

In the history of development of pediatric cardiac anesthesia, there is a long way between the baby in the icebath being prepared for DHCA and the complex technology necessary for ECMO resuscitation.

A significant challenge for the current generation of pediatric cardiac anesthesiologists is to help reduce the cost of care. One of the primary ways to reduce perioperative cost is limit ICU and ventilator time. This translates into increased demands and expectations for early extubation, preferably in the operation room.

Such changes in care have risks associated with them that will require careful assessment considering the advantages achieved with postoperative ventilation and sedation. For example, arrhythmias and cardiac arrest following endotracheal suctioning in the ICU postoperatively almost disappeared when heavy sedation with fentanyl prevented major swings in *PAP* with suctioning.[51,52] Careful selection of patients for early extubation and judicious use of shorter acting anesthetic agents may allow lengths of stay to be shortened without increasing risks. In some studies early extubation after relatively simple operations has in fact proven to be safe when using new short-acting anesthetic agents like sevoflurane and remifentanil, particularly when better pain control is also employed.

Other advances such as limiting the total dose of anesthetic agents by developing ways to monitor depth of anesthesia, so as to give sufficient doses to prevent awareness and attenuate stress responses while avoiding awareness during CPB, are being explored, but remain elusive.[53]

**Fig. 1.2** Infant on extracorporeal membrane oxygenation in the cardiac intensive care unit.

In the past the outcome criterion most emphasized for treatment of CHD has been survival. Now that survival rates are very good and getting better for almost all forms of CHD, attention has turned to the quality of that survival. As part of that trend, the patient care group increasing most rapidly at most centers is the adult with CHD. This is the somewhat unexpected result as care in childhood improves and more and more of these patients survive to adulthood and even into old age. At many institutions special programs have been created to treat these patients and the problems they face. These problems include complications, reoperations, and socio-economic barriers to normal education, employment, and creation of families. The question of pregnancy and anesthetic management of delivery for these patients is also evolving. It is unclear who is most qualified to provide anesthesia for such patients during labor and delivery. But suddenly the pediatric cardiac anesthesiologist may have to care for adults.[54]

Although much progress has been in the development of pediatric cardiac anesthesia to provide safe anesthetic care and improve outcome of treatment of CHD in the OR and catheterization laboratory for patients of all ages, much remains to be done. One can say with certainty that the intimate connection between advances in therapy, surgical or medical, and the anesthesia support services required to make those therapeutic advances possible will continue to present new challenges to the pediatric cardiac anesthesiologist. The pediatric cardiac anesthesiologists will in turn meet those challenges and in the process find ways to make still more improvements. Thus we progress in our art and science.

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# 2 Teaching and learning in congenital cardiac anesthesia

Alan Jay Schwartz

"Pedantic" is a description teachers wish to avoid. In the interest of doing this, I offer a fifth grader's biography of the great teacher Socrates: "Socrates was a man. Socrates was a Greek. Socrates went around telling people what to do. They poisoned him!"

## Education

This chapter about education on anesthesia for patients with congenital heart disease (CHD) is not intended in such a manner that I risk Socrates' fate but rather is intended to be provocative and to give cause for thought to an important subject not often reflected upon. All of anesthesia education can be easily considered in the following question (DE Greenhow, pers. comm., 1982):

> "How shall who teach what to whom for what purpose now and in the future?!"

Anesthesia education is presented using this question as the framework for consideration. This chapter provides a philosophy of teaching anesthesia and a detailed proposal for anesthesia education in pediatric cardiac anesthesiology.

Teaching, in a narrow sense, the way most of us think about it, is an activity by an individual aimed at causing another person to know some new fact or to know how to accomplish some new task. The focus appears to rest on the teacher and the activity of teaching. It does not take long to realize, however, that this way of looking at the teaching/learning activity has misplaced emphasis. If not with the teaching activity, where does the emphasis belong? The answer to this question lies in understanding the definition of education.

Education is an all-encompassing process (not merely a specific activity) resulting in a change in behavior on the part of the student/learner. The focus of education is the learner, not the teacher. It is the student who is educated by interacting with an environment that provides experience(s). Education is a change in behavior based on experiences. The experiences most often include the student interacting with a teacher but are almost never limited to that alone. The entire milieu defines the total experience. When the milieu changes, so may the education; that is, the change in behavior exhibited by the student may vary dramatically if the milieu is varied.

Picture the educational setting in which a cardiac or pediatric anesthesiology resident is learning how to use epinephrine when weaning a patient from cardiopulmonary bypass (CPB). The knowledge and skills that must be learned include application of the pharmacological principles of catecholamines to the pathophysiology of cardiovascular disease by turning on a mechanical infusion pump to deliver the indicated dose of a medication while technically monitoring for dose response and toxicity. Learning these facts and the skills sufficient to employ them is much different when done from a textbook or a preoperative conference with a faculty preceptor than when done during the operating room (OR) interaction between the surgeon and anesthesiologist, where varied opinions may consider dopamine a more sound physiologic choice or intermittent boluses a better administration technique. The interposition of the concerned surgeon and real-time patient setting between the student and the knowledge and skills to be learned changes the learning environment and, hence, the educational experience for the resident. More is learned than the facts and psychomotor skills. As the attitudes of both the anesthesiologist and the surgeon are displayed during the resolution of the questions about the "best" drug to use and the "right" way to give it, the resident learns how these two types of practitioners are supposed to relate to one another.

It seems obvious, therefore, that there is more to consider than just teaching. What more is there to the anesthesiologist's responsibility than just teaching those around her or him? Answering the component parts of the question posed at the beginning of this chapter provides the answer.

## Anesthesia education and congenital heart disease

Care of the child or adult with a congenital cardiac lesion has been an important part of cardiac surgical and cardiology practice since the beginning of the 20th century. In 1907, for example, Munro described ligation of a patent ductus arteriosus.[1] In 1946, Alfred Blalock, a surgeon, and Helen Taussig, a pediatrician, recognized that surgically creating an arterial–pulmonary shunt palliated patients with congenital cardiac defects that reduced pulmonary blood flow.[2] Use of deep hypothermia and circulatory arrest or low flow techniques has allowed surgeons to perform corrective "open heart" procedures on children and adults with cyanotic CHD. In 1967, Rashkind and colleagues described the balloon atrial septostomy to palliate babies with transposition of the great arteries.[3] In the 1980s and 1990s, Norwood and others developed cardiac surgical operations to palliate children with hypoplastic left heart syndrome.[4]

In less than 100 years, cardiac surgical and cardiology practice became highly sophisticated with respect to the care of patients with congenital cardiac lesions.

The rapid growth of sophisticated cardiac surgical and cardiology non-surgical diagnostic and therapeutic procedures for congenital cardiac lesions logically mandated comprehensive education of anesthesiologists specializing in the cardiac and/or pediatric anesthesiology subspecialties. The 3-year core anesthesiology residency program does not permit sufficient in-depth education about anesthesia for patients with congenital cardiac problems. The knowledge and skills necessary for the care of patients with congenital cardiac disease are different than those required for the care of patients with acquired valvular and ischemic cardiac diseases.

The "complete cardiac anesthesiologist" devoted to the care of patients with congenital cardiac lesions must immerse her/himself in a systematic program of clinical and didactic education about congenital cardiac anesthesia. This can only be achieved within a subspecialty residency (fellowship) in either cardiac or pediatric anesthesiology. Ideally, this is best achieved through the implementation of a standardized curriculum (see below). Understanding cardiovascular and pulmonary physiology is essential for the safe delivery of anesthesia patient care to patients with congenital cardiac lesions.

## The scope of anesthesia patient care for patients with congenital cardiac disease

Cardiac anesthesia is that care required to safely facilitate all indicated surgical and medical diagnostic and/or therapeutic procedures performed on patients with cardiac disease. Three essential requirements must be met for adequate performance of these procedures: (i) patient safety; (ii) "ideal" operating conditions; and (iii) patient comfort. The ideal anesthetic intervention accomplishes all three requirements at the same time. The reality of safe anesthetic practice mandates that patient safety be paramount followed in order of priority by operating conditions and comfort.

The surgical, therapeutic and diagnostic interventions that require cardiac anesthesia patient care can be classified in several ways. Procedure site, anatomic alterations or physiologic derangements are some of the commonly utilized classification schema. A classification system that includes all cardiothoracic interventions, surgical and medical, requiring an associated anesthetic intervention best defines the scope of cardiac anesthesiology.

Non-surgical interventions that require the care of an anesthesiologist or anesthesia care team to ensure patient safety, optimal conditions for the intervention to take place and patient comfort are more common for patients with congenital cardiac disease than those with acquired and ischemic heart disease. Non-surgical diagnostic and therapeutic interventions often require both the monitoring vigilance and pharmacological and physiological manipulations that anesthesia patient care provides. Diagnostic and/or therapeutic procedures in the radiology and cardiac catheterization suites and cardiac non-invasive and electrophysiological laboratories are examples of areas where patients with CHD are frequently evaluated and treated. Participation of the fully educated cardiac anesthesiology expert in the care of patients with congenital cardiac lesions in these non-OR sites as well as the OR is essential.

## A proposed anesthesiology curriculum for care of patients with congenital heart disease

The cardiac and pediatric anesthesiology subspecialty fellow will care for a wide variety of patients with CHD. These patients will undergo surgical or non-surgical diagnostic and/or therapeutic procedures to evaluate, palliate or correct their congenital cardiac lesion or for some other primary disease process with an underlying congenital cardiac problem being a comorbidity. The suggested curriculum for learning/teaching cardiac anesthesiology for specific application to the care of patients with CHD is anchored in the curriculum for the core residency education of all anesthesiologists.

A standardized curriculum does not exist for a fellowship program for a resident who has completed the required core anesthesiology training and desires to become a specialist in cardiac anesthesia specifically focused at the care of patients with congenital cardiac disease. A review process evaluating the educational experience provided by these programs is not required. While this training may be and most often is of the highest quality, without an accepted set of standardized evaluation criteria and a review to see that the criteria are met, it is impossible to comment upon the depth, breath and quality of the education provided in these settings.

There are at least two reasons why an accepted structure for such a fellowship program does not exist. The major explanation is that without an agreed upon approach emanating from an "authority" such as the Anesthesiology Residency Review Committee (RRC), there is no need for any program to meet specified requirements. Until a standard for cardiothoracic anesthesiology education is defined, institutions will conduct their programs by their own definition. This has resulted in great variability between programs. The second reason why a standard curriculum does not exist is that programs train residents in areas where they have the resources, i.e. case material and faculty with teaching expertise. If they do not have the resources they will not include an aspect of cardiothoracic anesthesiology in their training program even though this may be a very important area of training that is critical to the "full" education of a cardiothoracic anesthesiology specialist.

Many believe that the educational standard would be enhanced if an accreditation mechanism were developed for cardiac anesthesiology training programs. To this end, the Society of Cardiovascular Anesthesiologists (SCA), the largest organization in the world representing practitioners of this subspecialty, has developed a proposal for accreditation of training programs in cardiothoracic anesthesiology. There is no initiative underway to develop a certification process for cardiothoracic anesthesiologists (a process whereby a physician becomes certified as a specialist in anesthesiology when he or she voluntarily elects to complete certification requirements defined by the American Board of Anesthesiology [ABA]).

The SCA proposal for accreditation of training programs in cardiothoracic anesthesiology includes a "Pediatric Cardiac Anesthesiology Track" that is applicable to both children and adults with CHD.

## "**Pediatric cardiothoracic anesthesiology residency track** (pers. comm. with permission, SCA, Richmond, VA)

### Required core

1 Six months OR clinical activity providing a minimum of 80 surgical procedures on pediatric patients requiring CPB and 60 patients undergoing cardiac surgical procedures not requiring the use of CPB. At least 25% of these patients should be neonates, and 50% of all patients should be infants up to 1 year of age. The resident should be actively involved in the management of patients on extracorporeal membrane oxygenation (ECMO) and with ventricular assist devices.
2 It is strongly recommended that the resident have experience in the management of pediatric patients for cardiac pacemaker and automatic implantable cardiac defibrillator placement, surgical treatment of cardiac arrhythmias, cardiac catheterization, and cardiac electrophysiologic diagnostic/therapeutic procedures.
3 Three months of experience combining evaluation of pediatric patients utilizing echocardiography and cardiac catheterization. This will also include the anesthetic management of pediatric patients in the cardiac catheterization laboratory. Cardiac evaluation should also include cardiac magnetic resonance imaging (MRI) and exercise testing to evaluate a pediatric patient's functional capacity. Echocardiography, cardiac catheterization, and other non-invasive cardiac evaluation training may be done in conjunction with OR clinical activity or as independently designed rotations.
4 It is strongly recommended that the resident have a 1-month experience managing pediatric cardiothoracic surgical patients in a critical care setting. This experience may include the management of non-surgical cardiothoracic patients.

### Elective rotations

1 Two months of elective rotations (none < 2 weeks in duration) from the following pediatric categories: inpatient or outpatient cardiology, invasive cardiology, inpatient or outpatient pulmonary medicine, medical or surgical critical care, and extracorporeal perfusion technology."

The SCA proposal also recommends a didactic curriculum that covers topics applicable to both adult and pediatric cardiac anesthesiology education. The suggested didactic curriculum includes the following:

"The didactic curriculum, provided through lectures, conferences and workshops should supplement clinical experience as necessary for the subspecialty resident to acquire the knowledge to care for cardiothoracic patients and conditions outlined in the guidelines for the minimum clinical experience for each resident. The didactic components should include the following areas, with emphasis on how cardiothoracic diseases affect the administration of anesthesia and life support for cardiothoracic patients. The didactic program for the adult and pediatric cardiothoracic anesthesiology residency tracks will focus primarily on topics pertinent to their respective patient populations. The following represents guidelines for the minimum didactic experience and academic project (see below) for each resident. Some of the topics listed constitute components of the Core Residency in Anesthesiology. They are included in the requirements for the Cardiothoracic Anesthesiology Residency to emphasize their importance to the foundation of the discipline of cardiothoracic anesthesiology and stress the need to reinforce and enrich them in the subspecialty residency educational program:

1 Embryological development of the cardiothoracic structures.
2 Pathophysiology, pharmacology and clinical management of patients with cardiac disease including cardiomyopathy, heart failure, cardiac tamponade, ischemic heart disease, acquired and congenital valvular heart disease,

CHD, electrophysiologic disturbances, and neoplastic and infectious cardiac diseases.

3 Pathophysiology, pharmacology and clinical management of patients with respiratory disease including pleural, bronchopulmonary, neoplastic, infectious and inflammatory diseases.

4 Pathophysiology, pharmacology and clinical management of patients with thoracic vascular, tracheal, esophageal and mediastinal diseases, including infectious, neoplastic and inflammatory processes.

5 Non-invasive cardiovascular evaluation: electrocardiography, transthoracic echocardiography, transesophageal echocardiography (TEE), stress testing, cardiovascular imaging.
   (a) TEE training must be based upon the advanced echocardiography training objectives of the American Society of Echocardiography and the SCA *Guidelines for Training in Perioperative Echocardiography*.[5]

6 Cardiac catheterization procedures and diagnostic interpretation; invasive cardiac catheterization procedures including angioplasty, stenting, and transcatheter laser and mechanical ablations.

7 Non-invasive pulmonary evaluation: pulmonary function tests, blood gas and acid-base analysis, oximetry, capnography, pulmonary imaging.

8 Pre-anesthetic evaluation and preparation of cardiothoracic patients.

9 Pharmacokinetics and pharmacodynamics of medications prescribed for medical management of cardiothoracic patients.

10 Peri-anesthetic monitoring: non-invasive and invasive (intra-arterial, central venous, pulmonary artery, mixed venous saturation, cardiac output).

11 Pharmacokinetics and pharmacodynamics of anesthetic medications prescribed for cardiothoracic patients.

12 Extracorporeal circulation including myocardial preservation, effects of CPB on pharmacokinetics and pharmacodynamics, cardiothoracic, respiratory, neurological, metabolic, endocrine, hematological, renal and thermoregulatory effects of CPB, and coagulation/anticoagulation before, during and after CPB.

13 Pharmacokinetics and pharmacodynamics of medications prescribed for management of hemodynamic instability: inotropes, chronotropes, vasoconstrictors, vasodilators.

14 Circulatory assist devices: intra-aortic balloon counterpulsation, left and right ventricular assist devices, and biventricular assist devices.

15 Cardiac surgical procedures: adult and pediatric, minimally invasive, myocardial revascularization, valve repair and replacement, pericardial, neoplastic procedures, and heart and/or lung transplantation.

16 Thoracic aortic surgery: ascending, transverse and descending aortic surgery with circulatory arrest, CPB employing low flow and/or retrograde perfusion.

17 Esophageal surgery: varices, neoplastic, colon interposition, foreign body, stricture.

18 Pulmonary surgery: thoracoscopic or open; lung reduction, bronchopulmonary lavage, one lung ventilation, lobectomy, pneumonectomy and bronchoscopy; fiberoptic, rigid, laser resection.

19 Post-anesthetic critical care of cardiothoracic surgical patients.

20 Ventilators.

21 Pain management of cardiothoracic surgical patients.

22 Research methodology/statistical analysis.

23 Quality assurance/improvement.

24 Ethical and legal issues.

25 Practice management.

Cardiothoracic anesthesiology subspecialty conferences, including lectures, interactive conferences, hands-on workshops, morbidity and mortality conferences, cardiac catheterization and echocardiography conferences, cardiothoracic surgery case review conferences, journal reviews, and research seminars should be regularly attended. Active participation of the cardiothoracic anesthesiology resident in the planning and production of these conferences is essential. However, the faculty should be the conference leaders in the majority of the sessions. Attendance by subspecialty residents at multidisciplinary conferences especially in cardiovascular medicine, pulmonary medicine, cardiothoracic surgery, vascular surgery, and pediatrics relevant to cardiothoracic anesthesiology is encouraged.

The resident must complete a minimum of one academic assignment. Academic projects may include grand rounds presentations, preparation and publication of review articles, book chapters, and manuals for teaching or clinical practice, clinical research investigation or similar scholarly activities. A faculty supervisor must be in charge of each project."

The clinical cardiac and pediatric anesthesiology fellowship programs are customarily 1 year in duration. A significant portion of the 1-year fellowship (e.g. 6 months) can be devoted to education focused on anesthesia for patients with CHD and provide a broad exposure to the clinical experiences outlined above coupled with the didactic program that systematically covers the listed topical areas. The sequencing of the clinical experiences is less important than the inclusion of enough variety so that patients with CHD are cared for.

Dedicated time is ideally set aside for other experiences that amplify the clinical anesthesia experience, e.g. rotations through the cardiac catheterization and the pulmonary function testing laboratories. Time devoted to the perfusion team will greatly enhance the fellow's mastery of the principles and practice of CPB and its related topics such as management of the intra-aortic balloon pump.

Every fellow learning cardiac and/or pediatric anesthesiology should be provided education about education.[6] The fellow can serve as "junior faculty" when supervising a core

resident caring for a patient with CHD. The fellow should be expected to conduct teaching conferences, present lecture topics, and teach in other appropriate settings. Only in this way will the quality of the future teachers of anesthesiology for patients with congenital cardiac lesions be assured.

If research experience is added to the subspecialty training of a cardiac and/or pediatric anesthesiology fellow, a variable additional time period, over and above the 1-year clinical experience, will be defined based upon the research project requirements. Every subspecialty trainee should be expected to complete an academic project as defined in the proposal cited above.

## How to learn: The principles of education

From a teaching perspective, there are three areas of learning: (i) cognitive, (ii) psychomotor, and (iii) affective. It is very useful to conceptualize teaching and learning cardiac anesthesiology using this type of classification.

Cognitive learning centers on the knowledge base. The content learning that this represents is usually well defined by educators. Textbook after textbook has been written to provide the learner with what the teachers deem essential content for cognitive learning. Content learning, however, entails more than just memorizing facts. Cognitive learning has been defined by Bloom in his well-accepted taxonomy.[7] Learning and teaching in the cognitive domain follows a hierarchy of six increasingly more complex levels:

**1** Knowledge—recall.
**2** Comprehension—understanding.
**3** Application—use of abstractions.
**4** Analysis—break down; seeing the relationship of parts.
**5** Synthesis—put together; creating a new entity.
**6** Evaluation—judgement of value.

Knowing facts about pressures and oxygen saturations within the cardiac chambers, for example, is basic content necessary for understanding the physiology of congenital cardiac lesions. It is the higher levels of cognitive learning that are needed to develop a differential diagnosis and safe anesthetic plan. Understanding the cardiac chamber pressure and oxygen saturation data, application of it to a specific anatomic and clinical situation, and analysis of the physiological data for a particular patient allows the creation of an anesthetic prescription, for example, that does not result in a specific patient developing ventricular failure or systemic hypoxia.

The fundamentals of a knowledge base for pediatric cardiac anesthesiology exist within the *Content Outline* of the Joint Council on In-Training Examinations of the ABA and American Society of Anesthesiologists (ASA).[8] The full outline is divided into sections on physiological, physical and clinical sciences. Within each of these sections are specific subsections directly related to cardiac anesthesiology for patients with CHD. In the section on physiological sciences, for example, determinants and regulation of cardiac output and pharmacology of cardiovascular drugs are outlined. In the section on physical sciences, topics such as cardiovascular anatomy and physics of monitoring methods are included. The section on clinical sciences covers topics such as CHD and circulatory arrest. The Appendix to this chapter is an abridged form of the ABA/ASA Outline listing the topical areas that define the content of cardiothoracic anesthesiology.[9]

As in many educational endeavors, knowledge is well defined. Agreement on what constitutes the psychomotor domain of learning, however, is often poorly defined or non-existent. A clear, written definition of the psychomotor skills that must be mastered when learning cardiothoracic anesthesiology is not available. Many psychomotor skills that are essential for learning cardiothoracic anesthesiology are obvious. Intra-arterial and pulmonary artery monitoring, for example, are techniques that must be learned by the student of cardiothoracic anesthesiology. When these techniques should be mastered during the education of the anesthesiologist, however, is not agreed upon.

It would be of educational benefit if all of the psychomotor skills that encompass cardiothoracic anesthesiology were catalogued. Once the full scope of the skills is defined, the next appropriate step would be to decide what must be included in the core anesthesiology residency training program and what should be deferred for the more advanced educational program for those electing training as subspecialists in cardiac and pediatric anesthesiology.

The last category for learning is the affective domain. Affective refers to the "emotional" aspect of education. Specifically, the affective domain covers those aspects of learning that enable the student to interact with others and understand relationships. The goal is to enable the learner to understand their own personal values and those of others in order to develop interactions that will be most efficient and effective. While psychological sciences in general are well defined, this is a specific psychological area of learning that is not as well developed. A taxonomy of the affective learning domain exists in general form.[9] The taxonomy defines the following levels of affective learning and teaching:

**1** Receiving.
**2** Responding.
**3** Valuing.
**4** Organizing.
**5** Value complexing.

As students and educators, we are usually quite good at learning and teaching knowledge and skills. As pupils and professors, we are much less adept at the educational process for affective learning and teaching. Organized curricula exist for content and, in some instances, skill learning. Rarely does a curriculum exist for affective learning. Teachers most often do not set out to teach affective topics like they do knowledge and skill lessons. Affective learning most often takes place not from a curriculum, but rather, when the student observes

the teacher's behavior. An enormous amount of passive teaching and learning takes place in the affective arena, in ways much more subtle than for content and psychomotor skills. By just being themselves, teachers role model "good, bad, and ugly" behaviors and students learn them all, quite well.

By not consciously planning the teaching of affective topics, i.e. behavior, the student of cardiothoracic anesthesiology is deprived of the opportunity to learn such essentials as how best to relate to a surgeon, cardiologist, nurse, and patient. Effective relationships between physician professionals that are not passive, passive–aggressive or aggressive, but rather open, forthright, and communicative need to be more formally taught and will intuitively benefit patient care. Think, for example, how different the affective learning by the resident will be in the weaning from CPB scenario described in the introduction to this chapter. Instead of arguing with the surgeon about the medication choices and vying for control of the selection process in front of the observing residents from both the anesthesiology and surgical services, a joint collaborative effort can be planned, role modeled and taught. Worse yet would be the anesthesiologist–teacher telling the cardiac surgeon of the use of one drug while in fact using another drug known to the cardiothoracic anesthesiology resident but not the surgical team. Such passive–aggressive behavior must not be consciously or unintentionally role modeled and therefore taught to cardiac and/or pediatric anesthesiology residents.

## Essential/desirable educational resource needs and paraprofessional relationships

In order to have cardiac and/or pediatric anesthesiology fellowship training that is of adequate quality, a number of specific institutional resources are essential. There must be a cardiothoracic surgical program that cares for patients with CHD. Ideally this will include a training program accredited by the Accreditation Council for Graduate Medical Education (ACGME). The surgical case volume and mix must include all of the areas listed in the curriculum section above.

In addition to the surgical program, accredited general pediatrics and pediatric subspecialty programs are essential and an adult CHD division is desirable. To fully support the diagnostic and therapeutic needs of patients with CHD, clinical laboratory facilities must exist in the institution. Cardiothoracic and pulmonary non-invasive laboratories and a cardiac catheterization suite are essential. Consultation from general pediatric and all other appropriate pediatric subspecialties as well as an adult cardiology service with expertise in the management of adult CHD patients must be readily available for cardiothoracic surgeons and anesthesiologists.

Imaging is a very important part of the diagnostic and therapeutic needs of those caring for patients with CHD. A full service radiology department with radioisotope capability must be available. The pediatric cardiology and pulmonary medicine departments may be equipped to meet many of the imaging and isotope needs. It is less important which service provides the imaging than that it be fully available.

A very important aspect of having the pediatric and adult cardiology services available and their equipment needs met is that this will then allow collaboration between these departments and the cardiothoracic surgeons and anesthesiologists. Joint clinical care and teaching conferences, educational programs and research projects will enhance the residency training programs for all of the services and most certainly the subspecialty fellowships in cardiac and pediatric anesthesiology.

When anesthesiology fellows complete their training in cardiac or pediatric anesthesiology many will enter clinical practice settings. In these environments they will undoubtedly interact with or even hire paraprofessionals. It is inevitable that cardiac and pediatric anesthesiologists will work side-by-side with perfusionists, cardiothoracic nurse practitioners, respiratory therapists, surgical physician's assistants and the many other categories of paraprofessionals that care for this patient population. While it may never have been considered an important part of the educational experience for cardiac and pediatric anesthesiology trainees in the past, all residencies should give serious consideration to this issue. Patient care settings will present physician–paraprofessional interactions. Better that these relationships be understood and made part of the education of the residents and fellows than not. If "taught," patient care will benefit and these relationships will most likely be more positive than if ignored.

## Who learns and who teaches: Cardiac and pediatric anesthesiology fellowship education in the USA

### The programs and the learners

There are 132 accredited "core" residency programs in anesthesiology in the USA educating 4296 trainees.[10] A core residency is defined as a program that provides 3 years of clinical anesthesia training broadly defined in the "Program Requirements for Residency Education in Anesthesiology."[11] The Program Requirements are published by the Anesthesiology RRC of the ACGME. The RRC is comprised of representatives from the ABA, ASA and American Medical Association (AMA). A program is accredited when it voluntarily elects to be reviewed by the RRC and is determined to be in compliance with the published Program Requirements. Cardiothoracic and pediatric anesthesiology education as a part of the core residency is conducted in all 132 ACGME accredited programs. This education undergoes quality review as part of the entire accreditation/reaccreditation process for anesthesiology residencies.

The Program Requirements for residency education during the first 2 years of the core clinical anesthesiology training program call for a balance of clinical experiences and didactic presentations that include all aspects of peri-anesthetic care in basic anesthesia and subspecialty disciplines. Cardiac and pediatric anesthesiology are included in the list of subspecialties for which ". . . identifiable 1-month rotations . . ." must be provided.[11] An additional requirement for ". . . a 2-month rotation in critical care"[10] provides the trainee with an opportunity for learning many of the principles of cardiac anesthesiology, especially as they apply to patients in the critical care unit setting.

"The program must provide 12 months of experience in advanced and complex anesthesia assignments in the CA-3 year."[11] The Anesthesiology RRC has recently implemented new Program Requirements that blend advanced and subspecialty clinical experiences for the CA-3 year into one 12-month experience in advanced anesthesia case management during which no subspecialty training may be more than 6 months in length.[11] This precludes most core residents from gaining sufficient subspecialty expertise to be fully educated in cardiac and/or pediatric anesthesiology for patients with CHD.

There are currently 41 accredited pediatric anesthesiology specialty programs educating 61 trainees.[10] Program requirements for pediatric anesthesiology fellowship education have been defined by the Anesthesiology RRC.[10] Cardiothoracic anesthesiology is not an RRC accredited program, hence standardized program requirements do not exist. Program reporting of cardiothoracic anesthesiology programs by the AMA does not occur. Cardiothoracic anesthesiology subspecialty education as a CA-4 program is offered in 70 institutions.[12] These programs have been identified by the SCA Education Committee through their questionnaire about training opportunities in this subspecialty. Utilizing the responses, an SCA booklet, *Training Opportunities in Cardiovascular Anesthesia* has been published on a periodic basis to make this information available for prospective trainees.[12]

The ASA (Committee on Anesthesia Subspecialties, Park Ridge, IL 60068), under the guidance of JG Reves, MD, has collected information on the numbers of trainees who have elected to "specialize" during the last 12 months (CA-3 year) of the 36-month core residency and who have elected to gain subspecialty training in an additional non-required year of education after the completion of the core residency. The most recent data is from the 2000–01 academic year and represents responses to questionnaires mailed to 151 institutions. The information represents an 86.7% response rate (130 completed questionnaires).

Figure 2.1 displays the total number of CA-3 residents training in core anesthesiology programs in the USA from 1989 to 2001. Figure 2.2 displays the number of individuals who have elected to complete an additional non-required

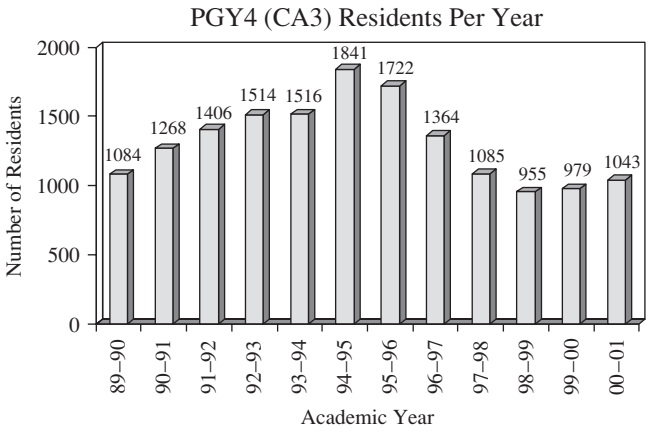


**Fig. 2.1** Number of CA-3 residents in core anesthesiology training programs in the USA from 1989/90 to 2000/01. Reproduced with permission, American Society of Anesthesiologists (ASA), Committee on Subspecialties, Park Ridge, IL 60068. Excerpted from *Committee Work of the ASA Committee on Anesthesia Subspecialties. CA-3 and CA-4 Subspecialty Education Data for the 2000–2001 Academic Year*, of the American Society of Anesthesiologists (ASA). A copy of the full text can be obtained from ASA, 520 N. Northwest Highway, Park Ridge, IL 60068-2573.

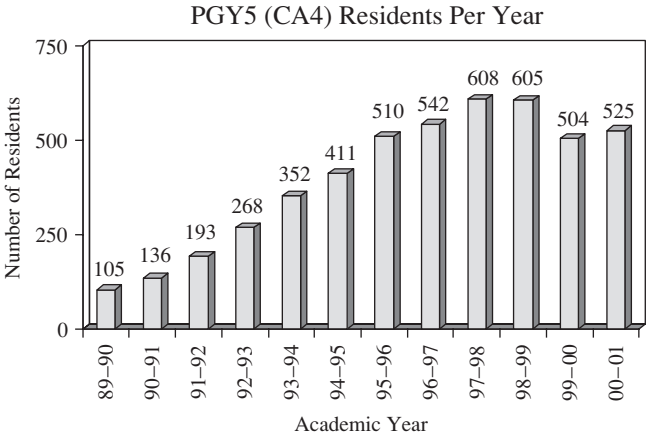


**Fig. 2.2** Number of CA-4 residents in elective anesthesiology training programs in the USA from 1989/90 to 2000/01. Reproduced with permission, ASA Committee on Subspecialties, Park Ridge, IL 60068. Excerpted from *Committee Work of the ASA Committee on Anesthesia Subspecialties. CA-3 and CA-4 Subspecialty Education Data for the 2000–2001 Academic Year*, of the American Society of Anesthesiologists (ASA). A copy of the full text can be obtained from ASA, 520 N. Northwest Highway, Park Ridge, IL 60068-2573.

year of training (CA-4) after completing the core residency program from 1989 to 2001. Figures 2.3 and 2.4 depict the distribution of subspecialties for CA-3 and CA-4 residents in 2000–01. There has been a relatively steady increase in the number of individuals who have elected additional CA-4 subspecialty training. Many trainees believe that additional education and the resultant "credential" will make them more competitive when obtaining practice positions. Table 2.1 summarizes the percentage of core residents since the 1989–90 academic year that selected subspecialty education

**Table 2.1** Percentage of anesthesiology residents in subspecialty education for 6 or more months during the required CA-3 (PGY 4) training period.

| Year | 1989–90 | 1990–91 | 1991–92 | 1992–93 | 1993–94 | 1994–95 | 1995–96 | 1996–97 | 1997–98 | 1998–99 | 1999–2000 | 2000–01 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 6–11 months subspecialty education | 46 | 40 | 36 | 27 | 27 | 23 | 20 | 8 | 6 | 7 | 5 | 3 |
| 12 months subspecialty education | 11 | 4 | 5 | 4 | 2 | 2 | 1 | 2 | 2 | 4 | 2 | 4 |
| No subspecialty education | 44 | 55 | 59 | 69 | 71 | 75 | 79 | 91 | 93 | 90 | 93 | 94 |

Excerpted from *Committee Work of the ASA Committee on Anesthesia Subspecialties. CA-3 and CA-4 Subspecialty Education Data for the 2000–2001 Academic Year*, of the American Society of Anesthesiologists (ASA). A copy of the full text can be obtained from ASA, 520 N. Northwest Highway, Park Ridge, IL 60068-2573. Reproduced with permission, ASA Committee on Subspecialties.

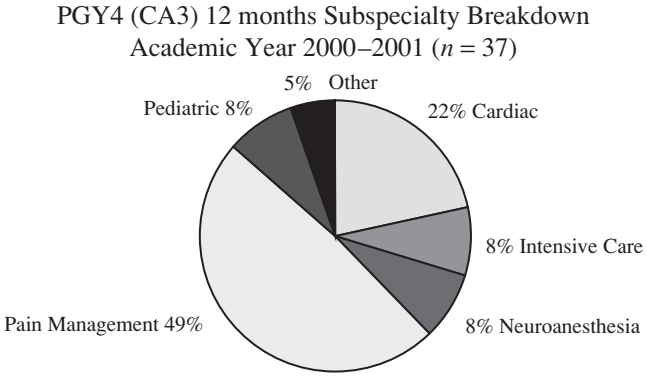


**Fig. 2.3** Subspecialty breakdown for 12-month training of CA-3 residents in core anesthesiology training programs in the USA in 2000–01. Excerpted from *Committee Work of the ASA Committee on Anesthesia Subspecialties. CA-3 and CA-4 Subspecialty Education Data for the 2000–2001 Academic Year*, of the American Society of Anesthesiologists (ASA). A copy of the full text can be obtained from ASA, 520 N. Northwest Highway, Park Ridge, IL 60068-2573. Reproduced with permission, ASA Committee on Subspecialties.

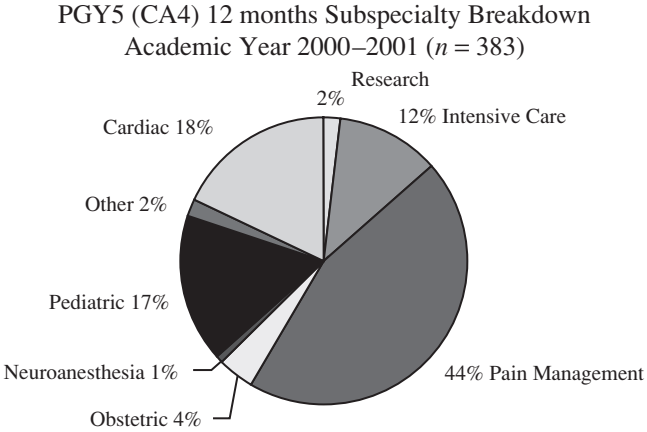


**Fig. 2.4** Subspecialty breakdown for 12-month training of CA-4 residents in elective residency training programs in the USA in 2000–01. Excerpted from *Committee Work of the ASA Committee on Anesthesia Subspecialties. CA-3 and CA-4 Subspecialty Education Data for the 2000–2001 Academic Year*, of the American Society of Anesthesiologists (ASA). A copy of the full text can be obtained from ASA, 520 N. Northwest Highway, Park Ridge, IL 60068-2573. Reproduced with permission, ASA Committee on Subspecialties.

for 6 or more months in their required CA-3 year. There has been a clear trend away from subspecialty training in the CA-3 year of the core anesthesiology residency training program. The opposite trend has been documented in the totally elective CA-4 year (Table 2.2).

Figures 2.5–2.8 summarize the number and percentage of residents who selected cardiothoracic and pediatric anesthesiology subspecialty education to fulfill their required CA-3 year training or elected it in their CA-4 year. The trends for cardiothoracic and pediatric subspecialty training is similar to the more general trend for all subspecialty education, i.e. fewer CA-3 residents are selecting cardiothoracic or pediatric anesthesiology and a larger number are electing a CA-4 year in cardiothoracic or pediatric anesthesiology. Cardiothoracic and pediatric anesthesiology each accounted respectively for 22% and 8% of the CA-3 and 18% and 17% of the CA-4 subspecialty trainees in 2000–01 (Figs 2.9 & 2.10). The popularity of pain management has resulted in erosion in the total number of residents selecting training in cardiothoracic and pediatric anesthesiology. This is documented by the fact that in 2000–01, 171 CA-4 residents (CA-4 n = 383 in 2000–01) selected a 12-month subspecialty training program in pain management (Figs 2.9 & 2.10).

## The teachers

The faculty who teach cardiac and pediatric anesthesiology are anesthesiologists who have vast clinical experience in the

**Table 2.2** Percentage of anesthesiology residents in subspecialty education for 6 or more months during an elective CA-4 (PGY 5) training period.

| Year | 1989–90 | 1990–91 | 1991–92 | 1992–93 | 1993–94 | 1994–95 | 1995–96 | 1996–97 | 1997–98 | 1998–99 | 1999–2000 | 2000–01 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 6–11 months subspecialty education | 27 | 23 | 24 | 18 | 18 | 20 | 12 | 12 | 4 | 6 | 10 | 10 |
| 12 months subspecialty education | 59 | 67 | 69 | 75 | 75 | 76 | 83 | 83 | 90 | 87 | 86 | 73 |
| No subspecialty education | 13 | 10 | 7 | 7 | 7 | 4 | 5 | 4 | 6 | 8 | 5 | 18 |

Excerpted from *Committee Work of the ASA Committee on Anesthesia Subspecialties. CA-3 and CA-4 Subspecialty Education Data for the 2000–2001 Academic Year*, of the American Society of Anesthesiologists (ASA). A copy of the full text can be obtained from ASA, 520 N. Northwest Highway, Park Ridge, IL 60068-2573. Reproduced with permission, ASA Committee on Subspecialties.

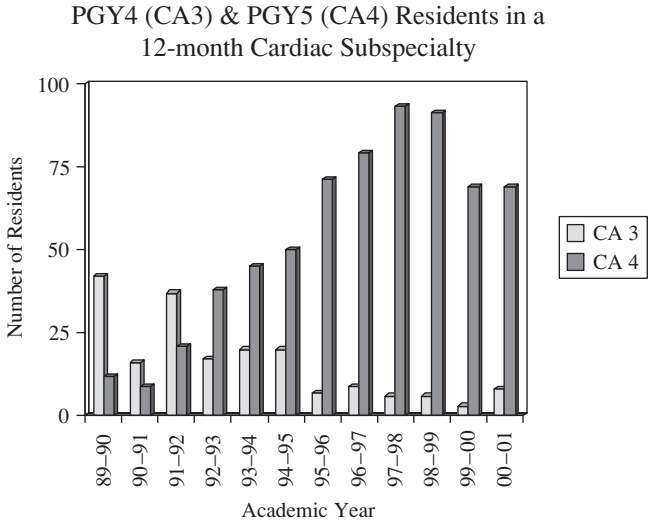


**Fig. 2.5** Number of CA-3 and CA-4 residents in anesthesiology training programs participating in a 12-month cardiac subspecialty education in the USA from 1989/90 to 2000/01. Excerpted from *Committee Work of the ASA Committee on Anesthesia Subspecialties. CA-3 and CA-4 Subspecialty Education Data for the 2000–2001 Academic Year*, of the American Society of Anesthesiologists (ASA). A copy of the full text can be obtained from ASA, 520 N. Northwest Highway, Park Ridge, IL 60068-2573. Reproduced with permission, ASA Committee on Subspecialties.

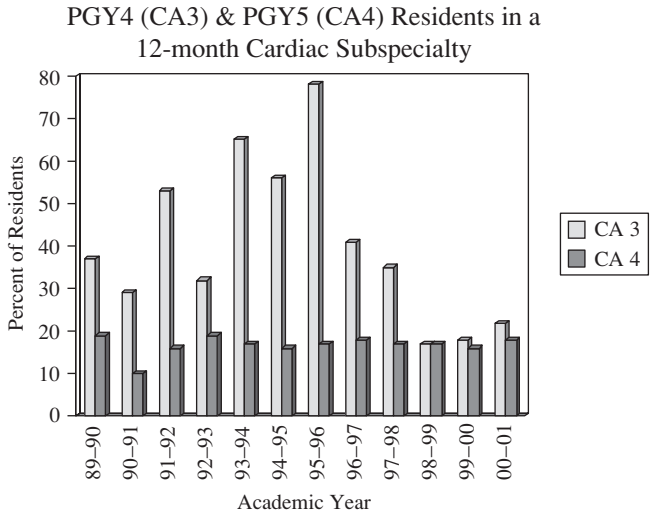


**Fig. 2.6** Percentage of CA-3 and CA-4 residents in anesthesiology training programs participating in a 12-month cardiac subspecialty education in the USA from 1989/90 to 2000/01. Excerpted from *Committee Work of the ASA Committee on Anesthesia Subspecialties. CA-3 and CA-4 Subspecialty Education Data for the 2000–2001 Academic Year*, of the American Society of Anesthesiologists (ASA). A copy of the full text can be obtained from ASA, 520 N. Northwest Highway, Park Ridge, IL 60068-2573. Reproduced with permission, ASA Committee on Subspecialties.

care of these patients. Within this group are faculty members who have completed specialized training in cardiac, pediatric or both subspecialties of anesthesiology. There is no requirement for a teacher of cardiac or pediatric anesthesiology to have completed a subspecialty training program in the discipline. The RRC Program Requirements comment on subspecialty teachers in the following way: "The faculty should have varying interests, capabilities, and backgrounds, and must include individuals who have specialized expertise in a significant majority of the recognized subspecialties. . . . Fellowship training; several years practice, primarily within a subspecialty; and membership and active participation in national organizations related to the subspecialty may signify expertise."[11]

It is fair to state that cardiac and pediatric anesthesiology is taught by physicians who are primarily clinicians, not teachers. These individuals, like the overwhelming majority of physician educators, have had little to no education about being an educator. As such, clinical anesthesiologists who teach anesthesiology in general and cardiac and/or pediatric anesthesiology in particular are often the least adept at the teaching tasks they have prime responsibility for effecting.

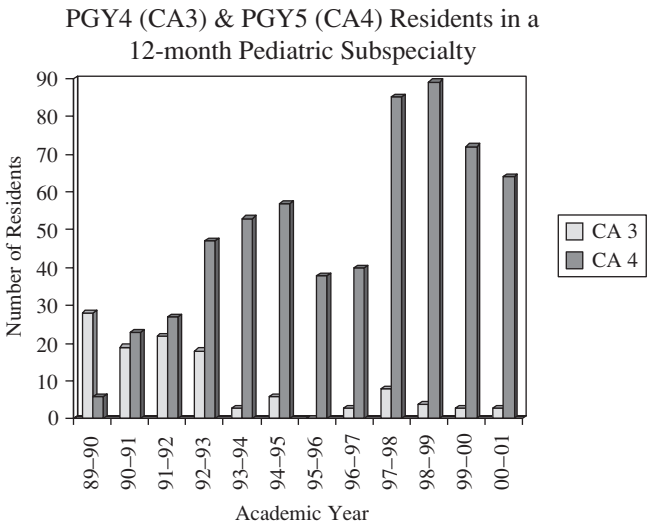


**Fig. 2.7** Number of CA-3 and CA-4 residents in anesthesiology training programs participating in a 12-month pediatric subspecialty education in the USA from 1989/90 to 2000/01. Excerpted from *Committee Work of the ASA Committee on Anesthesia Subspecialties. CA-3 and CA-4 Subspecialty Education Data for the 2000–2001 Academic Year*, of the American Society of Anesthesiologists (ASA). A copy of the full text can be obtained from ASA, 520 N. Northwest Highway, Park Ridge, IL 60068-2573. Reproduced with permission, ASA Committee on Subspecialties.

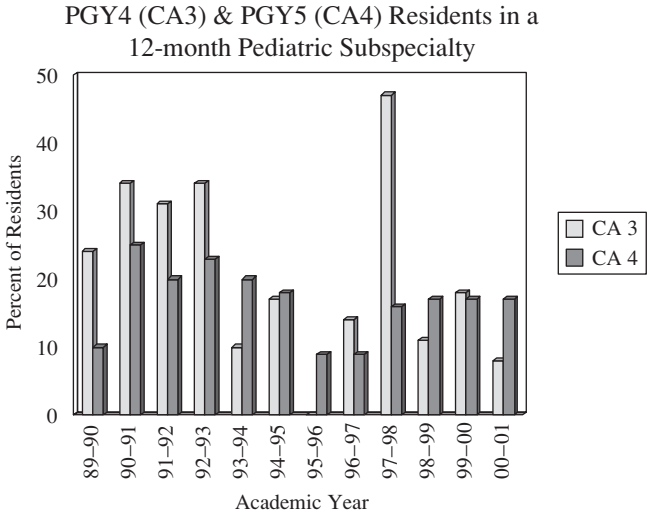


**Fig. 2.8** Percentage of CA-3 and CA-4 residents in anesthesiology training programs participating in a 12-month pediatric subspecialty education in the USA from 1989/90 to 2000/01. Excerpted from *Committee Work of the ASA Committee on Anesthesia Subspecialties. CA-3 and CA-4 Subspecialty Education Data for the 2000–2001 Academic Year*, of the American Society of Anesthesiologists (ASA). A copy of the full text can be obtained from ASA, 520 N. Northwest Highway, Park Ridge, IL 60068-2573. Reproduced with permission, ASA Committee on Subspecialties.

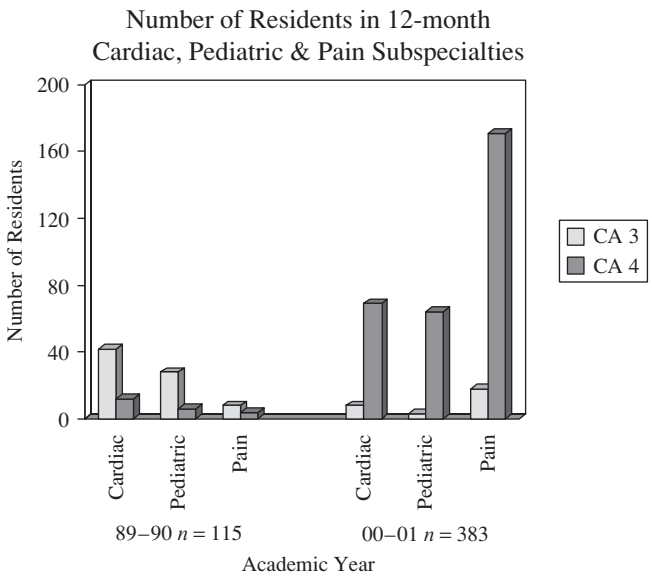


**Fig. 2.9** Number of CA-3 and CA-4 residents in 12-month cardiac, pediatric and pain anesthesiology subspecialty residency programs in 1989–90 and 2000–01. Excerpted from *Committee Work of the ASA Committee on Anesthesia Subspecialties. CA-3 and CA-4 Subspecialty Education Data for the 2000–2001 Academic Year*, of the American Society of Anesthesiologists (ASA). A copy of the full text can be obtained from ASA, 520 N. Northwest Highway, Park Ridge, IL 60068-2573. Reproduced with permission, ASA Committee on Subspecialties.

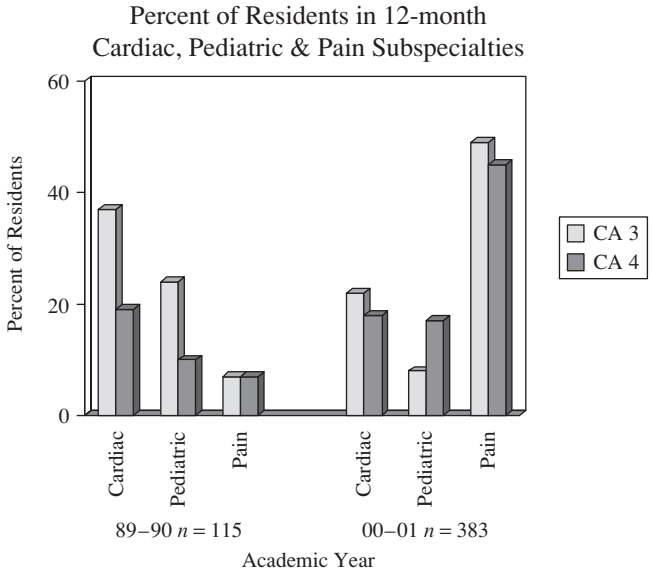


**Fig. 2.10** Percentage of CA-3 and CA-4 residents in 12-month cardiac, pediatric and pain anesthesiology subspecialty residency programs in 1989–90 and 2000–01. Excerpted from *Committee Work of the ASA Committee on Anesthesia Subspecialties. CA-3 and CA-4 Subspecialty Education Data for the 2000–2001 Academic Year*, of the American Society of Anesthesiologists (ASA). A copy of the full text can be obtained from ASA, 520 N. Northwest Highway, Park Ridge, IL 60068–2573. Reproduced with permission, ASA Committee on Subspecialties.

Information is available that points out what constitutes effective teaching traits and how to become a better physician educator.[6,13–16] Exposure to and adoption of these principles and techniques will markedly improve the entire educational process and outcome for anesthesiology education.

### Program evaluation—educational analysis

Analysis of the educational program is the logical and essential outgrowth of the teaching process. The teaching process consists of: (i) identifying a target (student) population, i.e. the core anesthesiology and subspecialty cardiac and pediatric anesthesiology resident trainees; (ii) agreeing upon program goals and objectives; (iii) developing a curriculum, i.e. knowledge, skills, and attitudes, based upon the goals and objectives; and (iv) facilitating the activity of teachers who implement the curriculum using various clinical and didactic instructional methods.

Evaluation of the success of this process is accomplished in a variety of ways. The faculty evaluate the students to assure that they have learned the content, skills and attitudes. The trainees and program are evaluated by the ability of the residents to pass certifying exams (when they exist) and secure professional positions in which they become credentialed to provide specific medical care. Patient outcome statistics can be analyzed to demonstrate that the educational program does not result in unacceptable morbidity and mortality and in fact may improve these parameters. An institution's CQI (continuous quality improvement) program serves as an effective method for continuing medical education and evaluation of the success of the educational program as well as the clinical care provided to patients. The resident trainees assess the faculty's effectiveness and accomplishments as educators and role models. The RRC evaluates the core anesthesiology and pediatric anesthesiology subspecialty residency programs based upon their ability to meet the published Program Requirements. If an accreditation mechanism is established for subspecialty education in cardiothoracic anesthesiology, a similar RRC evaluation will assess these programs. Until formal accreditation of cardiothoracic anesthesiology residencies becomes a reality, informal evaluation must take place via internal institutional reviews and by peers from involved professional organizations like the SCA.

Analysis of all of the evaluation data mentioned allows reaffirmation or modification of the program goals and objectives, curriculum, faculty, and teaching methods. In this way, the educational loop is completed, quality education is provided, and public trust assured.

## Practical advice on learning anesthesia for the care of patients with congenital heart disease—pearls to consider

Education is a change in behavior based upon experiences. The first and foremost perspective that the resident/fellow must have is to fully engage in experiences related to this subspecialty.

**Pearl I**: To gain experiences, immerse yourself in every conceivable clinical and didactic activity related to anesthesia for patients with CHD.

Enhance every experience by raising its cognitive level. Full understanding of anesthesia for patients with CHD can only come from questioning each scenario.

**Pearl II**: Seek the answer to the most important question related to your learning, i.e. why?

In order to assure that the resident/fellow has had sufficient experiences from which to learn and has asked "why" to fully understand, insist that the resident becomes a teacher.

**Pearl III**: Learn how to teach cardiothoracic anesthesiology to others and you will assure that you have learned it!

### Acknowledgements

I wish to thank George E. Miller, MD, for the insight on Socrates.

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## Appendix—Content outline [abridged—to include cardiothoracic and pediatric anesthesiology topics]

### Joint Council on In-training Examinations

*American Board of Anesthesiology*
*American Society of Anesthesiologists*

Revised January, 1996

I. Physiological sciences
  A. Physiology
    1 Respiration
      Lung volumes
      Lung mechanics
      Ventilation–perfusion
      Diffusion
      Blood gas transport
      Regulation of ventilation
      Non-respiratory functions of lungs
    2 Cardiovascular
      Cardiac cycle
      Ventricular function
      Venous return
      Blood pressure
      Micro-circulation
      Organ perfusion
      Regulation of circulation and blood volume
    3 Central and peripheral nervous system
      Autonomic nervous system
    4 Hepatic function
    5 Renal function
    6 Endocrine function
    7 Temperature regulation
  B. Pharmacology
    1 General concepts
    2 Anesthetics—gases and vapors
    3 Anesthetics—intravenous
    4 Anesthetics—local
    5 Muscle relaxants
    6 Autonomic drugs
    7 Cardiovascular drugs
    8 Diuretics
    9 Drug interactions

II. Physical sciences
  A. Anatomy
    1 Topographical anatomy as landmarks
    2 Radiologic anatomy
    3 Respiratory system
    4 Cardiovascular system
  B. Biochemistry
    1 Normal body metabolism
    2 Acid-base regulation
    3 Water and electrolytes
  C. Physics
    1 Mechanics
    2 Flow velocity
    3 Uptake and distribution of inhalation anesthetics
    4 Physics of breathing systems
    5 Monitoring methods
    6 Instrumentation
    7 Ventilators
    8 Defibrillators
    9 Pacemakers

III.
  A. Anesthesia procedures, methods, and techniques
    1 Evaluation of the patient and preoperative preparation

2 General anesthesia
3 Intravenous fluid therapy during anesthesia
4 Complications
Trauma
Temperature
Bronchospasm, laryngospasm
5 Special techniques
Controlled hypotension
Controlled hypothermia

B. Disease states—clinical problems and their management
1 Respiratory
Obstructive disease
Restrictive disease
Management of the patient with respiratory disease
2 Cardiovascular
Ischemic heart disease
Valvular heart disease
Rhythm disorders and conduction defects
Heart failure and cardiomyopathy
Cardiac tamponade and constrictive pericarditis
Circulatory assist
Myocardial preservation
Pulmonary embolism
Hypertension
Peripheral circulatory failure
Vascular diseases
Cardiopulmonary resuscitation
3 Other entities
Pediatric anesthesia
Neonatal physiology
Congenital heart disease
Emergencies in the newborn
4 Special problems in
Laparoscopic surgery
Thoracoscopy

Based on ABA–ASA. *Content Outline*. Joint Council on In-Training Examinations. American Board of Anesthesiology–American Society of Anesthesiologists (ASA), 1996. A copy of the full text can be obtained from ASA, 520 N. Northwest Highway, Park Ridge, IL 60068-2573.

# 3 Physiology and molecular biology of the developing circulation

Dean B. Andropoulos
Monique L. Ogletree

## Introduction

The circulatory system in congenital heart disease (CHD) continually changes and develops in response to both normal and pathologic stimuli. Response to anesthetic and surgical interventions must be understood in this framework, and is often radically different from the usual, expected pediatric and adult situations with a "normal" cardiovascular system. This chapter will review developmental changes of the cardiovascular system from fetal life through adulthood, both in the normal and pathophysiologic states associated with CHD. Not much is known about the development of the normal and diseased human heart. Much of the information discussed in this chapter was derived from animal models, and undoubtedly new information will be discovered as human myocardial tissue is studied.

## Development from fetus to neonate

### Circulatory pathways

The fetus receives oxygenated and nutrient-rich blood from the placenta via the umbilical vein, and ejects desaturated blood through the umbilical arteries to the placenta, and thus the placenta, not the lung, serves as the organ of respiration. Blood flow thus largely bypasses the lungs *in utero*, accounting for only about 7% of the fetal combined ventricular output.[1] Pulmonary vascular resistance (*PVR*) is high, and the lungs collapsed and filled with amniotic fluid. This is the basis for the fetal circulation, which is a parallel circulation, rather than the series circulation seen postnatally. Three fetal circulatory shunts exist to carry better-oxygenated blood from the umbilical vein to the systemic circulation: the ductus venosus, ductus arteriosus, and foramen ovale (Fig. 3.1a). Approximately 50% of the umbilical venous blood, with an oxygen tension of about 30–35 mmHg, passes through the ductus venosus, and then into the right atrium. There it streams preferentially across the foramen ovale, guided by the valves of the sinus venosus and Chiari network into the left atrium. Thus the brain and upper body preferentially receive this relatively well-oxygenated blood, which accounts for 20–30% of the combined ventricular output. Blood returning in the inferior vena cava represents about 70% of the total venous return to the heart, and two thirds of this deoxygenated blood passes into the right atrium and ventricle. About 90% of the blood flows through the ductus arteriosus to supply the lower fetal body.

After birth, there is a dramatic fall in *PVR* and increase in pulmonary blood flow, with inflation and oxygenation of the lungs (Fig. 3.2). The placental circulation is removed, and all of these changes lead to closure of the ductus venosus, constriction of the ductus arteriosus, and reversal of pressure gradients in the left and right atria, leading to closure of the foramen ovale. This leads to a state called the transitional circulation (Fig. 3.1b), characterized by high pulmonary artery pressures and resistance (much lower than *in utero*, however), and a small amount of left-to-right flow through the ductus arteriosus. This is a labile state, and failure to maintain lower *PVR* can rapidly lead to reversion to fetal circulatory pathways, and right-to-left shunting at the ductus arteriosus and foramen ovale. This maintenance of fetal circulatory pathways is necessary for survival in many CHD patients, particularly those dependent on a patent ductus arteriosus for all or a significant portion of systemic or pulmonary blood flow, or atresia of atrioventricular valves. Maintenance of ductal patency with prostaglandin $E_1$ ($PGE_1$) is crucial in these lesions. In a two ventricle heart with large intracardiac shunts, maintenance of the fetal circulation leads to right-to-left shunting at the foramen and ductal levels, and thus hypoxia. Conversion to the mature circulation (Fig. 3.1c) in the normal heart occurs over a period of several weeks, as *PVR* falls further, and the ductus arteriosus closes permanently by thrombosis, intimal proliferation, and fibrosis. Factors favoring the transition from fetal to mature circulation include normal oxygen tensions and physical expansion of the lungs, normal pH, nitric oxide (NO), and prostacyclin ($PGI_2$). Factors favoring reversion to

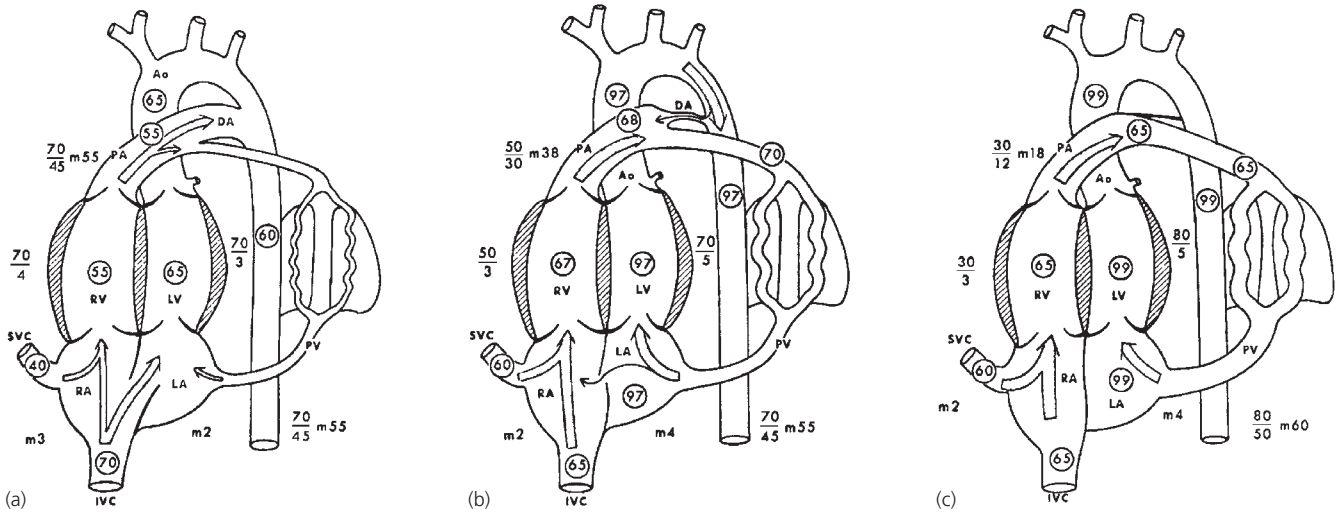



**Fig. 3.1** Transition from fetal to mature circulation. (a) Fetal circulation. (b) Transitional circulation. (c) Mature circulation. Circled numbers are oxygen saturations; uncircled numbers are pressures in mmHg. Ao, aorta; DA, ductus arteriosus; IVC, inferior vena cava; LA, left atrium; LV, left ventricle; m, mean pressure; PA, pulmonary artery; PV, pulmonary vein; RA, right atrium; RV, right ventricle; SVC, superior vena cava. Reproduced with permission from Rudolph AM. *Congenital Diseases of the Heart*. Chicago: Year Book Medical Publishers, 1974.

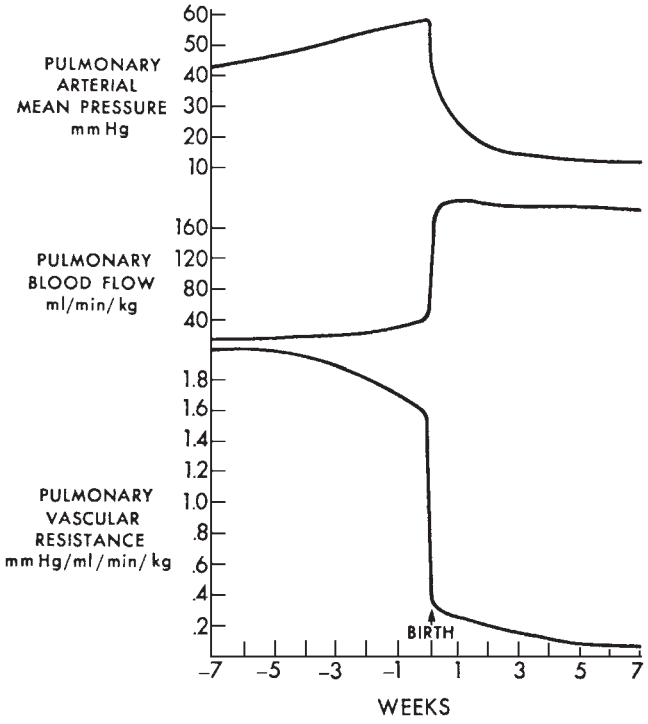



**Fig. 3.2** Changes in pulmonary artery pressure, pulmonary blood flow, and pulmonary vascular resistance in the lamb after birth. Reproduced with permission from Rudolph AM. *Congenital Diseases of the Heart*. Chicago: Year Book Medical Publishers, 1974.

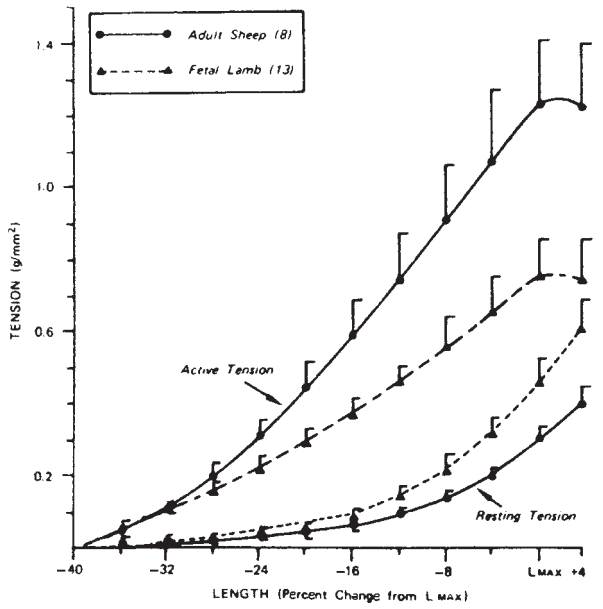
fetal circulation include low oxygen tension, acidotic pH, lung collapse, and inflammatory mediators (leukotrienes, thromboxane $A_2$, platelet-activating factor) as seen in sepsis and other related conditions, and endothelin-A receptor activators.[2]

### Myocardial contractility

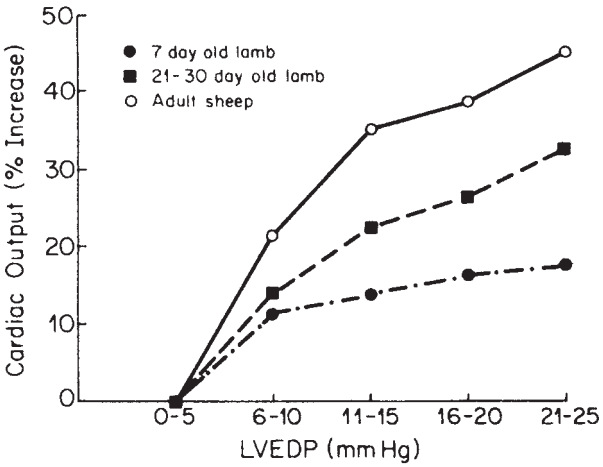
The fetal myocardium is characterized by poorly organized cellular arrangements, and fewer myofibrils with a random orientation, in contrast to the parallel, well organized myofibrillar arrangement of the adult myocardium (see below). Fetal hearts develop less tension per gram than adult hearts because of increased water content and fewer contractile elements. Calcium cycling and excitation contraction coupling are also very different, with poorly organized T-tubules and immature sarcoplasmic reticulum (SR), leading to more dependence on free cytosolic ionized calcium for normal contractility. Despite this immature state, the fetal heart can increase its stroke volume in a limited fashion up to left atrial pressures of 10–12 mmHg according to the Frank–Starling relationship, as long as afterload (i.e. arterial pressure) is kept low.[3] These features continue throughout the neonatal and early infancy period.

## Development from neonate to older infant and child

At birth the neonatal heart must suddenly change from a parallel circulation to a series circulation, and the left ventricle in particular must adapt immediately to dramatically increased preload from blood returning from the lungs, and increased afterload as the placental circulation is removed. The very high oxygen consumption of the newborn necessitates a high cardiac output for the first few months of life. However, animal models have demonstrated that the fetal and newborn myocardium develops less tension in response to increasing




(a)




(b)

**Fig. 3.3** (a) Isometric resting and active length–tension relationships in fetal and adult lamb cardiac muscle strips. Reproduced with permission from Friedman WF. The intrinsic physiologic properties of the developing heart. *Prog Cardiovasc Dis* 1972; **15**: 87–111. (b) Response to volume load of normal saline at 5 mL/kg/minute, at constant heart rate. *LVEDP*, left ventricular end-diastolic pressure. Reproduced with permission from Friedman WF, George BL. Treatment of congestive heart failure by altering loading conditions of the heart. *J Pediatr* 1985; **106**: 697–706.

preload (sarcomere length), and that cardiac output increases less to the same degree of volume loading (Fig. 3.3).[4,5] Resting tension, however, is greater in the newborn compared to the mature heart. This information suggests that the newborn heart is operating near the top of its Frank–Starling curve, and that there is less reserve in response to both increased afterload and preload. This observation is borne out clinically in newborns after complex heart surgery, who are often intolerant of even small increases in left atrial pressure or mean arterial pressure. The newborn myocardium also has only a limited ability to increase its inotropic state in response to exogenous catecholamines, and is much more dependent on heart rate to maintain cardiac output than is the mature heart. One reason for this is the high levels of circulating endogenous catecholamines that appear after birth, necessary to make the transition to extrauterine life.[6] As these levels decrease in the weeks after birth, contractile reserve increases.

The neonatal myocardium is less compliant than the mature myocardium, with increased resting tension as noted above, and a significantly greater increase in ventricular pressure with volume loading.[7] This implies that diastolic function of the neonatal heart is also impaired compared to the mature heart. The neonatal myocardium also responds less to exogenous catecholamine administration than the mature heart.[8] This will be discussed further later in this chapter. The myofibrils of the newborn heart also appear to have a greater sensitivity to calcium, developing a greater tension than adult myofibrils when exposed to the same free $Ca^{2+}$ concentration *in vitro*.[9]

It must again be emphasized that nearly all of these data were obtained from animal models, and although the information appears to agree with what is observed clinically, there exists a need for non-invasive studies of normal human hearts from the neonatal period through adulthood to confirm these impressions of cardiac development.

## Gene expression in cardiac development

Genetic aspects of human cardiac development are beginning to be understood, and in contrast to the physiologic studies almost exclusively in animal models, small amounts of human cardiac tissue obtained from biopsy or autopsy specimens can be studied for differences in genetic expression of the structural components of the heart. Some aspects of these developmental changes will be reviewed here.

Myosin is the major protein component of the thick filaments of the cardiac myofibril, and developmental differences in the expression of this protein may play a significant role in changes in myocardial contractility. The myosin heavy chain makes up the backbone of the thick filaments of the contractile unit of the cardiac myocyte. Two major isoforms, the α and β, exist, with the genes found on chromosome 14. The β isoform predominates in cardiac muscle throughout development, and so does not change significantly with maturation.[10] The myosin light chain, however, has multiple isoforms, and the relative proportions of these isoforms change with development, and also in response to pressure overload of the heart. Phosphorylation of the myosin light chain increases the myofibrillar sensitivity to $Ca^{2+}$, and the isoforms that predominate in the newborn myocardium appear to confer a greater sensitivity to $Ca^{2+}$ than those seen in the mature heart.[11] This may be an important component of the

explanation for increased sensitivity of the neonatal heart to $Ca^{2+}$.

Troponin I, C, and T are critical proteins which bind $Ca^{2+}$ and regulate the interaction between myosin and actin, and thus directly affect the force of contraction. Troponin C, the $Ca^{2+}$ binding portion of the troponin moiety, does not change its isoform with development. Troponin I, however, has two major isoforms, a slow skeletal muscle type that is predominant in the heart in fetal and neonatal life, and the cardiac isoform, which is the only one expressed in the mature heart, both in normal and failing ventricles.[12] Only the cardiac (mature) isoform responds to β-adrenergic stimulation, which results in a faster twitch development and greater twitch tension in muscle experiments. And, the neonatal myofibrils containing the immature myosin light chain isoform are more resistant to acidosis than are mature myofibrils. Troponin T is expressed in multiple isoforms, with four being expressed in the fetal and neonatal heart, but only one in the mature heart. These isoforms exhibit different levels of adenosine triphosphatase (ATPase) activity and $Ca^{2+}$ sensitivity (see below), with greater ATPase activity and $Ca^{2+}$ sensitivity seen in the immature forms.[9] This again may contribute to the different myocardial function seen with development of the heart. Tropomyosin[13] has two and actin[14] has three isoforms which are expressed in different proportions as developmental changes occur, but the functional significance of these changes has yet to be elucidated.

The extracellular matrix of the heart is important in translating the force generated by the shortening of sarcomere length to the cardiac chambers, resulting in cardiac output. The major components of the extracellular matrix are collagen types I and II, glycoproteins, and proteoglycans. The expression of these elements changes with development, and this likely has important functional implications. The neonatal heart has a higher content of both total and type I collagen (which is stiffer and less compliant than type III collagen) when compared to the total protein content of the heart.[15] The collagen to total protein ratio reaches mature levels by about 5 months of life. This, along with greater water content of the myocardium, may partially explain the difference in diastolic function, and also the lesser ability of the neonatal myocardium to increase its inotropic state because of the relative lack of contractile elements. A network of collagen-based connections, called the weave network, develops rapidly after birth, connecting myocytes and capillaries and allowing greater functional integrity to develop in response to the greater afterload stress on the heart.[16] This development of the extracellular matrix, which appears to be complete by approximately 6 months of age, results in a much more efficient transfer of force generated by sarcomere shortening to the cardiac chambers (Fig. 3.4).

The cardiac myocytes have receptors on the outside of their sarcolemmal membranes called integrins. These receptors are specific for collagen and fibronectin, and cause the attachment of the extracellular matrix to the myocytes, allowing force transduction to occur.[17] Collagen and vinculin, another cytoskeletal protein, are attached to the sarcomere at the Z disk. The integrins have two subunits, α and β, which express several isoforms, the relative proportions of which change during development to those which afford greater adherence of the cytoskeletal proteins to the myocytes, resulting in greater structural integrity.

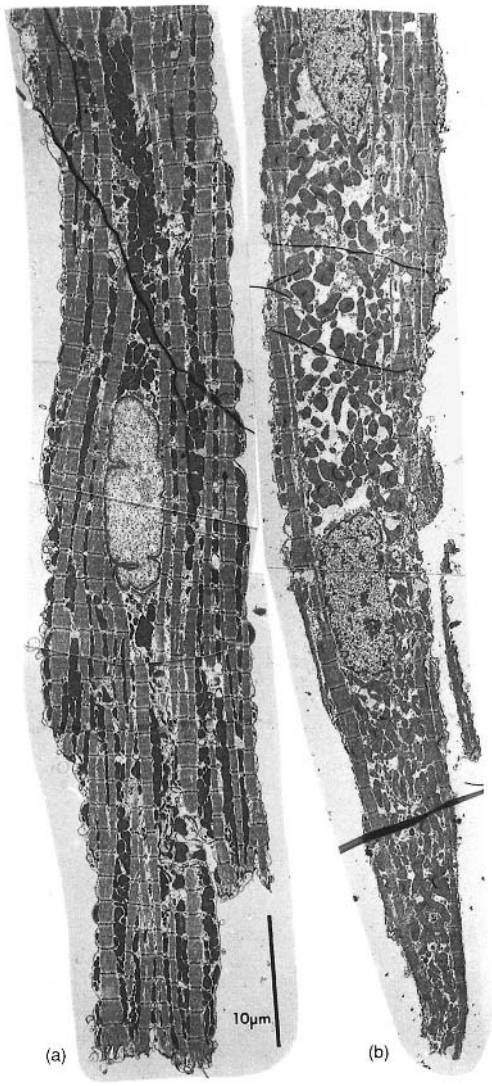



**Fig. 3.4** Longitudinal sections through an adult rabbit cardiac myocyte (a), and a 3-week-old rabbit cardiac myocyte (b). Note the differences between myofibril organization and structure, as well as cell size. Reproduced with permission from Nassar R, Reedy MC, Anderson PA. Developmental changes in the ultrastucture and sarcomere shortening of the isolated rabbit ventricular myocyte. *Circ Res* 1987; **81**: 465–83.

The preceding short review is meant to give the reader an idea of some of the aspects of the molecular biology of the developing circulation. The explosion of new information in this area will lead to a more thorough understanding of the

pathophysiology of disease states and will suggest avenues for future treatment. For a more complete treatment of this area, the reader is referred to several excellent reviews.[18–20]

Changes in receptor signaling and excitation contraction coupling are discussed below.

### Innervation of the heart

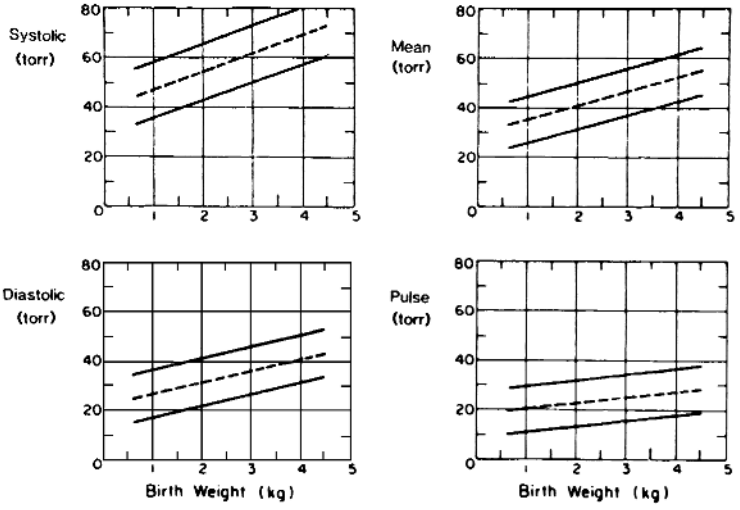
Clinical observations in newborn infants have led to the hypothesis that the sympathetic innervation and control of the cardiovascular system is incomplete in the newborn infant compared to older children and adults, and that the parasympathetic innervation is intact. Examples of this include the frequency of bradycardia in the newborn in response to a number of stimuli, including vagal and vagotonic agents, and the relative lack of sensitivity in the newborn to sympathomimetic agents. Histologic studies in animal models have demonstrated incomplete sympathetic innervation in the neonatal heart when compared to the adult, but no differences in the number or density of parasympathetic nerves.[21,22]

Autonomic cardiovascular control of cardiac activity can be evaluated using analysis of the electrocardiogram by measuring heart rate variability in response to both respiration and to beat-to-beat variability in systolic blood pressure.[23] The sympathetic and parasympathetic input into sinoatrial node activity contribute to well described heart rate variability changes; in general, the greater the heart rate variability, the greater the parasympathetic input into sinoatrial node activity.[24] Studies using these methodologies for normal infants during sleep suggest that the parasympathetic predominance gradually diminishes until approximately 6 months of age, coinciding with greater sympathetic innervation of the heart similar to adult levels.[25]

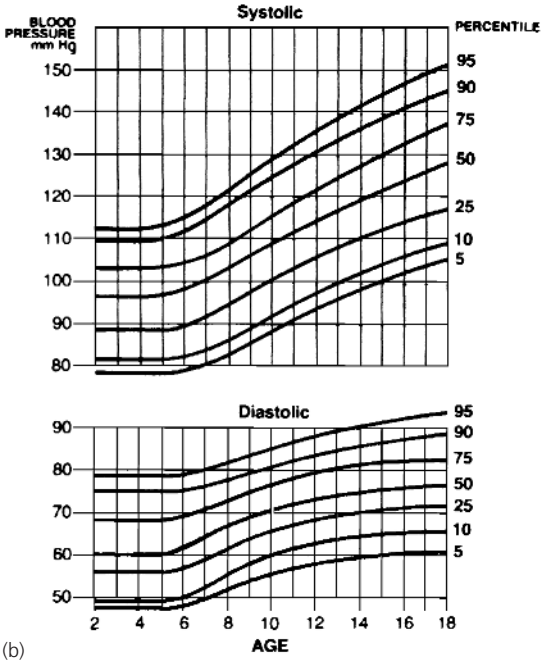
## Development from child to adult

Beyond the transition period from fetal to newborn life and into the first few months of postnatal life, there is not much human or animal information concerning the exact nature and extent of cardiac development at the cellular level. Most studies compare newborn or fetal to adult animals.[26] In the human infant, it is assumed that the cellular elements of the cardiac myocyte, i.e. adrenergic receptors (ARs), intracellular receptors and signaling, calcium cycling and regulation, and interaction of the contractile proteins, is similar to the adult by approximately 6 months of age. This corresponds with the age that depression of cardiac function by volatile agents appears to diminish to adult levels.[27]

It is useful for the anesthesiologist to be aware of normal ranges for physiologic variables in premature and full term newborns of all sizes, and in infants and children of all ages (Fig. 3.5). Obviously, acceptable ranges for these variables are




(a)




(b)

**Fig. 3.5** (a) Blood pressure measured in the umbilical artery of infants in the first 12 h of life weighing 600–4200 g. Reproduced with permission from Versmold HT, Kitterman JA, Phibbs RH, Gregory GA, Tooley WH. Aortic blood pressure during the first 12 hours of life in infants with birth weight 610 to 4220 grams. *Pediatrics* 1981; **67**: 607–13. (b) Blood pressure percentiles, age 2–18 years. Reproduced with permission from Blumenthal SC. Report of the task force on blood pressure control in children. *Pediatrics* 1977; **59** (Suppl.): 794–820.

highly dependent on the individual patient's pathophysiology, but the wide range of "normal" values may reassure the practitioner to accept "low" blood pressure; for example, if other indices of cardiac function and tissue oxygen delivery are acceptable.

## Myocardial sequelae of longstanding congenital heart disease

Hypertrophy of the cardiac chambers is a common response to a number of different chronic pathophysiologic states. Wall thickness increases though hypertrophy of the cardiac myocytes and non-contractile elements. The hypertrophy reduces wall stress in the dilated heart, but also serves to reduce ventricular function, particularly diastolic function, in chronic congestive heart failure and myocardial dysfunction. This reduction in function serves to reduce myocardial oxygen consumption in response to a wide variety of chronic stresses, both in pressure and volume overloaded ventricles.[28]

Pressure overload hypertrophy results in altered gene expression in the cardiomyocyte. Myosin isoform expression (see below) changes from the faster reacting α-myosin to the slower β-myosin, reducing myocardial function.[29] Altered expression or mutations of other genes that regulate production of cardiac cytoskeletal proteins, such as dystrophin, may occur in patients with end-stage cardiomyopathy.[30,31]

## Cardiomyocyte receptor function in normal and diseased hearts

### The adrenergic receptor

The ARs are a part of a large superfamily of receptors that mediate their biological responses through the coupling of a specific guanine nucleotide regulatory protein or G protein.[32] This superfamily of receptors shares a common structural motif, characterized by seven hydrophobic domains spanning the lipid bilayer. The seven domains are attached by three internal loops and three external loops between the amine terminus and the cytoplasmic carboxy terminus. The function of this receptor family is dependent on a specific agonist (or ligand) binding to the receptor, which causes a conformational change in the receptor. This structural change permits the interaction, between the intracellular portion of the receptor and guanine nucleotide regulatory protein (or G protein). This interaction, also referred to as coupling, inevitably links the activated receptor to a specific biological response. The regulation of the biological response is initiated by the specificity of the receptor for a particular extracellular agonist and the coupling of a specific G protein to that activated receptor.

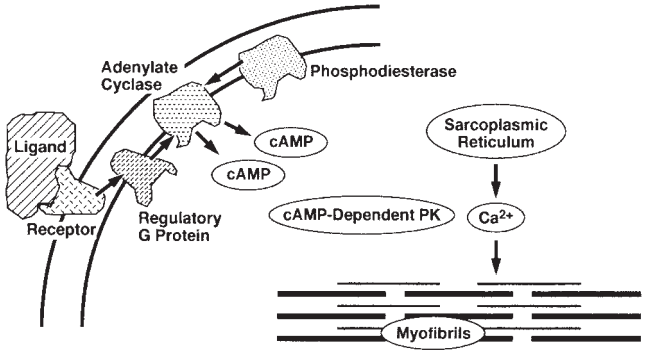



**Fig. 3.6** Adrenergic receptor activation produces conformational changes in the receptor, the G protein and its subunits, which increases adenylate cyclase activity and cyclic adenosine monophosphate (cAMP) activity. cAMP-dependent protein kinase (PK) activity increases, which results in the phosphorylation of many intracellular proteins, the net result of which is release of calcium from the sarcoplasmic reticulum, and activation of the actin–myosin complex by binding to troponin C. Phosphodiesterase breaks down cAMP and leads to the reduction of phosphorylation and thus all of the downstream cascade effects. Reproduced with permission from Fisher DJ, Feltes TF, Moore JW, Marcus B, Johnson G. Management of acute congestive cardiac failure. In: Garson A, Bricker JT, Fisher DJ, Neish SR, eds. *The Science and Practice of Pediatric Cardiology*, 2nd edn. Baltimore, MD: Williams & Wilkins, 1998.

Once an extracellular ligand (or agonist) is specifically recognized by a cell surface receptor, the receptor goes through a conformational changes that exposes a specific region of the receptor complex to the intracellular side of the plasma membrane (Fig. 3.6).[33] This confirmation change triggers the interaction of the G protein with the amino acids of the third intracellular loop of the receptor and hence leading to G protein activation. There are three different G proteins: stimulatory G protein ($G_s$), inhibitory G protein ($G_i$) and the $G_q$. Under normal conditions, all of the β-receptors interact with the $G_s$, the $\alpha_1$ interacts with the $G_q$, and $\alpha_2$ interacts with the $G_i$. Each G protein is a heterotrimer made up of three subunits: α, β, and γ. The activation of the G protein-coupled receptor causes an exchange of bound guanosine diphosphate (GDP) for guanosine triphosphate (GTP) within the α-subunit and initiates the disassociation of the β–γ-subunit from the α-subunit. The GTP-activated α-subunit modulates the activity of a specific effector enzyme within a specific signaling pathway by catalyzing the hydrolysis of GTP to GDP and inorganic phosphate. This causes the transference of a high-energy phosphate group to an enzyme and in turn causes the deactivation of the α-subunit. This process will eventually lead to the deactivation of the α-subunit and the reassociation with the β–γ complex. This cycle is continuously repeated until the agonist becomes unbound from the receptor. Downstream of enzyme activation, the production of a second messenger regulates the biological response.

Adrenergic receptors have been subdivided into two groups of receptors based on the results of binding studies

using a series of selective agonists and antagonists. In 1948 Ahlquist used the difference in rank orders of potency of a series of agonists to separate the ARs into two principal receptor groups, the α- and β-receptor groups.[34] These findings have been confirmed repeatedly with the development of drugs that function to selectively antagonize the α-receptor with no effect on the β-receptor. Soon after the distinction between the α- and β-receptor type was known, it became more evident that the separation of α- and β-receptors was not sufficient to explain pharmacological studies using rank order of potency for an antagonist differing from an agonist because it blocks the biological response. With the advent of radioligand labeled antagonists and new molecular cloning techniques examining receptor gene expression, it became clear that the two principal receptor groups could be further subdivided into additional subtypes.

To date, within the β-adrenergic group four different subtypes have been identified: $\beta_1$, $\beta_2$, $\beta_3$, and $\beta_4$. Pharmacologically $\beta_1$ and $\beta_2$ are differentiated by their affinities to different catecholamines: epinephrine, norepinephrine, and isoproterenol. Beta-1 has similar affinity for epinephrine and norepinephrine, while $\beta_2$ has a higher affinity for epinephrine than to norepinephrine. Both $\beta_1$ and $\beta_2$ have the same affinity for isoproterenol. The $\beta_3$- and $\beta_4$-receptors have minor roles in cardiovascular function and will not be further discussed.

The expression and distribution of each subtype is highly dependent on the organ, which adds another level of specificity. Distribution of a particular receptor in two different tissue types may result in two different functions. When examining cardiovascular response to adrenergic stimulation, the $\beta_1$-receptor is predominantly expressed in heart tissue. The stimulation of the receptor subtype leads to both inotropic and chrontropic effects on cardiac function, resulting in an increase in the myocardial contractile force and a shortening of contractile timing, respectively. While $\beta_2$ can also be found in the heart, it is mostly expressed in vascular smooth muscle tissue. The distribution and function relevance of this receptor subtype in the heart is controversial and may change with alterations in cardiac function. The percentage of $\beta_2$ in the non-failing heart averages about 20% in the ventricle[35] and 30% in the atrium. The ratio of $\beta_1$- to $\beta_2$-receptors is approximately 3 : 1 in younger hearts.[36,37]

Each signaling pathway is specific to each AR. Once the agonist binds to the $\beta_1$-receptor causing the coupling of the G protein, the G protein α-subunit becomes activated followed by an increase in adenylate cyclase (AC) activity, which induces the conversion of adenosine triphosphate (ATP) to cyclic adenosine monophosphate (cAMP). The second messenger, cAMP, phosphorylates protein kinase A (PKA). The function of a kinase is to phosphorylate other target proteins, which initiates a biological response (Fig. 3.6). Protein kinase A phosphorylates many effector proteins, and the phosphorylation of each functions to increase the concentration of intracellular calcium.

The $\beta_2$-receptor has also been shown to function through the cAMP signaling pathway causing the activation of PKA, but not nearly to the extent of $\beta_1$ in cardiomyocytes.[38] The response of this stimulation appears to have a larger effect on smooth muscle; for example, on the vascular smooth muscle. In this tissue type, the stimulation of $\beta_2$ and the subsequent increase in cAMP promotes the vasodilation of vascular smooth muscle and may lead to alterations in blood pressure. In these tissues, the effect of $\beta_1$ stimulation appears to be minimal, due to lack of $\beta_1$-receptors in the smooth muscle.

Similar to the β-receptor, the α-receptors can be pharmacologically subdivided into $\alpha_1$ and $\alpha_2$. The $\alpha_1$-receptor is distributed in most vascular smooth muscle and to a lesser extent in the heart. The $\alpha_2$-receptor has been found in some vascular smooth muscle; however, its major functional importance is as a presynaptic receptor in the central and peripheral nervous systems. The use of molecular techniques have identified three additional subtypes of the $\alpha_1$-receptor ($\alpha_{1A}$, $\alpha_{1B}$, and $\alpha_{1D}$) and three additional subtypes of the $\alpha_2$-receptor.[32] Binding of an agonist to an $\alpha_1$-receptor in the heart or vascular smooth muscle results in activation of the $G_q$ subunit of the G protein, which activates phospholipase C (see below), producing diacylglycerol and inositol-1,4,5-triphosphate, which releases $Ca^{2+}$ from the SR and increases vascular smooth muscle tone or cardiac contractility. A schematic classification of ARs incorporating recent knowledge of molecular pharmacology and signal transduction is presented in Fig. 3.7.[32]

The AR concentration in cardiac tissue is very small and measured as fentomoles per milligram of protein. However, the response to stimulation of the receptor is greatly amplified by the signal that occurs downstream of the receptor. In rat ventricular myocytes, the ratio between the β-receptors and the next two downstream signaling components (β-receptor : G protein : AC) is 1 : 200 : 3.[39] This demonstrates how a large response can be initiated by the activation of a small number of receptors. In addition, it also shows that the rate-limiting component that ultimately regulates intracellular production of cAMP is receptor density and the enzyme concentration of AC.

## Developmental changes in adrenergic receptor signaling

Information concerning changes in AR function during the transition from neonatal to more mature myocardial development is limited to a few animal studies, which will be summarized here. As noted above, the neonatal heart has a limited inotropic response to catecholamine administration.

Beta-adrenergic receptor density was higher in the ventricular myocardium of neonatal vs. adult rabbits, but the inotropic response to the same concentration of isoproterenol was significantly greater in the adult tissue.[40]

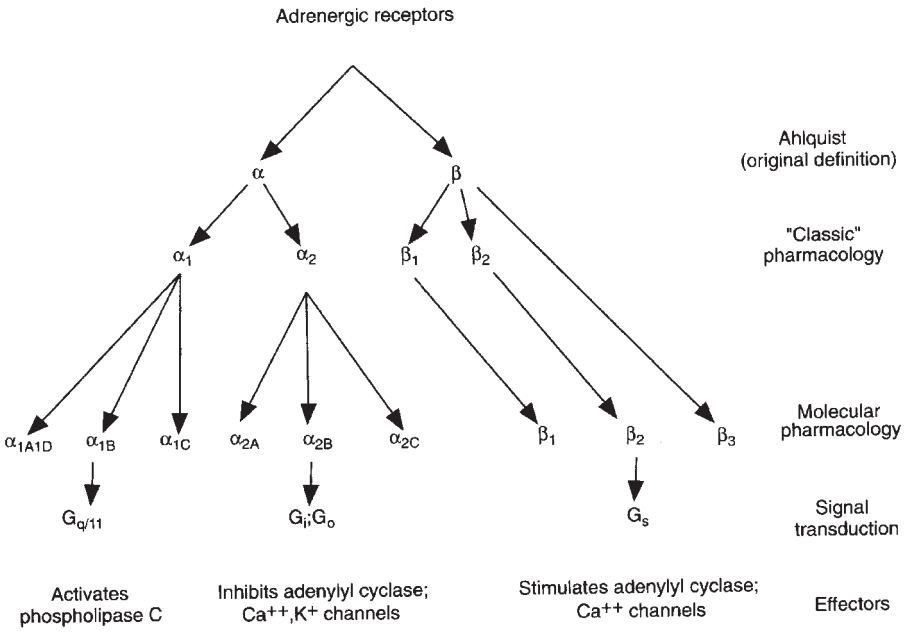



**Fig. 3.7** A modern schematic classification of adrenergic receptors. Reproduced with permission from Moss J, Renz CL. The autonomic nervous system. In: Miller RD, ed. *Anesthesia*, 5th edn. Philadelphia, PA: Churchill Livingstone, 2000: 523–77.

In the neonatal rat, the mechanism of β-adrenergic mediated increase in contractility was entirely due to $\beta_2$ stimulation, whereas in the adult rat it was due solely to $\beta_1$-receptor activation. Coupling of the $\beta_2$-receptor to $G_i$ protein action was apparently defective in the neonatal rat, because the ratio of $G_i$ to $G_s$ subunits was much higher in the neonate. The relative proportion of $\beta_1$- and $\beta_2$-receptors was the same in neonatal vs. adult hearts (17% $\beta_2$); this approximates the ratio measured in children with mild CHD, which is about 22%.[41]

There is animal and human evidence that α-adrenergic receptor-mediated chronotropic and inotropic effects on the cardiac myocyte change with development. In the neonatal animal model, α-stimulation produces positive inotropic and chronotropic effects, whereas in the adult it produces negative effects.[42,43] The chronotropic response to $\alpha_1$-stimulation diminished with increasing age in children being evaluated for autonomic dysfunction after vagal and sympathetic blockade.[44]

## Calcium cycling in the normal heart

Calcium assumes a central role in the process of myocardial contraction and relaxation, serving as the second messenger between depolarization of the cardiac myocyte, and its contraction mediated by the actin–myosin system. Calcium's role in this excitation–contraction coupling in the normal mature heart will be reviewed briefly before discussion of developmental changes and changes with heart failure.[45]

Cardiac muscle cell contraction depends on an increase in intracellular $Ca^{2+}$ above a certain threshold, and relaxation ensues when intracellular $Ca^{2+}$ falls below this threshold. Two major regions of $Ca^{2+}$ flux occur: across the sarcolemmal membrane (slow response), and release from internal stores

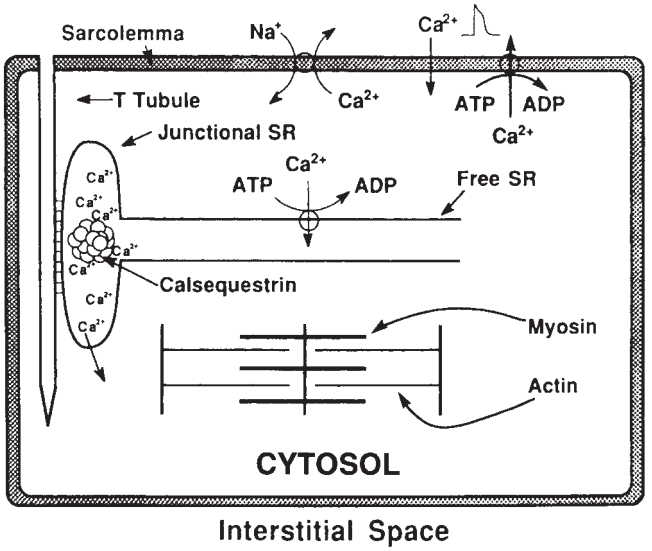



**Fig. 3.8** Schematic summary of major calcium fluxes in the cardiac myocyte. ADP, adenosine diphosphate; ATP, adenosine triphosphate; SR, sarcoplasmic reticulum. Reproduced with permission from Tate CA, Taffet GE, Fisher DJ, Hyek MF. Excitation–contraction coupling: Control of normal myocardial cellular calcium movements. In: Garson A, Bricker JT, Fisher DJ, Neish SR, eds. *The Science and Practice of Pediatric Cardiology*, 2nd edn. Baltimore, MD: Williams & Wilkins, 1998: 171–80.

in the SR (rapid release and reuptake) (Fig. 3.8).[46] The primary site of entry of $Ca^{2+}$ through the sarcolemmal membrane is through the L-type, or low-voltage-dependent $Ca^{2+}$ channel, which occurs in two types, a low-threshold, rapidly inactivating channel, and a higher threshold, more slowly inactivating channel.[47] Depolarization of the sarcolemmal membrane triggers opening of these channels, resulting in triggering of

release of large amount of $Ca^{2+}$ from the SR—the major internal $Ca^{2+}$ storage mechanism. $Ca^{2+}$ entry through the slowly inactivating channels serves to fill the SR with adequate $Ca^{2+}$ stores. Removal of $Ca^{2+}$ from the cytoplasm to the exterior of the cell occurs via two major mechanisms: the sodium–calcium (NaO–$Ca^{2+}$) exchanger, and the calcium ATPase pump. The NaO–$Ca^{2+}$ exchanger usually serves to exchange three sodium ions (moving into the cell) for one $Ca^{2+}$ (moving out of the cell), although the reverse action, as well as a 1 : 1 exchange are possible.[48] The $Ca^{2+}$–ATPase pump actively transports $Ca^{2+}$ (in a 1 : 1 $Ca^{2+}$–ATP ratio) out of the cell in an energy-dependent high-affinity but low-capacity manner.[49] The affinity of the sarcolemmal $Ca^{2+}$–ATPase pump is enhanced by calmodulin, binder of free cytoplasmic $Ca^{2+}$ (see below). An important concept concerning regulation of $Ca^{2+}$ flux by these mechanisms is that although they do play an important role in balancing internal and external $Ca^{2+}$ concentration and in supplying $Ca^{2+}$ to replenish SR $Ca^{2+}$ stores, and in initiating the $Ca^{2+}$-induced release of $Ca^{2+}$ from the SR (see below), the amount of $Ca^{2+}$ flux is far less than across the SR, the far more important mechanism for excitation–contraction coupling in the mature heart.[50] The sarcolemmal $Ca^{2+}$ flux mechanisms play a much more important role in the excitation–contraction coupling of the neonatal (immature) heart, as will be discussed below.

The massive release and reuptake of $Ca^{2+}$ responsible for activation and deactivation of the actin–myosin complex and cardiocyte contraction and relaxation occurs at the level of the SR. The SR is a closed, intracellular membranous network that is intimately related to the myofilaments responsible for contraction (Fig. 3.9).[51] The SR is connected to the sarcolemmal membrane via the transverse tubule (T-tubule) system. Depolarization of the sarcolemmal membrane results in transfer of charge down the T-tubules to the SR, resulting in the opening of SR $Ca^{2+}$ channels and the release of large amounts of $Ca^{2+}$ into the cyotoplasm, where it can then bind to troponin and initiate the actin–myosin interaction. The SR is divided into longitudinal SR and terminal cisternae; the latter connect to the T-tubules. The terminal cisternae are primarily involved in the release of $Ca^{2+}$, and the longitudinal SR in its reuptake.[52]

The primary $Ca^{2+}$ release mechanism of the SR is the ligand-gated $Ca^{2+}$ release channels (also known as the ryanodine receptors), that bind to the drug ryanodine. The channels are activated by two primary mechanisms: depolarization via the T-tubules, and binding of intracellular $Ca^{2+}$ itself; the predominance of one mechanism over the other differs in cardiac vs. skeletal muscle. The close proximity of the L-type sarcolemmal $Ca^{2+}$ channels in the T-tubules to the ligand-gated $Ca^{2+}$ release channels allows the depolarization to rapidly allow $Ca^{2+}$ into the cell and open the SR $Ca^{2+}$ channels. These ligand-gated $Ca^{2+}$ release channels close when the cytosolic $Ca^{2+}$ concentration increases—thus it opens at 0.6 μM $Ca^{2+}$ and closes at 3.0 μM $Ca^{2+}$.[46]

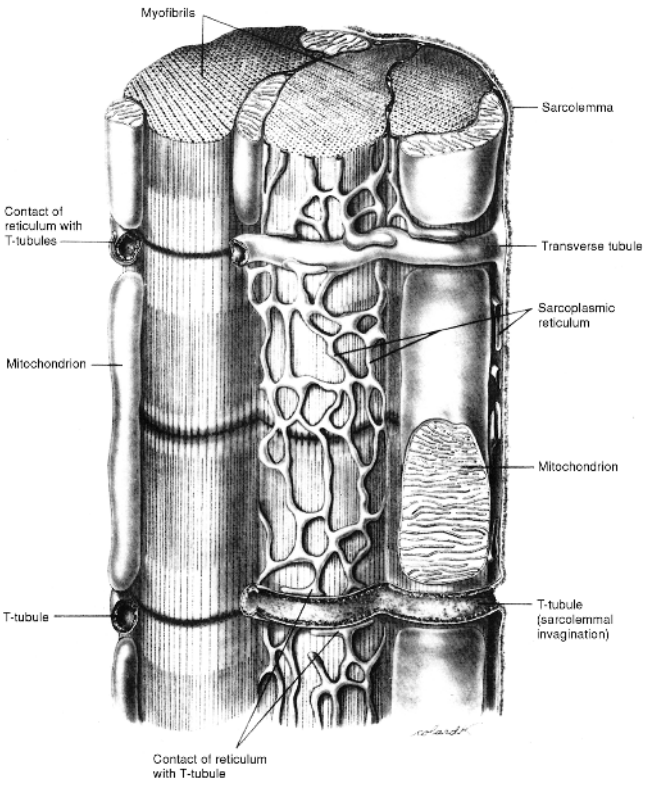



**Fig. 3.9** Normal, mature cardiac myocyte structure. Reproduced with permission from Bloom W, Fawcett DW. *A Textbook of Histology*. Philadelphia, PA: Saunders, 1968.

The reuptake and sequestration of $Ca^{2+}$ allows relaxation of the cardiac myocyte, and is an active transport mechanism, primarily involving hydrolysis of ATP by the SR $Ca^{2+}$–ATPase (SERCA), located in the longitudinal SR.[53] It binds two $Ca^{2+}$ with high affinity and rapidly transports them to the inside of the SR. This transport system differs from the sarcolemmal membrane: it has higher affinity, allows for more rapid transport, and is not sensitive to calmodulin. $Ca^{2+}$ is stored in the SR by calsequestrin, a high-capacity, low-affinity protein which acts as a $Ca^{2+}$ sink, which is reloaded, awaiting opening of the SR $Ca^{2+}$ channels with the next cardiac cycle.

There are two other proteins with essential roles in the regulation of $Ca^{2+}$ flux: phospholamban and calmodulin.[54,55] Phospholamban is associated with the SR $Ca^{2+}$–ATPase (SERCA), and can be phosphorylated by at least four different protein kinases (see above)—cAMP-dependent, $Ca^{2+}$/calmodulin-dependent, cGMP-dependent, or protein kinase C (PKC). When phosphorylated, phospholamban increases the affinity of the SERCA for $Ca^{2+}$, facilitating $Ca^{2+}$ flux back into the SR, and thus the inotropic and lusitropic state of the heart. Phospholamban plays an important role in the β-adrenergic mediated increase in the inotropic state of the heart. Calmodulin is a $Ca^{2+}$ storage protein with four binding sites, found in the cytoplasm, which interacts with the sarcolemmal $Ca^{2+}$–ATPase (increasing its affinity for $Ca^{2+}$), the

SR ligand-gated $Ca^{2+}$ release channel (inhibits its activity at optimal cytoplasmic $Ca^{2+}$), and binds to the $Ca^{2+}$/calmodulin-dependent protein kinase.[55]

The preceding review is a very simplified representation; there are many other details revealed by recent research, many issues that are unknown due to species differences, and many steps in the $Ca^{2+}$ cycling process that are simply not understood and require further research.

The increase in intracellular cytoplasmic $Ca^{2+}$ initiates the contractile process through a complicated series of interactions within the contractile protein system, which will be briefly reviewed. Myosin is the major component of the thick filaments, which make up the microscopic structure of the myofibril, and its interaction with actin (the major component of the thin filaments) provides the mechanical basis of cardiac muscle cell contraction.[56] Actin and myosin make up approximately 80% of the contractile apparatus, and are arranged in a parallel, longitudinal fashion, projecting from a Z-line or band (Fig. 3.10) to form the basic contractile unit called the sarcomere. A three-dimensional lattice, consisting of interdigitated thick and thin filaments in a hexagonal array with three thin filaments in close proximity to each thick filament, is formed. The actin and myosin are linked by projections on the myosin protein called S1 crossbridges, which bind to actin, and via an energy-dependent hinge-like mechanism, produce the sliding filament crossbridge action that is thought to produce sarcomere shortening and lengthening. The lattice is held together by connecting proteins such as titin, nebulin, and α-actinin.[57] The actin–myosin interaction is initiated when $Ca^{2+}$ binds to troponin, a protein closely connected to actin which consists of three subunits: a $Ca^{2+}$ binding subunit (TNC), a tropomyosin binding unit (TNT), and an inhibitory subunit (TNI). TNC can bind up to four $Ca^{2+}$ ions, and this produces a conformational change on the thin filament, which allows the S1 myosin head crossbridges to attach.[58] This also changes the TNI subunit's conformation, and allows tropomyosin, another protein integral in filament interaction, to move aside and expose the binding sites on actin, allowing the strong binding to the S1 crossbridges. With $Ca^{2+}$ present, actin causes myosin ATPase to hydrolyze one ATP molecule, providing energy that results in the S1 myosin head pulling on the thin filament, resulting in sarcomere shortening. Troponin C is the most important aspect of the regulation of cardiocyte contraction, and is exquisitely sensitive with a steep response curve to local levels of $Ca^{2+}$. When $Ca^{2+}$ levels decline rapidly, associated with its reuptake into the SR, the inhibitory form of the troponin, tropomyosin, actin complex, returns, and the result is reversal of the crossbridge binding and thus sarcomere relaxation.

Besides calcium, many other regulatory mechanisms exist to influence the interaction and sensitivity of $Ca^{2+}$ binding to troponin, including β-adrenergic stimulation, thyroid hormone, and phosphorylation by cAMP-dependent protein kinases. Some of these will be discussed below.

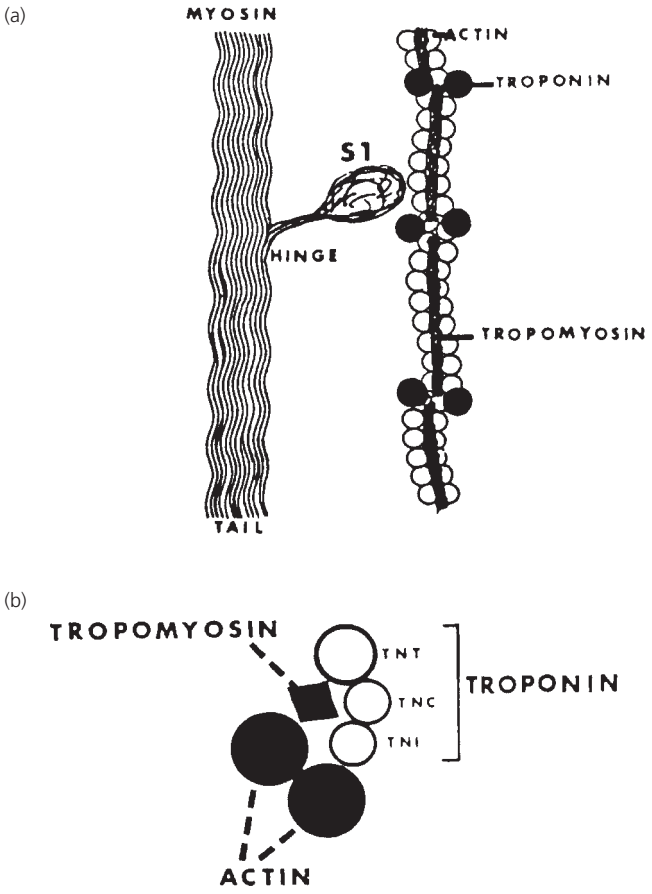



**Fig. 3.10** (a) Single thick and thin filament showing the S1 crossbridge and hinge mechanism. (b) Relationship of actin to tropomyosin and the three troponin subunits. See text for explanation. Reproduced with permission from Michael LH. Cardiac contractile proteins in the normal heart: The contractile process and its regulation. In: Garson A, Bricker JT, Fisher DJ, Neish SR, eds. *The Science and Practice of Pediatric Cardiology*, 2nd edn. Baltimore, MD: Williams & Wilkins, 1998: 181–92.

## Developmental changes in calcium cycling

Several aspects of the excitation–contraction system are different in the immature heart. In neonatal hearts the T-tubule is not fully formed.[59] The SR in neonatal animal models has been shown to have less storage capacity and less structural organization,[60] less mRNA expression,[60,61] and less functional responsiveness to chemical blockade.[62,63] There is some human evidence that the inhibitory subunit of troponin (TNI) changes from a predominately cAMP insensitive form to a cAMP responsive form by 9 months of age, giving a possible explanation for the increased responsiveness seen with β-adrenergic stimulation after the neonatal period.[64] All of this information has led to the theory that the neonatal cardiac myocyte is more dependent on free cytosolic $Ca^{2+}$ fluxes than is the mature heart, and more susceptible to blockade of

**Table 3.1** Summary of major differences between neonatal and mature hearts.

| | Neonatal | Mature |
|---|---|---|
| Physiology | | |
| Contractility | Limited | Normal |
| Heart rate dependence | High | Low |
| Contractile reserve | Low | High |
| Afterload tolerance | Low | Higher |
| Preload tolerance | Limited | Better |
| Ventricular interdependence | Significant | Less |
| $Ca^{2+}$ cycling | | |
| Predominant site of $Ca^{2+}$ flux | Sarcolemma | SR |
| Dependence on normal $iCa^{2+}$ | High | Lower |
| Circulating catecholamines | High | Lower |
| Adrenergic receptors | Downregulated<br>Insensitive<br>$\beta_2$, $\alpha_1$ predominant | Normal<br><br>$\beta_1$ predominant |
| Innervation | Parasympathetic predominates<br>Sympathetic<br>Incomplete | Complete |
| Cytoskeleton | High collagen and water content | Lower collagen and water content |
| Cellular elements | Incomplete SR<br>Disorganized<br>Myofibrils | Mature SR<br>Organized<br>Myofibrils |

$iCa^{2+}$, intracellular $Ca^{2+}$; SR, sarcoplasmic reticulum.

the L-type $Ca^{2+}$ sarcolemmal channels as a mechanism of depression of myocardial contractility. The latter is thought to be an explanation for the greater hemodynamic depression seen with halothane in neonatal rat myocytes than with sevoflurane, and thus an explanation for the same phenomenon seen clinically.[65] Since nearly all of this experimental evidence comes from various animal models, there is a need for studies in human tissue to determine if these explanations are valid in patients. The age of maturation of cardiac intracellular and extracellular maturity in humans is not clear because of this lack of information, but on clinical grounds it is thought to be approximately 6 months of age.

A summary of the major differences in cardiac development and function between the neonatal and mature heart is presented in Table 3.1.

## Thyroid hormone

Triiodothyronine ($T_3$) has recently been increasingly recognized as having a critical role in both the development of the cardiovascular system, but also in its acute regulation and performance. Normal $T_3$ levels are essential for normal maturation and development of the heart through expression of genes responsible for the production of the cardiac contractile proteins, elements of the calcium cycling apparatus, and development and density of β-adrenergic receptors.[66] The cell nucleus mediated effects of $T_3$ require an increase in protein synthesis and at least 8 h for effects to occur. These include an upregulation of β-adrenergic receptors, an increase in cardiac contractile protein synthesis, an increase in mitochondrial density, volume, and respiration, an increase in SR $Ca^{2+}$–ATPase mRNA, and changes in myosin heavy chain isoforms. Acute effects of $T_3$ on cardiac myocytes occur in minutes, result from interaction with specific sarcolemmal receptors, and include stimulation of L-type $Ca^{2+}$ pump activity, stimulation of SR $Ca^{2+}$–ATPase activity, increased protein kinase activity, and a decrease in phospholamban.[67] Cardiac surgery and cardiopulmonary bypass (CPB) interfere with the conversion of thyroxine ($T_4$) to $T_3$, and serum levels decrease significantly after cardiac surgery in infants and children.[68] Triiodothyronine infusion can improve myocardial function in children after cardiac surgery and reduce intensive care unit (ICU) stay.[69]

# Regulation of vascular tone in systemic and pulmonary circulations

The regulation of vascular tone is an important consideration in the understanding and treatment of CHDs. Both the

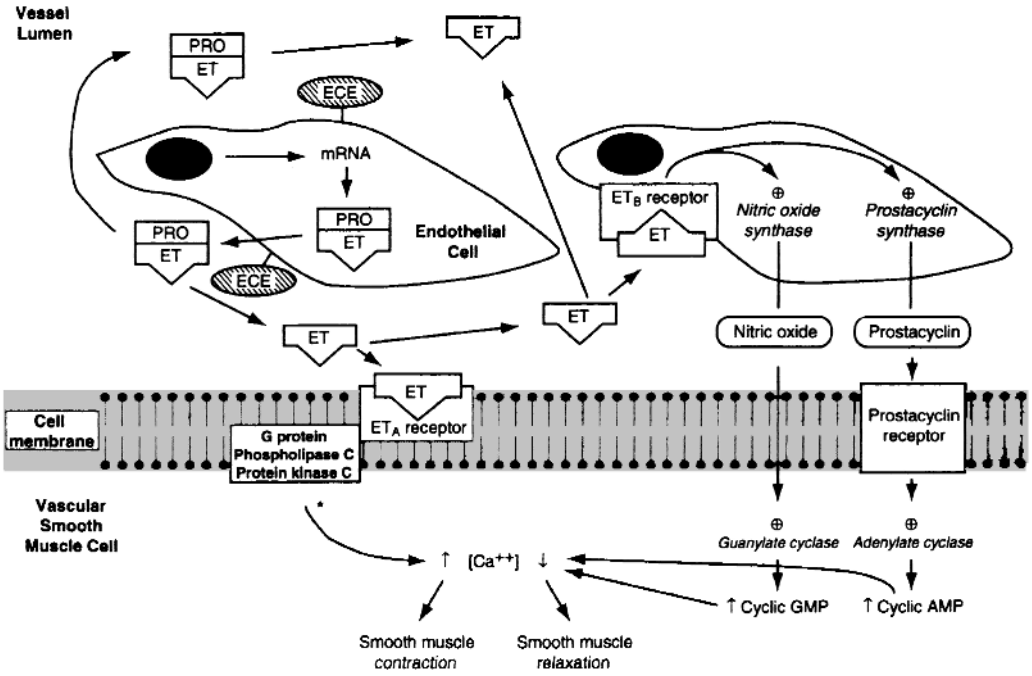



**Fig. 3.11** Schematic of some major mediators of vascular tone in the pulmonary circulation. See text for explanation. AMP, adenosine monophosphate; ECE, endothelin converting enzyme; ET, endothelin-1; GMP, guanosine monophosphate; PROET, proendothelin-1. Reproduced with permission from Haynes WG, Webb DJ. The endothelin family of peptides: Local hormones with diverse roles in health and disease? *Clin Sci (Lond)* 1993; **84**: 485–500. ©The Biochemical Society and the Medical Research Society.

systemic and pulmonary circulations have exceedingly complex systems to maintain appropriate vascular resistance, and a delicate balance between vasodilating and vasoconstricting mediators is seen in the normal patient. However, in response to a multitude of stimuli, abnormal responses may develop which lead to pulmonary or systemic hypertension, or conversely vasodilation. The latter is not a problem except in the case of systemic vascular resistance which is too low. We will summarize some of the systems involved in regulation of vascular tone, which will serve as a basis for understanding some of the pathophysiologic states and the approaches to some of the treatments outlined later in this book. A schematic representation of some of these mediators is shown in Fig. 3.11. To some extent, the control mechanisms reviewed are present in both the systemic and pulmonary circulations; however, certain mechanisms are perceived to be more important in one circulation vs. the other. For example, the endothelial-mediated systems (NO–cGMP pathways, etc.) seem to predominate in the pulmonary circulation (low resistance circulation), whereas the phospholipase systems seem to predominate in the systemic circulation (high resistance circulation).

## Pulmonary circulation

Vasoactive metabolites of arachdonic acid, called eicosanoids, are produced in cell membranes, via the lipoxygenase pathway to form leukotrienes, or the cyclo-oxygenase pathway to form the prostaglandins. Important vasodilating prostaglandins include $PGE_1$, which promotes and maintains patency of the ductus arteriosus and is life saving in ductus-dependent CHD. Prostacyclin, or $PGI_2$, is a potent pulmonary vasodilator.[70] Prostaglandins act in vascular smooth muscle of the systemic and pulmonary circulations by binding to receptors in the smooth muscle cell membrane, activating AC and increasing cAMP concentrations, which lead to lower $Ca^{2+}$ levels and to relaxation of vascular tone. Thromboxane $A_2$ is a potent leukotriene that has the opposite effects of the prostaglandins, producing vasoconstriction and platelet aggregation. Imbalance in this system caused by chronic hypoxia and high pulmonary artery pressures can lead to chronic pulmonary hypertension.

Nitric oxide is an endothelium-derived relaxant factor that causes relaxation of vascular smooth muscle cells by activating guanylate cyclase, increasing the concentration of cyclic guanosine monophosphate (cGMP), and thus reducing the local concentration of $Ca^{2+}$ and thus reducing vascular tone.[71] $Ca^{2+}$ sensitive potassium channels have been shown to contribute to the vasodilation caused by NO via a cGMP-dependent protein kinase.[72] Nitric oxide is formed from L-arginine by NO synthase, and quickly inactivated by binding to hemoglobin. Nitric oxide works by diffusing into the vascular smooth muscle cell, and stimulates guanylate cyclase to produce cGMP, which results in vasodilation.

Phosphodiesterase V breaks down cGMP, so the phosphodiesterase inhibiting drugs can potentiate NO mediated vasodilation. This is the basis for testing drugs such as sildenafil to treat pulmonary hypertension in CHD.[73]

Endothelin is a powerful endothelium-derived vasoactive peptide, of which endothelin-1 (ET-1) is the best characterized. Endothelin-1 is produced from proendothelin-1 by endothelin converting enzymes in the endothelial cells of systemic and pulmonary vasculature. Increased pressure, shear stress, and hypoxia can lead to increased production of ET-1 in the pulmonary circulation. Two ET-1 receptors, $ET_A$ and $ET_B$, mediate effects on smooth muscle vascular tone.[74] The $ET_A$ receptor is found on the smooth muscle cell membrane and mediates vasoconstriction, while the $ET_B$ receptor is located on the endothelial cell itself, and results in increased NO synthase activity, and thus increased NO and vasodilation. The primary activity of ET-1 appears to be to stimulate the $ET_A$ receptor, and indeed increased levels of ET-1 are found in many pulmonary hypertensive states such as Eisenmenger's syndrome and primary pulmonary hypertension.[75]

## Systemic circulation

There are multiple levels of control over the peripheral circulation. Neural control by the sympathetic and parasympathetic nervous systems consists of an afferent limb consisting of receptors such as stretch receptors within the walls of the heart, and baroreceptors in the walls of arteries, such as the aortic arch and carotid sinuses. Stimulation of the baroreceptors by stretch in the arterial wall leads to vasodilation and heart rate slowing mediated by the vasomotor centers of the medulla.[76] Stimulation of atrial stretch receptors inhibits secretion of vasopressin from the hypothalamus. The efferent limb of the autonomic nervous system consists of sympathetic and parasympathetic nerve fibers. The sympathetic nerves can be divided into vasoconstrictor and vasodilator fibers. The vasoconstrictor fibers release norepinephrine when stimulated, resulting in activation of α-adrenergic receptors and vasoconstriction. The vasodilator fibers release acetyolcholine or epinephrine, and are mainly present in skeletal muscle. Parasympathetic fibers are vital in control of heart rate and function, but have only a minor role in controlling the peripheral circulation.[77] Hormonal control and receptor mediated intracellular signaling are other important mechanisms, and will be discussed in more detail.

Norepinephrine primarily stimulates the peripheral α-receptors and causes intense vasoconstriction. It is secreted by the adrenal medulla and by sympathetic nerves in proximity to the systemic blood vessels. Epinephrine is also secreted by the adrenal medulla, but its primary action is to stimulate the $\beta_2$-receptors in the peripheral circulation, causing vasodilation through cAMP mediated reductions in intracellular $Ca^{2+}$ concentrations.

Angiotensin II is produced by activation of the renin–angiotensin–aldoseterone axis in response to low circulating blood volume and low blood pressure, sensed by the juxtaglomerular apparatus in the kidney. Renin produces angiotensin I by cleaving angiotensinogen, and angiotensin II is produced when angiotensin I passes through the lung by angiotensin-converting enzyme. Angiotensin II is a potent vasoconstrictor (see below), and also induces the hypothalamus to secrete vasopressin (antidiuretic hormone), which also has potent vasoconstrictor properties.

The arachodonic acid metabolites are discussed above, and appear to have a more central role in the control of the pulmonary circulation.

Atrial natriuretic factor (ANF) is released from atrial myocytes in response to stretch (elevation of right or left atrial pressure) on the atrium. Atrial natriuretic factor has vasodilatory and cardioinhibitory effects, and decreases tubular reabsorption of sodium in the kidney.[78] B-type natriuretic peptide (BNP) is released by ventricular myocardium, also in response to stretch, and causes an increase in cGMP, leading to vasodilation in both arterial and venous systems. In addition, it increases urinary sodium and water excretion.[79]

Extensive progress has been made in the last decade in elucidating the second messenger systems active in converting activation of receptors on systemic vascular cell membranes to changes in vascular tone. The phosphoinositide signaling system is the common pathway for many of these agonists (Fig. 3.12).[76] Membrane kinases phosphorylate phosphatidylinositol, which is an inositol lipid located mainly in the inner lamella of the plasma membrane. Phosphatidylinositol 4,5-biphosphate is produced. It is from this compound that the second messenger, inositol 1,4,5-triphosphate, is produced, by the action of the enzyme phospholipase C (PLC).[80] The sequence begins with the binding of an agonist, such as angiotensin II, vasopressin, norepinephrine, or endothelin, to a receptor with seven membrane spanning domains. This receptor is linked to an activated $G_q$-protein subunit, which in turn stimulates phosphatidylinositol-specific phospholipase C (PI-PLC) to produce inositol 1,4,5,-triphosphate, which acts to cause release of $Ca^{2+}$ from the SR, resulting in activation of the actin–myosin system in the smooth muscle cells, resulting in contraction and an increase in vascular tone. Another second messenger, 1,2-diacylglycerol, is also produced, which goes on to activate PKC, which in turn has a role in mitogenesis and thus proliferation of smooth muscle cells. There are many isozymes of PLC; the form implicated in this series of events is the PLCβ form. The PLCγ isoform is activated when cell growth factors such as platelet-derived growth factor bind to their receptors on the cell surface and active tyrosine kinases. This results in the production of phosphatidylinositol 3,4,5-triphosphate, which may also be implicated in mitogenesis.

Vasodilation of the systemic circulation results from the formation of NO by nitrovasodilators, or by activation of

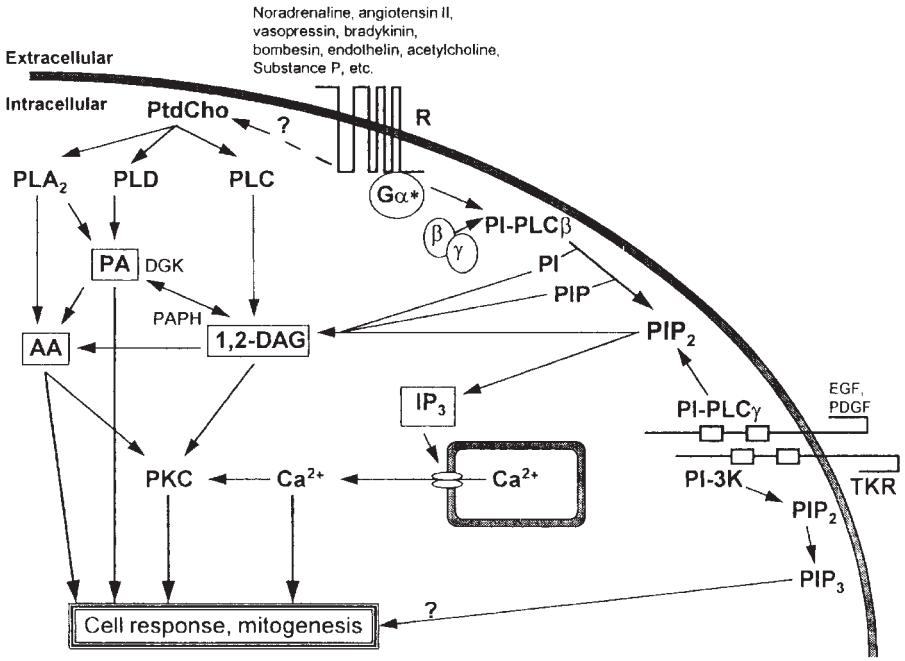



**Fig. 3.12** Phospholipase C (PLC) system. Diagram summarizing the major receptor-activated pathways for production of inositol 1,4,5-triphosphate ($IP_3$) and 1,2-diacyglycerol (1,2-DAG). The binding of an agonist to a receptor (R) with seven membrane-spanning domains results in activation of the phosphatidylinositol-specific phospholipase Cβ (PI-PLCβ), whereas the stimulation of tyrosine kinase receptors (TKRs) by polypeptide growth factors will activate phosphatidylinositol-specific phospholipase Cγ (PI-PLCγ). Both pathways will result in the hydrolysis of phosphatidylinositol 4,5-biphosphate ($PIP_2$) and the formation of $IP_3$ and 1,2-DAG. In addition, agonists that act on the heterotrimeric receptors may stimulate phosphatidylcholine (PtdCho) hydrolysis, and activation of TKRs will stimulate the production of phosphatidylinositol 3,4,5-triphosphate ($PIP_3$). AA, arachidonic acid; DGK, diacylglyceral kinase; EGF, epidermal growth factor; Gα*, activated G protein subunit β-subunits; PA, pulmonary artery; PAPH, phosphatidic acid phosphohydrolase; PDGF, platelet-derived growth factor; PI, phosphatidylinositol; PI-3K, phosphatidylinositol 3-kinase; PIP, phosphatidylinositol 4-phosphate; PKC, protein kinase C; $PLA_2$, phospholipase $A_2$; PLD, phospholipase D. Reproduced with permission from Izzard AS, Ohanian J, Tulip JR, Heagerty AM. The structure and function of the systemic circulation. In: Anderson RH, Baker EJ, Macartney F *et al*., eds. *Paediatric Cardiology*, 2nd edn. London: Churchill Livingstone, 2002: 95–109, with permission from Elsevier.

$\beta_2$-adrenergic receptors in the peripheral vasculature, both of which result in the activation of guanylate cyclase and the production of cGMP, which reduces intracellular $C^{2+}$ concentrations, and results in the relaxation of vascular smooth muscle.[81]

The vascular beds in various peripheral tissues differ in the amount of local metabolic control of vascular tone; for example, pH has much more influence on the pulmonary circuit, with low pH leading to vasoconstriction and higher pH leading to vasodilation, than in other tissues. Local carbon dioxide concentration is much more important to central nervous system vasculature, with high levels leading to vasodilation. Decrease in oxygen tension will often lead to vasodilation, as adenosine is released in response to the decreased oxygen delivery. Autoregulation, or maintaining relatively constant blood flow over a wide range arterial pressures, predominates in the cerebral circulation but is not as critical in other tissue beds. Autoregulation and carbon dioxide responsiveness are both blunted in the fetal and immature brain.[82]

## Receptor signaling in myocardial dysfunction, congenital heart disease, and heart failure

A discussion of receptor signaling and calcium cycling in myocardial dysfunction is useful to serve as the basis for understanding many of the therapies discussed later in this text. We will discuss receptor physiology and calcium flux in three settings: acute myocardial dysfunction as seen after cardiac surgery and CPB, changes seen as responses to chronic cyanotic heart disease, and those seen with chronic congestive heart failure and cardiomyopathy.

### Receptor signaling in acute myocardial dysfunction

Acute myocardial dysfunction, such as that sometimes seen after CPB, is often treated with catecholamines. These drugs can be ineffective if used in escalating doses. In children

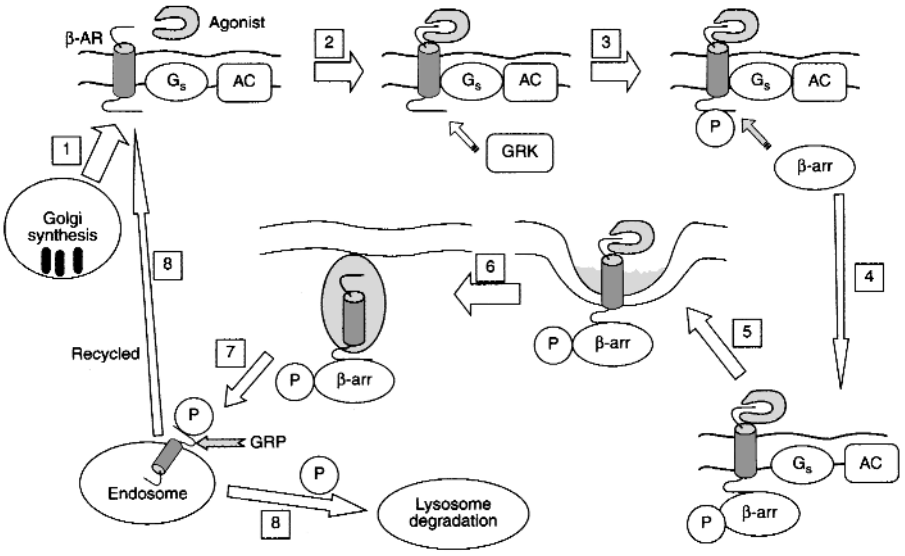



**Fig. 3.13** Desensitization and downregulation of the β-adrenoreceptor (β-AR). 1, agonist binding; 2, phosphorylation of the β-adrenoreceptor by G protein coupled receptor kinases (GRK); 3, β-arrestin binds to the GRK-phosphorylated β-adrenoreceptor, which is bound to the $G_s$ protein. The receptor is then sequestrated to the endosomal compartment (4–7), to be dephosphorylated, and then either recycled back to the sarcolemma (8), or translocated to lysosomes for further degradation (8). AC, adenlylate cyclase; β-arr, β-arrestin; GRP, G protein coupled receptor phosphatase; P, inorganic phosphate groups. Reproduced with permission from Booker PD. Pharmacological support for children with myocardial dysfunction. *Paediatr Anaesth* 2002; **12**: 5–25.

undergoing cardiac surgery with bypass, the number and subtype distribution of β-adrenergic receptors in atrial tissue was not affected; however, the activation of AC by isoproterenol was significantly less after bypass.[83] This suggests uncoupling of β-receptors from the $G_s$ protein–adenlyate cyclase complex as a mechanism for the reduced sensitivity to catecholamines. Another mechanism for densensitization to moderate or high doses of catecholamines may occur after only a few minutes of administration, because of increased cAMP concentrations, which result in receptor phosphorylation by PKA or PKC, or by G protein coupled receptor kinases (at high catecholamine doses) which results in uncoupling from the $G_s$ protein.[84]

Phosphorylated ARs produced by high doses of catecholamines may be inactivated by a process called sequestration, after only a few minutes. These receptors can be sequestered by endocytosis, in a process involving a protein called β-arrestin, which binds to the receptor and a sarcolemmal protein called clathrin (Fig. 3.13). These sequestered receptors may either be recycled back to the cell membrane surface, or destroyed by lysosomes.[85] This permanent destruction and degradation of receptors occurs after hours of exposure to catecholamines, and is accompanied by decreased mRNA and receptor protein synthesis, resulting in a prolonged decrease in AR concentrations, which is reversed by decreasing exogenous catecholamines, but only as fast as new receptors can be synthesized.

Neonatal hearts may exhibit a different response to the acute or prolonged administration of catecholamines. Instead of desensitization, neonatal animal models demonstrate an enhanced β-adrenergic receptor response, accompanied by an increase in AC activity.[86] Desensitization as described above occurs later in development. The exact translation of these data to humans is not clear.

Treatment with catecholamines may also increase the concentration of $G_i$ protein subunits, decreasing the sensitivity of the β-adrenergic receptor. This relative decrease in the ratio of $G_s$ to $G_i$ protein subunits has been demonstrated in rat and dog models.[87,88] Another possible mechanism of catecholamine-induced desensitization of the neonatal myocyte was demonstrated in a rat model, where prolonged exposure to norepinephrine caused an initial increase in functional L-type $Ca^{2+}$ channels on the sarcolemmal membrane. Continued exposure caused a decrease in L-type $Ca^{2+}$ channel mRNA to 50% of control values.[89] Sarcoplasmic reticulum $Ca^{2+}$–ATPase concentrations are reduced with chronic norepinephrine administration in the dog.[90] Finally, exposing adult or neonatal rat myocytes to high concentrations of catecholamines for 24 h leads to increased apoptosis of myocardial cells, a genetically programmed energy-dependent mechanism for cell death and removal.[91,92] This effect was mediated through β-adrenergic receptors in the adult model, and α-receptors in the neonatal model.

All of these studies provide the theoretical basis for the argument that administration of catecholamines to patients with acute myocardial dysfunction should be as limited in dose and duration as possible. Obviously, this is difficult to accomplish in the setting of weaning a difficult patient from CPB. Strategies that may limit catecholamine dose include administering low doses of catecholamines together with phosphodiesterase inhibitors, which may avoid some of the aforementioned problems.[93]

## Receptor signaling in congenital heart disease

In the past decade there is some new information available concerning AR signaling in patients with CHD who are treated and well compensated, i.e. do not have severe

myocardial dysfunction and congestive heart failure. In a study of 71 infants and children undergoing cardiac surgery, the right atrial appendage was studied for β-adrenergic receptor density, distribution of $\beta_1$- and $\beta_2$-receptor subtypes, and coupling to AC.[94] This study found that patients with severe, or poorly compensated acyanotic (e.g. congestive heart failure) or cyanotic (e.g. severe cyanosis) had significantly reduced β-adrenergic receptor densities. Outside of the newborn period, this downregulation was $\beta_1$ selective, but in newborns with critical aortic stenosis or transposition of the great arteries, there was additional significant downregulation of the $\beta_2$ subtype. In tetralogy of Fallot patients, those treated with propranolol had a significant increase in the number and density of β-adrenergic receptors when compared with untreated patients. Beta-adrenergic receptor downregulation correlated with increased circulating norepinephrine levels. Finally, in severely affected patients, AC activity was reduced, demonstrating a partial decoupling, as noted above. Other studies have determined that symptomatic tetralogy of Fallot patients, i.e. those with cyanotic spells, have a significantly greater number of β-adrenergic receptors in their right ventricular outflow tract muscle, and their AC activity was greater when compared to patients without cyanotic spells.[95] Alpha-1-adrenergic receptors are also affected by CHD. In a study of atrial tissue excised at surgery in 17 children, α- vs. β-adrenergic receptor stimulation was evaluated with pharmacologic agents, and the α-component was responsible for 0–44% of the inotropic response, and β-stimulation for 56–100% of the response, with the degree of right ventricular hypertrophy and pressure load correlating with the amount of a stimulation found.[96]

## Receptor signaling in congestive heart failure and cardiomyopathy

In children with congestive heart failure due to chronic left-to-right shunting and volume overload of the heart, circulating norepinephrine levels are elevated, as they are in adults with congestive heart failure. This leads to a downregulation in β-adrenergic receptor density.[97] The degree of elevation of pulmonary artery pressure and level of left-to-right shunting correlates with the plasma catecholamine levels, and is inversely correlated with β-adrenergic receptor density. All of these abnormalities return to normal control levels after corrective surgery. The degree of receptor downregulation in congestive heart failure may correlate with postoperative morbidity in infants and children. Children with a prolonged ICU stay of greater than 7 days or who died during the early postoperative course (nine of the 26) had significantly less $\beta_1$ and $\beta_2$ mRNA gene expression than those who had better outcomes.[98] In addition, the children receiving propranolol for treatment of their congestive heart failure had higher β-adrenergic receptor mRNA levels and tended to have improved outcomes. Finally, children with dilated cardiomyopathy and a depressed ejection fraction of 41% showed no significant increase in ejection fraction during the dobutamine stress test, with infusion of dobutamine at 5 and then 10 μg/kg/minute.[99]

The preceding has been a brief discussion of receptor signaling in pediatric heart disease. This emerging field has many implications for treatment strategies, and the reader is referred to excellent reviews for more detail information on this subject.[100]

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# 4 Anesthetic agents and their cardiovascular effects

Dean B. Andropoulos

## Introduction

A wide variety of anesthetic regimens is used for patients with congenital heart disease (CHD) undergoing cardiac or non-cardiac surgery, procedures in the cardiac catheterization laboratory, or other diagnostic or therapeutic procures such as magnetic resonance imaging. The goal of all of these regimens is to produce general anesthesia or adequate sedation, while preserving systemic cardiac output (*CO*) and oxygen delivery. Many of these patients have limited cardiac reserve, and if a cardiac arrest or other adverse cardiac event occurs, successful resuscitation is less frequent than in patients with normal hearts.[1] Thus, intelligent selection of regimen and dosage, with the patient's unique pathophysiology of their cardiac lesion in mind, along with requirements for the particular procedure they are undergoing, is essential. This chapter reviews the effects on hemodynamics and myocardial contractility of anesthetic agents and muscle relaxants commonly used for patients with CHD.

## Volatile agents

*In vitro* studies of effects on contractility in isolated adult human atrial fibers indicate that direct myocardial contractility depression is greatest with halothane and that sevoflurane is equal to isoflurane and desflurane (Fig. 4.1).[2] These studies of myocardium reveal that differences among these agents occur primarily from differing effects on calcium flux through L-type $Ca^{2+}$ channels, both trans-sarcolemmal, and in the sarcoplasmic reticulum (SR) (Fig. 4.2). Halothane reduces $Ca^{2+}$ flux through the sarcolemma more than isoflurane, with the net result that there is less intracellular $Ca^{2+}$ available to bind to the troponin–actin–myosin complex which produces myocyte contraction. Another mechanism of myocardial depression is that halothane, but not isoflurane, directly activates ryanodine-sensitive SR $Ca^{2+}$ channels, thereby reducing $Ca^{2+}$ storage in the SR and making less available for release during contraction. The effects of sevoflurane and desflurane on $Ca^{2+}$ flux are similar to isoflurane.[2]

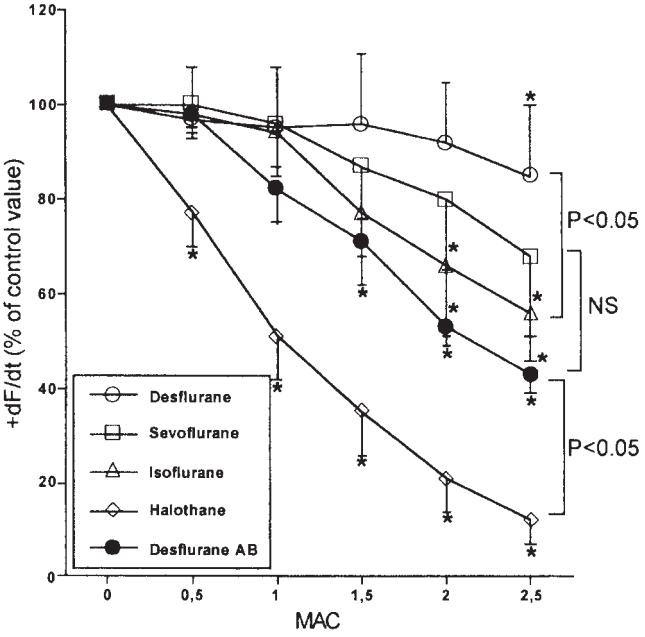


**Fig. 4.1** Force of contraction over time (+dF/dt) of isolated adult human atrial trabeculae in response to 0.0–2.5 minimum alveolar concentration (*MAC*) anesthetics. Desflurane AB is desflurane in the presence of α- and β-receptor blockade. Halothane depresses contractility significantly more than all other agents at every *MAC*. Reproduced with permission from Hanouz JL, Massetti M, Guesne G. *In vitro* effects of desflurane, sevoflurane, isoflurane, and halothane in isolated human right atria. *Anesthesiology* 2000; **92**: 116–24.

The effects of volatile anesthetic agents on myocardial contractility and hemodynamics in children with normal hearts reveal halothane to have a greater myocardial depressant effect than the other agents.[3–6] Holzman *et al*.[3] compared the effects of halothane and sevoflurane on echocardiographically derived indices of contractility, using stress-velocity and stress-shortening indices to eliminate the effects of loading conditions. Wodey *et al*.[4] performed a similar study on infants

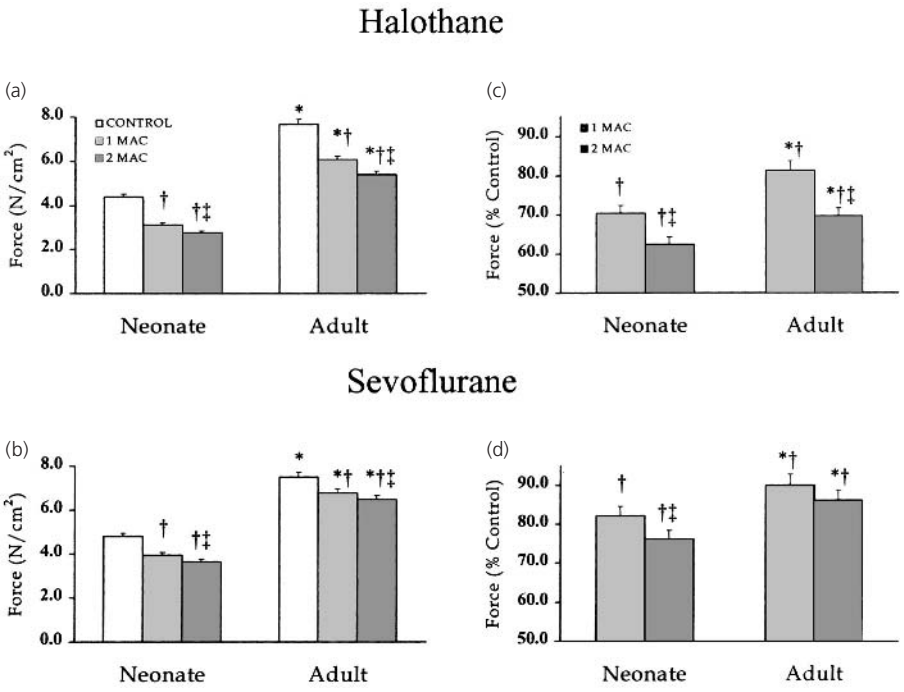


**Fig. 4.2** Force of contraction (N/cm$^2$) in neonatal vs. adult rat ventricular trabecular muscle. Baseline force of contraction is greater in adult tissue, and both halothane and sevoflurane depress contractility more in the neonatal than adult ventricular muscle. Halothane depresses contractility to a greater extent in both age groups. Figures (a) and (b) report raw data, (c) and (d) express results as a percentage of baseline contractility. Reproduced with permission from Prakash YS, Cody MJ, Hannon JD *et al*. Comparison of volatile anesthetic effects on actin–myosin crossbridge cycling in neonatal vs. adult cardiac muscle. *Anesthesiology* 2000; **92**: 1114–25.

and also compared Doppler-derived cardiac indices. In both studies, halothane caused a significantly greater decrease in contractility than sevoflurane at 1.0 and 1.5 minimum alveolar concentration (*MAC*). In the latter study, cardiac index (*CI*) was preserved with sevoflurane, but was significantly decreased with halothane. Isoflurane's effect has been studied echocardiographically in infants and young children with normal hearts,[5,6] and found to have a similar profile to halothane, namely a decrease in *CI* and systolic and mean blood pressure. It is important to note that infants from the newborn period up to an age of approximately 6 months exhibit an exaggerated degree of depression of myocardial contractility and blood pressure in response to all volatile agents, but especially halothane (Fig. 4.2).[7] This is likely due to the immaturity of the $Ca^{2+}$ release and reuptake system, necessitating higher levels of free cytosolic $Ca^{2+}$ to be available to bind to the troponin–actin–myosin complex to produce myocyte contraction. Recent evidence supports this theory. Sevoflurane, and to a greater extent, halothane, interfere with both L-type $Ca^{2+}$ channel and $Na^{+}$–$Ca^{2+}$ exchanger $Ca^{2+}$ flux at the plasmalemmal membrane more in neonatal than adult rat myocytes.[8] The volatile anesthetics interfered with $Ca^{2+}$ release from the SR more in adult rat myocytes. This information provides a mechanism for what is commonly observed clinically.

In a recent report of the Pediatric Perioperative Cardiac Arrest Registry halothane alone or in combination was deemed to be responsible for 67% of the medication-related cardiac arrests.[9] Isoflurane was responsible for none, and sevoflurane for 4% of the medication-related cardiac arrests.

In a study of 40 preterm neonates (mean post-conceptual age 32 weeks) undergoing a variety of procedures (9 patent ductus arteriosus ligations), Friesen *et al*.[10] found that after atropine and pancuronium (which increased heart rate [*HR*] 8–12%), both halothane and isoflurane maintained *HR*, and decreased systolic blood pressure by 25% and 30% respectively.

The effects of volatile agents on systemic vascular resistance (*SVR*) as measured by arterial blood pressure differ between agents. $Ca^{2+}$ flux in the smooth muscles of arterioles is reduced by all of these agents, resulting in less resting tone and thus lower blood pressure and vascular resistance. Halothane exhibits the most pronounced reduction of blood pressure, due to the combination of reduction in arterial tone, as well as the more pronounced depression of myocardial contractility.[11] Isoflurane and sevoflurane lower blood pressure primarily through reduction in *SVR*.[3–5,7,10]

In patients with CHD halothane also appears to have the most pronounced reduction in blood pressure.[12–16] Glenski *et al*.[12] used echocardiography to compare the effects of isoflurane and halothane on M-mode derived measures of contractility and showed that contractility was preserved with isoflurane and depressed with halothane (Fig. 4.3). A study using transthoracic echocardiography comparing halothane, isoflurane, and sevoflurane[15] in 54 children with CHD (Table 4.1) reported that at 1.0 and 1.5 *MAC* there was significant myocardial depression from halothane, resulting in a decline in mean arterial pressure (*MAP*, decline of 22% and 35%), ejection fraction (*EF*, decline of 15% and 20%) and *CO* (*CO* decline of 17% and 21%) in patients aged from 1 month to 13 years with two ventricles undergoing cardiac surgery. Sevoflurane maintained both *CO* and *HR*, and had less profound hypotensive (*MAP* decrease 13% and 20% at

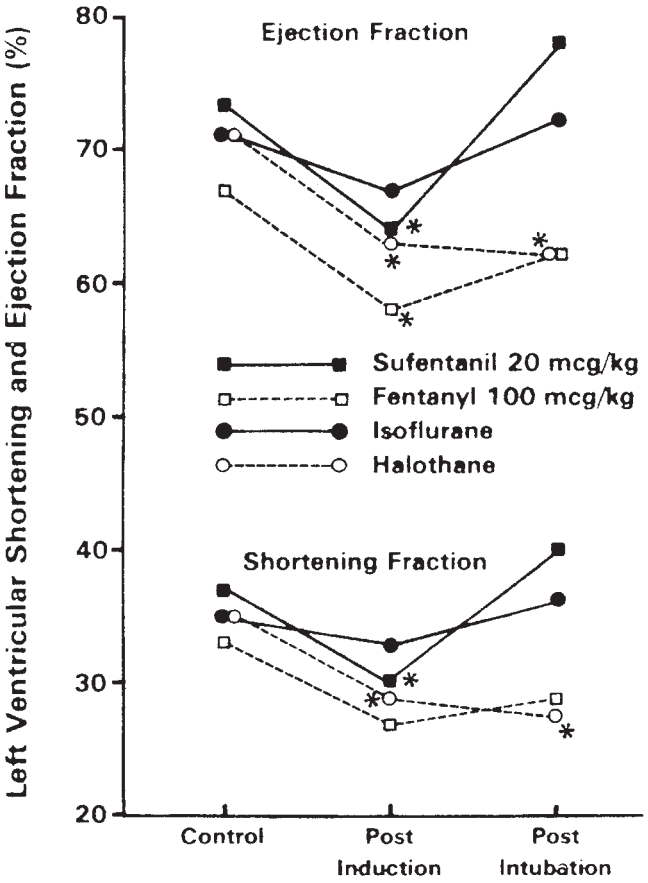


**Fig. 4.3** Echocardiographically measured contractility measures with different anesthetic regimens in children with congenital heart disease. Halothane depressed contractility more than isoflurane at both time periods. Large induction doses of narcotics depress contractility initially, but contractility returns to or near baseline after tracheal intubation. Reproduced with permission from Glenski JA, Friesen RH, Berglund NL, Henry DB. Comparison of the hemodynamic and echocardiographic effects of sufentanil, fentanyl, isoflurane and halothane for pediatric cardiovascular surgery. *J Cardiothorac Anesth* 1988; **2**; 147–55.

1.0 and 1.5 *MAC*) and negative inotropic (*EF* preserved at 1.0 *MAC*, 11% decrease at 1.5 *MAC*) effects compared with halothane. Isoflurane, in concentrations as high as 1.5 *MAC*, preserved *CO* and *EF*, had less suppression of *MAP* (*MAP* 22% and 25%) than halothane, increased *HR* (*HR* 17% and 20%) and decreased *SVR* (*SVR* 20% and 22%).

The effects of these agents on pulmonary (*Q*p) and systemic (*Q*s) blood flow in 30 biventricular patients and left-to-right shunts has also been assessed.[10] Halothane, isoflurane, and sevoflurane did not change *Q*p : *Q*s as measured by echocardiography.[16] Russell *et al*.[17] compared halothane with sevoflurane in the pre-bypass period in 180 children with a variety of cardiac diagnoses, including 14 with single-ventricle physiology. The incidence of significant hypotension, bradycardia, and arrhythmia requiring drug treatment with atropine, phenylephrine, epinephrine, or ephedrine was higher with halothane (two events per patient vs. one). Serum lactate also increased slightly with halothane.

In normal children desflurane commonly produces tachycardia and hypertension during the induction phase, followed by a slight reduction in *HR* and systolic blood pressure during steady state at 1 *MAC* anesthetic level.[11,18] There are no reports of its hemodynamic profile in patients with CHD. In a study of 47 children, mean age 12.8 years, undergoing electrophysiological study for supraventricular tachycardia (SVT), desflurane allowed induction of the SVT in all patients, and demonstrated no clinically important differences in any electrophysiologic measurement compared to a fentanyl-based anesthetic.[19] The arrythmogenic potential of desflurane has been demonstrated to be similar to that of isoflurane.[20]

Twenty-three to forty-eight percent of children with normal cardiac anatomy develop arrhythmias from the use of halothane, with up to 40% of these arrhythmias being ventricular in origin. This compares to an incidence of 6–12% in patients exposed to sevoflurane.[21,22] A study performed in infants, mean age 7.5 months, found sevoflurane induction caused a 20% incidence of junctional bradycardia (< 80 beats/minute). Isoflurane, when utilized in children for electrophysiologic studies and radiofrequency ablation for supraventicular tachycardia, does not affect sinoatrial or atrioventricular node conduction, and all arrhythmias were easily induced.[23]

Few studies to date have addressed the effects of the different anesthetics on two important groups of pediatric patients with congenital or acquired heart disease: patients with a single functional ventricle, and patients with cardiomyopathy or significantly decreased systolic ventricular function. Diastolic function with halothane and isoflurane has been studied in animal models of cardiomyopathy.[24,25] The two agents differ with halothane producing negative lusitropic effects, while isoflurane conserves or may even improve diastolic function. There are no reports of diastolic function in response to anesthetic agents in patients with CHD.

Some practitioners consider halothane to be indicated for use in patients with ventricular outflow tract obstruction, such as tetralogy of Fallot (TOF) or hypertrophic cardiomyopathy (HCM), where depressed contractility and maintenance of baseline *HR* is desirable to allow for a longer ejection time to reduce obstruction to outflow.[26] This theoretical advantage of halothane may well be offset by a greater decrease in *MAP*, which could increase right-to-left shunting in TOF, or the gradient across the left ventricular outflow tract in HCM. Loss of sinus rhythm, more likely with halothane, is poorly tolerated by many of these patients. However, halothane has been used for TOF with success,[27,28] and no controlled studies have addressed this question.

Of the three most commonly used volatile agents isoflurane and sevoflurane are most likely to maintain cardiovascular stability (contractility, *CO*, maintenance of normal sinus rhythm [NSR]) in biventricular patients with CHD. Halothane poorly preserves myocardial function in

**Table 4.1** Hemodynamic changes in response to four anesthetic regimens in 54 children with congenital heart disease with two ventricles.

| | | Measured and calculated hemodynamic and echocardiographic variables | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Agent** | ***MAC*** | ***HR*** **(beats/min)** | ***MAP*** **(mmHg)** | ***EF*** **(%)** | ***SF*** **(%)** | ***SVI*** **(mL/m²)** | ***LVEDVI*** **(mL/m²)** | ***CI*** **(L/min/m²)** | ***SVRI*** **(dyne · s · cm⁻⁵ · m²)** |
| Halothane | 0 | 129 ± 22 | 77 ± 15 | 63 ± 9 | 40 ± 5 | 36 ± 16 | 44 ± 19 | 4.49 ± 1.87 | 1425 ± 622 |
| | 1 | 130 ± 19 | 60 ± 11* | 54 ± 12* | 32 ± 7*† | 28 ± 11* | 38 ± 14 | 3.47 ± 1.17 | 1331 ± 529 |
| | 1.5 | 129 ± 17 | 49 ± 12* | 50 ± 13* | 30 ± 8*† | 26 ± 11* | 39 ± 12 | 3.34 ± 1.36* | 1132 ± 503* |
| Sevoflurane | 0 | 123 ± 32 | 67 ± 8 | 68 ± 11 | 44 ± 7 | 56 ± 41 | 37 ± 15 | 6.91 ± 4.32 | 1014 ± 653 |
| | 1 | 126 ± 26 | 58 ± 13* | 62 ± 9 | 39 ± 7 | 52 ± 31 | 36 ± 18 | 6.59 ± 4.04 | 883 ± 592 |
| | 1.5 | 128 ± 25 | 58 ± 13* | 58 ± 10* | 39 ± 9 | 46 ± 26 | 35 ± 14 | 5.78 ± 3.06 | 782 ± 390 |
| Isoflurane | 0 | 112 ± 27 | 69 ± 12 | 63 ± 7 | 39 ± 5 | 46 ± 22 | 46 ± 24 | 4.96 ± 2.74 | 1377 ± 809 |
| | 1 | 125 ± 16* | 54 ± 9* | 62 ± 8 | 37 ± 4 | 39 ± 17 | 40 ± 17 | 4.82 ± 2.20 | 1022 ± 601* |
| | 1.5 | 128 ± 13* | 50 ± 9* | 59 ± 9 | 36 ± 5 | 39 ± 17 | 42 ± 19 | 4.59 + 2.12 | 950 ± 513* |
| Fentanyl – | 0 | 106 ± 22‡ | 66 ± 8 | 63 ± 6 | 40 ± 6 | 46 ± 34 | 54 ± 25 | 5.16 ± 4.39 | 1261 ± 644 |
| midazolam | 1 | 87 ± 19*§ | 59 ± 11* | 60 ± 7 | 39 ± 5 | 42 ± 30 | 47 ± 25 | 3.79 ± 3.05* | 1540 ± 806 |
| | 1.5 | 82 ± 18*§ | 56 ± 11* | 59 ± 7 | 38 ± 7 | 43 ± 30 | 52 ± 24 | 3.67 ± 2.99* | 1559 ± 875 |

All values are mean ± SD.

*$P < 0.05$, one-way analysis of variance, different from 0 minimum alveolar concentration (*MAC*) within the same anesthetic group. †$P < 0.05$, two-way analysis of variance, halothane versus sevoflurane and fentanyl–midazolam at 1 and 1.5 *MAC*. ‡$P < 0.05$, two-way analysis of variance, fentanyl–midazolam versus halothane at 0 *MAC*. §$P < 0.05$, two-way analysis of variance, fentanyl–midazolam versus halothane, sevoflurane, and isoflurane at 1.0 and 1.5 *MAC*.

*CI*, systemic cardiac index; *EF*, ejection fraction; *HR*, heart rate; *LVEDVI*, left ventricular end-diastolic volume index; *MAP*, mean arterial pressure; *SF*, shortening fraction; *SVI*, stroke volume index; *SVRI*, systemic vascular resistance index.

Reprinted with permission from Rivenes SM, Lewin MB, Stayer SA, *et al.* Cardiovascular effects of sevoflurane, isoflurane, halothane, and fentanyl–midazolam in children with congenital heart disease: an echocardiographic study of myocardial contractility and hemodynamics. *Anesthesiology* 2001; **94**: 223–9.

this patient population. Halothane and sevoflurane cause minimal airway irritation and thus are preferable for inhaled induction of anesthesia; however, there is little evidence for the continued use of halothane for this purpose in patients with CHD. Isoflurane has even less effect on contractility and hemodynamics than sevoflurane, and thus is considered by many to be the best maintenance agent, especially in light of its lower cost.

## Nitrous oxide

Despite its ubiquitous use as an adjunct to anesthetic induction and maintenance in patients with CHD, information regarding the effect of nitrous oxide on hemodynamics in patients with CHD is very limited. Its use may be relatively contraindicated where increased $F_{IO_2}$ is indicated, or where enlargement of enclosed air collections is possible, such as in any intracardiac or intrathoracic surgery. Reports of increased pulmonary vascular resistance (*PVR*), sympathetic stimulation, or significantly decreased *CO* in response to $N_2O$[29,30] in adult patients have not been substantiated in children with or without cardiac disease.

In infants and small children with normal hearts, Murray *et al*.[31] found that addition of 30% and 60% $N_2O$ to 1 *MAC* halothane or isoflurane resulted in a decreased *HR* and *CI*, without changing *EF* and stroke volume measured echocardiographically. These authors also demonstrated that when 0.6 *MAC* halothane or isoflurane was substituted for 60% $N_2O$ during 0.9 *MAC* isoflurane or halothane anesthesia, *HR*, *MAP*, and *CI* were unchanged.[32]

In 14 patients with CHD recovering from surgery, Hickey *et al*.[33] administered 50% $N_2O$ and observed a decrease of 9% in *HR*, 12% in *MAP*, and 13% in systemic *CI*. However, mean pulmonary artery pressure (*PAP*) and *PVR* were not significantly changed in these well-ventilated patients with a $P_{ACO_2}$ of 34–35, and pH of 7.47–7.49, even in patients with elevated *PVR* at baseline. This single report represents the total number of patients with CHD in which $N_2O$ administration has been carefully studied. Despite this paucity of information, extensive clinical experience has demonstrated $N_2O$ to be safe and effective, particularly as an adjunct to inhaled induction of anesthesia for congenital heart surgery.

## Xenon

Xenon, a noble gas, has anesthetic properties and a blood : gas partition coefficient even lower than $N_2O$ (0.14 vs. 0.47).[34]

In clinical studies in adults, it reliably produces general anesthesia with very rapid induction and emergence, and is virtually devoid of cardiovascular effects. Dogs with induced cardiomyopathy demonstrate minimal effects on systemic and pulmonary hemodynamics, as well as systolic or diastolic left ventricular function, from inhalation of xenon.[35] The major drawbacks are a *MAC* of 70%, and high cost. Xenon also increases oxygen consumption, probably by directly stimulating the cellular metabolic rate.[36] No reports have been published about the use of xenon in pediatric patients, however the favorable hemodynamic and pharmacokinetic characteristics of this anesthetic would be ideal for patients with CHD, particularly those with compromised myocardial function undergoing procedures where other volatile agents, $N_2O$ or large doses of narcotics are undesirable.

## Opioids and benzodiazepines

Fentanyl and sufentanil have been studied as a sole anesthetic in patients with CHD. Hickey and Hansen *et al*.[37–40] provided the basis for this technique with a series of studies in neonates and infants less than 1 year of age undergoing complex repairs ranging from the Norwood operation to complete repair of biventricular lesions. Fentanyl doses of 50–75 μg/kg, and sufentanil doses of 5–40 μg/kg, administered with pancuronium 0.1–0.15 mg/kg, provided excellent hemodynamic stability with minimal changes in *HR* and blood pressure throughout the surgery. The increase in *PAP* and resistance in response to suctioning in infants recovering from cardiac surgery was eliminated with 25 μg/kg fentanyl. Moore *et al*.[41] demonstrated that 5, 10, or 20 μg/kg sufentanil in children 4–12 years of age had no effect on *EF* as measured by echocardiography, in patients undergoing repair of biventricular lesions. Increases in *HR*, blood pressure and stress hormones were more effectively blunted by the higher doses. Glenski *et al*.[12] reported M-mode echocardiographic measures of contractility, blood pressure, and *HR* response using fentanyl (at 100 μg/kg) or sufentanil (at 20 μg/kg) in children from 6 months to 9 years of age. Measurements were made at three different times: after a premedication with morphine and scopolamine, after induction, and after tracheal intubation. These opioids decreased both *EF* and shortening fraction after induction, but they returned to or above baseline after intubation (Fig. 4.3).

Midazolam is often added to fentanyl anesthesia to provide sedation and amnesia, as a substitute for low dose volatile anesthetic agent, particularly in hemodynamically unstable patients and young infants, where the myocardial depressant effects of volatile agents are more pronounced. Fentanyl and midazolam combinations have been studied in two different clinically utilized dose regimens (15–30 μg/kg fentanyl and 0.29–0.45 mg/kg midazolam) for induction and the pre-bypass period in congenital heart surgery in biventricular patients.[15] Vecuronium was used for muscle relaxation in order to isolate the effects of the other two agents on hemodynamics. Measurements of *CO* and contractility were made by echocardiography. Fentanyl/midazolam caused a significant decrease (22%) in *CO* despite preservation of contractility. That was predominantly due to a decrease in *HR*. Coadministration of a vagolytic agent such as atropine[42] or pancuronium would likely preserve *CO*. The added effect of midazolam on echocardiographic indices of contractility has not been previously reported; however, increased inotropic support requirements have been documented in infants undergoing cardiac surgery with the addition of midazolam bolus totaling 0.3 mg/kg, and infusion of 0.1 mg/kg/hour intraoperatively.[43]

The stress response to major cardiac surgery in infants and children has been the subject of considerable interest. Anand and Hickey[44] reported the use of high dose sufentanil at a total mean dose of 37 μg/kg as a sole anesthetic for complex neonatal surgery. The sufentanil was continued by infusion for 24 hours postoperatively. This regimen was compared to halothane plus morphine (mean dose of 0.35 mg/kg) intraoperatively, followed by intermittent morphine and diazepam postoperatively. Stress response, as measured by changes in adrenal hormones, cortisol, glucose, and lactate was significantly reduced in the sufentanil group, and mortality and major complications such as sepsis and necrotizing enterocolitis were also significantly reduced. A more recent study from the same institution of 45 infants averaging 3 months of age undergoing biventricular repair was reported.[45] A fentanyl total dose 100 μg/kg, either given as intermittent boluses of 25 μg/kg, or as boluses plus infusion, either with or without midazolam, resulted in a significant endocrine stress response to cardiac surgery. Despite this, outcome was excellent in all groups,[46] with no adverse outcomes related to the anesthetic technique nor to stress response. The sole hemodynamic difference between the regimens was a lower *MAP* during cooling on bypass in the group who received midazolam. Finally, Duncan *et al*.[46] reported a dose-response study of 2, 25, 50, 100, and 150 μg/kg fentanyl before bypass in 40 children averaging 13 months and 8.5 kg. The 2 μg/kg group had significant increases in pre-bypass norepinephrine, glucose, and cortisol, and significantly higher *HR* and blood pressure than all other groups. Doses of 25 μg/kg or higher eliminated changes in these parameters for the duration of the surgery. It is difficult to interpret the significance of these stress-response studies because they evaluated by different age groups and lesions. Also there was more than one decade between reports with improvements in surgical, bypass, and postoperative management. If any group of patients had benefited from attenuation of the stress response, it would appear to be neonatal patients undergoing complex surgery.

In choosing between fentanyl and sufentanil, there appear to be few if any specific differences between the agents. Cost considerations and familiarity lead most practitioners to select

fentanyl as the basis for most high or moderate complexity congenital heart surgeries.

Remifentanil is a synthetic ultra-short acting narcotic agent metabolized by plasma esterases with half-life 3–5 minutes that is independent of the duration of infusion.[47] It is particularly useful for short non-cardiac procedures with intense stimulation where narcotic-based anesthesia and its hemodynamic stability would be desirable, yet where rapid emergence is also important. Remifentanil at 0.25 μg/kg/minute provides equivalent analgesia and a similar hemodynamic profile to epidural bupivacaine when used with $N_2O$/isoflurane anesthesia for major abdominal or lower extremity surgery in children.[48] Donmez *et al*.[49,50] reported a series of 55 children undergoing cardiac catheterization with a remifentanil infusion of 0.1 μg/kg/minute. This regimen maintained excellent cardiovascular stability, with minimal changes in *HR*, blood pressure or oxygen saturation. Fifty-eight percent of patients required additional sedation with midazolam or ketamine. Apnea was infrequent, and the time to recovery score of five (10-point scale) was only 2–4 minutes. Patients undergoing long cardiac catheterization procedures could potentially benefit from this agent. Its use has been reported for atrial septal defect repair, where patients are extubated in the operating room (OR).[51] It apparently does not bind to the cardiopulmonary bypass (CPB) circuit,[52] and its clearance in children before and after CPB appears to be predictable within a narrow range, making it a potentially useful agent for "fast-track" anesthesia and early extubation for simple surgical procedures. Despite these advantages, nausea/vomiting and bradycardia/hypotension,[48] as with other synthetic μ-receptor agonists, are a prominent feature of the adverse event profile.

## Propofol

Propofol has become a popular agent for sedation and general anesthesia for cardiac catheterization procedures and for postoperative intensive care unit (ICU) sedation to facilitate early tracheal extubation. In plasma concentrations found in routine clinical use, propofol has minimal negative inoptropic effects in isolated animal cardiac preparations,[53] or in human adult atrial muscle strips.[54]

In children with normal hearts on induction propofol consistently decreases systolic and *MAP* by 5–25%,[55] without changing *HR*. There has been one published study using echocardiography to assess myocardial contractility and *CO* in infants with normal hearts induced with propofol.[55] The shortening fraction or *CI* was not changed, *SVR* decreased by 14% and 27% at 1 and 5 minutes after induction. Load independent measures of contractility (stress-velocity index and stress-shortening index) decreased significantly from baseline at 5 minutes after induction with propofol.

Williams *et al*.[56] measured the hemodynamic effects of propofol in 31 patients aged 3 months to 12 years at a dose of 50–200 μg/kg/minute undergoing cardiac catheterization (Fig. 4.4). They found that propofol significantly decreased *MAP* and *SVR*; however, systemic *CO*, *HR*, and mean *PAP*, as well as *PVR*, did not change. In patients with cardiac shunts, the net result was a significant increase in the right-to-left shunt, a decrease in the left-to-right shunt, and decreased *Q*p : *Q*s, resulting in a statistically significant decrease in $PaO_2$ and $SaO_2$, as well as reversal of the shunt from left-to-right to right-to-left in two patients. In another study of patients undergoing cardiac catheterization, Lebovic *et al*.[57] demonstrated that patients could experience a 20% decrease in *HR* or *MAP*.

Zestos *et al*.[58] studied patients undergoing congenital heart surgery with CPB who were selected for early extubation in the ICU ($n = 26$). A propofol infusion at 50 μg/kg/minute was begun after CPB, and compared to a placebo control group who received intralipid. The infusions were discontinued upon leaving the OR, and morphine was given as needed for pain. Both the time to tracheal extubation (33 vs. 63 minutes) and the number of morphine doses (1.0 vs. 2.3) were significantly less in the propofol group. No hemodynamic

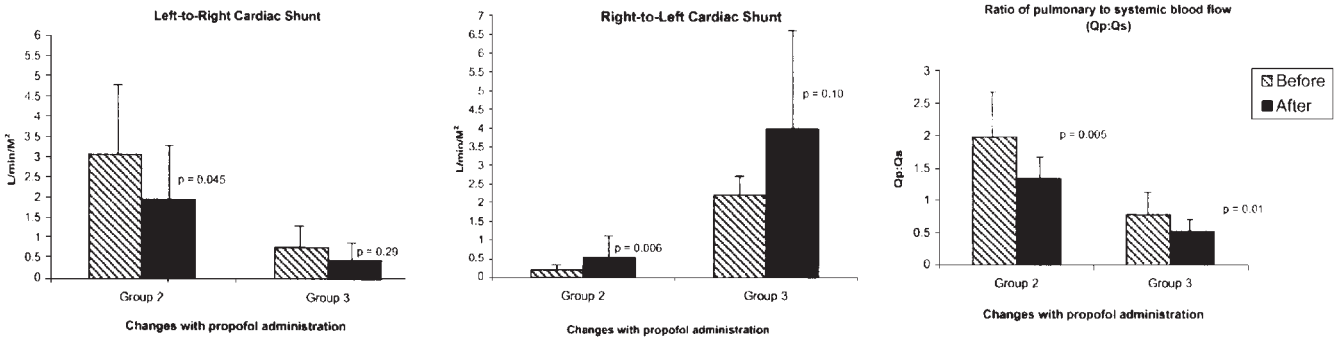


**Fig. 4.4** Changes in intracardiac shunting in response to propofol induction and infusion in children undergoing cardiac catheterization. Group 2, patients with net left-to-right cardiac shunting; Group 3, patients with net right-to-left cardiac shunting. *Q*p : *Q*s decreased significantly in both groups. Reproduced with permission from Williams GD, Jones TK, Hanson KA, Morray JP. The hemodynamic effects of propofol in children with congenital heart disease. *Anesth Analg* 1999; **89**: 1411–16.

depression was observed in this study. Another recent study with a similar protocol for propofol infusion after weaning from bypass demonstrated that 70% of children undergoing simple and complex surgery were extubated within 9 hours of ICU admission.[59]

Propofol has no significant effect on sinoatrial or atrioventricular node conduction, or on the ability to induce supraventicular tachycardia, and therefore is desirable as a primary agent during electrophysiologic studies and radiofrequency ablation.[23,60] However, ectopic atrial tachycardia may be suppressed by propofol.[61]

Although propofol is very useful for cardiac catheterization, short, stimulating procedures, and short term sedation after cardiac surgery, its use long term as an ICU sedative is controversial, with a report of unexplained metabolic acidosis and myocardial failure after long term (> 48 h) high dose use in pediatric patients.[62,63]

In summary, propofol can be utilized in patients with adequate cardiovascular reserve who can tolerate a mild decrease in contractility and *HR*, and a decrease in *SVR*. Propofol may cause an increased intracardiac right-to-left shunt, and reversal of shunt in some patients (i.e. acyanotic TOF), and thus hemodynamic data obtained in the cardiac catheterization laboratory should be interpreted accordingly.

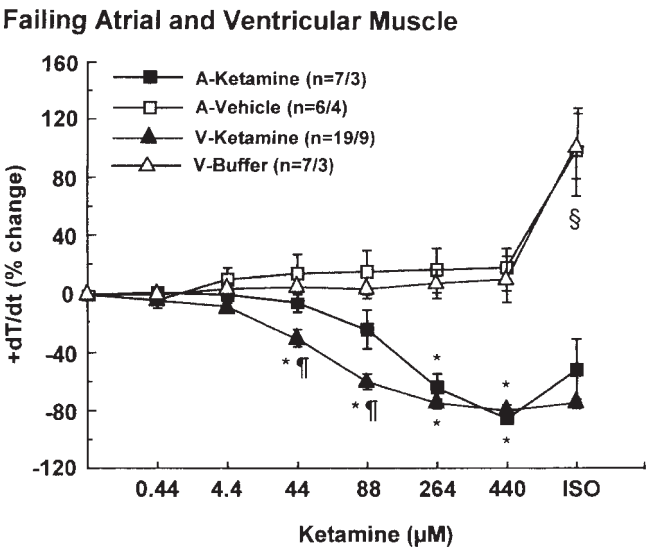


**Fig. 4.5** Developed tension over time (+dT/dt) in cardiac muscle trabeculae in explanted hearts from adults undergoing cardiac transplantation in response to increasing ketamine concentrations. The upper limit of clinical concentration is 44 μM after 2 mg/kg induction dose. A, atrial muscle; buffer, Krebs–Henseleit buffer control; ISO, change with addition of 1 μM isoproterenol; V, ventricular muscle; Vehicle, control solution without ketamine. Numbers in parentheses represent numbers of muscle strips/number of patients, respectively. Reproduced with permission from Sprung J, Schuetz SM, Stewart RW *et al*. Effects of ketamine on the contractility of failing and nonfailing human heart muscles *in vitro*. *Anesthesiology* 1998; **88**: 1202–10.

## Ketamine

The general anesthetic and analgesic effects of ketamine are thought to be mediated by its interaction with *N*-methyl D-aspartate receptors in the brain.[64] It increases *HR*, blood pressure, and *CO* through central nervous system mediated sympathomimetic stimulation and inhibition of the reuptake of catecholamines. It has been shown that ketamine is a direct myocardial depressant when studied in isolated myocyte preparations,[65] and in adult human failing atrial and ventricular muscle trabeculae (Fig. 4.5).[66] The direct myocardial depression caused by ketamine may be unmasked when administered to patients whose sympathomimetic responses are already maximally stimulated from cardiomyopathy, or other conditions leading to poor myocardial reserves, because further increase in catecholamine release is limited. Similarly, if the patient is chronically receiving β-adrenergic agonists, catecholamine receptors may be downregulated, resulting in a diminished response to endogenously generated catecholamines, again allowing the myocardial depressant effects of ketamine to predominate.

The mechanism of myocardial depression is by inhibition of L-type voltage-dependent $Ca^{2+}$ channels in the sarcolemmal membrane. An increased extracellular $Ca^{2+}$ concentration may enhance this effect.[65] This direct myocardial depression effect is greater than that produced by etomidate.[54] In a patient with end-stage cardiomyopathy awaiting heart transplant, hemodynamic collapse occurred after the induction of anesthesia with ketamine.[67] In a study of ketamine vs. sufentanil for induction of anesthesia in patients undergoing cardiac transplant, whose average *EF* was 14%, and who were all receiving inotropes and vasodilators preoperatively found that ketamine increased *MAP*, central venous pressure, and *PAP* significantly, and decreased stroke volume index and left ventricular stroke work index.[68] Cardiac index decreased slightly but not to a statistically significant degree. Systemic vascular resistance and *HR* were higher. The sum total of the hemodynamic effects of ketamine induction in these patients was less myocardial work at the expense of a higher myocardial wall tension. Sufentanil induction did not change any of these parameters from baseline.

Other well-recognized untoward effects associated with ketamine use do not differ among patients with CHD. These include emergence reactions, excessive salivation, and an increase in cerebral metabolism, intracranial pressure, cerebral blood flow and cerebral oxygen consumption.[64]

Despite the adverse effects of ketamine that are delineated above, this drug has been a mainstay of induction of general anesthesia in patients with CHD.[69,70] It can be administered intravenously or intramuscularly; and it will reliably maintain *HR*, blood pressure, and systemic *CO* at an induction dose of 1–2 mg/kg i.v., or 5–10 mg/kg i.m., and a maintenance dose of 1–5 mg/kg/hour in patients with a variety of

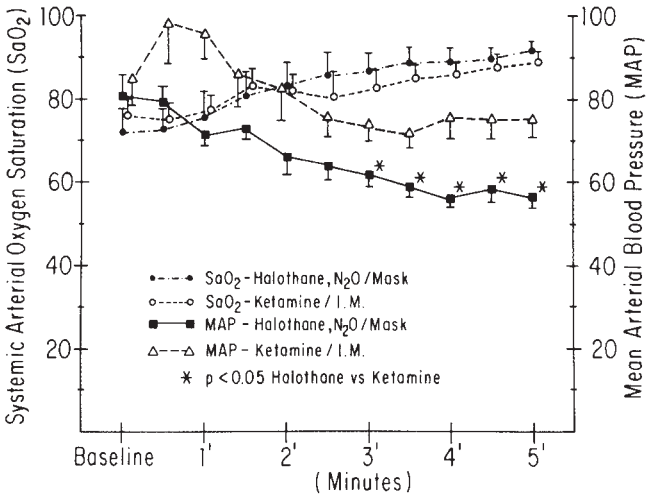


**Fig. 4.6** Oxygen saturation and mean arterial pressure in response to induction with intramuscular ketamine vs. halothane in patients with right-to-left cardiac shunting, most of whom had tetralogy of Fallot. Reproduced with permission from Greeley WJ, Bushman GA, Davis DP, Reves JG. Comparative effects of halothane and ketamine on systemic arterial oxygen saturation in children with cyanotic heart disease. *Anesthesiology* 1986; **65**: 666–8.

CHDs, including TOF (Fig. 4.6).[27,71] The question about exacerbation of pulmonary hypertension has been addressed in two important studies. Morray *et al*.[72] demonstrated that in cardiac catheterization patients, 2 mg/kg ketamine caused a minimal (< 10%) increase in mean *PAP*, and ratio of *PVR* to *SVR* (*R*p : *R*s), with no change in direction of shunting or *Q*p : *Q*s. Hickey *et al*.[38] studied postoperative cardiac surgery patients with normal $Paco_2$ and demonstrated that ketamine 2 mg/kg had no effect on *PAP* or calculated *PVR*, either in patients with normal or elevated baseline *PVR*. There have been two cardiac catheterization laboratory studies reporting increases in *PVR* in some patients; however, these studies were both performed at 5000 feet altitude, which contributed to these confounding results.[73,74]

Ketamine, supplemented with small doses of midazolam and/or morphine, has been used for interventional cardiac catheterization procedures[75] and for postoperative analgesia after cardiac surgery in children. Hemodynamic stability has been excellent, with few complications. The most notable adverse effect was transient apnea in 10% of spontaneously breathing newborns undergoing balloon atrial septostomy in the catheterization laboratory.

Intramuscular induction of anesthesia may be achieved with ketamine 5 mg/kg, succinylcholine 4 mg/kg, and atropine 20 μg/kg mixed in the same syringe. This regimen is useful for small patients who present to the OR without intravenous access in whom the inhalational induction of anesthesia may produce undesirable hemodynamic effects. Endotracheal intubation can usually be achieved in 3–5 minutes, and attention can be turned to establishing intravenous access with the airway secure and a stable hemodynamic state.

In summary, ketamine is an attractive choice for intravenous or intramuscular induction of anesthesia in patients with CHD with good or moderately limited hemodynamic reserve, including those with pulmonary hypertension or cyanosis. However, care must be taken in patients with severely limited cardiac reserve and depressed myocardial contractility. Such patients may be chronically receiving β-adrenergic or similar agents, or their own endogenous sympathomimetic system is maximally stimulated because of a low *CO* state. The myocardial depressant properties of ketamine may be unmasked and lead to hemodynamic compromise.

## Etomidate

Etomidate is an imidazole derivative introduced into clinical practice in 1972. It is thought to produce its hypnotic effects (without analgesia) by interaction with γ-aminobutyric acid receptors.[64] Besides having a desirable lack of effect on hemodynamics, etomidate reduces cerebral blood flow and cerebral metabolic rate for oxygen consumption (30–50%), and intracranial pressure. It has little effect on ventilation, does not release histamine, and does not change airway smooth muscle tone. Of all of the available intravenous induction agents, etomidate consistently demonstrates the smallest amount of direct myocardial depression in several *in vitro* models. Two well-designed studies using adult human atrial and ventricular tissue demonstrated no effect of etomidate on myocardial contractility in concentrations seen in clinical use (Fig. 4.7). In the same model, ketamine showed slight, and thiopental strong, negative inotropic effects in clinical concentration ranges. This was true even in abnormal myocardial samples of ventricular tissue taken from hearts removed for cardiac transplantation.[54,76]

All of these beneficial effects of etomidate are offset by a number of undesirable effects. Etomidate is water insoluble and thus is formulated in propylene glycol, and commonly produces pain on injection, which may be ameliorated by pretreatment with lidocaine, and 1 : 1 dilution with sterile water. Myoclonic movement, hiccoughs, and nausea and vomiting are frequent.[64] It should be noted that, as in adults, a single dose of etomidate used for induction in pediatric patients undergoing cardiac surgery with CPB suppresses the usual increase in plasma cortisol levels by inhibiting 11-β-hydroxylase, the enzyme that converts 11-deoxycortisol to cortisol.[50] Cortisol levels returned to normal 24 hours later.

There are few published reports of the hemodynamic effects of etomidate in children with CHD. Twenty patients with a variety of congenital defects were studied in the cardiac catheterization laboratory. These authors found that etomidate at 0.3 mg/kg bolus followed by an infusion of 26 μg/kg/minute had similar effects as ketamine 4 mg/kg

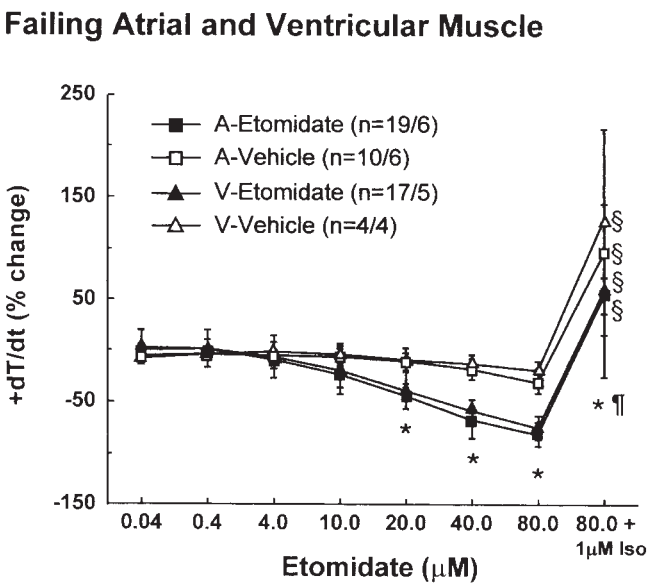


**Fig. 4.7** Developed tension over time (+dT/dt) in cardiac muscle trabeculae in explanted hearts from adults undergoing cardiac transplantation in response to increasing etomidate concentrations. The upper limit of clinical concentration is 4 μM. A, atrial muscle; Iso, change with addition of 1 μM isoproterenol; V, ventricular muscle; Vehicle, 35% propylene glycol, in which etomidate is solubilized. Numbers in parentheses represent numbers of muscle strips/number of patients, respectively. Reproduced with permission from Sprung J, Ogletree-Hughes ML, Moravec CS. The effects of etomidate on the contractility of failing and nonfailing human heart muscle. *Anesth Analg* 2000; **91**: 68–75.

followed by an infusion of 83 μg/kg/minute, namely a slight increase in *HR* but no change in *MAP* during induction or the 60-minute infusion.[77] Sarkhar *et al*.[78] studied etomidate bolus 0.3 mg/kg in 12 children undergoing cardiac catheterization for device closure of atrial septal defect, or radiofrequency ablation of atrial arrhythmias. There were no significant changes in any hemodynamic parameter, including *HR*, *MAP*, filling pressures, vascular resistances, *Q*p : *Q*s, or mixed venous oxygen saturation. A case report of stable hemodynamics in a pediatric patient with end-stage cardiomyopathy receiving a second anesthetic 4 weeks after cardiovascular collapse with ketamine induction (see above) demonstrates the utility of the drug in this population.[67] Etomidate has been utilized for induction of anesthesia in adults with congenital cardiac conditions such as ruptured aneurysm of the sinus of valsalva, and cesarean section in a patient with uncorrected coronary artery to pulmonary artery fistula, and has been demonstrated to be devoid of cardiovascular effects in these patients.[79,80]

Thus it would appear that etomidate is best utilized in patients with the most limited cardiac reserve. It seems to be particularly useful in teenagers or adults with poorly compensated palliated CHD presenting for cardiac transplantation, or revision of previous surgeries. New water soluble preparations, or other formulations of etomidate[81,82] may eliminate the troubling side effects of pain on injection and phlebitis.

## Barbiturates

An induction dose of thiopental[55] was studied with transthoracic echocardiography to determine cardiovascular responses in infants with normal hearts. In contrast to propofol, thiopental did not alter systolic or *MAP*, or *SVR*. Shortening fraction decreased significantly, and there was a mild decrease in load-independent measures of contractility as well. The *HR* and *CI* did not change significantly. Another study[83] comparing thiopental and propofol for induction in children found thiopental produced a decrease in *MAP* of 14–21%, and a 10–15% reduction in *CO*, which was possibly influenced by the inhalation of $N_2O$ and halothane.

The rapid acting barbiturates, including thiopental, are direct myocardial depressants. A recent study using adult human atrial muscle strips, found a reduction in contractility of 25–50% after exposure to thiopental at clinically relevant concentrations.[54] Thiopental also causes venodilation and pooling of blood in the periphery. The mechanism for these cardiovascular effects is related to both an interference of $Ca^{2+}$ flux across the sarcolemmal membrane, and an alteration of the nitric oxide synthase pathway.[84]

Hemodynamic homeostasis is mediated by baroreceptor reflex-induced sympathetic stimulation. Patients with limited reserves, and maximally stimulated sympathetic responses or downregulated β-adrenergic receptors will likely experience significant hypotension with barbiturate anesthetic inductions.

In summary, the intravenous induction of anesthesia with barbiturates in patients with CHD should be reserved for those patients with good cardiac reserves and intact baroreceptor reflexes, who can tolerate a reduction in contractility, and a possible reduction in arterial pressure.

## Special conditions effecting anesthetic pharmacokinetics and pharmocodynamics in congenital cardiac anesthesia

### Intracardiac shunts

The presence of a right-to-left intracardiac shunt decreases the rate of rise of the concentration of inhaled anesthetic in the arterial blood, as a portion of the systemic *CO* bypasses the lungs and then dilutes the anesthetic concentration in the systemic arterial blood.[85] The anesthetic concentration in the blood thus never equals the exhaled concentration. Huntington *et al*.[85] studied six children with right-to-left shunts from a fenestrated Fontan operation whose average pulmonary to systemic blood flow ratio was 0.58. These

patients achieved an arterial anesthetic concentration (*F*a) of only 55% of inspired halothane concentration (*F*I) after 15 minutes during washin of 0.8% halothane. After closure of the right-to-left shunt (occlusion of Fontan fenestration in the cardiac catheterization laboratory), the arterial concentration of halothane equaled the inspired concentration. This difference between *F*a and *F*I is greater during induction or washout; and greater with less soluble drugs such as sevoflurane, desflurane, and nitrous oxide, than with less soluble drugs such as halothane.

In the face of significant right-to-left intracardiac shunting, intravenous agents given by bolus may pass directly into the left side of the heart with less dilution by systemic venous blood and passage through the pulmonary vascular system. This may result in transient high arterial, brain, and cardiac concentrations of drugs such as lidocaine.[86] Intravenous induction agents and muscle relaxants may also achieve sufficient arterial and brain concentrations more rapidly with right-to-left intracardiac shunts.[87]

Left-to-right intracardiac shunts have little effect on the speed of induction with inhaled anesthetic agents.[88] The recirculation of blood through the lungs results in increased uptake of anesthetic and in a higher blood anesthetic concentration in the pulmonary capillaries, which in turn reduces the anesthetic concentration gradient between the alveolus and the pulmonary capillary blood, reducing anesthetic uptake. The two effects cancel each other. Only in the case of severe congestive heart failure from left-to-right shunt, with significant interstitial and alveolar edema, would left-to-right intracardiac shunting be expected to slow inhalation induction, from the combined effects of diffusion limitation and ventilation–perfusion mismatch resulting alveolar deadspace ventilation in which no new anesthetic agent is taken up.

## Cardiopulmonary bypass

The onset of CPB affects plasma levels of intravenous drugs by a number of different mechanisms.[89] Hemodilution of the patient's blood volume by a factor of 50% to 300%, depending on the size of the patient and the priming volume of the circuit, causes an immediate reduction in plasma levels. Many drugs also bind to the membrane oxygenator and other components of the bypass circuit, resulting in a further decrease in plasma levels. This effect is variable, and is dependent on the drug, the type of bypass circuit used (i.e. silicone vs. polypropylene), the age and size of the patient, and the plasma and bypass prime albumin concentrations. Hypothermia slows the metabolism of all drugs by reducing the rate of reaction of all enzymes involved in drug metabolism, whether they are in the liver (cytochrome P450 system), kidney, or plasma. Rewarming significantly increases the rate of metabolism of intravenous agents.

A constant, stable fentanyl plasma level[90] can be achieved in most children through the administration of a loading dose of 30–50 μg/kg followed by an infusion of 0.15–0.30 μg/kg/minute. Plasma fentanyl levels decrease by 70–75% immediately upon institution of CPB with a silicone membrane oxygenator. After cooling to 18–25°C, fentanyl metabolism decreases considerably and free drug concentrations change very little, even without added drug.[91] Metabolism then increases and drug levels decline in the plasma as rewarming proceeds. Data concerning common anesthetic adjuvants such as midazolam suggest similar changes in plasma concentrations.[89] Thus, without supplementation of intravenous agents such as fentanyl and midazolam, either just before or at the initiation of bypass, there is an increased risk of awareness. A similar risk would appear to be true during the final phases of the rewarming period. Indeed, this concept is borne out by recent studies using the bispectral index (see below) as an indicator of depth of sedation in children undergoing bypass with mild hypothermia.[92]

Neuromuscular blocking agents have an enhanced effect during hypothermic bypass,[89] both from decreased metabolism and clearance, and because of the effects of hypothermia to potentiate the pharmacodynamic effects of the drugs at the neuromuscular junction. These effects rapidly reverse themselves during rewarming. These drugs have a small volume of distribution and thus few tissue stores from which to re-equilibrate plasma levels. Thus, plasma levels would be expected to decline in proportion to the hemodilution factor of the pump prime, subject to changes in protein binding. This may be offset by reductions in the patient's plasma volume on bypass due to vasoconstriction. The action of these drugs in response to bypass is accordingly more variable than other commonly used intravenous anesthetic agents. There is limited pediatric information available. Monitoring of neuromuscular blockade with a twitch monitor is recommended if early reversal is desired.

Volatile agents may be used during bypass to supplement anesthetic depth, or as vasodilators. Isoflurane is most commonly utilized at a concentration of 0.5–2.0% inspired into the sweep gas of the bypass circuit. Multiple adult studies have demonstrated the effectiveness and relatively rapid washin of this agent.[89] However, pediatric data is limited, and because sweep gas flow rates are often less than 1 L/minute, uptake is probably much slower and it cannot be assumed that the desired blood anesthetic level is rapidly reached when volatile anesthetic agents are administered through the bypass circuit to infants and small children. Washout of volatile agents is also slower at low sweep gas rates, and volatile agents should be discontinued early during the rewarming period to avoid the myocardial depressant effects of these agents while attempting to wean the patient from bypass.

## Hypothermia

Studies performed on animal models reveal hypothermia reduces the *MAC* of volatile anesthetics.[93] Liu *et al*.[94] studied

the *MAC* of isoflurane in 33 children with left-to-right intracardiac shunts at 37, 34, or 31°C. They found *MAC* was reduced by 28% at 31°C when compared to normothermia, indicating a decrease in *MAC* of approximately 5% per degree Celsius cooling. The bispectral index (*BIS*) value has been demonstrated to correlate strongly with temperature during mild hypothermic bypass in children,[95] providing supporting evidence that hypothermia alone provides general anesthesia.

## Monitoring anesthetic depth and awareness

Until recently, the only means available to the clinician to monitor anesthetic depth and assess the risk of awareness was through a general knowledge of the pharmacokinetic and pharmacodynamic properties of anesthetics, along with measurement of the end-tidal anesthetic concentrations and clinical signs of depth of anesthesia. The clinical signs of inadequate anesthesia in the paralyzed cardiac surgical patient include autonomic signs such as papillary dilation, tearing, and tachycardia/hypertension. These signs are often unreliable, given the hemodynamic derangements common in this population, manipulation by the surgeon causing activation of baroreceptor reflex responses, and the use of vasoactive and chronotropic drugs, or drugs that block the autonomic response. Recently the *BIS*, a highly processed electroencephalogram, has become available.[92,95–97] Available pediatric data suggest that this modality correlates with end-tidal levels of volatile anesthetics and with *MAC* awake levels, with better correlation in children over 1–2 years of age, although interpatient variability is significant.[92] Studies in both infants and older children undergoing congenital heart surgery with CPB, demonstrate that the index (a dimensionless number 0–100) decreases with lower nasopharyngeal temperature, and increases during the rewarming phase. However, *BIS* did not correlate with hemodynamic, metabolic, or hormonal indices of light anesthesia. *BIS* has been demonstrated to be more sensitive to changes in the levels of volatile anesthetics and propofol, and less sensitive to narcotics and benzodiazepines. In our experience, we commonly find that *BIS* increases during rewarming on bypass to levels in the range for risk of awareness despite large doses of fentanyl and midazolam. Pediatric studies of *BIS* during cardiac surgery are limited, and larger prospective studies are needed to demonstrate the validity and utility of device.

## Neuromuscular blocking agents and antagonists

### Succinylcholine

Succinylcholine is rarely indicated for anesthesia for CHD because of its association with the development of malignant hyperthermia, hyperkalemic cardiac arrest, and bradycardia after intravenous bolus administration. Succinylcholine will produce a more rapid onset of muscle relaxation than non-depolarizing muscle relaxants,[98] and we have limited its use to full-stomach emergency indications, i.e. cardiac transplant, to treat layrngospasm, and as part of an intramuscular induction.

Infants and children frequently exhibit bradycardia, nodal rhythm, ventricular premature beats, and rarely, asystole, after intravenous dosing of 1–2 mg/kg without atropine pretreatment. The frequency of all of these arrhythmias increases with a second dose. A dose of 4 mg/kg i.m., either alone, or with atropine 20 μg/kg, and ketamine 5–10 mg/kg in the same syringe, rarely causes bradycardia.[99]

### Pancuronium

Pancuronium is frequently used in doses of 0.1–0.3 mg/kg for initial relaxation for CHD[100] and is particularly desirable in many small infants and young children because of the vagolytic and mild sympathomimetic effects, which preserve or increase *HR*, especially in the face of concomitant bradycardia from high dose narcotic anesthesia.

### Vecuronium

Vecuronium is devoid of cardiovascular effects in children.[101] It is a useful agent when increases in *HR* are undesirable, e.g. HCM. When no uncertainties about ability to manage the airway are evident, it is a useful alternate to succinylcholine in a dose of 0.3–0.4 mg/kg for modified rapid sequence induction.

### Rocuronium

Rocuronium is a moderately rapid onset intermediate duration non-depolarizing neuromuscular blocker that is useful at a dose of 0.6–1.2 mg/kg i.v. At the upper dose ranges it is an acceptable substitute for succinylcholine for modified rapid sequence induction. Cardiovascular effects are minimal, however, because it causes pain on injection, or because it is a weak vagolytic medication, an increase in *HR* is often observed after injection. This agent may be utilized for intramuscular administration in doses of 1.8–2.0 mg/kg, and when injected into the deltoid will produce suitable intubating conditions in 3–4 minutes.[102]

### Atracurium and cisatracurium

These agents are non-organ dependent for elimination and are attractive choices in the face of significant hepatic and renal dysfunction. Atracurium at high dosages frequently casues histamine release, resulting in hypotension when injected rapidly,[98] making it undesirable for many patients

with CHD. Cisatracurium is a stereoisomer of atracurium, also degraded by Hoffmann elimination, does not release histamine, and like vecuronium, is devoid of cardiovascular effects even when administered rapidly.[103]

## Antagonists

The muscarinic effects of neostigmine must be blocked by atropine or glycopyrrolate to prevent potentially serious decreases in *HR*. Because the onset of cardiovascular effects of neostigmine and glycopyrrolate are similar, a most useful regimen is to utilize neostigmine and glycopyrrolate in the same syringe in a 5 : 1 ratio of neostigmine : glycopyrrolate (i.e. 75 μg/kg : 15 μg/kg) injected slowly to minimize the small risk of arrhythmia with neostigmine.

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# 5 Cardiopulmonary bypass

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## Introduction

In order to facilitate the repair of congenital heart lesions, cardiopulmonary bypass (CPB) was developed. The earliest reported successes were in the 1950s with Gibbon and Lillehei performing intracardiac surgery using a variety of systems to oxygenate and pump the circulating blood in a surgical patient.[1] These systems posed significant risk of death not only to the patient, but also to the patient's parent who was being used as oxygenator and pump, using the technique of cross circulation.[2] Many improvements have been made upon the original artificial systems, but the fundamental principles of extracorporeal circulation have remained the same. The extracorporeal circuit takes venous blood from the patient, pumps it through an oxygenator and filter, and returns it to the arterial system of the patient, thus bypassing the heart and lungs. Variation exists between types of pumps, oxygenators, venous reservoirs, and the size and coating of tubing and cannulae. New technologies and current research continues to improve outcome from congenital heart disease (CHD) surgery, and the effects of CPB on the patient continue to be elucidated. To better understand the physiology of CPB in the infant and child, it is helpful to first understand the differences between pediatric and adult bypass.

## Differences between pediatric and adult cardiopulmonary bypass

The physiologic effects of CPB on neonates, infants, and children are significantly different than in adults (Table 5.1).[3] During CPB, pediatric patients are exposed to different biologic extremes not seen in adults, including deep hypothermia (15–20°C), hemodilution (three to 15-fold greater dilution of circulating blood volume), low perfusion pressures

**Table 5.1** Cardiopulmonary bypass differences between adult and pediatric patients.

| Parameter | Adult | Pediatric |
|---|---|---|
| Hypothermic temperature | Rarely below 25–32°C | Commonly 15–20°C |
| Use of total circulatory arrest | Rare | Common |
| Dilution effects on blood volume | 25–33% | 100–200% |
| Perfusion pressures | 50–80 mmHg | 20–50 mmHg |
| Influence of α- vs. pH-stat management strategy | Minimal at moderate hypothermia | Marked at deep hypothermia |
| Measured $Paco_2$ differences | 30–45 mmHg | 20–80 mmHg |
| Glucose regulation | | |
| Hypoglycemia | Rare–requires significant hepatic injury | Common—reduced hepatic glycogen stores |
| Hyperglycemia | Frequent–generally easily controlled with insulin | Less common—rebound hypoglycemia may occur |

Modified with permission from Davies LK. Cardiopulmonary bypass in infants and children: How is it different? *J Cardiothorac Vasc Anesth* 1999; **13**: 330–45.

(20–30 mmHg), wide variation in pump flow rates (ranging from highs of 200 mL/kg/minute to total circulatory arrest), and differing blood pH management techniques (α-stat or pH-stat, or both sequentially). These parameters significantly differ from normal physiology and affect preservation of normal organ function during and after CPB. In addition to these prominent changes, subtle variations in glucose supplementation, cannula placement, presence of aortopulmonary collaterals, and patient age may also be important factors affecting organ function during CPB. Adult patients are infrequently exposed to these biologic extremes. In adult cardiac patients, temperature is rarely lowered below 25°C, hemodilution is more moderate, perfusion pressure is generally maintained at 50–80 mmHg, flow rates are maintained at 50–65 mL/kg/minute, and pH management strategy is less influential because of moderate hypothermic temperatures and rare use of circulatory arrest. Variables such as glucose supplementation rarely pose a problem in adult patients due to large hepatic glycogen stores. Venous and arterial cannulae are larger and less deforming of the atria and aorta, and their placement more predictable. Although superficially similar, the conduct of CPB in children is considerably different from that in adults. One would therefore expect marked physiologic differences in the response to CPB in the child.

## Temperature

Hypothermic CPB is used to preserve organ function during cardiac surgery. Four distinct methods of CPB are used: normothermic CPB, moderate hypothermic CPB (25–32°C), deep hypothermia with low-flow CPB (15–20°C), or deep hypothermic circulatory arrest (DHCA). The choice of method of bypass to use is based on the required surgical conditions, patient size, the type of operation, surgeon preference, and the potential physiologic impact on the patient.

Moderate hypothermic CPB is the principal method of bypass employed for older children and adolescents. In these patients, venous cannulae are less obtrusive, and the heart can easily accommodate superior and IVC cannulation. Bicaval cannulation reduces right atrial blood return, and improves the surgeon's ability to visualize intracardiac anatomy. Moderate hypothermia may also be chosen for less demanding cardiac repairs in infants, such as an atrial septal defect or an uncomplicated ventricular septal defect. Most surgeons are willing to cannulate the inferior and superior vena cavae in neonates and infants. However, in these patients this approach is technically more difficult and likely to induce brief periods of hemodynamic instability. Additionally, the pliability of the cava and the rigidity of the cannulae may result in caval obstruction, impaired venous drainage, and elevated venous pressure in the mesenteric and cerebral circulation.

Deep hypothermic CPB is generally reserved for neonates and infants requiring complex cardiac repair. However, certain older children with complex cardiac disease or severe aortic arch disease benefit from deep hypothermic temperatures. For the most part, deep hypothermia is selected to allow the surgeon to operate under conditions of low-flow CPB or total circulatory arrest. Low pump flows (25–50 mL/kg/minute) improve the operating conditions for the surgeon by providing a near bloodless field. Deep hypothermic circulatory arrest allows the surgeon to remove the atrial and/or aortic cannula. Utilizing this technique, surgical repair is more precise because of the bloodless and cannula-free operative field. Arresting the circulation, even at deep hypothermic temperatures, introduces the concern of how well deep hypothermia preserves organ function, with the brain being at greatest risk.

Recent reports have reconsidered the use of normothermic CPB in pediatric patients. In a study comparing hypothermic with normothermic CPB, no difference was detected in two biochemical markers for brain injury.[4] Normothermic CPB requires higher pump flow rates and hematocrit to meet the metabolic demand of normothermic tissues. These adjustments may lead to more blood in the surgical field, and may reduce the margin of safety for preventing ischemic injury should mechanical failure occur with the CPB system.[5]

## Hemodilution

Although hemoconcentrated blood has an improved oxygen-carrying capacity, its viscosity reduces efficient flow through the microcirculation. With hypothermic temperatures, blood viscosity increases significantly and flow decreases.[6] Hypothermia, coupled with the non-pulsatile flow of CPB, impairs blood flow through the microcirculation. Blood sludging, small vessel occlusion, and multiple areas of tissue hypoperfusion may result. Therefore, hemodilution is an important consideration during hypothermic CPB. The appropriate level of hemodilution for a given hypothermic temperature, however, is not well defined. Experimental evidence suggests that reducing hematocrits to as low as 15% provides a sufficient quantity of oxygen delivery to the myocardium at normothermia, provided intravascular volume, colloid osmotic pressure, and normotension are maintained.[7] At hypothermic temperatures, hematocrits reduced to as low as 10% provide adequate oxygen delivery during CPB, as long as flow rates and perfusion pressure are maintained.[8,9] Since red blood cells serve as the major reservoir of oxygen during circulatory arrest, hematocrit values closer to 20% are generally preferred for deep hypothermia when this technique is contemplated. Most centers maintain hematocrit levels at 20 ± 2% during deep hypothermia (15–20°C) and will allow the hematocrit to drift as low as 18% before transfusing additional red blood cells. Although this is an arbitrary limit, lower hematocrit values have not been systematically evaluated to ensure adequate oxygen delivery to tissue. Cerebral oxygen delivery is an especially important consideration,

since cerebral autoregulation is impaired at deep hypothermic temperatures and after DHCA.

In order to achieve a hematocrit of 20–25% in neonates and infants, banked blood should be added to the priming solution. The mixed hematocrit on CPB (Hct CPB = the hematocrit of the patient's blood volume plus the total priming volume of the circuit) can be calculated by the formula:

$$\text{Hct CBP} = \frac{\text{Hct preop} \times \text{BV}}{\text{TPV} + \text{BV}}$$

Where Hct CPB is mixed Hct (*TPV + BV*), *BV* is patient's blood volume (estimated blood volume based upon the patient's weight), *TPV* is total priming volume of the CPB circuit, and Hct preop is the starting hematocrit of the patient. This calculation allows an estimate of the hematocrit of the patient using an asanguinous prime and is therefore useful for older children and adolescents. In neonates and infants, the perfusionist must add blood to the pump prime in order to achieve a desired hematocrit during hypothermic CPB.

Currently, no evidence exists for defining the optimal hematocrit after weaning from CPB. Decisions concerning post-CPB hematocrits are made based on the patient's post-repair function and anatomy. Patients with residual hypoxemia or those with moderate to severe myocardial dysfunction benefit from the improved oxygen carrying capacity of hematocrit levels of 40% or higher. Patients with a physiologic correction and excellent myocardial function may tolerate hematocrit levels of 20–25%.[7] In children with mild to moderate myocardial dysfunction, accepting hematocrit levels between these extremes seems prudent. Therefore, in patients with physiologic correction, moderately good ventricular function, and hemodynamic stability, the risks associated with blood and blood product transfusion should be strongly considered during the immediate post-bypass period.

### Prime composition and volume

The priming solutions used in pediatric CPB take on great importance because of the disproportionately large prime volume to blood volume ratio in children and the resulting effects on procoagulants (see Chapter 10). In adults the priming volume is equivalent to 25–33% of the patient's blood volume, whereas in neonates and infants the priming volume may exceed the patient's blood volume by 200%. Even contemporary low-volume bypass circuits rarely reduce this figure much below 150% in the smallest neonates. Therefore, care must be taken to achieve a physiologically balanced prime and limit the volume as much as possible. Most pediatric priming solutions, however, have quite variable levels of electrolytes, calcium, glucose, and lactate. Electrolytes, glucose, and lactate levels may be quite high if the prime includes large amounts of banked blood, or quite low if a minimal amount of banked blood is added. Calcium levels are generally very low in pediatric prime solutions; this may contribute to the rapid slowing of the heart with the initiation of bypass. The main constituents of the priming solution include: crystalloid, banked blood (to maintain a temperature-appropriate hematocrit), and colloid. Other supplements that may be added to the prime are mannitol, a buffer (sodium bicarbonate or tromethamine), and steroids. Many institutions add colloid or fresh frozen plasma to the pump prime in neonates and small infants or use whole blood in the priming solution. Low concentrations of plasma proteins have been shown experimentally to impair lymphatic flow and alter pulmonary function by increasing capillary leak.[10,11] Although adding albumin to pump prime has not been shown to alter outcome in adults during CPB, one study has suggested that maintaining normal colloid osmotic pressure may improve survival in infants undergoing CPB.[12,13] The addition of fresh frozen plasma or whole blood is an attempt to restore the level of procoagulants which are severely diluted with CPB in infants. Priming with fresh frozen plasma instead of 5% albumin significantly reduces chest tube drainage in infants undergoing complex surgery.[14] For neonates and infants, blood must be added to the priming solution. Most institutions use packed red blood cells in their prime solution; however, some use whole blood. The use of whole blood supplements both red blood cells and the coagulation factors with a single donor exposure. In fact, low-volume bypass circuits may enable perfusionists and anesthesiologists to share a single unit of whole blood thereby limiting the donor exposure to one throughout the entire perioperative course. The addition of any blood products will cause a much higher glucose load in the prime. Hyperglycemia may increase the risk of neurologic injury if brain ischemia occurs. Mannitol is added to promote an osmotic diuresis and to scavenge oxygen-free radicals from the circulation. Steroids are added to stabilize membranes to produce the theoretical advantage of reducing ion shifts during periods of ischemia. Steroids, however, may raise glucose levels and this may be detrimental if there is a period of cerebral ischemia. Steroids remain one of the more controversial additives in priming solutions.

## Centrifugal vs. roller pumps

A roller pump consists of a semicircular raceway with a central axis from which extends at least two arms that are 180° from one another, and rotate at an adjustable speed as measured in revolutions per minute (RPM). At the end of the arm is a roller which compresses the tubing against the raceway wall, creating a pressure difference between the inflow and outflow limbs as the roller rotates. The speed of rotation and the diameter of the tubing determine the pump flow. Roller pumps are commonly used for cardiotomy suction, and in pediatric bypass are the more common pump used for systemic perfusion. An advantage of roller pumps is the

reduced priming volume and ease of priming compared to centrifugal pumps. There are several potential disadvantages of roller pumps which may be significant. The occlusion of the roller/tubing/raceway apparatus must be adjusted carefully to maximize forward flow by minimizing leak, while not being too occlusive and leading to blood trauma and to breakdown of the inner wall of the tubing (spallation). Also, should the arterial line become occluded, the pump may create enough pressure behind the occlusion to cause rupture of the tubing.

The centrifugal pump involves a sealed chamber with inflow and outflow limbs. The chamber must be primed and de-aired. Within the chamber is a fanned impeller or a series of cones which are magnetically coupled to an electric motor. When the impellers spin, a pressure differential is created and blood can be propelled in this manner. Unlike the roller pump apparatus, a centrifugal pump's flow is dependent upon resistance downstream, and a flowmeter must be used in the arterial line to measure blood flow. When turned off, the pump permits free flow, and so the venous and arterial lines must be clamped to prevent patient exsanguination. The centrifugal pump may have several advantages over the roller pumps. If the pump were to entrain air from the venous reservoir, it would become de-primed and would not pump the air to the patient; it may be less harmful to formed elements of blood and less thrombogenic. Should the arterial line be occluded, the pressure buildup between pump and patient would be less that that required to rupture the tubing. Suggested pump flow rates for neonates, infants and children differ from those in adults and are given in Table 5.2.

**Table 5.2** Cardiopulmonary bypass flow rates.

| Weight (kg) | Flow range (patient warm) | Flow range (patient cold) |
|---|---|---|
| | *mL/kg/min* | *mL/kg/min* |
| 0–5 | 125–175 | 75–100 |
| 5–10 | 100–150 | 75–100 |
| | *L/min* | *L/min* |
| 10–20 | *BSA* × [2.6–3.0] | *BSA* × [2.0–2.2] |
| 20–40 | *BSA* × [2.4–3.0] | *BSA* × [2.0–2.2] |
| > 40 | *BSA* × [2.2–2.6] | *BSA* × [2.0–2.2] |

*BSA*, body surface area (in $m^2$).

## Miniaturization of the cardiopulmonary bypass circuit

Minimizing the volume of pump prime for neonates and infants has been a priority due to the difficult balance between severe hemodilution and immunological and infectious risks associated with transfusion. A schematic of the CPB circuit is shown in Fig. 5.1. The ultimate goal of miniaturization of the circuit volume should be to provide a range of pump prime that would allow for adequate hemodilution and eliminate the need for supplemental banked blood for the smallest patients. Thus far efforts to reduce circuit size and volume have met limitations, which include increasing resistance to flow in narrower tubing, length of tubing limitations due to physical proximity of the CPB machine to the

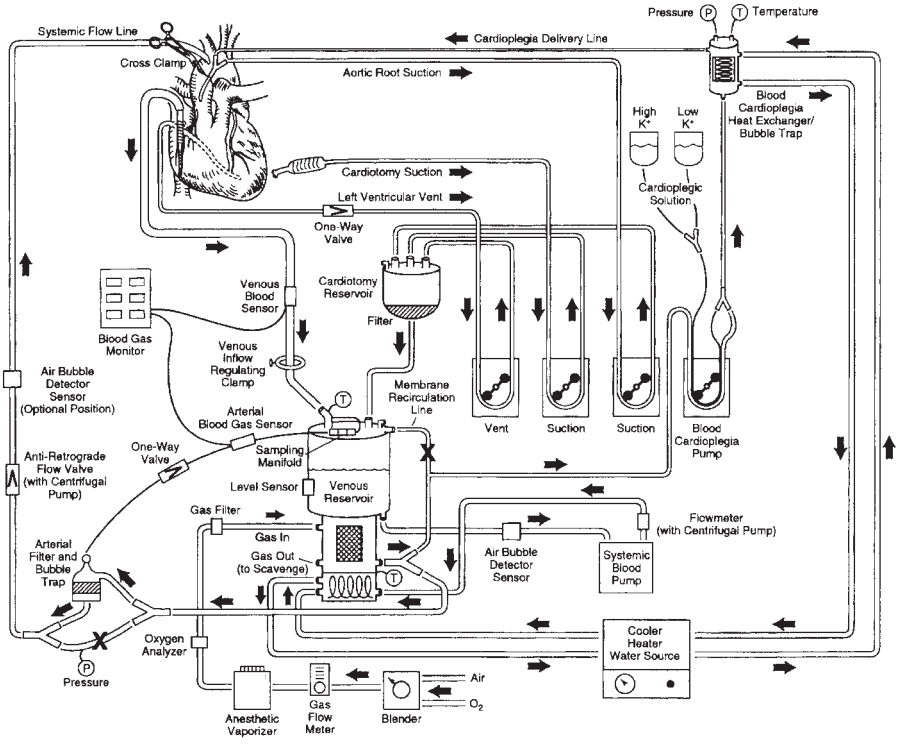


**Fig. 5.1** Schematic diagram of cardiopulmonary bypass circuit. This scheme depicts a membrane oxygenator with integral hard-shell venous reservoir and external cardiotomy reservoir. Many circuits have the cardiotomy reservoir, venous reservoir, and oxygenator integrated into one single unit. The systemic blood pump may be either a roller or centrifugal pump. Most pediatric venous cannulations are bicaval with two separate venous cannulae instead of the single venous cannula depicted here. Carbon dioxide can also be added to the inspired gas to facilitate pH-stat blood gas management. Arrows indicate direction of flow; P, pressure sensor; T, temperature sensors; X, placement of tubing clamps. Reproduced with permission from Hessel EA, Hill AG. Circuitry and cannulation techniques. In: Gravlee GP, Davis RF, Kurusz M, Utley JR, eds. *Cardiopulmonary Bypass: Principles and Practice*, 2nd edn. Philadelphia, PA: Lippincott, Williams & Wilkins, 2000: 69–97.

operative field, and minimum oxygenator membrane surface area. Additionally, the venous reservoir represents a safety net for periods of reduced venous drainage. While progress has allowed pump primes of as little as 150–180 mL, this volume does not permit an asanguinous prime to be used safely for most neonates. In order to reduce the volume necessarily remaining in the venous reservoir, centers have successfully employed actively assisted venous drainage.

## Vacuum assisted bypass

Considerations regarding the disadvantages of severe hemodilution and therefore the need for sanguinous pump prime have led to many changes in circuit size including integration of circuit components to limit prime volume, and efforts to limit circuit volume by actively assisted venous drainage.[15] This technique permits a decrease in the height difference between the patient and the venous reservoir as compared to passive (standard) venous drainage, thus shortening the length of venous and arterial tubing, limiting circuit volume. The use of active drainage also permits venous tubing and cannulae of smaller diameter to be utilized, again limiting circuit volume. However, active venous drainage involves risks that must be weighed against potential advantages.[16]

There are two general ways in which suction may be applied to the venous system for augmented drainage. A sealed, hard-shelled venous reservoir may be connected to a controlled suction device. This exposes the patient to the considerations of a hard reservoir such as a blood–air interface which is procoagulant/proinflammatory, and it permits the possibility of massive air entrainment into the arterial limb of the circuit should the reservoir fall below a critical level. The second method of active venous drainage involves the placement of a pump on the venous limb. Although this would permit the use of a soft-reservoir, limiting the blood gas interface, the problems inherent in both systems would still apply. The concerns for augmented venous drainage are twofold: first, the vacuum created may lyse red blood cells, increasing free hemoglobin in the circuit and increasing the risk of renal injury; and second, the flow of venous blood must be carefully regulated or there is a risk of inadequate drainage leading to increased superior vena cava (SVC) or inferior vena cava (IVC) pressures and the ascites or tissue edema that can follow, or too much suction which could lead to entrainment of air into the CPB circuit.[17]

## Pulsatile cardiopulmonary bypass

Pulsatile perfusion has been used succesfully for pediatric congenital heart surgery.[18–20] Although the use of non-pulsatile bypass is much more common, there exists evidence that indicates areas of potential advantage of using pulsatile perfusion during phases of CPB. In a comparison of conventional vs. pulsatile perfusion around a period of DHCA for congenital heart surgery, the pulsatile group showed more rapid cooling and rewarming, and increased urine production during bypass.[19,20] One study also showed a decreased total pump time in the pulsatile perfusion group.[20] There also seems to be decreased systemic vascular resistance during pulsatile perfusion. In animal studies, pulsatile perfusion enhances cerebral and renal blood flow during bypass in a piglet model of perfusion and DHCA.[21] In a randomized crossover study there was no difference in cerebral perfusion by near-infrared spectroscopy comparing pulsatile and non-pulsatile bypass, and in another comparison, no difference in plasma cortisol and adrenocorticotropic hormone (ACTH) was detected during and after perfusion of children using moderate hypothermia.[22,23] Controversy remains over the advantages for application in humans as various pump/oxygenator and filter combinations yield inconsistent results and a universal standard for comparison between pumps and techniques has not yet been achieved.[24–26]

## Management of cardiopulmonary bypass

### Initiation of cardiopulmonary bypass

Arterial and venous cannulation of the heart prior to initiating CPB may result in significant problems in the peri-bypass period. A malpositioned venous cannula has the potential for vena caval obstruction. The problems of venous obstruction are magnified during CPB in the neonate because arterial pressures are normally low (20–40 mmHg), and large relatively stiff cannulae easily distort these very pliable venous vessels. A cannula in the IVC may obstruct venous return from the splanchnic bed, resulting in ascites from increased hydrostatic pressure and/or directly reduced perfusion pressure across the mesenteric, renal, and hepatic vascular beds. Significant renal, hepatic, and gastrointestinal dysfunction may ensue and should be anticipated in the young infant with unexplained ascites. Similar cannulation problems may result in SVC obstruction. This condition may be more ominous during bypass. Under these circumstances, three problems may ensue: (i) cerebral edema; (ii) a reduction in regional or global cerebral blood flow (*CBF*); and (iii) a reduced proportion of pump flow reaching the cerebral circulation causing inefficient brain cooling. In the operating room it is advisable either to monitor SVC pressures via an internal jugular catheter or by looking at the patient's head for signs of puffiness or venous distension after initiating bypass. Neurological monitoring, such as near-infrared cerebral oximetry or transcanial Doppler ultrasound, can rapidly detect decreases in *CBF* due to SVC obstruction.[27,28] Discussions with the perfusionist regarding adequacy of venous return and/or large cooling gradients between the upper and lower

body should alert the anesthesiologist and the surgeon to potential venous cannula problems. Patients with anomalies of the large systemic veins (persistent left SVC or azygous continuation of an interrupted IVC) are at particular risk for problems with venous cannulation and drainage.

Problems with aortic cannula placement also occur. When the cannula is placed, pressure in the arterial side of the circuit should be measured. The pressure should be between the mean and the systolic pressure of the patient. Transfusion of 10–50 mL of bypass prime should be given slowly, while pressure in the arterial circuit is measured. Pressure should remain low, signifying a cannula placement in the center of the lumen of the aorta. The aortic cannula may slip beyond the takeoff of the innominate artery and, therefore, selectively flow to the right side of the cerebral circulation. Also, the position of the tip of the cannula may promote preferential flow down the aorta or induce a Venturi effect to steal flow from the cerebral circulation. This problem has been confirmed during *CBF* monitoring by the appearance of large discrepancies in flow between the right and left hemisphere after initiating CPB.[28] Other clues to cannula misplacement include better cooling in the lower body than in the upper body. The presence of large aortic to pulmonary collaterals, such as a large patent ductus arteriosus (PDA), may also divert blood to the pulmonary circulation from the systemic circulation thereby reducing *CBF* and the efficiency of brain cooling during CPB.[29] The surgeon should gain control of the ductus either prior to or immediately after instituting CPB to eliminate this problem and, if possible, large aortopulmonary collaterals should be embolized in the cardiac catheterization laboratory prior to the operative procedure. Neonates with significant aortic arch abnormalities (e.g. aortic atresia, interrupted aortic arch) may require radical modifications of cannulation techniques, such as placing the arterial cannula in the main pulmonary artery and temporarily occluding the branch pulmonary arteries to perfuse the body via the PDA, or even dual arterial cannulation of both the ascending aorta and main pulmonary artery. Some centers utilize two arterial catheters, one in a radial artery, and one in the femoral or umbilical artery, to demonstrate adequate pressure in the lower body during bypass for interrupted or hypoplastic aortic arch.[30] Such adaptations require careful vigilance to ensure effective, thorough cooling of vital organs.

Once the aortic and venous cannulae are positioned and connected to the arterial and venous limb of the extracorporeal circuit, bypass is initiated. The arterial pump is slowly started and once forward flow is assured, venous blood is drained into the oxygenator. Pump flow rate is gradually increased until full circulatory support is achieved. If venous return is diminished, arterial line pressure is high, or mean arterial pressure is excessive, pump flow rates must be reduced. High line pressure and inadequate venous return are usually due to malposition or kinking of the arterial and venous cannulae, respectively. The rate at which venous blood is drained from the patient is determined by the height difference between the patient and the oxygenator inlet and the diameter of the venous cannula and line tubing. Venous drainage can be enhanced by increasing the height difference between the oxygenator and the patient or by using a larger venous cannula. Venous drainage can be reduced by either decreasing the height difference between the oxygenator and the patient or by partially clamping the venous line.

In neonates and infants, deep hypothermia is commonly used. For this reason, in some institutions the pump prime is kept cold (18–22°C). When the cold perfusate contacts the myocardium during the institution of CPB, heart rate slows immediately and contraction is impaired. Other centers prefer to avoid this perceived stress on the myocardium and keep the prime temperature very close to the patient's temperature. The contribution of total blood flow pumped by the infant's heart rapidly diminishes. Therefore, to sustain adequate systemic perfusion at or near normothermic temperatures, the arterial pump must reach full flows quickly. Cardiopulmonary bypass is initiated in neonates and infants by beginning the arterial pump flow first. Once aortic flow is ensured, the venous line is unclamped and blood is siphoned out of the right atrium into the inlet of the oxygenator. Flowing before unclamping the venous line prevents the potential problem of exsanguination if aortic dissection or misplacement of the aortic cannula occurs. Neonates and infants have a low blood volume to prime volume ratio, and intravascular volume falls precipitously if the venous drainage precedes aortic inflow. Once aortic cannula position is verified, pump flow rates are rapidly increased to maintain effective systemic perfusion. Since coronary artery disease is rarely a consideration, the myocardium should cool evenly unless distortion caused by the cannulae compromises the coronary arteries. When a cold prime is used, caution must be exercised in using the pump to infuse volume prior to initiating CPB. Infusion of cold perfusate may result in bradycardia and impaired cardiac contractility before the surgeon is prepared to initiate CPB. This again is a reason why many centers do not utilize cold prime.

Once CPB begins, careful observation should be focused to ensure appropriate circuit connections, myocardial perfusion and optimal cardiac decompression. Ineffective venous drainage can rapidly result in ventricular distension. This is especially true in infants and neonates where ventricular compliance is low and the heart is relatively intolerant of excessive preload augmentation. If ventricular distension occurs, pump flow must be reduced and the venous cannula repositioned. Alternatively, the heart may be decompressed by placing a cardiotomy suction or small vent in the appropriate chamber.

## Pump flow rates

Recommendations for optimal pump flow rates for children

have historically been based both on the patient's body mass and evidence of efficient organ perfusion as determined by arterial blood gases, acid-base balance, and whole body oxygen consumption during CPB.[31,32] At hypothermic temperatures metabolism is reduced. Pump flow rates can therefore be reduced and still meet or exceed the tissues' metabolic needs (see the discussion of low-flow CPB in the Deep hypothermic circulatory arrest section below). Some centers utilize higher flows of 150–200 mL/kg/minute at all temperatures, combined with vasodilation produced by α-receptor blockade, with the goal of preservation of organ function and capillary integrity.[33,34] Outcome data proving one approach superior to the other are lacking.

## Deep hypothermic circulatory arrest

Neonates and infants who require extensive repair of complex congenital heart defects may have these procedures performed using DHCA. This technique facilitates precise surgical repair under optimal conditions, free of blood or cannulae in the operative field, providing maximal organ protection, and often resulting in shortened total CPB time. The scientific rationale for the use of deep hypothermic temperatures rests primarily upon a temperature-mediated reduction of metabolism. Induced hypothermia decreases the metabolic rate, as well as whole body and cerebral oxygen consumption by a factor of 2–4 for every 10°C reduction in temperature in neonates and infants.[35,36] These results are consistent with *in vitro* models, which relate temperature reduction to a decrease in the rate constant of chemical reactions. The reduction in oxygen supply during deep hypothermic low-flow CPB (DHCPB) is associated with preferential increases in vital organ perfusion (e.g. to the brain) and by increased extraction of oxygen.[37]

Therefore, to some extent DHCPB exerts a protective effect by reducing the metabolic rate for oxygen, promoting preferential organ perfusion and increasing tissue oxygen extraction.

Extensive clinical experience using DHCA has shown the duration of the safe circulatory arrest period may last up to 45 minutes.[38,39] Beyond this duration, the incidence of permanent and transient neurologic sequelae may increase. Both the duration of the arrest period and variations in perfusion technique during cooling and rewarming influence the development of these problems. However, the effect of deep hypothermia on tissue metabolism and oxygen consumption and extraction clearly does not explain the entire protective effect of "safe" DHCA. Cortical $P_{O_2}$ and $P_{CO_2}$ levels indicate basal cerebral metabolic activity continues during DHCA (i.e. anaerobic metabolism develops after local tissue oxygen stores are consumed). During brain ischemia, excitatory amino acids (EAAs) such as glutamate and aspartate are released and are putative mediators of ischemic damage.[36,40,41] Hypothermia has been shown to significantly decrease the release of EAAs, potentially contributing to the central nervous system protective effect.[42] In addition, hypothermia transforms a normal semiliquid cellular membrane to a semisolid, which may act to prevent calcium influx during reperfusion and thereby account for additional protection noted in some experimental models.[43]

Although all organ systems are at risk for the development of ischemic and reperfusion injury, as manifested by lactate and pyruvate production during DHCA, the brain appears to be the most sensitive and the least tolerant of these effects. Brain stem and cortical evoked potentials as well as processed electroencephalographs (EEGs) are altered after DHCA.[44–46] The abnormalities in the evoked potentials appear to be related to the duration of DHCA and are attributed to altered metabolism. During reperfusion after the arrest period *CBF* and metabolism remain depressed in neonates and small infants (Figs 5.2–5.4).[47] Importantly, during the use of these extremes of temperature, it appears that autoregulation is lost and cerebral perfusion becomes highly dependent on the conduct of extracorporeal perfusion and presumably post-bypass hemodynamic performance (Fig. 5.5).

Current controversy exists regarding the immediate-term and long-term neuropsychologic effects of DHCA. Early reports regarding the long-term consequences of DHCA on brain development and intelligence were conflicting.[48] Transient neurologic dysfunction and other reversible cerebral injuries have been reported. These transient, subtle neuropsychologic disturbances have led investigators to examine more systematically the long-term outcome after DHCA.

More recently a number of more sophisticated studies examining the outcome after DHCA have been performed. In a recent randomized clinical trial comparing the incidence of brain injury following DHCA or low-flow CPB, DHCA was demonstrated to have longer EEG recovery times and a higher incidence of clinical seizures in the early postoperative period.[49] The DHCA group also had a higher incidence of neurologic abnormalities and poor motor function at 1 year of age, and poor expressive language and motor development at 2.5 years of age, particularly in those who exhibited early postoperative seizures.[50] Recent reports from the same clinical trial have shown that the DHCA cohort has continued to have worse motor coordination and planning and speech abnormalities at 4 years of age.[51–53] Of interest, both the DHCA and low-flow CPB groups have lower cognitive and motor performance compared to a general population. This latter finding suggests factors outside DHCA and low-flow bypass but within the perioperative period are associated with poor neuropsychologic development.

A recent clinical study has suggested pH-stat blood gas management strategy during CPB to be associated with an improved neuropsychologic outcome in children.[52] This study was a retrospective developmental study with a core of patients who have undergone surgery for transposition of the

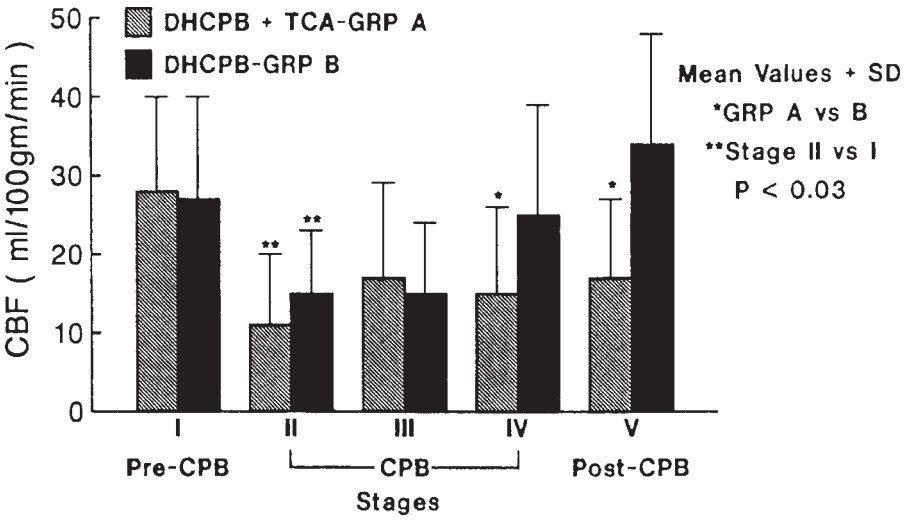


**Fig. 5.2** Cerebral blood flow measurements using xenon washout technique in 25 infants and children aged from 2 days to 5 years. Group A was cooled to 18°C with deep hypothermic circulatory arrest (DHCA), and Group B cooled to 18°C without DHCA. Stage I, before cardiopulmonary bypass (CPB); stage II, stable hypothermic conditions at 5 minutes; stage III, stable hypothermic conditions at 25 minutes or just after DHCA; stage IV, rewarmed on CPB; stage V, after CPB. Cerebral blood flow did not return to baseline after DHCA. Reproduced with permission from Greeley WJ, Ungerleider RM, Smith LR, Reves JG. The effects of deep hypothermic cardiopulmonary bypass and total circulatory arrest on cerebral blood flow in infants and children. *J Thorac Cardiovasc Surg* 1989; **97**: 737–45.

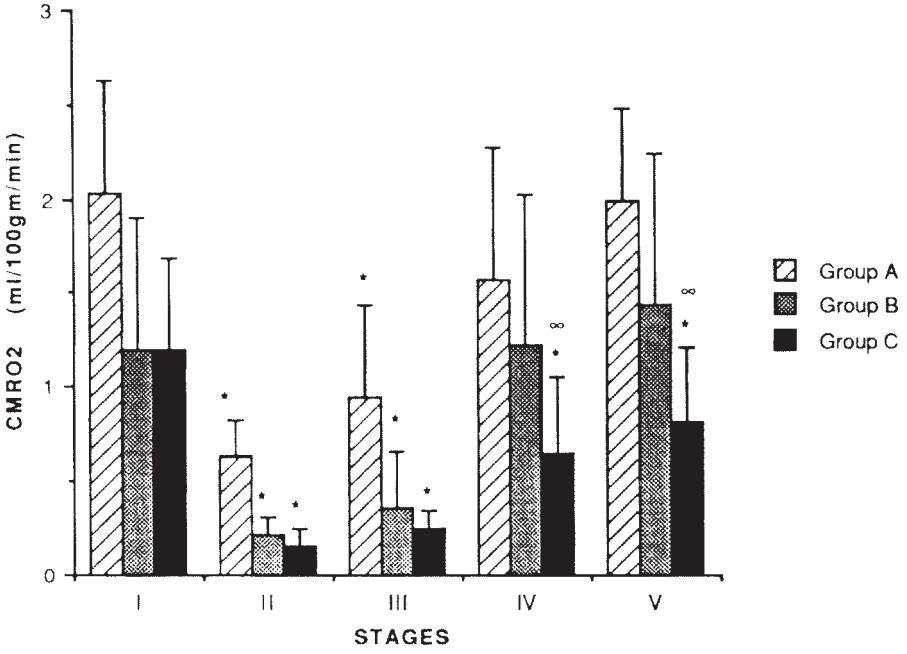


**Fig. 5.3** Cerebral metabolic rate for oxygen ($CMRO_2$) ratio during cardiac surgery in 46 pediatric patients aged from 1 day to 14 years. Stage I, before cardiopulmonary bypass (CPB); stage II, stable hypothermic conditions at 5 minutes; stage III, stable hypothermic conditions at 25 minutes or just after deep hypothermic circulatory arrest (DHCA); stage IV, rewarmed on CPB; stage V, after CPB. Group A was cooled to 28°C without DHCA, Group B was cooled to 18°C without DHCA, and Group C cooled to 18°C with DHCA. All groups had a significant decrease in $CMRO_2$ during hypothermic bypass. $CMRO_2$ in group C was significantly decreased during stages IV and V compared with baseline (I) and groups A and B at stages IV and V. $*P < 0.001$, stages II–V vs. stage I; $\infty p < 0.01$, group C vs. A. Reproduced with permission from Greeley WJ, Kern FH, Ungerleider RM *et al*. The effect of hypothermic cardiopulmonary bypass and total circulatory arrest on cerebral metabolism in neonates, infants, and children. *J Thorac Cardiovasc Surg* 1991; **101**: 783–94.

great arteries. The authors found a strong positive correlation between arterial $P_{CO_2}$ during cooling before circulatory rest and developmental score. This suggested that children undergoing α-stat blood gas management strategy had a worse developmental outcome than where a pH-stat strategy was employed. In a recent randomized clinical trial of neonates undergoing cardiac surgery using DHCA, pH-stat management was noted to have faster EEG recovery times and fewer postoperative seizures compared to an α-stat bypass group.[54,55] Therefore pH-stat management may be beneficial.

Experimental studies have also suggested the superiority of pH-stat strategy. Using pH-stat strategy, animals had greater *CBF* during cooling and better recovery of cerebral adenosine triphosphate (ATP) and intracellular pH after arrest and reperfusion,[56] which suggests that pH-stat blood gas management may have protective mechanisms due to an increased rate of brain cooling. In a study comparing the effects of pH-stat and α-stat management on cerebral oxygenation and blood flow, the cerebral protective effect of pH-stat management was demonstrated and indicated that the kinetics of cerebral deoxygenation might contribute to the mechanism of protection.[57–59] Because of the potential for neurologic dysfunction after DHCA, some institutions use low-flow deep hypothermic CPB as an alternative technique.[60] Since low-flow bypass can produce ischemia if flow is too low and because it lengthens the CPB time, compared

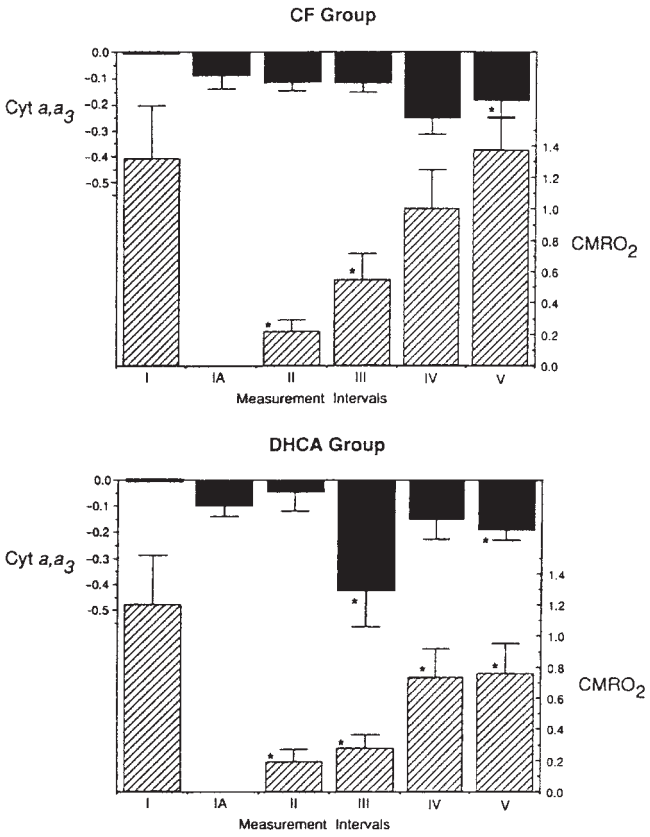


**Fig. 5.4** Recovery of cerebral metabolic rate for oxygen ($CMRO_2$) in mL/100g/minute measured by xenon washout, and cytochrome c oxidase activity (cyt $a,a_3$) measured by near-infrared spectroscopy during deep hypothermic bypass at 18°C in 15 patients aged from 1 day to 6 years. Stage I, before cardiopulmonary bypass (CPB); IA, normothermia at start of CPB; stage II, stable hypothermic conditions at 5 minutes; stage III, stable hypothermic conditions at 25 minutes or just after deep hypothermic circulatory arrest (DHCA); stage IV, rewarmed on CPB; stage V, after CPB. CF group, continuous flow group; DHCA group, deep hypothermic circulatory arrest group. Dark bars are a decrease in cyt $a,a_3$ activity from baseline; hatched bars are $CMRO_2$. *$P < 0.05$ for $CMRO_2$ and cyt $a,a_3$ vs. control. Reproduced with permission from Greeley WJ, Bracey VA, Underleider RM *et al*. Recovery of cerebral metabolism and mitochondrial oxidation state is delayed after hypothermic circulatory arrest. *Circulation* 1991; **84**: III400–6.

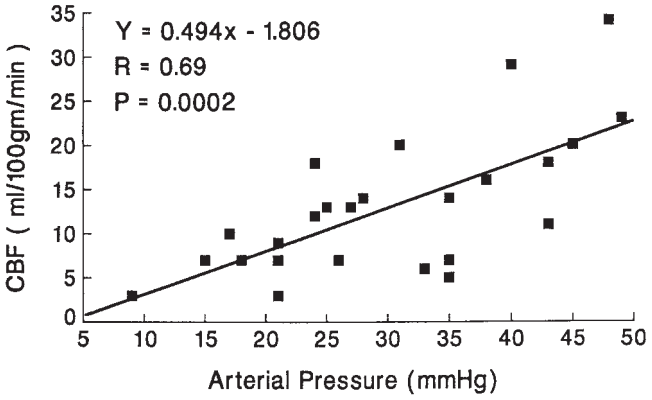


**Fig. 5.5** The effect of perfusion pressure on cerebral blood flow (*CBF*) measured using xenon clearance, during deep hypothermic bypass at 18–22°C in 25 infants and children. There was a significant association between arterial pressure and *CBF*, demonstrating a loss of cerebral autoregulation. Reproduced with permission from Greeley WJ, Ungerleider RM, Smith LR, Reves JG. The effects of deep hypothermic cardiopulmonary bypass and total circulatory arrest on cerebral blood flow in infants and children. *J Thorac Cardiovasc Surg* 1989; **97**: 737–45.

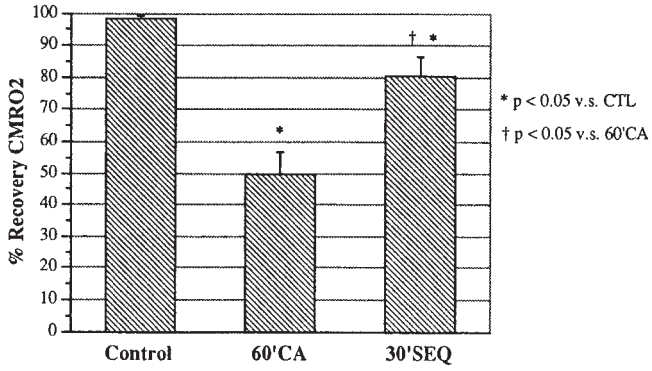


**Fig. 5.6** Percent recovery of cerebral metabolic rate for oxygen ($CMRO_2$) in a neonatal piglet model of hypothermic cardiopulmonary bypass (CPB) at 18°C. Control (CTL) animals did not undergo any deep hypothermic circulatory arrest (DHCA), 60′CA animals underwent 60 continuous minutes of DHCA, and 30′SEQ animals underwent two sequential 30-minute periods of DHCA separated by a 30-minute period of full CPB flow. Reproduced with permission from Mault JR, Whitaker EG, Heinle JS *et al*. Cerebral metabolic effects of sequential periods of hypothermic circulatory arrest. *Ann Thorac Surg* 1994; **57**: 96–101.

to DHCA, serious concerns over this technique have also arisen.[61,62] A recent experimental study demonstrated worse brain injury with low-flow bypass than with DHCA.[63] Other alternative techniques are intermittent perfusion (Fig. 5.6) and selective cerebral perfusion (see below and Chapter 8). One strategy with potential for determining the safe duration of DHCA in the individual patient using neurologic monitoring found that a near-infrared cerebral oximetry (NIRS) nadir time of less than 30 minutes was associated with no neurologic morbidity or pathology in a neonatal piglet model of DHCA.[64] A higher hematocrit of 30, lower temperature of 18°C, and pH-stat blood gas management all significantly delayed the decay in cerebral oxygenation and the onset of the nadir, lengthening the period of "safe" DHCA. This suggests a clinical strategy for DHCA monitoring and management using NIRS.

Other factors such as surface cooling, anesthetic agents, and cerebral protective agents may influence and modify the central nervous system protective effects of DHCPB

and DHCA. However, the potential added protection from anesthetic drugs, barbiturates, lidocaine, or calcium channel blockers is unknown. There are no clinical studies in children systematically examining the influence of these pharmacological agents on cerebrovascular physiology or neurologic outcome. Therefore, the use of these agents remains entirely speculative and unfounded. Clearly, further controlled study of the long-term effects of DHCA with added pharmacologic agents on neuropsychologic outcome in children is necessary. Equally important, the manner in which the patient is cooled and rewarmed may affect outcome,[65,66] and merits further investigation, even before the testing of pharmacological drugs. It has been demonstrated that rapid cooling to deep hypothermic temperatures in less than 20 minutes is associated with higher incidence of acute and long-term neurologic morbidity.[67,68]

## Selective cerebral perfusion

Because of the concern that prolonged DHCA may lead to neurologic morbidity, alternative techniques have been developed that limit or eliminate DHCA for some types of surgery, particularly neonatal aortic arch reconstructive surgery such as the Norwood stage I palliation for hypoplastic left heart syndrome, or aortic arch reconstruction for hypoplastic or interrupted aortic arch. Selective cerebral perfusion provides blood flow to the brain, while the remainder of the body is not perfused, providing a bloodless operating field similar to DHCA.[69] One such technique is called regional low-flow cerebral perfusion (RLFP), and utilizes a 3.0 or 3.5 mm polytetrafluoroethylene (PTFE) graft sutured to the right innominate artery before bypass.[70] This graft serves as the arterial inflow during bypass, and as a modified Blalock–Taussig shunt if needed after bypass. A standard arterial cannula is placed in the distal end of the PTFE graft, and a single venous cannula in the atrium. Full-flow bypass is instituted in this manner, the patient is cooled, usually to deep hypothermic temperatures, and during the period of aortic reconstruction, snares are placed around the base of the right innominate, left carotid, and left subclavian arteries, as well as the descending thoracic aorta. The brain is perfused via the right innominate artery and right vertebral artery (via the right subclavian artery), and the circle of Willis to the left cerebral hemisphere. Bypass flow rates during this technique are less than full flow, and have ranged from 20 to 90 mL/kg/minute. Neurologic monitoring in the form of near-infrared cerebral oximetry and transcranial Doppler ultrasound have been utilized to determine adequate flow during RLFP (see Chapter 8).[71] Regional low-flow cerebral perfusion delivers oxygenated blood to both cerebral hemispheres,[72] and also has the potential advantage of providing some limited blood flow to subdiaphragmatic viscera in the neonate, through an extensive arterial collateral system.[73] Using RLFP, the period of DHCA during the Norwood stage I palliation is limited to that needed for atrial septectomy and moving the cannula to the neoaorta after its reconstruction, a total of less than 10 minutes. Despite the theoretical advantages of selective cerebral perfusion, to date there are no published outcome studies comparing it to DHCA.

## Discontinuation of cardiopulmonary bypass

When weaning from CPB, blood volume is assessed by direct visualization of the heart and monitoring right atrial or left atrial filling pressures. When filling pressures are adequate, the patient fully warmed, acid-base status normalized, hematocrit optimized, heart rate adequate and sinus rhythm achieved, the venous drainage is gradually occluded and the patient can be weaned from bypass. The arterial cannula is left in place so that a slow infusion of residual pump blood can be used to optimize filling pressures. Myocardial function is assessed by direct cardiac visualization and either a transthoracic left or right atrial catheter, a percutaneous internal jugular catheter, or by the use of intraoperative echocardiography. Pulse oximetry can also be used to assess the adequacy of cardiac output,[74] systemic arterial saturation, or the inability of the oximeter probe to register a pulse may be a sign of very low output and high systemic resistance.[75]

After the repair of complex congenital heart defects, the anesthesiologist and surgeon may have difficulty separating patients from CPB. Under these circumstances, a diagnosis must be made and includes: (i) an inadequate surgical result with a residual defect requiring repair; (ii) pulmonary artery hypertension; and (iii) right or left ventricular dysfunction. Two general approaches are customarily used, either independently or in conjunction with one another. An intraoperative "cardiac catheterization" can be performed to assess isolated pressure measurements from the various great vessels and chambers of the heart (i.e. catheter pullback measurements or direct needle puncture to evaluate residual pressure gradients across repaired valves, sites of stenosis and conduits, and oxygen saturation data to examine for residual shunts).[76] Alternatively, echo-Doppler may be used to provide an intraoperative image of structural or functional abnormalities to assist in the evaluation of the postoperative cardiac repair.[77,78] If structural abnormalities are found, CPB can be reinstituted and residual defects repaired prior to leaving the operating room. Leaving the operating room with a significant residual structural defect adversely affects survival and increases morbidity.[77,78] The echo-Doppler can rapidly identify right and left ventricular dysfunction and suggest the presence of pulmonary artery hypertension. In addition, echo-Doppler can identify regional wall motion abnormalities due to ischemia or intramyocardial air that will direct specific pharmacological therapy and provide a means of assessing the results of these interventions (see Chapter 7).[79]

## The inflammatory process and the effects of cardiopulmonary bypass

Cardiopulmonary bypass leads to the release of inflammatory and anti-inflammatory mediators. Exposure of blood elements to the extracorporeal circuit, hypothermia, tissue injury, reperfusion, and non-pulsatile flow all may contribute to mediator release. Patients with severe cyanosis may also have elevated levels of proinflammatory cytokines preoperatively. Studies have shown that some reduction in the inflammatory reaction may be possible by pre-treating the patient with dexamethasone, and the use of modified ultrafiltration (MUF) has shown reduction of inflammatory mediators as well as other benefits. Interleukin 6 (IL-6), IL-8 and tumor necrosis factor (TNF) have all been shown to increase in the bypass and post-bypass period; their levels are reduced by hemofiltration on bypass.[80]

## Glucose regulation

In recent years, a substantial amount of clinical and experimental data has shown conclusive evidence of the detrimental effect of hyperglycemia during complete, incomplete, and focal cerebral ischemia.[81–83] The role of glucose in potentiating cerebral injury appears to be due to two factors: ATP utilization and lactic acidosis.[84,85] The anaerobic metabolism of glucose requires phosphorylation and the expenditure of two molecules of ATP before ATP production can occur. This initial ATP expenditure may result in a rapid depletion of ATP and may explain why hyperglycemia worsens neurologic injury. Lactic acidosis is also important in glucose-augmented cerebral injury. An important role, however, may be as a glycolytic enzyme inhibitor. Lactate slows anaerobic ATP production, by inhibiting glycolysis immediately after ATP is consumed in the phosphorylation of glucose.[86]

### Hyperglycemia

Although a strong scientific argument can be made for the detrimental effects of hyperglycemia during ischemia, there is very little evidence supporting worsening neurologic outcome from hyperglycemia during CPB and/or DHCA in children. A retrospective review of 34 children undergoing DHCA suggested a worse neurologic outcome in the hyperglycemic children; however, the results were reported as a non-significant statistical trend.[87] A pathologic review of acquired neurologic lesions in patients undergoing the stage I repair of hypoplastic left heart syndrome suggested hyperglycemia as a significant associated finding in patients with extensive cerebral necrosis or intraventricular hemorrhage. Although associated, a host of other potentially damaging factors (e.g. periods of hypoxia, low diastolic and systolic pressure, and thrombocytopenia) were statistically associated with the observed neuropathology.[88] Since hyperglycemia accompanies a generalized stress response, the literature has failed to distinguish whether glucose directly contributes to neurologic injury or merely serves as a marker for a high-risk population who ultimately suffer neurologic insult as a result of other factors.

### Hypoglycemia

Hypoglycemia is a frequent concern in neonates during the perioperative period. Reduced hepatic gluconeogenesis coupled with decreased glycogen stores place the newborn at increased risk of hypoglycemic events. In newborns with CHD, reduced systemic perfusion (e.g. critical coarctation, hypoplastic left heart syndrome, critical aortic stenosis) may result in worsening hepatic biosynthesis, further impairing glucose production. These patients may be fully dependent on exogenous glucose; therefore, it is not uncommon for them to require 20–30% dextrose infusions to maintain euglycemia in the pre-bypass period. Older children are not immune to hypoglycemic events and are therefore susceptible to hypoglycemic-induced neurologic injury. Patients with low cardiac output states (cardiomyopathies, pre-transplant patients, critically ill postoperative patients) requiring reoperation and substantial inotropic support are at risk of reduced glycogen stores and intraoperative hypoglycemia.[89]

The impact of hypoglycemia during bypass is further complicated by the consequences of hypothermia, carbon dioxide management, and other factors that may modify normal cerebrovascular responses during bypass. In a dog model, insulin-induced hypoglycemia to 30 mg/dL did not alter the EEG findings; however, after 10 minutes of hypocapnic hypoglycemia, the EEG became flat.[90] When regional blood flow was examined in these animals, cortical and hippocampal blood flow remained normal, whereas other regions of the brain had reduced flow. The loss of EEG activity from hypoglycemia alone does not normally occur above glucose levels of 8 mg/dL.[90]

During deep hypothermic CPB and DHCA, *CBF* and metabolism are altered. The additive effect of hypoglycemia, even if mild, may cause alterations in cerebral autoregulation and culminate in increased cortical injury.[88,91] The common practice of using hyperventilation to reduce pulmonary vascular resistance in neonates and infants during weaning from CPB and in the early post-bypass period could further exacerbate hypoglycemic injury. Glucose monitoring and rigid maintenance of euglycemia are an important part of CPB management in the congenital heart patient.

## Renal effects

After CPB, the combined effects of hypothermia, non-pulsatile

perfusion, and reduced mean arterial pressure causes release of angiotensin, renin, catecholamines, and antidiuretic hormone[92–94]. These circulating hormones promote renal vasoconstriction and reduce renal blood flow. Yet despite the negative impact of CPB on renal function, studies have been unable to link low-flow, low-pressure, non-pulsatile perfusion with postoperative renal dysfunction.[93,95] The factors that best correlate with postoperative renal dysfunction are preoperative renal dysfunction and profound reductions in post-CPB cardiac output. Preoperative factors include primary renal disease, low cardiac output, and dye-related renal injury after cardiac catheterization.[94]

The incidence of acute renal insufficiency after pediatric cardiac surgery is 3–8%.[94,96,97] Multiple causative factors are involved whose final common pathway is oliguria and an elevated serum creatinine. Diuretics have been the mainstay of promoting urine flow after pediatric CPB. Furosemide in a dose of 1–2 mg/kg and/or ethacrynic acid 1 mg/kg every 4–6 h induces a diuresis and may reverse renal cortical ischemia associated with CPB. After DHCA, it is not unusual to observe a 24-h period of oliguria or anuria that resolves over the next 12–24-h period. The use of diuretics is effective only after these patients have initiated spontaneous urine output.

Glomerular filtration rate, creatinine clearance, and medullary concentrating ability are substantially reduced in neonates and young infants. Therefore, the use of CPB in these patients is associated with greater fluid retention than is typically seen in older children and adult patients. The net result may be increased total body water, increased organ weight (e.g. lungs, heart), and greater difficulty with postoperative weaning from ventilatory support. The use of ultrafiltration during rewarming or after CPB is effective in reducing total body water, limiting the damaging effects of CPB, and decreasing the postoperative ventilation period.[98,99]

### Pulmonary effects

While cardioplegia protects the heart, there is no parallel protection afforded the lung during bypass. Pulmonary dysfunction is common after CPB and its pathogenesis is poorly understood. In broadest terms, lung injury is mediated in one of two ways: first, an inflammatory response due to leukocyte and compliment activation, and, secondly, a mechanical effect culminating in surfactant loss, atelectasis with resultant ventilation-to-perfusion mismatch, loss of lung volumes, and altered mechanics of breathing.

Pulmonary function after CPB is characterized by reduced static and dynamic compliance, reduced functional residual capacity, surfactant deficiency and an increased A–a gradient.[100,101] Atelectasis and increased capillary leak due to hemodilution, and hypothermic CPB are the most likely etiologies. Hemodilution reduces circulating plasma proteins, reducing intravascular oncotic pressure, and favors water extravasation into the extravascular space. Hypothermic CPB causes complement activation and leukocyte degranulation.[102] Leukocytes and complement are important in causing capillary–alveolar membrane injury and microvascular dysfunction through platelet plugging and release of mediators which increase pulmonary vascular resistance. The technique of MUF may reduce lung water and pulmonary morbidity during the postoperative period.

## Neurologic effects

The true incidence and severity of neurologic injury related to CPB is difficult to determine, as injury may have occured due to the lesions or an event in the perinatal period that can be difficult to recognize preoperatively.[103,104] Furthermore, neurodevelopmental abnormalities in children with CHD may be due to one or all of the following: genetic or metabolic factors, the cardiac lesions themselves, the stresses of the perinatal period with a greatly reduced cardiac reserve, or direct injury from the CPB/perioperative interventions. Injuries related to CPB may include intracranial hemorrhage, embolic injury, inadequate preservation during periods of low flow or total circulatory arrest, and reperfusion-related injuries.[105,106] Injury may include stroke, developmental delay, and seizure activity.[107] Attempts to reduce injury caused by CPB have included filters, membrane oxygenators, pulsatile perfusion, and pharmacologic additives. Filters may be used to reduce bubbles, thrombi, emboli, or leukocytes. Only a few years ago, bubble oxygenators were standard practice in major institutions, without the use of arterial line filters.[105] However, this practice has been abandoned because a significant reduction in the number of cerebral emboli can be demonstrated using membrane oxygenators and arterial filters.[108,109] Leukocyte depletion has been advocated as an adjunct in order to reduce morbidity related to the inflammatory response. In a piglet study, no benefit to *CBF* was noted with the use of a leukocyte depleting filter.[110] For infants, there was no significant benefit noted when undergoing bypass with the aid of a leukocyte filter.[111]

## Use of modified ultrafiltration

The overall morbidity and mortality after cardiac surgery in children is influenced by the effects of CPB. During the initiation of CPB considerable hemodilution occurs.

This hemodilution is the result of the priming volume required for the CBP circuit. Under many circumstances this hemodilutional effect is intentional, decreasing blood viscosity and thereby preventing sludging when the patient is cooled to temperatures below 20°C. After CPB, hemodilution is associated with tissue edema and organ dysfunction. Because blood elements are exposed to the non-endothelialized

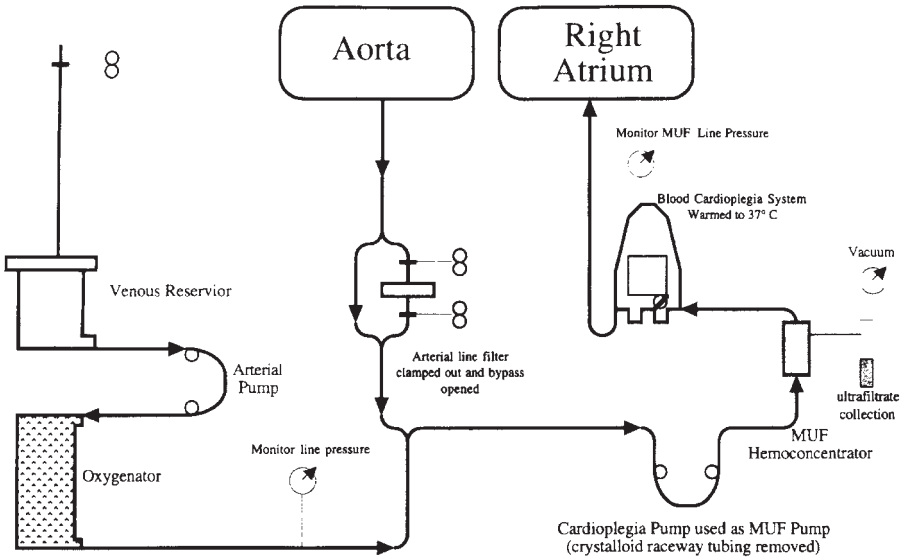


**Fig. 5.7** Schematic diagram of the modified ultrafiltration (MUF) circuit. After cardiopulmonary bypass, blood is removed from the aortic cannula, pumped through the ultrafilter using a CPB roller head, ultrafiltrate is removed and the hemoconcentrated fluid is returned to the patient through a venous cannula into the right atrium. The blood in the venous reservoir can also be oxygenated and pumped through the MUF circuit and returned to the patient after hemoconcentration. Reproduced with permission from Darling E, Nanry K, Shearer I *et al*. Techniques of paediatric modified ultrafiltration: 1996 survey results. *Perfusion* 1998; **13**: 93–103.

circuitry of CPB, there is also a significant inflammatory response as a result of CPB. Both these effects of hemodilution and inflammation are exaggerated in neonates, infants and young children due to their disproportionate exposure to the circuit relative to their body size. This inflammatory response leads to an increase in capillary permeability, leading to an overall increase in total body edema postoperatively.

Efforts to reduce the hemodilution and inflammatory effects of CPB include reducing priming volume, pharmacologic anti-inflammatory and diuretic therapies, and the use of postoperative peritoneal dialysis, and ultrafiltration.

Modified ultrafiltration was first used clinically as an alternative method to reduce the adverse effects of CPB in children.[99] Modified ultrafiltration is performed after CPB and allows filtration of both the patient's blood and the remaining contents of the CPB circuit including the venous reservoir (Fig. 5.7).[112–114] Using the MUF technique, an ultrafilter is interposed in the CPB circuit between the aortic arterial line and the venous cannula, which is located in the right atrium. After weaning from CPB, the blood is removed from the patient via the aortic cannula and fed through the ultrafilter along with blood from the venous reservoir and oxygen. The outlet of the ultrafilter is fed to the right atrium of the patient. Blood flow through the ultrafilter approximates 200 mL/minute which is maintained by a roller pump. Suction is applied to the filter port of the ultrafilter resulting in an ultrafiltration rate of 100–150 mL/minute. A constant left atrial or right atrial pressure is maintained achieving continued hemodynamic stability in most patients. Ultrafiltration is carried out until endpoints are reached, either time (15–20 minutes) or achieving a hematocrit value of approximately 40%.[113]

Ultrafiltration appears to offer two major advantages. First, total body water is reduced as a direct result of removing the ultrafiltrate.[99] This effect counteracts the hemodilution effects associated with the institution of CPB. In addition, the hematocrit is raised after CPB enhancing oxygen delivery to the tissues. Secondly, MUF has been shown to remove some of the deleterious vasoactive substances associated with inflammatory response to CPB.[115,116] This effect is mediated by reducing circulating cytokines, which are associated with capillary leak syndrome. Examination of the ultrafiltrate shows that it contains low molecular weight, inflammatory mediators including C3A, C5A, IL-6A, IL-8A, TNF, myocardial depressant factor, and various other cytokines. Several studies have shown that compared to control patients, patients that have MUF after CPB have substantially less total body water, less compliment, and IL release, require less blood transfusions, and show a faster recovery of systolic blood pressure.[99,113,117] Other studies have shown direct clinical benefit after ultrafiltration; MUF has been shown to increase left ventricular systolic function, decreasing end-diastolic pressure, thereby improving left ventricular compliance.[118] Modified ultrafiltration improves *CBF*, metabolic activity and oxygen delivery (Fig. 5.8),[119] acutely improving cerebral metabolism, which may reduce and reverse the known deleterious effects of DHCA. Modified ultrafiltration reduces postoperative blood use, chest tube drainage, plural effusions, and hospital stay in patients after cavopulmonary operations.[120]

An alternative to MUF is conventional filtration during the rewarming period of CPB. In an experimental model examining MUF vs. conventional ultrafiltration, MUF alone was effective in reducing weight gain and myocardial edema, and was associated with improving left ventricular function.[121] Outcomes with MUF vs. conventional ultrafiltration are not different with regard to fluid balance, hematocrit, mean arterial pressure, left ventricular function, duration of ventilation, intensive care or hospital stay, or mortality.[122] Possible

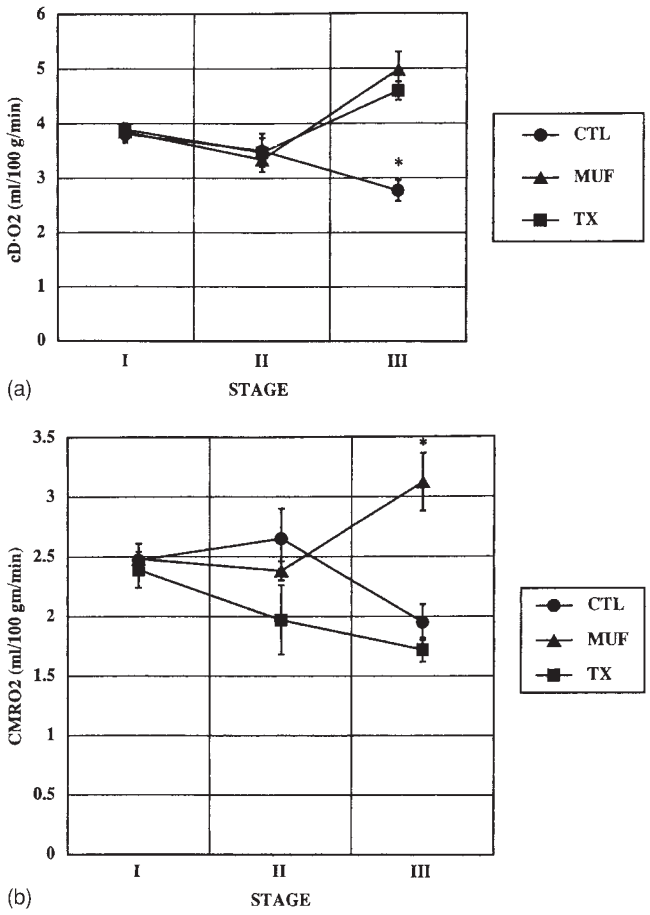


**Fig. 5.8** (a) Cerebral oxygen delivery ($cDO_2$), and (b) cerebral metabolic rate for oxygen ($CMRO_2$) before and after deep hypothermic circulatory arrest (DHCA) in neonatal piglets. There was a significant decrease in $cDO_2$ and $CMRO_2$ in control (CTL) group animals compared with those receiving modified ultrafiltration (MUF) or transfusion (TX). Stage I, before cardiopulmonary bypass (CPB); stage II, 5 minutes after CPB; stage III, 25 minutes after CPB. Reproduced with permission from Skaryak LA, Kirshbom PM, DiBernardo LR *et al.* Modified ultrafiltration improves cerebral metabolic recovery after circulatory arrest. *J Cardiothorac Vasc Anesth* 1995; **109**: 744–51.

complications of MUF include air embolus, patient cooling during ultrafiltration, and bleeding.[113] These theoretical and technical potential complications appear not to be of substantial concern. It is the view of most groups that the benefits of MUF far exceed the risk.[114]

## Stress response and cardiopulmonary bypass

The release of a large number of metabolic and hormonal substances including catecholamines, cortisol, growth hormone, prostaglandins, complement, glucose, insulin, β-endorphins, and other substances characterizes the stress response during hypothermic CPB.[123–125] The likely causes for the elaboration of these substances include contact of blood with the non-endothelialized surface of the pump tubing and oxygenator, non-pulsatile flow, low perfusion pressure, hemodilution, hypothermia, and response to surgical stress. Other factors that may contribute to elevations of stress hormones include delayed renal and hepatic clearance of proinflammatory mediators during hypothermic CPB, myocardial injury, and exclusion of the pulmonary circulation from bypass. The lung is responsible for metabolizing and clearing many of these stress hormones. The stress response generally peaks during rewarming from CPB. There is strong evidence that the stress response to surgical trauma can be blunted through the use of high dose opioid anesthesia.[123–125]

It is unclear at what level elevated circulating stress hormones become detrimental, since this is a normal neonatal adaptive response. There is little question that these substances could mediate undesirable effects such as myocardial damage (catecholamines), systemic and pulmonary hypertension (catecholamines, prostaglandins), pulmonary endothelial damage (complement, prostaglandins), and pulmonary vascular reactivity (thromboxane). The benefits of controlling the stress response with fentanyl in premature infants undergoing PDA ligation and with sufentanil in neonates with complex CHD has been demonstrated.[126,127] Although blunting the stress response seems warranted, there is additional evidence suggesting that the newborn stress response, especially the endogenous release of catecholamines, may be an adaptive metabolic response necessary for survival at birth.[128] Thus the complete elimination of an adaptive stress response may not be desirable. To what extent acutely ill neonates with CHD are dependent on their stress response for maintaining hemodynamic stability is currently unknown.

It is therefore prudent to maintain a depth of anesthesia adequate to attenuate the stress response, but to attempt to block the response all together may not be necessary. Acceptable anesthesia during CPB may be best accomplished by either the continuous administration of an inhalation anesthetic via a vaporizer connected to the pump oxygenator, careful titration of incremental doses of opioids, or the precise administration of an opioid or opioid and benzodiazepine by a continuous infusion technique. Primary opioid anesthetic techniques result in reduced stress hormone release and decreased postoperative metabolic acidosis and lactate production when compared with primary halothane anesthesia, and are therefore a preferred technique in complex CHD.[126] If depth of anesthesia is accomplished by the administration of large doses of opioids (e.g. fentanyl or sufentanil), postoperative mechanical ventilation will be necessary. By contrast, residual levels of inhalation anesthetic drugs (e.g. halothane or isoflurane) can produce transient myocardial depression at the termination of CPB, complicating separation from CPB.

In conclusion, there have been dramatic improvements in the morbidity and mortality for congenital heart surgery in neonates, infants and children. While much of this success has been due to improved surgical techniques, preoperative assessment, and postoperative care, nonetheless our understanding of the pathophysiologic effects of CPB and their reduction have also contributed to this success. Continued improvements in perfusion techniques and strategies are expected to further improve outcomes during and after pediatric cardiac surgery.

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# 6 The inflammatory response and its modification

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> Nature's reaction to every injury, whether physical, chemical, or bacterial, is inflammation, or in other words, congestion with its resulting benefits.
>
> (E.H. Beckman, MD, Southern Minnesota Medical Association, Saint Mary's Hospital, Mayo Clinic, August 1907).

## Introduction

The normal human response to an abnormal allergen or environment is the triggering of a defense mechanism, mediated through a humoral or cellular immune response. This is no more obvious than the response of the body to cardiopulmonary bypass (CPB) and the abnormal environment of extracorporeal circulation (ECC).[1]

Despite significant advances in cardiac surgery in the past 50 years, and major strides in improving the outcome of congenital cardiac defect repair, CPB remains an integral part of most operations. Cardiac surgery continues to carry an inherent risk of triggering a cascade of reactions leading to the systemic inflammatory response syndrome (SIRS), and manifested as multisystem organ failure (MSOF), especially in small infants and children.[2,3]

Clinically, the inflammatory response is manifested as reduced pulmonary function, with decreased compliance, worsening oxygenation, and prolonged need for postoperative mechanical ventilation. Cardiovascular dysfunction, requiring inotropic support, and occasionally the use of mechanical assist devices, occurs in more than 50% of children following cardiac surgery. In addition, 3–7% of children experience renal and hepatic dysfunction; in some series neurologic morbidity occurs in up to 30% of patients; and a high percentage have significant tissue edema and weight gain.[4]

## Mechanisms of activation

The inflammatory response is triggered with the initiation of CPB, from contact of blood with the non-endothelial surface of ECC, activating the coagulation and complement cascades. Other triggers of inflammation include bowel hypoperfusion with endotoxemia, and organ ischemia and reperfusion injury with release of the aortic cross-clamp and termination of bypass. Multiple triggers, mediators, and effectors interact to initiate, propagate, and maintain the inflammatory response and produce end-organ damage (Table 6.1).

Blood contact with the artificial surface activates the intrinsic coagulation pathway (increased factor XIIa), as well as the extrinsic pathway (factor VII contact with tissue factor). Despite the use of high dose systemic heparin, and maintaining an adequate activated clotting time (ACT > 480 seconds), markers of thrombin generation (prothrombin $F_{1+2,}$ fibrinopeptide A) increase with the progression of bypass. The fibrinolytic system is also activated, with increased kallikrein, bradykinin, and tissue plasminogen activator (tPA).[5]

The complement system is a series of 19 functionally linked plasma proteins which, once activated, interact to effect humoral immunity and inflammatory response. The complement proteins generally are inactive until activated by the antigen–antibody complex (classic pathway) or by infectious

**Table 6.1** Inflammatory triggers and mediators during cardiopulmonary bypass.

| | |
|---|---|
| Complement | C3a, C5a, C5b-9 |
| Leukocyte and adhesion molecules | CD11b/CD 18, E-selectin, ICAM-1, integrins |
| Arachidonic acid metabolites | Thromboxane $A_2$, prostaglandins |
| Endotoxin | |
| Cytokines | TNF-α, IL-6, IL-8, IL-10 |
| PAF | |
| NO | |
| Endothelins | Endothelin-1 |
| Oxygen free radicals | Superoxide anion, singlet oxygen, hydroxyl radicals, hydrogen peroxide |

ICAM-1, intercellular adhesion molecule-1; IL, interleukin; NO, nitric oxide; PAF, platelet-activating factor; TNF-α, tumor necrosis factor-α.

organisms (alternate pathway). The main event in complement activation is the generation of C3a and C3b from C3 by the action of C3 convertases, and increased C5a (neutrophil attractant) at the onset of bypass.[6] The classic pathway is activated at the end of bypass by the protamine–heparin complex and increased C4a concentration. The end result is release of activated anaphylotoxins (C3a, C4a, and C5a) that in turn cause histamine release, increased vascular permeability, and neutrophil activation. C5a is the most potent of the anaphylotoxins, and acts directly on the endothelial cells, stimulating contraction, vascular leak, and exocytosis. The combined effect of actions of C5a, C3a, and C4a on mast cells, endothelial cells, and neutrophils determines the inflammatory response at the site of complement activation, and thus the degree of organ damage. In a group of 29 children undergoing cardiac surgery, Seghaye *et al*.[7] showed a significant increase in C3a and C5a at the initiation of CPB, significant transpulmonary neutropenia, and correlation between the degree of complement activation with postoperative morbidity. The elevation of C3a and C5a is proportional to the duration of CPB and the increasing age of patients. Infants have a more pronounced increase in C3a and C5a when compared to neonates.[8]

The initiation of CPB is associated with decreased gastric mucosal pH, intestinal hypoperfusion, and increased permeability. The absorption of ingested monosaccharides (L-rhamnose), dependent on transcellular transport, is decreased during and following CPB, due to intestinal cellular edema. Meanwhile, paracellular transport and urinary excretion of disaccharides (cellobiose) is increased up to the third postoperative day.[9]

Levels of circulating endotoxin and the need for inotropic support correlate with increased intestinal mucosal permeability. The severity of necrotizing enterocolitis (NEC) in newborns correlates with the amount of endotoxin and mediators of inflammation (proinflammatory interleukins [IL] IL-1β and IL-8) in the circulation.[10] The lipopolysaccharide (LPS) bacterial outer membrane of Gram-negative organisms, and circulating endotoxin, bind to macrophages and monocytes, initiating release of mediators of inflammation.

The final trigger to the inflammatory cascade is the ischemia-reperfusion injury that occurs with unclamping the aorta, discontinuing CPB, and resuming pulsatile perfusion. Both in clinical observations[11] and experimental models[12] of ischemia and reperfusion, there is significant increase in neutrophil count, plasma granulocyte elastase, serum IL-6 and IL-8, associated with pulmonary leukocyte sequestration, myocardial and cerebral neutrophil infiltration, and organ dysfunction.

## Pathophysiology of the inflammatory response

Following activation by surface contact, complement, endotoxemia, and reperfusion, the inflammatory response is mediated by expression and secretion of tumor necrosis factor-α (TNF-α), various cytokines and arachidonic acid metabolites.[13]

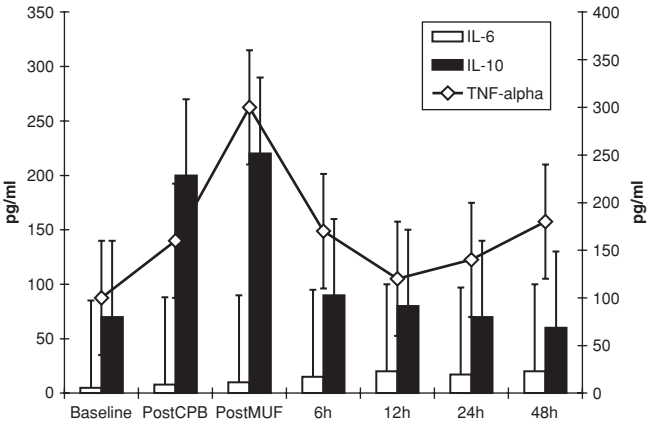


**Fig. 6.1** Proinflammatory and anti-inflammatory cytokine responses to cardiopulmonary bypass (CPB) in children. IL, interleukin; MUF, modified ultrafiltration; TNF-α, tumor necrosis factor-α. Reproduced with permission from Chew MS, Brandslund I, Brix-Christensen V *et al*. Tissue injury and the inflammatory response to pediatric cardiac surgery with cardiopulmonary bypass: A descriptive study. *Anesthesiology* 2001; **94**: 745–53.

Macrophages and monocytes, which are already primed by C5a, release TNF-α (also known as cachexin due to its prominent presence in cachexia of chronic illness) in response to stimulation by endotoxin. Plasma levels of TNF-α have been shown to increase during and after CPB with a bimodal peak at 2 and 18–24 hours postoperatively.[14] Tumor necrosis factor-α release is the initial event in the release of further pro- and anti-inflammatory cytokines (Fig. 6.1).[15] Tumor necrosis factor-α acts on mononuclear phagocytes, and on the vascular endothelium, to stimulate secretion of a cascade of pro- and anti-inflammatory cytokines that share many biologic activities.

Cytokines are polypeptide or glycopeptide hormones of low molecular weight (5–28 kDa) that are produced by various cell types. They mediate and regulate the immune and inflammatory response to external stimuli, and facilitate the communication between leukocytes (hence the name "interleukins" or IL). The cell types producing cytokines include macrophages, monocytes, lymphocytes, and endothelial cells. Cytokines are not stored as pre-formed molecules, and their synthesis is initiated by new gene transcription. Once synthesized, cytokines are rapidly secreted, resulting in a burst of serum cytokine release. Cytokines often influence the synthesis and release of other cytokines, leading to a cascade-like increase of their plasma concentrations in a series of successive waves. Positive and negative regulatory mechanisms mediate the biologic effects and concentration of the various cytokines. The wave of release begins with an increase in serum TNF-α, followed by release of several proinflammatory

interleukins (IL-1β, IL-6, and IL-8) and anti-inflammatory (IL-10) cytokines.

Tumor necrosis factor-α, C3a, and C5a stimulate macrophage and monocyte IL-1β production and release. Interleukin-1β levels have been shown to increase after CPB and to reach its peak levels at 24 hours postoperatively. Interleukin-1β also activates neutrophils and endothelial cells to cause adhesion between them. Interleukin-1β stimulates the production of IL-6 and IL-8 and thus plays a central role in the inflammatory process. It has been shown to cause decreased myocardial β-adrenergic receptor (BAR) response to catecholamine stimulation. It also causes fever by the production of prostaglandin $E_2$ in the hypothalamus, thus known as the endogenous pyrogen.

Interleukin-6 is produced by various cell types, including macrophages, monocytes, endothelial cells, lymphocytes, and fibroblasts in response to TNF-α. It is known as the acute phase interleukin. The acute phase response consists of fever, leucocytosis, altered vascular permeability, decreased synthesis of albumin, and increased synthesis of acute phase proteins, like C-reactive protein (CRP) by the liver. Interleukin-6 levels peak 3–6 hours after CPB and correlate with postoperative organ dysfunction. In one study, plasma IL-6 levels in children undergoing ventricular septal defect repair (105 ± 12 pg/mL) were significantly lower than levels in patients who underwent complex surgical repairs (220 ± 25 pg/mL).[14] Elevated levels of IL-6 after bypass may be related to the severity of the preoperative condition, the duration of CPB, or myocardial compromise postoperatively. Interleukin-6 seems to be the best indicator of outcome after sepsis or CPB-induced multiorgan failure.

Interleukin-8 is the chemokine that attracts neutrophils to the site of inflammation. The same cell types that produce other cytokines also produce IL-8, through stimulation by endotoxin and TNF-α. Levels of IL-8 begin to rise at rewarming, and peak at 1–3 hours after CPB, and are present after 24 hours. Interleukin-8 attracts neutrophils to the site of inflammation and causes upregulation of adhesion molecules necessary for neutrophil adhesion to endothelial cells. It also stimulates neutrophils to release oxygen free radicals and proteolytic enzymes which enhance endothelial damage.

Another group of proinflammatory cytokines, the β-chemokines monocyte chemoattractant protein (MCP-1), are significantly increased following CPB, and correlate with duration of bypass, longer surgical time, and increased need for inotropes.[16]

Interleukin-10 is an anti-inflammatory cytokine as opposed to IL-6 and IL-8, which are proinflammatory cytokines. Interleukin-10 levels also increase and peak around 3 hours after CPB (Fig. 6.1). Interestingly IL-6 stimulates the release of IL-10 by macrophages, endothelial cells, and monocytes. Interaction between pro- and anti-inflammatory cytokines likely determines the severity of the inflammatory response and multi-organ dysfunction following CPB in children.[17]

There are conflicting reports regarding the time of release, the degree of increase in plasma levels, and the relative ratio between pro- and anti-inflammatory cytokines in the literature. These discrepancies may stem from the source of sampling (arterial or venous blood), the timing of when blood is sampled, and the various measurement techniques (enzyme-linked immunosorbent assay, radioimmunoassay, or *in vitro* cell cytotoxicity assay). However, it is clear that the initial response is a release of TNF-α with an early and late peak, followed by a series of waves of interleukin release.

Other important mediators of inflammation are the leukotrienes, arachidonic acid metabolites, endothelin, and oxygen free radicals. The leukotrienes and arachidonic acid metabolites are humoral inflammatory mediators produced by macrophages, neutrophils, and monocytes after stimulation by C5a and IL-8. Leukotriene $B_4$ causes chemotaxis, release of proteolytic enzymes and generation of oxygen free radicals from neutrophils. Other leukotrienes cause arteriolar constriction and induce a profound increase in vascular permeability. Thromboxane $A_2$ and prostaglandins are arachidonic acid metabolites. Thromboxane $A_2$ has strong vasoconstrictor and platelet-aggregating properties. Thromboxane $A_2$ has been shown to cause myocardial dysfunction and pulmonary hypertension after CPB in animal models. Prostaglandins ($PGE_{1+2}$ and prostacyclin) on the other hand have vasodilating and antiplatelet-aggregating properties, and therefore counter balance the effect of thromboxane $A_2$.[18]

Endothelin is released from the endothelial cells, and is a potent vasoconstrictor. It thus regulates arterial blood pressure and influences cardiac output. Increased levels of endothelin have been demonstrated in patients who develop pulmonary hypertension. Elevated levels of endothelin occur after CPB and correlate with postoperative renal dysfunction. Endothelin release after CPB may also cause myocardial ischemia and the development of pulmonary edema.

These mediators of the inflammatory response (TNF-α, interleukins IL-1β, IL-6 and IL-8, and arachidonic acid metabolites), modulate the response of the body to the inflammatory trigger of bypass through neutrophil-endothelial adhesion, BAR downregulation, and inducible nitric oxide synthase (iNOS) production.

Once activated, neutrophils adhere to endothelial cells, and eventually migrate out of the vessel wall into the tissues (Fig. 6.2). There are specific adhesion molecules on the surface of neutrophils and endothelial cells.[19] These molecules include selectins (present on leukocytes, *L-selectin*, endothelial cell, *E-selectin*, and platelets, *P-selectin*), integrins (neutrophil only), and the immunoglobulin superfamily (endothelial cells only).[20,21] One study found that atrial and skeletal muscle E-selectin mRNA levels increase significantly following CPB in children. ELAM-1 (endothelial leukocyte adhesion molecule-1) presents on the endothelial surface after stimulation of TNF-α or IL-1, and plays a key role in the binding of neutrophils to endothelium.

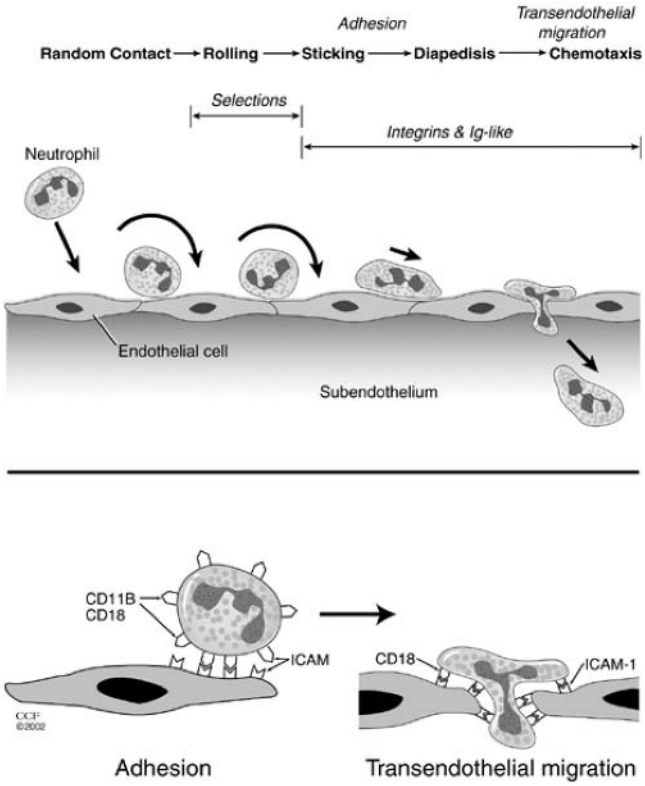


**Fig. 6.2** Neutrophil adhesion, diapedesis, transendothelial migration and chemotaxis. See text for explanation. ICAM, intercellular adhesion molecule.

The integrins are receptors, responsible for cellular interactions and have α- and β-subunits. The $\beta_2$-subunit of integrins facilitates the adhesion of neutrophils to other cells and also plays a key role in the inflammatory response. The common $\beta_2$-subunit is called CD18 and the α-subunits are called CD11a, CD11b, and CD11c. Upregulated CD11b expression on neutrophils likely contributes to neutrophil sequestration in the heart and lungs after bypass.

The immunoglobulin superfamily of receptors include ICAM-1 and ICAM-2 (intercellular adhesion molecule-1 and 2); the expression of these molecules on the endothelial surface is induced by C5a, TNF-α, IL-1β, or endotoxin. Plasma concentrations of soluble adhesion molecules increase significantly after CPB in cyanotic children, in younger patients, and with longer bypass times.[22] Interleukin-8 promotes neutrophil interaction with ICAM-1 receptors on the endothelial cells and neutrophil migration to the extravascular tissues.

The neutrophils extend pseudopods that probe for the path of least resistance at the interendothelial junctions. Increased vascularity, blood stasis, and endothelial injury allows the neutrophils to crawl between the endothelial cells. The proteolytic enzymes from the neutrophil granules digest the basement membrane to allow migration to subendothelial tissues. Once in the subendothelial space, neutrophils cause tissue injury by releasing proteases, elastases, toxic oxygen radicals, and arachidonic acid metabolites. The released elastase causes damage to endothelial cells, underlying basement membrane, subendothelial matrix, and parenchyma of various organs, and plasma levels are significantly elevated after CPB.

Platelets become activated during CPB from the action of C5a and also by platelet-activating factor (PAF) secreted by endothelial cells, which leads to the expression of platelet P-selectin. Platelets attached to the vascular endothelium play an important role in neutrophil adhesion and transmigration by attracting more neutrophils to the endothelium from the expression of P-selectin.[23]

Endothelial cells are responsible for the permeability barrier through which the exchange of substances takes place by transcytosis. The endothelium also promotes structural changes of the blood vessel in response to a local change in environment. The vascular endothelium is exposed to various inflammatory stimuli including endotoxin, cytokines, and the physical injury of surgical trauma. These stimuli may cause a disruption of the barrier function, vasoconstriction, abnormal coagulation, leukocyte adhesion, smooth muscle proliferation, and they release of more mediators of inflammation, like cytokines released from the cytoplasmic vacuoles called Weibel–Palade bodies.

Another mechanism by which the inflammatory response is mediated is through BAR downregulation. Discontinuation of CPB is a critical event, often associated with transient myocardial dysfunction, requiring increasing inotropic support. Canine transmyocardial left ventricular biopsies reveal the density of BAR to be significantly decreased following bypass.[24] The response of BAR in the myocardium or bronchial smooth muscles to non-selective β-agonists (isoproterenol), or selective $\beta_2$-agonists (zinterol), is impaired following CPB. The decreased density, and desensitization of BAR, is reproducible with TNF-α exposure, and correlates with the post-CPB increase in serum cytokines.[25]

The endothelium-derived relaxing factor, nitric oxide (NO), is a natural regulator of vasomotor tone and blood flow to organs. Under normal conditions, picomolar concentrations of NO are formed in the circulation, by the effect of constitutive nitric oxide synthase (cNOS). However, at the start of CPB, hemodilution, non-pulsatile flow, and circuit contact activate endothelial inducible nitric oxide synthase (iNOS), to produce excessive (nanomolar) concentrations of NO. Nitric oxide will modulate vasodilation, neutrophil adhesion, and tissue injury by TNF-α, cytokines, and other mediators of inflammation.[26]

The negative inotropic effect of TNF-α on isolated papillary muscle contraction, was blocked in the presence of *N*-monomethyl-L-arginine (L-NMMA), a specific NOS inhibitor. The concentration-dependent, reversible myocardial depression of TNF-α reappears with the addition of L-arginine.[27] Neuronal apoptosis following hypothermic circulatory arrest, especially in the hippocampus and neocortex, is significantly reduced by neuronal NOS inhibition.[28] Nitric oxide regulates

P-selectin expression, neutrophil adhesion and sequestration on CPB, and further propagation of the bypass-induced inflammatory response.[29]

## Clinical effects of the inflammatory response

Complications following CPB due to the systemic inflammatory response remain common and obvious, despite significant improvement in equipment, material, and the conduct of surgery. Following prolonged surgery, children may present to the intensive care unit with marked whole-body edema and multiple organ failure, especially those patients who require greater pharmacologic and mechanical support (Fig. 6.3).

High fever, thrombocytopenia, cardiorespiratory insufficiency, and failure of one or more vital organ systems, occur in more than 3.5% of children after open heart surgery.[30]

One study found 13/24 neonates developed capillary leak syndrome (CLS), which was associated with higher complement (C5a) and cytokine (TNF-α) levels postoperatively (Fig. 6.4). Plasma albumin fell significantly, and histamine release during CPB was more pronounced in patients with CLS.[31]

There is a strong association between triggering the inflammatory response and the development of coagulopathy following bypass. An inverse correlation is present between *in vitro* platelet aggregation and plasma IL-1β or IL-6 levels. Cytokines are important mediators of disseminated intravascular coagulopathy, fibrinolysis, and bleeding associated with CPB and sepsis.[32] Cardiac surgery still consumes more than 20% of the nation's blood supply, and almost 80% of all transfusions are used in only 15% of patients, who commonly show other signs of MSOF and systemic inflammatory response.

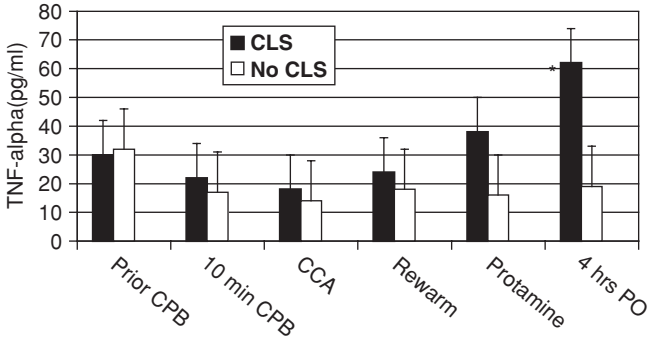


**Fig. 6.4** Course of tumor necrosis factor-α (TNF-α) before, during and after cardiopulmonary bypass (CPB) in neonates with (*black*), and without (*white*) capillary leak syndrome (CLS). CCA, complete circulatory arrest; PO, postoperatively (*$P < 0.05$). Adapted from Seghaye MC, Grabitz RG, Duchateau J *et al*. Inflammatory reaction and capillary leak syndrome related to cardiopulmonary bypass in neonates undergoing cardiac operations. *J Thorac Cardiovasc Surg* 1996; **112**: 687–97, with permission from Elsevier.

Myocardial dysfunction requiring inotropic support is common in the immediate postoperative period. The severity of cardiac depression appears to be associated with the extent of stimulation of the inflammatory response. In adults presenting for myocardial revascularization on CPB, a bimodal increase in TNF-α and IL-6 is noted postoperatively that is proportional to the duration of cross-clamp. Left ventricular wall motion abnormalities, episodes of myocardial ischemia, and inotropic requirements, correlated with cytokine expression.[33] Cardiac index and systemic vascular resistance are

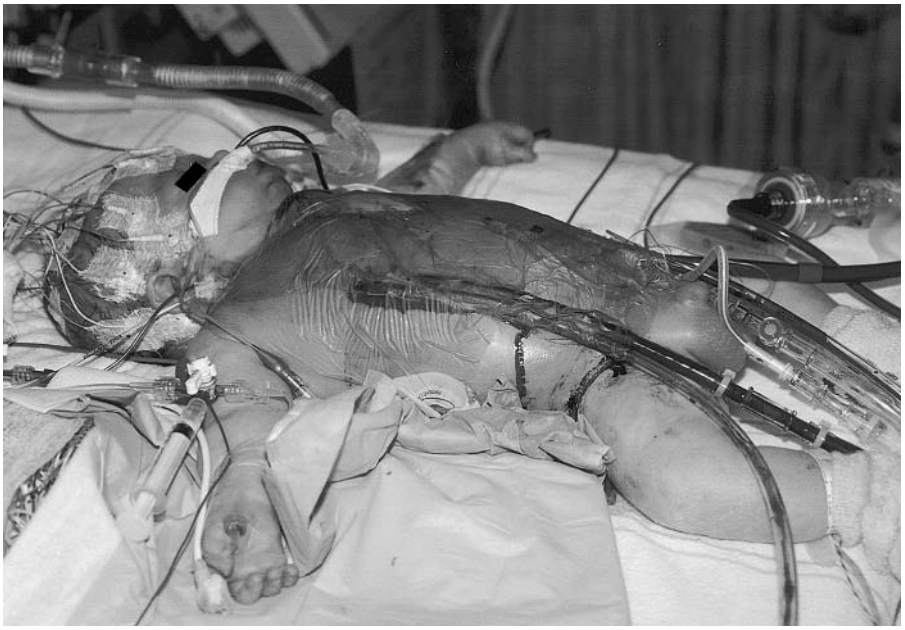

**Fig. 6.3** Systemic inflammatory response syndrome following extracorporeal circulation, leading to multisystem organ failure in a neonate with congenital heart disease.

inversely related, while pulmonary capillary wedge pressure was directly related to IL-6 increase postoperatively.[33,34] Preoperative depression of cardiac function appears to predispose the patient to develop an accentuated inflammatory response, with a significant increase in post-pump cytokines in patients with an ejection fraction of less than 0.45 preoperatively, compared to those with normal cardiac function.[34]

Myocardial damage appears to occur up to the fourth postoperative day in children following repair of congenital heart defects, and the changes in serum troponin, creatine kinase, and procalcitonin correlate with the increases in markers of inflammation.[35]

The pulmonary injury following CPB is one of the major causes of morbidity after cardiac surgery in children, and is known as "pump-lung". Pulmonary edema, microatelectasis, increased alveolar–arterial oxygen gradient (A–a$O_2$ gradient), and increased pulmonary vascular resistance, are common postoperatively. Duration of CPB in children correlates with decreases in surfactant, transpulmonary neutropenia, and neutrophil-lung sequestration. Granulocyte adhesion molecule expression (CD11b/CD18, MCP-1), and increase in serum IL-8, correlate with a deterioration in oxygenation in children after sugery.[36] Serum and alveolar epithelial IL-6 increase significantly following CPB in children, and correlated with intraoperative blood transfusion, fluid gain, Pediatric Risk of Mortality Score (PRISM), and survival (Fig. 6.5).[37]

Neurologic injury occurs frequently in children following repair of congenital heart disease (CHD), with gross deficits (strokes, seizures) found in 3%, and psychomotor and neurodevelopmental dysfunction found in 30% of children. Despite a relation between adhesion molecules, TNF-α, and cognitive dysfunction in other disease states, these markers of systemic inflammatory response showed no relationship with neurologic outcome at 5-day and 3-month performance tests.[38]

The risk of acute renal failure (2.7%) and gastrointestinal complications (1%) in children following CPB is associated with triggering the inflammatory response.[39,40] In patients with severe end-stage cardiomyopathy, five out of 16 developed fulminant hepatic failure despite adequate hemodynamic support by a left ventricular assist device. Markers of inflammation (CRP, IL-6, and IL-8) were significantly increased in patients who developed hepatic dysfunction.[41]

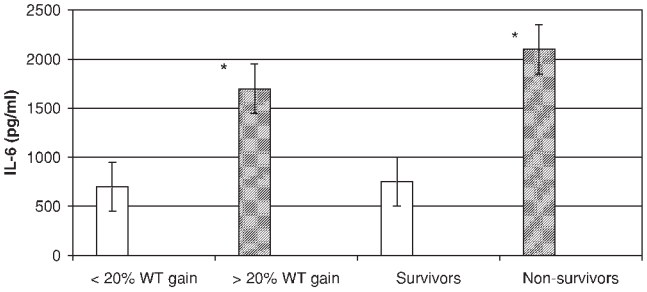


**Fig. 6.5** Relation of serum interleukin-6 (IL-6) levels to fluid retention and survival in children at 2 hours following cardiopulmonary bypass (*$P < 0.05$). WT, weight. Adapted from Hauser GJ, Ben-Ari J, Colvin MP *et al*. Interleukin-6 levels in serum and lung lavage fluid of children undergoing open heart surgery correlate with postoperative morbidity. *Intensive Care Med* 1998; **24**: 481–6, with permission from Springer-Verlag.

## Modification of the inflammatory response

Multiple treatment modalities and interventions are used in an attempt to limit the generation and extent of inflammation after bypass and avoid organ dysfunction.[42] One obvious method to decrease the triggering of inflammation is to avoid CPB, and currently over 16% of coronary artery bypass graft surgeries are performed without bypass. However, the use of ECC remains essential for all intracardiac repairs of congenital heart defects. Thus the interventions needed to limit the inflammatory response to CPB include: (i) preoperative therapies (intestinal decontamination, pre-surgical inotropes, and anesthetics); (ii) modifications of circuit biocompatability (heparin-coating, pulsatile flow, prime solution); (iii) changes in CPB conduct (temperature, leukocyte depletion, hemofiltration); and (iv) pharmacologic interventions (steroids, aprotinin, monoclonal antibodies). The treatment modalities and therapies are used in concert to treat the multifaceted inflammatory response to bypass (Fig. 6.6).

### Digestive decontamination

Endotoxemia in children with CHD is present in 40% of patients preoperatively, and 96% following CPB. Plasma levels of IL-6, unstable hemodynamics, and mortality are higher in children with more significant endotoxemia.[43] The use of selective digestive decontamination (polymyxin E, tobramycin, and amphotericin B) for 72 hours preoperatively reduces gut content of enterobacteria, and lowers endotoxin and cytokine concentrations post-bypass.[44]

### Inotropic support

Perioperative administration of low dose milrinone improves splanchnic perfusion on CPB, thus limiting intestinal mucosal ischemia and injury, thereby decreasing translocation of intestinal flora and endotoxemia. The use of milrinone 0.5 μg/kg/minute improves gastric intramucosal acidosis, reduces hepatic venous congestion, and reduces postoperative IL-6.[45]

### Prime solution and blood transfusion

The use of plasma expanders and the maintenance of colloidal osmotic pressure in prime solution limits activation of the alternative and common complement pathways.[46]

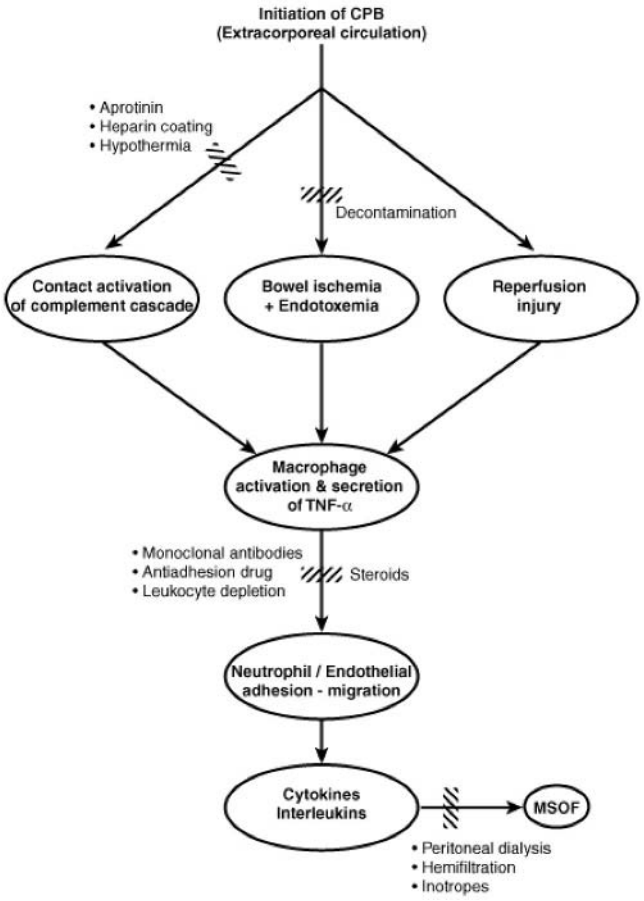


**Fig. 6.6** Treatment options of the inflammatory response to cardiopulmonary bypass (CPB). MSOF, multisystem organ failure; TNF-α, tumor necrosis factor-α.

Despite allogeneic blood transfusion causing more immunosuppression than autologous blood,[47] exposure to any transfusion, especially platelet concentrates, leads to a significant increase in markers of inflammation (C3a, C5a, TNF-α, and IL-6).[48] The magnitude of the interleukin response to CPB correlates with blood transfusion and duration of bypass.[49]

## Oxygenators and perfusion mechanics

Compared to bubble oxygenators, the use of membrane oxygenators in pediatric cardiac surgery is associated with better cardiac performance, better postoperative pulmonary compliance, and decreased shunt fraction, free hemoglobin, blood loss, postoperative pyrexia, and length of hospitalization. When extracorporeal perfusion lasts more than 2 hours, membrane oxygenators reduce the release of granulocyte adhesion molecules, lactoferrin, myeloperoxide, and pro-inflammatory cytokines.[50,51]

The use of non-pulsatile flow is associated with a progressive increase in systemic vascular resistance, decreased tissue oxygen consumption, metabolic acidosis, and the expression of inflammatory markers. Pulsatile perfusion (although less popular) and non-occlusive centrifugal pumps can be used during pediatric CPB, and may limit complement activation and reduce the inflammatory response.[52,53]

## Temperature control

The use of hypothermic CPB appears to offer a protective effect from the inflammatory response. One study compared maintaining a core temperature of 28°C vs. 36°C, and found markers of inflammation to be significantly reduced.[54] In an *in vitro* pediatric CPB circuit preparation, neutrophil activation and upregulation of adhesion molecules was significantly increased on normothermic (35°C) compared to hypothermic (17°C) bypass.[55] Even though a predominance of literature supports the concept that moderate or deep hypothermic bypass attenuates the inflammatory response and decreases histologic organ damage,[56] some investigators have shown no difference in those markers with changing temperature.[57,58]

## Heparin-coated circuits

The use of a heparin-coated (HC) or bonded extracorporeal circuit reduces heparin requirements during cardiac operations, and improves oxygen tension (HC 597.2 ± 31.2 vs. control 220.5 ± 42.3 mmHg), and pulmonary vascular resistance (HC 408.6 ± 69.4 vs. control 1159.8 ± 202.4 dyne · s · $cm^{-5}$) 2 hours after CPB.[59] Heparin bonding of the entire circuit, or the oxygenator (which forms > 80% of the circuit surface area in children), significantly reduces postoperative central hyperthermia and respiratory index. Plasma levels of terminal complement complexes, and expression of neutrophil adhesion molecules and serum cytokines are markedly reduced in children managed with HC circuits.[60–62] Two different processes of coating circuits with heparin have been described. The Carmeda process (Medtronic, Inc., Minneapolis, MN) deposits a polymer coating on the circuit surface, followed by covalently bonding heparin fragments to that coating. The Duraflo II process (Baxter Healthcare Corp., Irvine, CA) modifies the physicochemical properties of unfractionated heparin with a binding agent, giving it a high affinity for synthetic surfaces.[63] Although the Carmeda equipment appears more effective in reducing complement activation, both methods were similar in blunting the expression of cytokines and the inflammatory response.

## Leukocyte depletion

The use of a blood cell separator can limit the triggering of the inflammatory response and its deleterious effects. Leukocyte and platelet depletion (LPD) decrease leukocyte and platelet counts; and serum elastase, thromboxane, and thrombin–antithrombin III (TAT) complex are also lowered. This therapy leads to higher arterial oxygen tension and a lower

respiratory index, improved maximum stroke work index, and use of lower catecholamine doses.[64,65]

## Conventional and modified ultrafiltration

The hemodilutional effects of CPB are pronounced in children due to the disproportionately large priming volume and surface area of the circuit. Hemoconcentration applies a hydrostatic pressure gradient to a semipermeable membrane, removing excess water, low-molecular-weight substances, and inflammatory mediators. The filter can be used during rewarming, and placed between the oxygenator and the venous reservoir (in conventional ultrafiltration [CUF]), or after CPB, and placed between the arterial cannula and the right atrium (in modified ultrafiltration [MUF]). The suction pressure should not exceed 200 mmHg, removing fluid at a rate less than 50 mL/kg/minute. Both methods are effective in reducing proinflammatory cytokines, complement activation (C3a, C5a), and weight gain.[66,67]

Cytokine removal strategies using CUF or MUF are limited to the intraoperative period and are unable to limit the inflammatory response due to reperfusion injury in the postoperative period. The use of a Tenckhoff catheter for removal of peritoneal fluid was shown to remove significant amounts of IL-6 and IL-8, and may be beneficial in improving the pro- to anti-inflammatory (IL-6/IL-10) serum cytokine balance.[68]

## Intravenous anesthetics

The use of intravenous anesthetics to modulate the inflammatory response to CPB is an interesting and evolving area of investigation. The effect of pharmacologic concentrations of intravenous anesthetics on the expression of leukocyte adhesion molecules and release of cytokines has been studied in a cultured whole blood sample incubated with LPS endotoxin.[69] Compared to control, the LPS-stimulated TNF-α response was inhibited by thiopentone (12.8%) and ketamine (46.4%), augmented by propofol (172.3%), and unchanged with midazolam or fentanyl.

### Aprotinin

Aprotinin reduces endotoxin activation of the plasma kallikrein–kinin and complement system.[70] Aprotinin is a serine protease inhibitor commonly used in adult and pediatric cardiac surgery to decrease blood loss and transfusion requirements. Aprotinin shortens sternal closure times, decreases 24-hour chest tube drainage, transfusion of packed red blood cells and platelets, and overall hospital expense in children with cyanotic heart disease.[71,72] Aprotinin is an expensive medication, with known risk of anaphylaxis. Exposure to topical aprotinin in fibrin sealant resulted in developing aprotinin-specific immunoglobulins E and G in 8–39% of children.[73] However, only aprotinin blocks kallikrein and plasmin, thus preventing contact activation, the release of cytokines, and the inflammatory response to CPB. In a bronchial epithelial cell line, aprotinin blocks the expression of iNOS and the production of injurious concentrations of NO in response to cell stimulation with TNF-α and other cytokines.[74,75]

## Corticosteroids

The beneficial effects of steroid administration before CPB to attenuate the "post-pump syndrome" have long been investigated. Earlier studies focused on the hemodynamic effects of methylprednisolone (MPSS at 10–30 mg/kg) or dexamethasone (DXM at 1–6 mg/kg). Both glucocorticoids increased cardiac index, reduced peripheral vascular resistance, and improved microcirculation and visceral perfusion.[76] Steroid use has an equal and even a synergistic effect with other agents, such as aprotinin, in blunting the inflammatory response. Methylprednisolone improved oxygenation, cardiac index, and cytokine balance following CPB, when added to high dose aprotinin.[77,78]

Several investigations have shown that steroid pretreatment modulates different aspects of the inflammatory response, and the most recent studies are summarized in Table 6.2.[79–90] Steroids blunt the endotoxin-mediated increases in CD11b/CD18, and neutrophil surface adhesion-receptor expression.[77] They reduce the expression of proinflammatory cytokines, and LPS-stimulated production of IL-1β and TNF-α by macrophages. Methylprednisolone has been shown to block the upregulation of neutrophil integrin adhesion receptors, and preserve chemotactic properties, as well as attenuate complement activation with protamine administration.[82] Dexamethasone decreases proinflammatory cytokines, and the expression of ELAM-1 (endothelial leukocyte adhesion molecule-1) and ICAM-1 adhesion receptors.[86] The net results of steroid pretreatment appear to include improvement in hemodynamics, pulmonary mechanics, and recovery of cerebral perfusion and metabolism following deep hypothermic circulatory arrest.[80,86,88] Steroids cause attenuation of capillary leak and weight gain, and reduce postoperative pyrexia through limiting the inflammatory response.

The type, timing, and dose of steroid used are controversial, and may explain the discrepancy in outcome of some studies.[90] Administration of steroids 1–8 hours prior to incision appears to have a stronger impact on cytokines and acute phase-reactants (CRP), than does the same dosage used in the pump prime.[79,84] The administration of MPSS 20–30 mg/kg prior to surgical incision significantly improved the anti- to proinflammatory cytokine balance, and maintained a favorable postoperative clinical outcome (Fig. 6.7).[87]

## Anticytokine and monoclonal antibodies

Experimental studies have shown a benefit for strategies to block cytokines in sepsis-like syndromes using soluble

**Table 6.2** Recent randomized evaluations of steroid effect on inflammatory response to cardiopulmonary bypass.[79–90]

| Study | Steroid use: type, dose, and time | Subjects | Biochemical markers | Clinical effects |
|---|---|---|---|---|
| Wan *et al*.[79] (1996) | MPSS 500 mg preop. (GP-I) or 1.5 h post-clamp (GP-II) | 20 adult transplants | ↓ TNF & IL-8<br>↑ IL-10 (GP-I) | |
| Butler *et al*.[80] (1996) | MPSS 10 mg/kg Pump prime | 24 children | ↓ IL-6, CRP | ↓ Postop. fever |
| Tabardel *et al*.[81] (1996) | MPSS 30 mg/kg vs DXM 1 mg/k 4 h pre-CPB | 22 adults | ↓ IL-8, TNF-α<br>↑ IL-10 | No difference between MPSS and DXM |
| Loubser[82] (1997) | MPSS 30 mg/kg pre-CPB | 16 adults | ↓ C3a, C4a after protamine | |
| Mayumi *et al*.[83] (1997) | MPSS 20 mg/kg pre- and post-CPB | 24 adults | ↓ IL-2, CRP, T & B cells | |
| Lodge *et al*.[84] (1999) | MPSS 30 mg/kg 8 h & 1.5 h preop. vs.pump prime | 18 neonatal piglets | | ↑ Compliance<br>↓ A–a gradient, *PVR*, fluid gain |
| Dernek *et al*.[85] (1999) | MPSS 30 mg/kg preop. | 50 adults | ↓ Complement<br>↓ Ig activation | ↓ Pulmonary neutrophil sequestration |
| Bronicki *et al*.[86] (2000) | DXM 1 mg/kg 1 h prior to CPB | 29 children | ↓ IL-6, TNF-α<br>↔ C3a, neutrophil count | ↓ Rectal temp.<br>↓ A–a gradient<br>↓ Mechanical ventilation |
| Mossad *et al*.[87] (2000) | MPSS 20 or 30 mg/kg prior to incision | 47 infants | ↓ IL-6, IL-8<br>↑ IL-10 | ↓ PD drainage |
| Langley *et al*.[88] (2000) | MPSS 30 mg/kg i.m. 8 h & 2 h preop. | 16 neonatal piglets on DHCA | | ↑ Recovery of regional & global *CBF* & $CMRO_2$ |
| Volk *et al*.[89] (2001) | MPSS 15 mg/kg preop. | 39 adults | ↓ IL-1β, IL-6, IL-8, TNF-α response to LPS<br>↑ IL-10 | |
| Mott *et al*.[90] (2001) | MPSS 1 mg/kg × 4 doses preop. & 24 h postop. | 246 children | | ↑ Risk of PPS |

A–a gradient, alveolar-to-arterial oxygen gradient; *CBF*, cerebral blood flow; $CMRO_2$, cerebral metabolic rate for oxygen; CPB, cardiopulmonary bypass; CRP, C-reactive protein; DHCA, deep hypothermic circulatory arrest; DXM, dexamethasone; GP-I, Group I; GP-II, Group II; Ig, immunoglobulin; IL, interleukin; LPS, lipopolysaccharide; MPSS, methylprednisolone sodium succinate; PD, peritoneal dialysis; PPS, post-pericardiotomy syndrome; *PVR*, pulmonary vascular resistance; TNF, tumor necrosis factor.

TNF-α receptors and neutralizing factors, and IL-1β-receptor antagonists.[91] Inhibition of neutrophil adhesion using monoclonal antibodies and anti-selectins leads to improved recovery of ventricular function, myocardial oxygen consumption, and attenuates myocardial neutrophil proliferation following cold cardioplegic ischemia.[92–94] Clinical studies have shown the safety and efficacy of a humanized, recombinant, single chain antibody specific for human C5 in limiting the inflammatory response to bypass. Patients receiving 1–2 mg/kg i.v. of the complement inhibitor preoperatively had effective inhibition of the proinflammatory complement by-products (sC5b-9) and reduced surface adhesion molecules (CD11b/CD18).[95] Those patients had a 40% reduction in myocardial injury, improved scores on a mini-mental state examination, and a significant reduction in blood loss. There is ongoing investigation in this area, especially in children, to identify anti-adhesion molecules and cytokine inhibitors that limit the response of the body to the stress of bypass.

The inflammatory response to CPB is a cascade of events, with multiple triggers, mediators, and modulators, culminating in end-organ injury and poor outcome. The treatment modalities to this inflammatory response need to be preemptive, multifaceted, and used in combination to prevent the response, blunt its degree of expression, or limit the severity of organ dysfunction.[77,96] In one study, the use of four anti-inflammatory strategies (methylprednisolone, aprotinin,

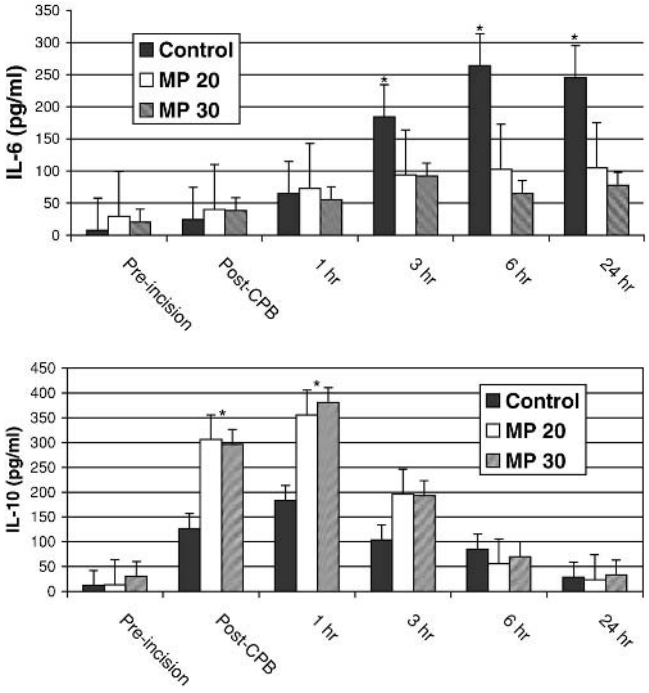


**Fig. 6.7** Serum interleukin-6 (IL-6) (a) and IL-10 (b) concentrations before and after cardiopulmonary bypass (CPB) (*$P < 0.05$). Control, no steroids; MP 20, methylprednisolone 20 mg/kg; MP 30, methylprednisolone 30 mg/kg. Reproduced with permission from Mossad E, Appachi E, Kapural M *et al*. Effects of methylprednisolone on the inflammatory response to cardiopulmonary bypass in children. *Anesth Analg* 2000; **90**: SCA 28.

leukocyte depletion, or HC circuit) effectively attenuated markers of the inflammatory response to ECC, and decreased mortality to 2.3%, compared to a 5.7% risk stratification predicted mortality of the population studied.[96]

## Unanswered questions

Although the etiology of the systemic inflammatory response in cardiac surgery appears to be related to the contact-activation and exposure to the extracorporeal circuit, markers of inflammation have been detected in operations done without bypass. The combined stress of surgical trauma, vascular injury, and anesthesia may contribute significantly to the CPB-induced inflammatory response. In children operated upon with and without CPB, the activation of the alternate complement pathway, cytokines, and adhesion molecule expression were seen in both groups (C3d: 8.16 ± 3.6 vs. 4.12 ± 1.43 mg/L, peak IL-6: 164.4 vs. 277.8 pg/mL, ICAM-1: 241 ± 35 vs. 325 ± 29 pg/mL, E-selectin: 56.1 ± 32.8 vs. 42.4 ± 17.7 pg/mL, CPB vs. no CPB respectively).[97] Avoiding bypass will not completely eliminate the risk of triggering the inflammatory response to surgical stress.[98]

The response to surgical stress and CPB varies significantly between patients, with a wide range of cytokine release and adhesion molecule expression, in response to the same triggers. The patient's preoperative cardiac function appears to contribute to the extent of inflammatory response. Patients with severe end-stage heart failure have elevated serum TNF-α levels, which correlates with their New York Heart Association Status and degree of ventricular dysfunction. The proinflammatory cytokines play an important role in the pathogenesis of heart failure, but may also be triggered and released in the circulation from poor visceral perfusion.[99] The increase in serum IL-6 and TNF-α was more pronounced in patients with depressed preoperative cardiac function and lower ejection fraction.[34]

Similar to other disease states, the inflammatory response may have a spectrum of genetic expression responsible for the variability in response to the stimulus of CPB.[100] The expression of adhesion molecules in response to transient cerebral ischemia can be genetically modulated, and this presents a new target site for therapy of post-ischemic reperfusion injury.[101]

Treatment modalities to the inflammatory response may have side effects that supercede their benefits. Glucocorticoids cause postoperative hyperglycemia, and may aggravate ischemic neuronal damage. Despite effective suppression of the complement and interleukin response, DXM increased the size of cerebral infarct by 10-fold using a middle cerebral artery occlusion model.[102] There is evidence that steroids may worsen neurological outcomes in neonatal patients following a 42-day tapering course of steroids in ventilator-dependent low-birth-weight infants. One-year follow-up showed a significant increase in intracranial abnormalities, and a greater risk of developing cerebral palsy.[103]

The synergistic immunosuppression caused by high-dose MPSS and CPB (suppression of IL-2 helper T-cell function, and increased natural killer cells) may be detrimental.[83] The use of preoperative digestive decontamination, leukocyte depletion, and steroids may also increase the risk for postoperative infection.

Finally, stimulation of the inflammatory response is a complex process necessary for wound healing and immune defense. Therefore the goal of any therapy must not be the complete suppression of the inflammatory response to CPB. In fact, despite an abolished complement and adhesion-molecule response to CPB in a complement-deficient animal model, bypass-associated lung injury still occurrs.[104] Patients with leukocyte adhesion deficiency syndrome (LADS I and II), manifest absence of cell surface expression adhesion molecules, and have a significant risk of recurrent bacterial infections, skin lesions with impaired pus formation, and delayed wound healing. Replacement therapy with granulocyte–macrophage colony-stimulating factor increases cytokine and integrin expression, and improves their clinical condition.[105]

The inflammatory response is a natural defense mechanism which protects the body from foreign antigens and

limits their injury to a local site. However, when the stimulus is excessive, the response becomes exaggerated and harmful, and requires multimodal therapy to limit end-organ injury, but not to abolish it completely.

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# 2 Monitoring

# 7 Vascular access and monitoring

Dean B. Andropoulos

## Introduction

Hemodynamic assessment and treatment through invasive access to the circulation is crucial for every patient undergoing surgery for congenital cardiac disease. Secure, reliable venous and arterial access is necessary for accurate beat-to-beat monitoring of pressures and waveforms, and frequent sampling for blood gases, hematocrit, coagulation studies, and metabolic parameters. In this manner, pathophysiologic processes associated with the patient's underlying disease or the surgical procedure can be detected and treated as early as possible, with the goal of lessening morbidity. Central venous access is critical to directly infuse vasoactive medications and to deliver bolus drugs to achieve the desired hemodynamic effects in as short a time as possible. Large bore peripheral venous access is important to infuse crystalloids, colloids, and blood products with minimal resistance to flow. All of these procedures may be technically difficult, time consuming, and have significant morbidity, especially in newborns or small infants who comprise an increasingly large portion of the patients presenting for surgery. Meticulous attention to the details of vascular access by the pediatric cardiac anesthesiologist can maximize the benefits and minimize the risks to the patient. This chapter will review the techniques of vascular access in congenital cardiac surgery patients, emphasizing newer imaging modalities to guide successful placement, and strategies to avoid complications.

## Venous access

### Peripheral veins

Any visible peripheral vein, and many that are not visible, may be utilized for peripheral venous access. One strategy in pediatric cardiac patients is to cannulate a small superficial vein on the hand or foot with a small catheter (24 or 22 gauge) before induction, or during inhalation induction of anesthesia to facilitate the early administration of muscle relaxants and provide expeditious airway management. Later, with the airway secure and with an immobile patient, larger bore peripheral venous access can be achieved. Recommended sizes are 22-gauge 1″ (25.4 mm) catheters for infants newborn through 6 months, 20-gauge 1.25″ catheters for 6 months to 3 years, 18-gauge 1.5″ for 3–12 years, and 16 or 14-gauge 2″ catheters for teenage or adult patients. Resistance to fluid flow predicted by Pousielle's law is proportional to the length of the catheter and the viscosity of the fluid, and inversely proportional to the fourth power of the catheter radius. When rapidly infusing the more viscous colloids or packed red blood cells, it is important to use a large bore, short catheter in a large peripheral vein. Central venous catheters (CVCs) are usually less desirable for this use due to their smaller lumens and much longer lengths.

Any unusual resistance to infusion through a peripheral intravenous catheter must be immediately investigated. If the catheter is inaccessible, immediately change to a functioning catheter to avoid extravasation. Caustic or vasoactive substances, e.g. calcium chloride, dopamine, epinephrine, etc., should not be injected through peripheral veins unless no other alternative exists because of the risk of extravasation and tissue necrosis—such drugs should all be injected centrally.

The saphenous vein at the ankle is large and in a constant anatomic position in patients of all ages. It can usually be cannulated even if it cannot be seen or palpated. A recommended technique is to apply a tourniquet below the knee, prepare the site antiseptically, and extend the ankle at the medial malleolus with one hand while puncturing the skin at a shallow angle of 10–30° with an angiocatheter 0.5–1.0 cm lateral and about 1 cm inferior to the medial malleolus. Advance the catheter slowly in the groove between the malleolus and the tibialis tendon until blood return through the needle is established. Advance the needle and catheter together several millimeters, then advance the catheter over the needle into the vein with the index finger of the same hand that made the skin puncture, while maintaining extension of the ankle so that the saphenous vein is tethered straight

in its course, to minimize the possibility of puncturing the vein wall due to kinking of the vein. If the vein can be entered but the catheter will not advance its full length into the vein, a small flexible guidewire of 0.015″ (0.381 mm) or 0.018″ (0.457 mm) may be used to assist in cannulation of the saphenous or any other peripheral vein.[1]

Other large peripheral veins may be found in infants and children on the dorsum of the hand, at the wrist superficial to the radial head, as branches of the cephalic or brachial venous system in the antecubital fossa, or on the dorsolateral aspect of the foot. The latter site is especially prominent in many newborns. The principles of the techniques of cannulation are the same as for the saphenous vein, emphasizing extension of the underlying extremity, slow careful cannulation with one hand, and the use of a small guidewire if necessary. Multiple attempts may be required for veins that are not visible or palpable. Often, very small adjustments in direction or depth of cannulation attempts of a millimeter or less result in successful cannulation. It is sometimes necessary to attempt cannulation of several sites, and occasionally it is not possible to obtain peripheral access due to previous indwelling peripheral catheters in chronically ill children.

The external jugular vein is almost always visible in infants and children undergoing cardiac surgery, and is often enlarged and easily cannulated due to elevated right heart pressures. A recommended technique is to choose the larger external jugular vein, place a small rolled towel under the shoulders and place the patient in 30° Trendelenberg position, prepare the site antiseptically, and have an assistant compress the vein gently with pressure just above the clavicle to further distend it. Rotation of the head 45–90° away from the side of cannulation, and slight extension of the neck and traction of the skin over the vein with one hand will tether the vein into a straighter course to facilitate successful cannulation. The vein is punctured high in its visible course with an angiocatheter attached to a syringe filled with heparinized saline, and with the needle bent upwards 10–20° to facilitate the very flat, superficial angle of incidence necessary to cannulate the vein without puncturing its back wall. With constant, gentle aspiration of the syringe, the vein is entered and catheter advanced into the vein. Short peripheral catheters of the same size as recommended above should be used. A catheter advanced too far into the venous plexus beneath the clavicle will often exhibit resistance to the free, gravity driven, flow of fluid, and traction or withdrawal of the catheter a few millimeters may be necessary. External jugular catheters are often difficult to secure to the skin on the neck, and suturing them in place is recommended. This will enhance stability postoperatively as the patient begins moving. One advantage of using the external jugular vein for a peripheral venous catheter is that it is easily accessible under the surgical drapes, and can be frequently monitored for extravasation or kinking of the catheter, which is more common with this site than with the other commonly used peripheral veins.

## Intraosseous access

Intraosseous access to the venous circulation has been described for use during a crisis when no other venous access is available, e.g. during cardiopulmonary resuscitation or shock.[2] Rarely, it may be required for emergency resuscitation in the cardiac operating room, and therefore it is necessary for the pediatric cardiovascular anesthesiologist to be familiar with the technique. Normally this procedure is used only in small children, and the flat surface of the proximal tibia is used. Commercially available 14- or 16-gauge intraosseous needles, or 16-gauge bone marrow aspiration needles may be used. The site is aseptically prepared, the skin is punctured and the outer bony cortex is contacted. With a boring motion, the needle is advanced thought the outer cortex into the marrow space, heralded by a sudden loss of resistance. Infants have active marrow production in long bones, and when the stylet is removed and the needle aspirated bone marrow should appear in the hub. Rapid infusion of 10 ml normal saline without extravasation confirms proper placement, and emergency drugs and fluids may be administered. They reach the central circulation via the bone marrow sinusoids, which connect to the emissary veins from the bony cortex, and then to the larger veins draining into the central circulation. Drugs injected intraosseously, e.g. epinephrine, reach the heart slightly more slowly than when injected into a central vein, but the peak drug levels are not different.[2] Intraosseous needles should be available for the rare crisis in the operating room or intensive care unit (ICU). Intraosseous needles should be replaced as soon as possible with conventional peripheral or central venous access.

## Central venous access

### Umbilical vein

The umbilical vein in the fetus is a conduit to carry oxygenated and detoxified blood from the placenta, through the abdominal wall, through the liver and patent ductus venosus to the inferior vena cava (IVC) and the right atrium (RA) (Fig. 7.1).[3] This vessel can usually be cannulated at the umbilical stump for the first 3–5 days of postnatal life. Passage into the IVC depends on the patency of the ductus venosus, which often exists for the first few days, just as the ductus arteriosus. Sterile technique without a guidewire is used to pass the catheter blindly a premeasured distance. If no resistance to passage is met and free blood return is achieved, the catheter tip is usually in the high IVC or RA, and functions as a CVC. Catheter tip position must be determined by radiography as soon as possible to determine if it is through the ductus venosus into the IVC or the RA. Often, the ductus venosus is not patent, and the catheter tip passes into branches of the hepatic veins, and is visible in the liver radiographically. In this location the catheter must not be used except for

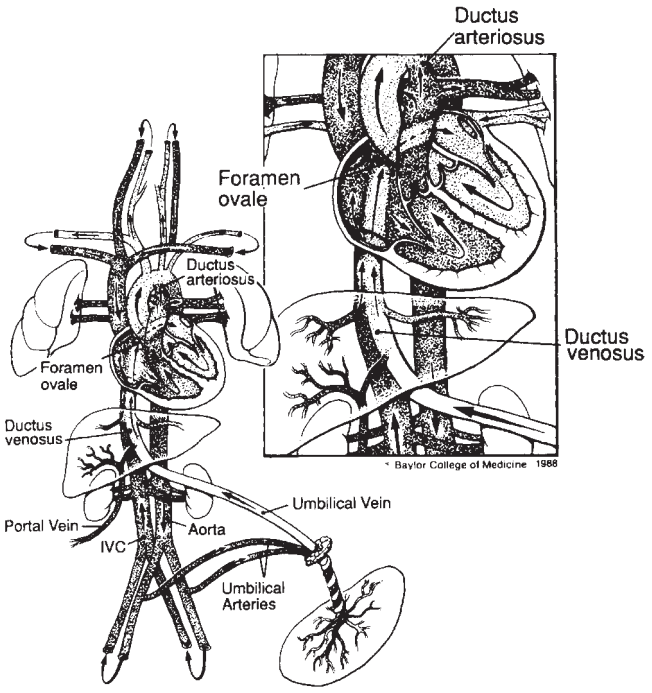


**Fig. 7.1** The fetal circulation. A catheter placed in the umbilical vein should have its tip through the ductus venosus into the inferior vena cava (IVC) at or near its junction with the right atrium. The tip of an umbilical artery catheter should lie at the level of the third lumbar vertebral body, between the origin of the renal arteries and the bifurcation of the aorta. Reproduced with permission from Parellada JA, Guest AL. Fetal circulation and changes occuring at birth. In: Garson A, Bricker JT, Fisher DJ, Neish SR, eds. *The Science and Practice of Pediatric Cardiology*, 2nd edn. Baltimore, MD: Williams & Wilkins, 1998: 349–58.

emergencies. Central venous pressure (CVP) monitoring is inaccurate in this position, and portal vein thrombosis, and liver and intestinal necrosis has been reported with the infusion of hyperosmolar or vasoactive drugs such as sodium bicarbonate and dopamine.[4] An alternative site for central access must be chosen.

Recently, 5 French size (Fr) double and triple lumen umbilical venous catheters (UVCs) have become available.[5,6] The multiple lumens allow concomitant CVP monitoring, vasoactive infusions, and a large 18-gauge lumen for volume infusion. If a single-lumen 5-Fr UVC is present preoperatively, it can be exchanged in the operating room for a triple-lumen catheter using a 70–80 cm long (0.018″ (0.457 mm) or 0.021″ (0.533 mm)) guidewire.

Every neonate with cardiac disease for whom surgery is planned in the first 2 weeks of life should have a multilumen UVC placed as soon as possible, before the ductus venosus closes. The umbilical vein is a central venous access site that is easily cannulated, will not be available for subsequent interventions, and will reduce the time required for vascular access in the operating room. Most importantly, other sites will be spared, i.e. femoral, jugular, and subclavian veins will not be exposed to the risk of thrombosis and permanent occlusion. This complication in the neonate carries a high rate of morbidity and mortality (see below). Umbilical venous catheter cannulation is especially important for patients with planned multiple interventions such as single-ventricle patients, who often require at least two cardiac catheterizations and two additional surgeries. A UVC can be left in place for as long as 14 days if no complications are suspected. When the umbilical vein is utilized, transthoracic right atrial catheters with their attendant risks of bleeding and pericardial or pleural effusions may not be necessary.

## Percutaneous central venous access

Percutaneous central venous access is the standard approach in many cardiac surgery programs.[7] The author recommends using a double lumen central line of the smallest acceptable size for percutaneous CVC placement. For all sites, either audio Doppler or two-dimensional ultrasound is used to facilitate insertion (see discussion below). The larger distal lumen is used for CVP monitoring and drug injection, and the smaller proximal lumen for vasoactive infusions. The smallest available double lumen catheter is currently 4 Fr in size. Superior vena cava (SVC) catheters should be used with caution or not at all in patients weighing less than 4 kg because of the increased risk of thrombosis (see Complications of vascular access section below). Recommended sizes and lengths are shown in Table 7.1.

Sterile technique using gown and wide draping leads to a "cleaner" insertion technique with fewer infectious complications.[8] In cardiac patients, the left side SVC lines should generally be avoided. The risk of erosion/perforation is greater (see below), and 5–15% of patients with congenital cardiac disease have a persistent left SVC, which most often drains either to the coronary sinus or left atrium, neither of which is a desirable location for a catheter tip. So, if left-sided line placement is contemplated, ascertain by echocardiography or cardiac catheterization report the presence of left SVC. If this is not known, choose an alternate site, i.e. femoral or intracardiac (see below).

The following general discussion of the Seldinger technique in pediatric patients can be applied to all percutaneous vascular access sites, either venous or arterial. The Seldinger

**Table 7.1** Recommended central venous catheter sizes and lengths.

| Patient weight | Internal jugular/ subclavian vein | Femoral vein |
|---|---|---|
| < 10 kg | 4 Fr, 2 lumen, 8 cm | 4 Fr, 2 lumen, 12 cm |
| 10–30 kg | 4 Fr, 2 lumen, 12 cm | 4 Fr, 2 lumen, 12–15 cm |
| 30–50 kg | 5 Fr, 2 lumen, 12–15 cm | 5 Fr, 2 lumen, 15 cm |
| 50–70 kg | 7 Fr, 2 lumen, 15 cm | 7 Fr, 2 lumen, 20 cm |
| > 70 kg | 8 Fr, 2 lumen, 16 cm | 8 Fr, 2 lumen, 20 cm |

technique is used for all percutaneous central venous cannulations. After wide sterile skin preparation with iodine or chlorhexidine-based solution, wide draping is carried out, preferably with a clear, fluid-impermeable adhesive aperture drape so that the underlying anatomy is clearly visible. Slow, controlled, careful needle manipulation, especially in small infants, must be emphasized. The slight movement in or out of only 1 mm or less may be enough to prevent passage of the guidewire. It is very important to have the guidewire prepared to insert and immediately accessible when the vein is entered, so the anesthesiologist does not have to look away from the puncture site to reach for the wire on a distant tray, often resulting in enough movement of the needle to prevent successful guidewire passage. After the desired vein is entered, the needle position is fixed by stabilizing it against the patient's body with the heel of the non-dominant hand, and the guidewire is carefully advanced into the RA. The resistance to wire passage should be minimal. Experienced operators learn to recognize the "feel" of a guidewire passing successfully. If any resistance is encountered, the wire must be carefully withdrawn, and another approach made if the needle is still in the vessel, ascertained by free aspiration of blood. Forcing a guidewire in the face of resistance can lead to significant complications. The electrocardiogram (ECG) should be carefully observed as the guidewire is slowly advanced. Premature atrial contractions (PACs) are usually observed as the first guidewire-induced dysrythmia, signifying atrial location. If no PACs are observed, the operator should suspect that the guidewire is not in the atrium. If ventricular extrasystoles are the first observed dysrythmia, especially if they are multifocal in nature, the wire is very likely in an artery, and the left ventricle has been entered retrograde. The wire must be withdrawn immediately, or the position ascertained by imaging, e.g. transesophageal echocardiography (TEE). In difficult or questionable cases TEE may be utilized to visualize the guidewire, and this is strongly recommended before the passage of a vessel dilator or the catheter. After guidewire passage, a very small skin incision with a no. 11 scalpel is made. Finally, careful dilation and catheter passage follows. The dilators in the prepackaged CVC kits are often one size larger than the catheter, i.e. 5-Fr dilator for 4-Fr catheter. This may be undesirable for small infants, and either passage of the catheter without dilation, or use of a dilator the same size as the catheter is preferable to make the smallest possible hole in the vein to minimize bleeding and trauma to the vessel wall, both of which may lead to an increased incidence of thrombosis or vascular insufficiency. Meticulous attention must be paid to blood loss in small infants during catheterization procedures, with direct compression of bleeding puncture sites using the heel of the non-dominant hand, while threading dilators, catheters, etc. Use of an assistant may be necessary in difficult catheterizations. After passage of the catheter to the desired depth, it is secured with sutures and a dressing. If more than 1 cm of catheter is outside the patient, additional suturing or catheter holding devices are necessary.

### Internal jugular vein

The right internal jugular (IJ) vein is the most common site chosen for central venous access in pediatric cardiac surgery. It is large, and runs in close proximity superficial to the carotid artery along most of its length. The primary advantage of using the IJ vein is that it provides a direct route to RA, and thus a high rate of optimal catheter positioning if the vessel can be cannulated. Various studies report only a 0–2% incidence of catheter tip outside the thorax, in contrast to the subclavian route (see below). The primary disadvantage comes from difficulty in cannulation in small infants, who have large heads and short necks, and thus there is difficulty in obtaining the shallow angle of approach necessary to access the vessel. Also some series report a 10–15% incidence of carotid artery puncture in infants and ultrasound studies of neck vessel anatomy reveal the partial or complete overlap of the IJ vein anterior to the carotid artery.[9,10] This site is also not comfortable for some awake infants, and tip migration may be significant with turning the head or flexion/extension of the neck.[11] All insertion techniques involve placing a small roll under the shoulders, using steep Trendelenberg position, and rotating the head no more than 45° to the left—greater rotation will produce more overlap of the IJ vein and carotid artery, and increase the risk of carotid puncture.[12] Recent studies have demonstrated that liver compression and simulated valsalva maneuver also increase the diameter of the IJ vein, possibly increasing the success rate of cannulation.[13]

There are numerous approaches to the IJ vein, some of which are described here (Fig. 7.2):

1. Muscular "triangle" method: puncture at the top of the junction where the sternal and clavicular heads of the sternomastoid muscle meet, lateral to the carotid impulse, directing the needle at the ipsilateral nipple. These landmarks are often not well defined in infants.
2. Puncture exactly halfway along a line between the mastoid process and the sternal notch, just lateral to the carotid impulse.
3. Use the cricoid ring as a landmark, and puncture just lateral to the carotid impulse.
4. Jugular notch technique: puncture just lateral to the carotid impulse, just above the jugular notch on the medial clavicle—a low approach.

An ultrasound technique (see below) should be used to clearly identify the course of the vessel and to detect any significant overlap with the carotid artery. There is no need to use a finder needle for small catheters where the access needle is 20 gauge or smaller. Surface landmarks are often inaccurate for estimating the correct depth of insertion for SVC lines, i.e. locating the tip midway between the sternal

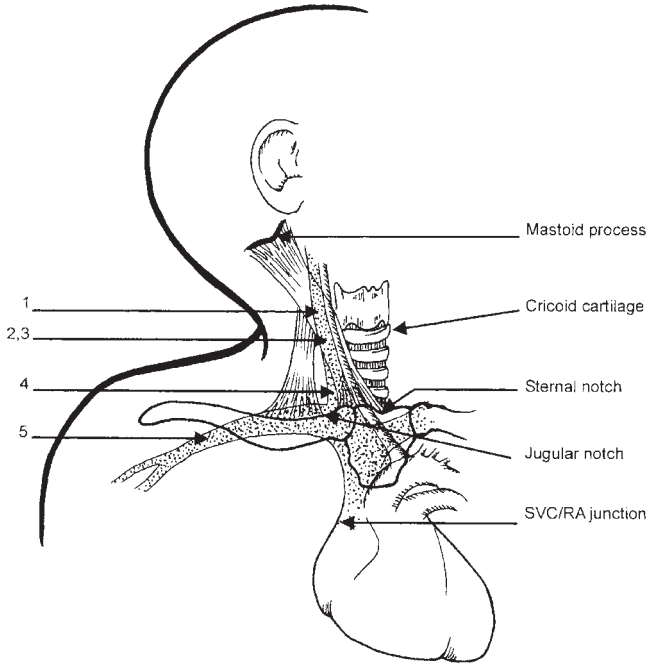


**Fig. 7.2** Sites for central venous cannulation of the superior vena cava (SVC). (1) High approach, midway between mastoid process and sternal notch. (2,3) Middle approach using apex of muscular triangle or cricoid cartilage. (4) Low approach using jugular notch. (5) Lateral approach to subclavian venipuncture. RA, right atrial. Reproduced with permission from Andropoulos DB, Bent ST, Skjonsby B, Stayer SA. The optimal length of insertion of central venous catheters for pediatric patients. *Anesth Analg* 2001; **93**: 883–6.

notch and nipple. See the discussion below for the method to ascertain the correct placement for all sites.

### Subclavian vein

The subclavian vein is positioned immediately behind the medial third of the clavicle.[14,15] Advantages of this route include the subclavian vein's relatively constant position in all ages in reference to surface landmarks, stability, less tip migration with patient movement, and comfort for the awake patient.[16,17] Disadvantages include an incidence of pneumothorax, especially with an inexperienced operator, and an occasional inability to dilate the space between the clavicle and first rib. Also in 5–20% of patients subclavian catheters will enter the contralteral brachiocephalic vein or ipsilateral IJ vein, instead of the SVC.[18]

#### *Technique*

A small rolled towel is positioned vertically between the scapulae, the steep Trendelenberg position is used, and the arms are restrained in neutral position at the patient's sides. This position maximizes the length of subclavian vein overlapping the clavicle, and moves the vein anterior, bringing it in close proximity to the posterior surface of the clavicle.[13] The right subclavian vein should always be the first choice (see below). Turn the head toward the side being punctured (i.e. toward right for the right-sided line). This position will compress the IJ vein on that side and prevent the guidewire from entering it, especially in infants,[19] which may lead to complications such as dural sinus thrombosis.[20] It will not, however, prevent the guidewire from crossing the midline and entering the contralateral brachiocephalic vein.[19] The needle is bent upwards in mid-shaft at a 10–20° angle to assure a very shallow course. In the author's experience the puncture site that is most successful is 1–2 cm lateral to the midpoint of the clavicle,[13] directly lateral from the sternal notch, with the needle directed at the sternal notch. Contact the clavicle first to assure a shallow angle of incidence to minimize the risk of pneumothorax. Then, the needle is "walked" carefully underneath the clavicle and advanced slowly with constant aspiration until blood return is achieved. Advancing the needle only during expiration is recommended to minimize the risk of pneumothorax. Having an assistant manually ventilate the patient will facilitate this process. If not successful, the needle is withdrawn slowly with gentle aspiration, because about 50% of infant subclavian veins are cannulated during withdrawal due to compression or kinking of the vein during needle advancement. Slow, controlled, careful needle manipulation, especially in small infants, must be emphasized. After the vein is entered, advance the guidewire—there should be no resistance. Look for PACs, sometimes only one or two, as a sign that the wire is in the heart. If no dysrythmias are seen, withdraw the wire, rotate it 90° clockwise, and advance it again until PACs are seen. Use a dilator (be very careful not to advance it too far—only far enough to expand the space between the clavicle and first rib) and pass the catheter to the desired depth using the one of the guidelines noted below.

Complications during subclavian catheterization occur when a needle angle of incidence is too cephalad, resulting in arterial puncture, or too posterior, resulting in pneumothorax. If the needle course remains shallow, just underneath the clavicle, and directed straight horizontally at the sternal notch, complications are rare. Advancing the needle too far in infants may result in puncture of the trachea.

### External jugular vein

Advantages of this approach are its superficial location and thus low risk of arterial puncture. The disadvantage is that the younger the patient, the less likely it is that the guidewire will pass into the atrium; the success rate is less than 50% if the patient is less than 1 year of age, and only 59% in patients less than 5 years of age.[21,22] Positioning is the same as the IJ approach, the vein is punctured high in its course, and the guidewire is passed. Often it can be observed turning medially toward the SVC. If no resistance is felt, and PACs are seen, or the guidewire is visualized on the TEE, then passage has been successful. Because of the low success rate of central

cannulation from the external jugular vein approach, our practice is to use the IJ vein first in all patients.

### Femoral vein

The femoral vein has long been used for central venous catheterization in pediatric patients, with no greater infection or other complication rate compared to other sites.[23,24] This is the site of choice for single ventricle patients through the first 6 months of life, because of the increased thrombosis risk in this population. A successful cavopulmonary connection will depend on a patent SVC circulation to provide over half of their pulmonary blood flow. Thus, SVC thrombosis will lead to inadequate drainage from the upper half of the body to the pulmonary circulation and cause SVC syndrome.

The left side is preferred because it avoids the cardiologists' favorite site, the right femoral vein. The single ventricle patient will receive multiple interventions, e.g. catheterizations and surgeries, so preserving vascular patency is extremely important.

*Technique*

The patient is positioned with a rolled towel under the hips for moderate extension. The puncture site should be 1–2 cm inferior to the inguinal ligament (line from the anterior superior iliac spine to the symphysis pubis), and 0.5–1.0 cm medial to the femoral artery impulse, with the needle directed at the umbilicus. Ultrasound guidance (see below) is important for the greatest chance for first pass, atraumatic placement. The guidewire is passed, ensuring no resistance. A vessel dilator is used, then the catheter is passed all the way to the hub to position the tip in the mid-IVC. It is important to puncture the vessel well below the inguinal ligament, to minimize the risk of unrecognized retroperitoneal bleeding. Bleeding below the inguinal ligament is easily recognized and treated with direct pressure.

Several studies have conclusively demonstrated that in the absence of increased intra-abdominal pressure or IVC obstruction, mean CVP as measured in the IVC below the diaphragm is identical to that measured in the RA in patients with and without congenital heart disease.[25–29] The only caveat is in the patient with interrupted IVC with azygous vein continuation into the SVC, a condition commonly encountered in patients with the heterotaxy syndromes. The equivalence of IVC and right atrial pressures under these conditions has not been evaluated, but the catheter can be used as any other central line for infusion of drugs and fluids.

## Direct transthoracic intracardiac vascular access

These are catheters placed by the surgeon directly into the right or left atrial appendages or upper pulmonary vein and threaded into the left atrium, secured by a pursestring suture.[30] Pulmonary artery (PA) catheters are placed high in the right ventricular outflow tract, through the pulmonary valve, or into the main PA. Some institutions employ continuous mixed venous oxygen saturation monitoring with PA catheters.[31] Transthoracic catheters are usually placed during rewarming on cardiopulmonary bypass. They may be used for pressure monitoring or vasoactive drug infusion. Advantages of this approach include saving time before bypass because percutaneous central lines are not placed, tip location is assured by direct vision, and vessel injury from percutaneous catheters is avoided. Disadvantages are that no central access is available before bypass, which may be important for unstable patients, and there is a low risk of cardiac tamponade when these catheters are removed. For this reason many institutions do not remove the mediastinal drainage tube postoperatively until the intracardiac lines are removed, or wait 3–5 days, to minimize the risk of bleeding. This either limits the lifespan of these lines and may leave the patient without adequate venous access, or may delay discharge from the ICU or hospital while waiting to remove these catheters.

A left atrial catheter is frequently utilized when a degree of postoperative left ventricular dysfunction is anticipated, as in complex newborn surgery such as the arterial switch operation, or after mitral valve surgery. Pulmonary artery catheters are utilized in the face of known significant preoperative and anticipated postoperative pulmonary hypertension, i.e. obstructed total anomalous pulmonary venous return, some complete atrioventricular canal patients, or patients with severe mitral valve disease.

In the largest series reported detailing the use and complica-tions of transthoracic catheters, there was overall a 0.6% incidence of serious complications, defined as significant bleeding or catheter retention out of 6690 transthoracic catheters. This risk was greatest for PA catheters (1.07% with three severe cardiac tamponades and one death out of 1680 catheters), followed by left atrial catheters, then right atrial catheters.[30] More recent reports give similar results, documenting a higher risk of bleeding with platelet counts of less than 50 000/L, and a 0.6% incidence of atrial thrombus in a study of 523 transthoracic catheters.[32] To date there are no outcome studies comparing transthoracic and percutaneous catheters.

## Continuous superior vena cava oxygen saturation monitoring after the Norwood operation for hypoplastic left heart syndrome

Continuous monitoring of mixed venous saturation ($SvO_2$) in the SVC using near-infrared oximetric catheters has recently been demonstrated to be very useful in post-bypass management of neonates undergoing the Norwood operation for hypoplastic left heart syndrome.[33] Therapy is directed at maintaining $SvO_2$ at 50% or greater, and when this goal is achieved as part of an overall management strategy, 30 day survival has been greater than 95% in recent reports. $SvO_2$ less

than 30% confers a significant risk of anaerobic metabolism and increased risk for poor outcome.

These catheters are placed by the surgeon transthoracically during rewarming, a short distance into the SVC. They remain in place for 2–5 days, and are removed exactly like other transthoracic catheters. Complication rate, e.g. bleeding or thrombosis, has been zero in the series reported thus far.

## Tunneled Broviac type percutaneous or intracardiac lines

In patients with difficult venous access who are anticipated to have a prolonged postoperative course, tunneled silicone catheters may be used to ensure necessary access. These can be placed percutaneously in standard fashion, i.e. in subclavian, jugular, or femoral veins, by cutdown, or placed transthoracically into the RA, as with a standard transthoracic catheter, but with a subcutaneous tunnel placing the skin exit site several centimeters from the chest wall entry site. These catheters often necessitate an additional anesthetic for removal, but in certain patients are cost effective, and preserve other access sites for future interventions, and are less thrombogenic than standard polyurethane transthoracic catheters.[34]

## Ascertainment of correct position of CVCs

Correct placement of CVCs is essential to prevent complications (see below), and to give accurate intravascular pressure information. The tip of a CVC should lie in the SVC, parallel to the vein wall, to minimize the perforation risk. Many authorities recommend placement in the upper half of the SVC, where the tip will be above the pericardial reflection in most patients, thus minimizing the risk of tamponade if perforation occurs.[35] In small patients the SVC is often short, i.e. 4–5 cm total length, and the pericardium is usually opened during cardiac surgery in these patients, providing drainage in case of perforation. In addition, the risk of arrhythmias is present as well with a catheter positioned in the RA. Various methods to determine correct placement are discussed below.

### Radiography

The chest radiograph is considered the gold standard for correct placement, but obtaining and processing a chest radiograph is time consuming, costly, and usually not necessary in the operating room. A chest radiograph should be obtained immediately postoperatively (Fig. 7.3), position of intravascular catheters ascertained, and adjustments made by the anesthesiologist if necessary. It is important to note that an anteroposterior radiograph may miss malposition in one of several ways. The most common is for an SVC catheter to be directed posteriorly down the azygous vein, which may not be detected by anteroposterior radiograph alone.

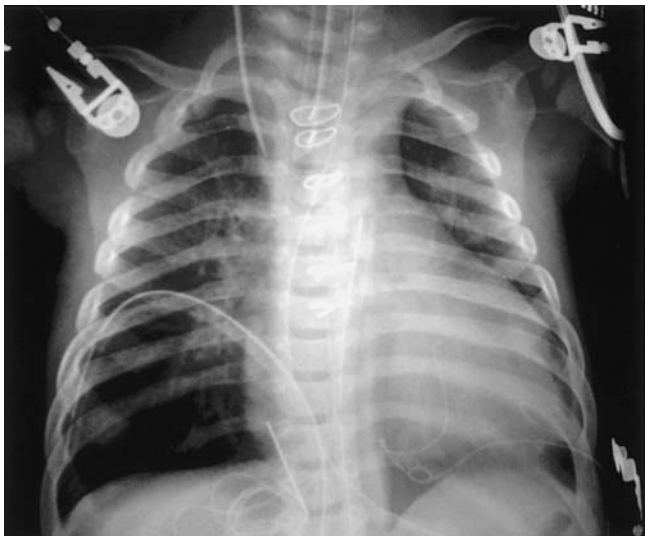

**Fig. 7.3** Postoperative chest radiograph with the tip of a right internal jugular vein catheter in the mid-superior vena cava.

### Transesophageal echocardiography

Transesophageal echocardiography is used for many congenital heart operations. Catheter tips and guidewires are easily imaged with TEE (Fig. 7.4), and one recent study using TEE-guided CVC placement demonstrated a 100% success rate for correct placement in the SVC when TEE was used, vs. 86% when surface anatomical landmarks were used in infants and children undergoing congenital heart surgery.[18] The TEE probe is placed before CVC attempts are made, and the SVC–right atrial junction in the 90° plane is imaged. When the vessel is punctured and the guidewire passed, it should be visualized passing from the SVC into the RA. Then the catheter is passed to its full length, the guidewire removed, and the tip of the CVC identified. Flushing the CVC with saline creates an easily visible stream of contrast which identifies the tip. The CVC is then pulled back until it is above the RA, in the distal SVC 1–2 cm above the crista terminalis. Using this technique, immediate, accurate confirmation of placement is obtained before final securing, and before the surgery. The proximal SVC, which is more than 2 cm above the RA, is difficult to image using TEE, so this method is most accurate in placing CVC in the distal SVC. Also, the commonly accepted radiographic SVC–RA junction is often higher than the SVC–RA junction noted by TEE.[18]

### Electrocardiographically-guided placement

The intravascular ECG may be used in children to guide correct CVC placement.[33,36,37] Either a 0.9% or 3% saline-filled lumen with special ECG adaptor, or a guidewire within the lumen attached to a sterile alligator clip and leadwire substituted for the right arm surface ECG lead may be used. Entry

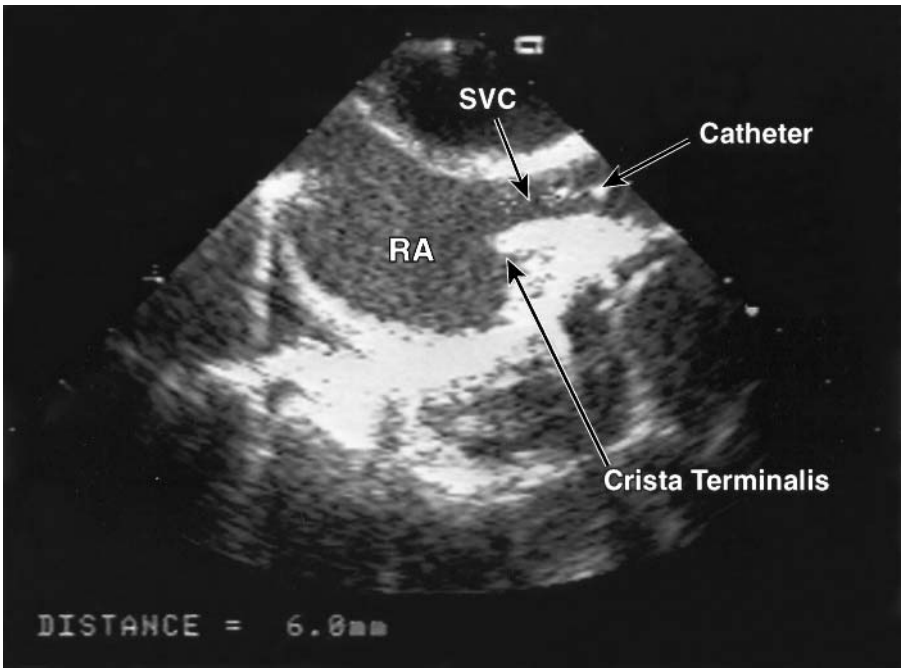


**Fig. 7.4** Transesophageal echocardiographic image of the superior vena cava (SVC)–right atrial (RA) junction in sagittal plane in an infant. The tip of the right internal jugular catheter is in the SVC, 6 mm above the RA. Reproduced with permission from Andropoulos DB, Stayer SA, Bent ST. A controlled study of transesophageal echocardiography to guide central venous catheter placement in congenital heart surgery patients. *Anesth Analg* 1999; **89**: 65–70.

of the catheter tip into the RA is signified by the sudden appearance of a P atriale, an exaggerated, large, upright P wave. The catheter tip is then pulled back 1–2 cm into the desired position in the SVC. Success rate for proper placement in the reported studies has been 80–90%, but there have been no controlled studies in children comparing this method to other methods. This method also requires special equipment not always available.

### Height- and weight-based formulae

A recent large study of CVC placement in infants and children undergoing congenital heart surgery developed formulae for correct insertion depth based on height and weight (Table 7.2).[38] Central venous catheters were inserted in the right IJ or subclavian vein and the postoperative radiograph studies were used to determine the tip position in reference to the SVC–RA junction. The length of catheter inside the patient was added to this distance to determine the position of the SVC–RA junction, and formulae developed that would predict placement above the RA, in the SVC 97.5% of the time (95% confidence interval 96–99%). All catheter tips predicted to be in the atrium using this data would be high in the RA within 1 cm of the SVC–RA junction, minimizing any perforation risk. The formulae are simple and easily implemented because weight and height are known on all patients undergoing cardiac surgery.

For patients with height less than 100 cm: (Height ÷ 10)—1 cm is the correct insertion distance (i.e. a 75-cm patient would have the catheter secured at 6.5 cm for either the IJ or the subclavian route).

**Table 7.2** Recommended length of superior vena cava central venous catheter (CVC) insertion in pediatric patients based on weight: right-sided internal jugular or subclavian.

| Patient weight (kg) | Length of CVC insertion (cm) |
|---|---|
| 2.0–2.9 | 4 |
| 3.0–4.9 | 5 |
| 5.0–6.9 | 6 |
| 7.0–9.9 | 7 |
| 10.0–12.9 | 8 |
| 13.0–19.9 | 9 |
| 20.0–29.9 | 10 |
| 30.0–39.9 | 11 |
| 40.0–49.9 | 12 |
| 50.0–59.9 | 13 |
| 60.0–69.9 | 14 |
| 70.0–79.9 | 15 |
| 80 and above | 16 |

For patients with height 100 cm or greater: (Height ÷ 10)—2 cm is the correct distance.

The caveats to this seemingly useful technique are that for the IJ vein, the puncture site was high, exactly midway between the mastoid process and the sternal notch; and for the subclavian, a puncture site 1–2 cm lateral to the midpoint of the clavicle. If different puncture sites are utilized, the operator must adjust the formulae accordingly. Also, the formulae have not yet been evaluated for accuracy in a prospective fashion.

## Percutaneously inserted central catheters

Percutaneously inserted central catheters (PICCs) have been utilized in the neonatal nursery for more than a decade, and have become standard practice for ill newborns expected to require prolonged venous access. The complication rate for these catheters is very low, and they are usually relatively easy to insert into the central circulation via the antecubital, saphenous, scalp, hand, axillary, or wrist veins, when placed by experienced, skilled personnel. Such personnel include nurses[39] or physicians placing them at the bedside, or in the interventional radiology suite[40] with ultrasound and fluoroscopic guidance. The key to successful placement is early access, before all large visible superficial veins are injured from attempts at peripheral intravenous placements. For this reason, the PICC line is optimally placed in the critically ill newborn with congenital heart disease in the first 12–24 hours after admission. Like all CVCs they occasionally cause complications such as perforation of the atrium, or embolization of a portion of the catheter.[41] The infection rate is very low.

***Technique***

A suitable vein should be identified. The branches of the basilic vein on the medial half of the antecubital fossa offer the highest success rate because of the large size and direct continuation with the axillary and subclavian veins. The cephalic vein tributaries can also be used, but are less likely to pass into the axillary vein. Other sites, e.g. the saphenous, hand, and scalp veins are cannulated as for a peripheral intravenous catheter. The site is prepared and draped, and appropriate local anesthesia and/or intravenous analgesia are administered. The vein is entered using a large breakaway needle or angiocatheter, and a 2-Fr non-styleted silicone catheter flushed with heparinized saline is passed with forceps a distance measured from the entry site to the SVC–RA junction. Continued easy passage without resistance, and continuous ability to aspirate blood signify proper placement. A radiograph, with injection of diluted contrast if needed, should be obtained prior to use. Proper catheter tip position is in the SVC or IVC, not in the RA. Occasionally the PICC line will not pass centrally, i.e. into the intrathoracic portion of the subclavian vein or further, or into the IVC. In this case it should be considered no differently to that of a peripheral venous line. For central PICC lines, any centrally delivered medication or fluid may be used, i.e. parenteral nutrition, dopamine, CaCl, etc. The 2-Fr PICC lines are too small for rapid fluid boluses or blood products, therefore inadequate as the sole pre-bypass access for cardiac surgery. Alternatively, 3-Fr PICC lines, placed with the aid of ultrasound and fluoroscopic guidance with a guidewire in the interventional radiology suite, may be used in newborns with caution, especially in the SVC position, because of the risk of thrombosis.[42] In older infants and children these larger catheters are preferred.

**Table 7.3** Recommended arterial catheter sizes: radial, dorsalis pedis (DP), posterior tibial (PT), and brachial arteries.

| Weight | Radial/DP/PT arteries | Brachial artery |
|---|---|---|
| < 2 kg | 24 g | Not recommended |
| 2–5 kg | 22 g | 24 g |
| 5–30 kg | 22 g | 22 g |
| > 30 kg | 20 g | 22 g |

**Table 7.4** Recommended arterial catheter sizes: femoral and axillary arteries.

| Weight | Femoral/axillary arteries |
|---|---|
| < 10 kg | 2.5 Fr, 5 cm long |
| 10–50 kg | 3 Fr, 8 cm long |
| > 50 kg | 4 Fr, 12 cm long |

# Arterial access

Tables 7.3 and 7.4 display recommended catheter sizes for arterial access based on site and patient weight.

## Radial artery

This is the preferred location in the newborn if an umbilical artery line is not possible or needs to be replaced, and in virtually all other patients. Placement on the same side of an existing or planned systemic to PA shunt is avoided, e.g. a right-sided modified Blalock–Taussig shunt.

***Technique***

The wrist is extended slightly with rolled gauze, the fingers taped loosely to an armboard, with the thumb taped separately in extension to tether the skin surface over the radial artery. An angiocatheter flushed with heparinized saline is used to increase the rapidity of flashback of blood into the hub of the needle after aseptic preparation. The skin is punctured at a 15–20° angle at the proximal wrist crease at the point of maximal impulse of the artery. Palpation is the usual method of identifying the artery, but audio Doppler localization can be helpful if the pulse is weak. Lighter planes of anesthesia provide stronger pulses and increase the success rate of cannulation. The first attempt, before any hematoma formation, always yields the greatest chance for success, so the operator should optimize conditions, e.g. positioning, lighting, and identification of the vessel. Puncture of the artery with the needle is signified by brisk flashback. The needle and catheter are then advanced 1–2 mm into the artery, and an attempt is made to thread the catheter primarily over the needle its full length into the artery. Threading should have minimal resistance and is signified by the continuing flow of blood into hub of needle. If threading is not successful, the

needle is replaced carefully in the angiocatheter, and the needle and catheter can be passed through the back wall of artery. Then the needle is removed, and a 0.015″ guidewire with flexible tip can be used to assist threading of catheter. The catheter is pulled back very slowly, and when vigorous arterial back flow occurs, the guidewire is passed, and the catheter threaded over the guidewire into the artery. Minimal resistance signifies successful threading. If unsuccessful, further attempts may be made at the same site, or at slightly more proximal sites to avoid areas of arterial spasm, thrombosis, or dissection. The circulation distal to the catheter should be assessed by inspection of color and capillary refill time of fingertips and nailbeds, and quality of signal from a pulse oximeter probe. A recommended technique for securing the catheter is with a clear adhesive dressing and transparent tape so that the insertion site and hub of the catheter are visible at all times.

## Femoral artery

The superficial femoral artery is a large vessel that is easily accessible in almost all patients,[43] and is a logical second choice when radial arterial access is not available. In infants, especially patients with trisomy 21, transient arterial insufficiency develops in up to 25% of patients after arterial catheterization when 20-gauge (3-Fr) catheters are used.[43] For this reason, in the author's institution, the smallest commercially available catheter, 2.5 Fr (equal to 21 gauge), is used in patients weighing less than 10 kg (see Table 7.4).

***Technique***

A small towel is placed under the patient's hips to extend the leg slightly to a neutral position. Slight external rotation, with the knees restrained by taping to the operating room bed fixes adequate position. After sterile preparation and draping, the course of the superficial femoral artery is palpated and punctured 1–2 cm inferior to the inguinal ligament, to avoid puncturing the artery above the pelvic brim, where a retroperitoneal hematoma could develop. If the pulse is weak, as in the case of aortic arch obstruction, use of audio Doppler effectively identifies the course of the vessel. The puncture technique varies, and may include direct puncture with an angiocatheter, or Seldinger technique using the needle in the commercially supplied kit, or a 21-gauge butterfly needle with the extension tubing removed. All of these are flushed with heparinized normal saline to increase the rapidity of flashback. A small flexible guidewire, 0.015″ (0.381 mm) or 0.018 (0.457 mm)″, is used. It is normally possible to thread a polyethylene catheter over the guidewire without making a skin incision, and under no circumstances is dilating the tract and artery with a dilator recommended, which could cause arterial spasm, dissection, or bleeding around the catheter if the puncture site is large. The catheter is secured by suturing around the entry site of catheter and wings around the hub. Distal perfusion is immediately assessed, and a pulse oximeter probe is placed on the foot for continuous monitoring and early warning of arterial perfusion problems.

## Brachial artery

The brachial artery has been successfully used for monitoring for cardiac surgery in children,[44] but using this site for arterial monitoring should generally be avoided because it has poor collateral circulation compared to the radial, femoral, and axillary arteries. Theoretically, there should be a higher incidence of arterial insufficiency with this site, but no studies document this. It should only be used in situations when there are limited other options, e.g. a right upper extremity arterial line is required to monitor pressure during cross-clamping for repair of coarctation of the aorta, or during bypass for aortic arch hypoplasia or interruption.

***Technique***

A 24-gauge catheter should be used in patients under 5 kg. The arm is restrained in neutral position on an armboard, and the arterial impulse is palpated above the elbow crease, well above the bifurcation into the radial and ulnar arteries. Cannulation proceeds as for the radial artery. Meticulous attention to distal perfusion must be paid at all times, and the catheter removed for any signs of ischemia. Pulse oximeter monitoring of distal pulses will provide early detection of perfusion problems. The catheter should be removed or replaced with a catheter in a site with better collateral circulation as soon as possible after the repair.

## Axillary artery

The axillary artery is large and well collateralized, and several series in critically ill children have demonstrated this to be a viable option with a low complication rate when other sites are not accessible.[45,46] However, given the potential morbidity of an ischemic arm and hand, and the theoretical problem of intrathoracic bleeding, this puncture site should be considered a site of last resort when there are limited options.

***Technique***

The arm is abducted 90°, and extended slightly at the shoulder to expose the artery. The artery is palpated high in the axilla, and punctured using an angiocatheter, then exchanged over a guidewire for a longer catheter, or by primary Seldinger technique. A catheter that is too short (e.g. 22-gauge 1″ (25.4 mm) long) will often be pulled out of the vessel with shoulder extension. Therefore, the shortest recommended catheter is 1.97″ (5 cm) long (see Table 7.4). Careful attention must be paid to distal perfusion, as with the brachial artery. Tip position should ascertained by chest radiograph, and should not lie inside the first rib. The proximity to the

brachiocephalic vessels makes it imperative that the catheter be flushed very gently by hand after blood draws, and that no air bubbles or clots ever be introduced, because of the risk of retrograde cerebral embolization.

## Umbilical artery

The umbilical artery is accessible for the first few days of life, and is the site of choice for newborns requiring surgery in the first week of life (see Fig. 7.1). The complication rate is low with low positioning, i.e. tip at the level of third lumbar vertebral body below take off of the renal arteries. The catheter can be left in place for 7–10 days. A relationship to intestinal ischemia and necrotizing colitis has been demonstrated,[47] and enteral feeding with an umbilical artery catheter (UAC) in place is controversial.[48] Umbilical catheters are most commonly inserted by the neonatal staff in the delivery room or neonatal ICU shortly after birth. The technique involves cutting off the umbilical stump with an umbilical tape encircling the base to provide hemostasis, dilating the umbilical artery, and blindly passing a 3.5-Fr catheter a distance based on weight, then assessing position as soon as possible radiographically. Lower extremity emboli, vascular insufficiency, and renal artery thrombosis have all been described;[49] however, the overall risk is low and this site is highly desirable because it is a large central artery yielding accurate pressure monitoring[50] during all phases of the surgery, and preserves access for future interventions.

## Temporal artery

The superficial temporal artery at the level just above the zygomatic arch is large and easily accessible in newborns, particularly the premature infant. It was widely used in the 1970s in neonatal nurseries,[51] but rapidly fell out of favor with the realization that significant complications, e.g. retrograde cerebral emboli, were disturbingly common.[52,53] It should only be used when a brachiocephalic pressure must be measured for the surgery in the face of an aberrant subclavian artery, so that the only way to measure pressure during cross-clamping or on bypass is via direct aortic pressure, or temporal artery pressure. Examples are coarctation of the aorta, aortic arch interruption or hypoplasia, with aberrant right subclavian artery that arises distal to the area of aortic obstruction.[54] The catheter must be used only during the case, blood drawing and flushing should be minimized, and it must be removed as soon as possible after the repair.

***Technique***

A 24-gauge catheter is used for newborns. The artery is palpated just anterosuperior to the tragus of the ear, just superior to the zygomatic arch. A very superficial angle of approach, i.e. 10–15°, is used, and the artery is cannulated in the same way as described for the radial artery.

## Dorsalis pedis/posterior tibial arteries

Superficial foot arteries should not be used for bypass cases, because of the well-known peripheral vasoconstriction and vasomotor instability in the early post-bypass period, which is more pronounced with these arteries than with the radial artery. It is frequently not possible to obtain an accurate arterial pressure waveform in the early post-bypass period. These arteries may be used for non-bypass cases, and in the ICU.

***Technique***

Dorsalis pedis—the foot is plantar flexed slightly to straighten the course of the artery, which is palpated between the second and third metatarsal. A superficial course is taken and the artery cannulated. Posterior tibial—the foot is dorsiflexed to expose the artery between the medial malleolus and the Achilles' tendon. The artery is often deep to the puncture site, so a steeper angle of incidence is required.

## Ulnar artery

The ulnar artery should only be used as a last resort in a desperate situation when other options are not available, because its use is only considered when radial artery attempts have been unsuccessful or thrombosed by past interventions. There is a high risk of ischemia of the hand if both the radial and ulnar artery perfusion is significantly compromised. Despite this, one series of 18 ulnar artery catheters in critically ill infants and children had an ischemia rate not different from radial and femoral artery catheters—5.6%.[55]

## Arterial cutdown

Cutdown of the radial artery is a reliable and often efficient method to establish access for congenital heart surgery. Some centers use this method as the first and primary method of securing arterial access, while others only resort to it when all other attempts fail. Despite the speed and ease of access for a cutdown, available literature indicates a higher rate of bleeding at the site, infection, failure, distal ischemia, and long-term vessel occlusion compared to percutaneous techniques.[56,57] It is for these reasons that the author's institution uses cutdowns only when percutaneous methods have failed.

***Technique***

The arm is positioned as for percutaneous radial catheterization. After surgical preparation and draping, an incision is made at the proximal wrist crease between the styloid process and the flexor carpi radialis tendon, either parallel or perpendicular to the artery. Sharp and blunt dissection is carried out until the artery is identified, and it is isolated with a heavy silk suture, vessel loop or right angle forceps. It is no longer considered necessary to ligate the artery distally to prevent bleeding, and in fact the artery may remain patent

after a cutdown if not ligated distally. The simplest and very effective technique is to cannulate the exposed artery directly with an angiocatheter, in the same manner as for percutaneous radial artery catheter placement. The catheter is then sutured to the skin at its hub, and the incision closed with nylon sutures on either side of the catheter. Removal entails cutting the suture at the hub of the catheter, removing the catheter, and applying pressure for a few minutes until any bleeding stops. The remaining skin sutures can be removed at a later date.

## Percutaneous pulmonary artery catheterization

Percutaneous PA catheterization has a limited role in congenital heart surgery for several reasons. The small size of many patients precludes placement of adequately sized sheaths and catheters, and most patients have intracardiac shunting, invalidating results of standard thermodilution cardiac output measurements and confusing mixed venous oxygen saturation ($SvO_2$) measurements. In addition, the frequent need for right-sided intracardiac surgery makes PA catheterization undesirable. Thus, when PA pressure or $SvO_2$ monitoring is indicated, transthoracic PA lines are the most common method in congenital heart surgery.

The most common indications for percutaneous PA catheterization in congenital heart surgery are in patients over 6 months of age able to accept a 5- or 6-Fr introducer sheath in the femoral or IJ vein. Patients having surgery on left-heart structures who do not have intracardiac shunting, who are at risk for left ventricular dysfunction, or pulmonary hypertension may benefit from the information available from a PA catheter. Examples include aortic surgery, aortic valve repair or replacement, subaortic resection or myomectomy for hypertrophic cardiomyopathy, mitral valve repair or replacement.

### *Technique*[58]

An oximetric catheter is recommended. Commercially available models are 5.5 or 8.5 Fr, and thus require a 6- or 9-Fr sheath, respectively. The 5.5-Fr catheter should be used in patients under 50 kg, and the 8.5 Fr in patients over 50 kg. The sheath is placed into the IJ, femoral, or subclavian veins as described above. The preferred sites of insertion are: (i) right IJ; (ii) left subclavian; or (iii) femoral vein because of the direct path and curvature of the catheter. If an oximetric catheter is used, it is calibrated prior to insertion. The balloon integrity should be tested before insertion by inflating the recommended volume of air or carbon dioxide, and the sterility sleeve is inserted before placement. The PA and CVP ports are connected, flushed, and calibrated before insertion. The PA catheter is inserted 10–15 cm with the balloon deflated, depending on patient size. The balloon is inflated, and the catheter advanced slowly toward the tricuspid valve, whose position is indicated by enlarging V waves on the CVP trace. The catheter is advanced through the tricuspid valve by advancing during diastole until the characteristic right ventricular trace is visible, with no dichrotic notch, and a diastolic pressure of 0–5. Then, the catheter is advanced carefully through the pulmonary valve during systole, until the characteristic PA tracing is visible, with a dichrotic notch and higher diastolic pressure. The catheter is then advanced gently until the pulmonary capillary wedge pressure (PCWP) tracing is obtained, at which time the balloon is deflated so the PA tracing rapidly returns. Difficulty with advancing through the pulmonary valve may be assisted by counterclockwise rotation of the catheter while advancing, positioning the patient right side down and giving a fluid bolus, or by using TEE to visualize the tip and guide subsequent attempts.[59] The catheter must not be left in the wedge position except during brief periods because of the risk of PA rupture and lung ischemia distal to the catheter. During bypass, the catheter can be pulled back several centimeters to reduce the risk of perforation on bypass.

Information obtainable with a PA catheter includes: RA, PA, and PCW pressures. In the absence of mitral valve stenosis or pulmonary venous or arterial hypertension, PA diastolic ~ PCWP ~ left atrial pressure (LAP) ~ left ventricular end-diastolic pressure, which is proportional to left ventricular end-diastolic volume, the classic measure of preload.[60] Despite the presence of pulmonary hypertension or residual mitral stenosis (diagnosed with postoperative TEE), information from the PA catheter can still be used to direct therapy.

The cardiac index may be measured by standard thermodilution methods, with care taken to input the correct calculation constant into the monitor software according to the catheter size and length, and volume and temperature of injectate. The average of three consecutive injections made in rapid succession at the same point in the respiratory cycle, i.e. expiration, will optimize conditions to achieve an accurate measurement during steady state conditions. Vascular resistances and stroke volume can also be calculated, using the formulae in Table 7.5.[61,62]

Hemodynamic data represent only half of the information available from an oximetric PA catheter. The other half consists of oxygen delivery and consumption measurements and calculations, which may also be used to guide therapy in the critically ill patient with low cardiac output syndrome. In the author's opinion, if the decision has been made to incur the risk and expense of percutaneous PA catheterization, the catheter should be used to its full extent by obtaining all of the information possible to direct therapy, which includes measurement of oxygen delivery and consumption (Table 7.6).[61,62] They require either measurement of mixed venous and systemic arterial saturations from blood samples from the tip of the PA catheter and arterial line (measured by cooximetry, not calculated), or substitution of these values with $SvO_2$ from the oximetric catheter (a valid assumption if

**Table 7.5** Derived hemodynamic parameters.

| Formula | Normal values | | |
|---|---|---|---|
| | **Adult** | **Infant** | **Child** |
| $CI = \frac{CO}{BSA}$ | 2.8–4.2 L/min/m$^2$ | 2–4 | 3–4 |
| $SVI = \frac{SV}{BSA}$ | 30–65 mL/beat/m$^2$ | 40–75 | 40–70 |
| $LVSWI = \frac{1.36 \cdot (MAP - PCWP) \cdot SVI}{100}$ | 45–60 g/m/m$^2$ | 20–40 | 30–50 |
| $RVSWI = \frac{1.36 \cdot (PAP - CVP) \cdot SI}{100}$ | 5–10 g/m/m$^2$ | 5–11 | 5–10 |
| $SVRI = \frac{(MAP - CVP) \cdot 80}{CI}$ | 1500–2400 dyn · s · cm$^{-5}$ · m$^2$ | 900–1200 | 1300–1800 |
| $PVRI = \frac{(PAP - PCWP) \cdot 80}{CI}$ | 250–400 dyn · s · cm$^{-5}$ · m$^2$ | < 200 | < 200 |

*BSA*, body surface area; *CI*, cardiac index; *CO*, thermodilution cardiac output; *CVP*, central venous pressure; *LVSWI*, left ventricular stroke work index; *MAP*, mean arterial pressure; *PAP*, pulmonary artery pressure; *PCWP*, pulmonary capillary wedge pressure; *PVRI*, pulmonary vascular resistance index; *RVSWI*, right ventricular stroke work index; *SI*, stroke index; *SV*, stroke volume; *SVI*, stroke volume index; *SVRI*, systemic vascular resistance index.

**Table 7.6** Derived oxygen delivery/consumption parameters.

| Formula | Normal values | | |
|---|---|---|---|
| | **Adult** | **Infant** | **Child** |
| Arterial $O_2$ content<br>$Cao_2 = (1.39 \cdot Hb \cdot Sao_2) + (0.0031 \cdot Pao_2)$ | 18–20 mL/dL | 15–18 | 16–18 |
| Mixed venous $O_2$ content<br>$Cvo_2 = 1.39 \cdot Hb \cdot Svo_2 + 0.0031 \cdot Pvo_2$ | 13–16 mL/dL | 11–14 | 12–14 |
| Arteriovenous $O_2$ content difference<br>$avDo_2 = Cao_2 - Cvo_2$ | 4.0–5.5 mL/dL | 4–7 | 4–6 |
| Pulmonary capillary $O_2$ content<br>$Cco_2 = 1.39 \cdot Hb \cdot Sco_2 + 0.0031 \cdot Pco_2$ | 19–21 mL/dL | 16–19 | 17–19 |
| Pulmonary shunt fraction<br>$Q_s/Q_t = 100 \cdot (Cco_2 - Cao_2)/(Cco_2 - Cvo_2)$ | 2–8% | 2–8 | 2–8 |
| $O_2$ delivery index<br>$Do_2I = 10 \cdot CO \cdot Cao_2/BSA$ | 450–640 mL/min/m$^2$ | 450–750 | 450–700 |
| $O_2$ consumption index<br>$Vo_2I = 10 \cdot CO \cdot (Cao_2 - Cvo_2)$/BSA | 85–170 mL/min/m$^2$ | 150–200 | 140–190 |

*BSA*, body surface area; $Cao_2$, oxygen content of arterial blood; $Cco_2$, oxygen content of pulmonary capillary blood; $Cvo_2$, oxygen content of mixed venous blood; *CO*, thermodilution cardiac output; $Do_2I$, $O_2$ delivery index; Hb, hemoglobin; $Pao_2$, partial pressure of oxygen in arterial blood; $Pco_2$, partial pressure of oxygen in pulmonary capillary blood; $Pvo_2$, partial pressure of oxygen in mixed venous blood; $Q_s$, pulmonary shunt blood flow; $Q_t$, total pulmonary blood flow; $Sao_2$, measured arterial oxygen saturation; $Sco_2$, measured pulmonary capillary oxygen saturation; $Svo_2$, measured mixed venous oxygen saturation, $Vo_2I$, $O_2$ consumption index.

properly calibrated), and the pulse oximeter value instead of measured systemic saturation. There are data from adult and pediatric critical care literature suggesting that the ability to increase and maximize both oxygen delivery and consumption may improve outcome, and is a predictor of survival from critical illness, including postoperative cardiac surgery.[63–66]

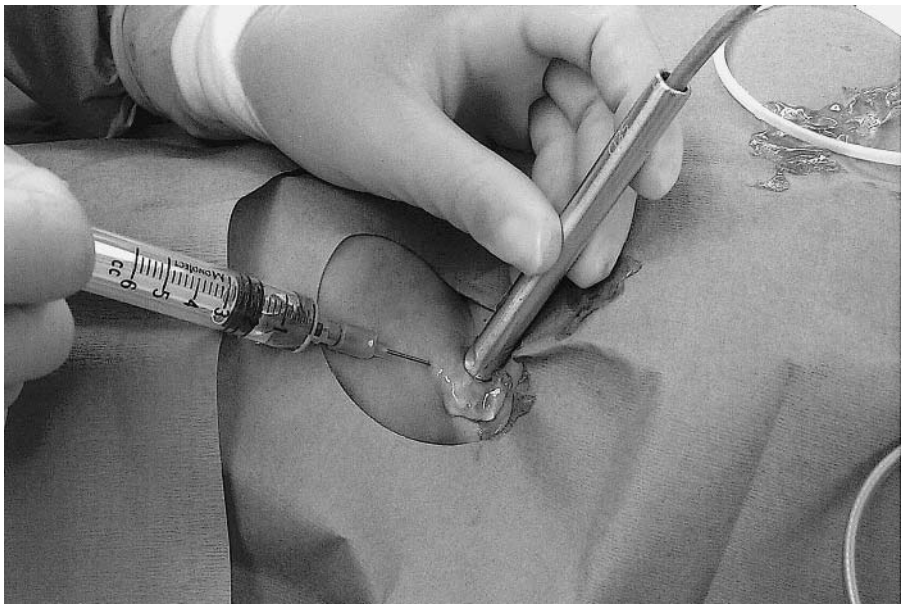

**Fig. 7.5** Audio Doppler-guided puncture of the internal jugular vein in an infant.

## Ultrasound guidance for vascular access in congenital heart surgery

Numerous studies find ultrasound guidance, either two-dimensional visual ultrasound,[67] or audio Doppler ultrasound, improves the outcome of central venous cannulation, in both children and adults.[68,69] Use of these methods leads to fewer attempts, decreased insertion time, fewer unintended arterial punctures, and fewer unintended arterial catheter placements. The consensus of many experts in the field of vascular access is that use of these guidance techniques should be considered the standard of care.

A 9.2 MHz pencil thin audio Doppler probe can be gas sterilized and reused (Fig. 7.5). The probe is applied to the site, and the course of the artery and vein are ascertained by their characteristic audio profiles—high pitched, intermittent, systolic flow for the artery, and a low-pitched, continuous venous hum for the vein. The probe is centered over the loudest signal, perpendicular to the skin surface, and the vessel is punctured exactly in the axis of the center of the probe. A "pop" followed by the continuous sound of blood aspiration can often be heard when the vessel is entered. The guidewire, dilator, and catheter are then passed as above. A variation of the audio Doppler technique is a device with the Doppler probe within the needle.[70] However, these needles are expensive, direct comparison has not shown them to be superior to visual ultrasound for cannulation, and because the lumen of the needle is partially occluded with the Doppler probe, flashback of blood is slow and unreliable.

Two-dimensional echocardiography, either in the form of commercially available devices for CVC cannulation only (Site-Rite), or surface probes on standard echocardiography machines, can be used to image large vessels. The color Doppler feature on the latter may be particularly useful to identify desired vessels during difficult vascular access. The desired vessel is localized, e.g. the IJ vein (Fig. 7.6) superficial to and lateral to the carotid artery. The IJ vein is also easily compressible with the probe and is gently pulsatile, while the

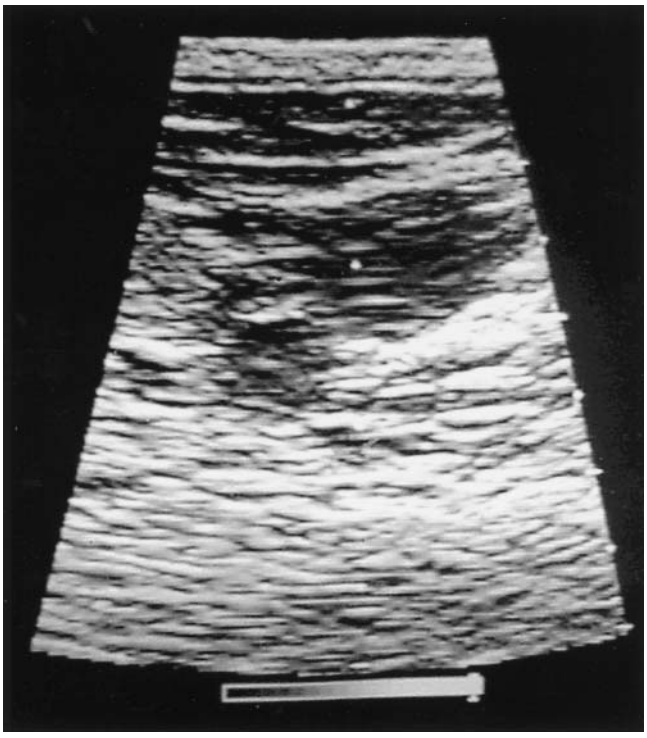

**Fig. 7.6** Two-dimensional ultrasound view of the internal jugular vein (larger circle, above and to the right of the smaller carotid artery).

carotid artery is round, difficult to compress with probe pressure, and very pulsatile. The commercially supplied needle guide or midline projection on the screen is used to insert the needle as the probe is held directly over the desired vessel, with the goal of puncturing it exactly in the midline. The needle can be seen indenting and then puncturing the vessel during correct placement. Visual ultrasound is particularly useful to clarify the anatomy after several previous attempts have been made. One can identify the vessel in the midst of a hematoma that has formed, or recognize overlap of the artery and vein. Once the vessel has been punctured and the guidewire passed, the ultrasound can be used to visualize the guidewire in the lumen of the vessel by scanning closer to the heart. Ultrasound methods are most useful for the IJ vein and femoral veins, and less useful for the subclavian.[71] Audio Doppler can be used to assist in the cannulation of any artery, and is particularly useful when pulses are diminished.

## Interpretation of intravascular pressure waveforms

The normal systemic arterial pressure waveform changes with progression distally from the central arterial circulation, e.g. ascending aorta, distally to the abdominal aorta and femoral arteries, and then to the peripheral arterial such as the radial and foot arteries (Fig. 7.7).[60] In general, the more central sites will produce less peaked systolic pressure waves with slightly lower systolic pressure readings. The dichrotic notch is pronounced in the central arteries. With distal progression, pulse wave amplification will produce a higher peaked systolic pressure wave with a slightly higher systolic pressure. This is most pronounced in the arteries of the foot, where the systolic pressure may be 5–15 torr higher than the ascending aorta. The mean and diastolic pressures change very little with progression. This concept is very important in interpreting arterial pressure tracings. The post-bypass arterial tracing is frequently dampened with catheters in small distal arteries, e.g. radial or foot arteries.[72] This usually resolves within a few minutes after bypass. For particularly long and difficult operations with long bypass and cross-clamp times, it may be useful to place catheters in larger arteries, e.g. femoral or umbilical, or to measure the pressure directly in the aortic root immediately after bypass to ascertain an accurate arterial pressure.

The arterial pressure tracing can yield more information than simply the systolic and diastolic blood pressures.[73] The slope of the upstroke of the pressure wave may be an indicator of systemic ventricular contractility, i.e. the steeper the upslope, the better the contractility. Significant reductions in contractility flatten the upslope. The position of the dichrotic notch may give an indication of peripheral vascular resistance. In infants, the normal dichrotic notch is in the upper half of the pressure wave. With low peripheral resistance, as in arterial runoff through a patent ductus arteriosus, the dichrotic notch is lower on the descending limb of the waveform, due to diastolic runoff into the PA, resulting in a relatively longer period of ventricular systole. The area under the curve of the systolic portion of the arterial tracing increases with increased stroke volume. Finally, a hypovolemic patient will often exhibit more pronounced respiratory variation during positive pressure ventilation, as the stoke volume decreases when positive pressure impedes an already limited venous return (Fig. 7.8). Despite common clinical experience demonstrating the utility of the arterial tracing to assess the hemodynamic status of pediatric patients, a recent study[74] compared cardiac index measured by computerized pulse contour analysis of the arterial catheter tracing to transpulmonary thermodilution cardiac index in 16 children after corrective congenital heart surgery. A total of 191 data points were obtained, and a relatively poor correlation of 0.72 with a wide scatter of measurements was found, suggesting that this method is not reliable in estimating cardiac output.

Recently developed technology uses an arterial catheter and a CVC, along with an injection of contrast, to measure cardiac output by either thermodilution or lithium dilution.[75] Both methods have demonstrated good correlation with standard thermodilution via a PA catheter, but are less invasive. Technical limitations exist for pediatric patients but these

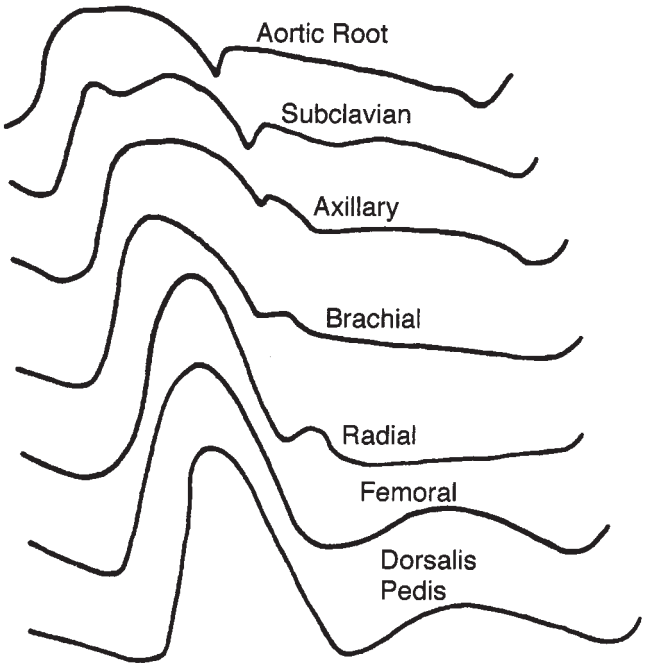


**Fig. 7.7** Progression of the arterial pressure tracing from the root of the aorta to more peripheral arteries. Pulse wave amplification produces a higher systolic peak and slightly lower diastolic pressure in the smaller distal arteries, especially the dorsalis pedis. Reproduced with permission from Reich DL, Moskowitz DM, Kaplan JA. Hemodynamic monitoring. In: Kaplan JA, Reich DL, Konstadt SN, eds. *Cardiac Anesthesia*. Philadelphia, PA: Saunders, 1999: 321–58.

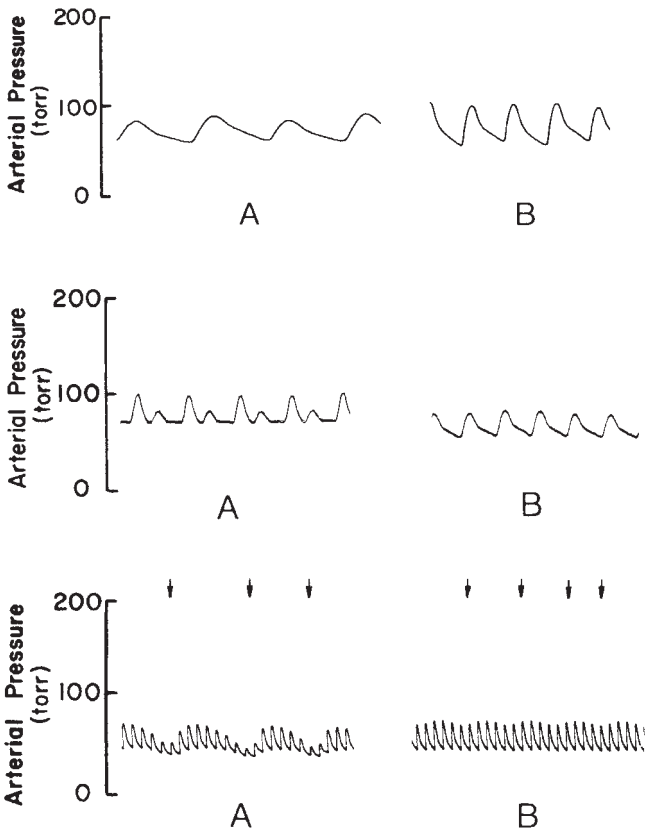


**Fig. 7.8** Top panel—the arterial pressure tracing with depressed (A), and normal (B) myocardial contractility. Middle panel—low (A), and normal (B) systemic vascular resistance. Lower panel—hypovolemia (A), and normovolemia (B)—arrows represent positive-pressure ventilations. Reproduced with permission from Gregory GA. Monitoring during surgery. In: Gregory GA, ed. *Pediatric Anesthesia*. New York: Churchill Livingstone, 2002: 249–65.

would not appear to be insurmountable, and these methods may become more widely available in the future.

Mechanical and electronic components of the intravascular pressure measurement system are important considerations when interpreting waveforms.[65] The shortest possible large bore, stiff plastic tubing should be used. Minimizing the number of stopcocks and connections will also improve the fidelity of the transmitted pressure wave. Thorough flushing before use to produce a bubble- and clot-free fluid path is critical. Periodic recalibration at the right atrial level is important to account for "drift" in the transducer setting. When ringing or overdamping is recognized, some monitor models offer adjustment of electronic filter frequency. The routine setting should be 12 Hz. If the arterial tracing is underdamped, e.g. overshoot producing an artificially high spike as the systolic pressure, filter frequency may be decreased as low as 3 Hz to compensate. Conversely, if overdamped, the filter frequency may be increased to as high as 40 Hz. Mechanical devices (ROSE, Accudynamic) may also be inserted to change the resonance frequency and/or damping factor of the system. Under no circumstances should a bubble be intentionally introduced into the system to produce an increased damping effect. Appropriateness of resonance frequency may be tested by flushing the system from a pressurized bag of heparinized saline, stopping suddenly, and observing the number and amplitude of oscillations required to return to baseline waveform. Proper damping is signified by one oscillation below, and one above, the mean before return to normal waveform.[76,77]

Failure of arterial pressure monitoring systems is always possible during congenital heart surgery. Causes of monitoring failure include kinking or clotting of the catheter, or spasm of the artery. Additional causes may include compression of an aberrant right subclavian artery from a TEE probe, or compression of an axillary artery from a sternal retractor. A back-up oscillometric blood pressure cuff should always be present. In addition, a reasonable precaution is to have the groins prepped into the field so the surgeon can place a catheter in the femoral artery percutaneously or by cutdown.

### Central venous, right and left atrial waveforms

Normal atrial (i.e. central venous) pressure waveforms consist of the A, C, and V waves corresponding to atrial contraction, closure of the tricuspid or mitral valves, and ventricular contraction. Normal right atrial A-wave pressure is lower than V-wave pressure, which is usually less than 10 mmHg. Changes from the normal tracing can give important information about the hemodynamic status and cardiac rhythm of the patient. For example, when atrioventricular synchrony is lost, as in junctional ectopic tachycardia or supraventicular tachycardia, the A wave disappears, and the V wave enlarges considerably, reflecting backwards transmission of ventricular pressure through an ineffectively emptied atrium (Fig. 7.9). Determining the cardiac rhythm from the ECG is often difficult at rapid heart rates because the P wave of the ECG is indiscernible. The left or right atrial waveform can give crucial added information in this situation, clearly retaining the A wave in cases of sinus tachycardia. Competency of the atrioventricular (AV) valves can also be assessed from the atrial tracing. Mitral or tricuspid regurgitation will produce a large V wave on the atrial tracing. It is often very useful to record the vascular pressure tracings in sinus rhythm at baseline for later comparison.

## Vascular access in newborns requiring cardiac surgery

Many patients requiring surgery in the first 2 weeks of life will need future surgery or cardiac catheterization. The goals for vascular access in this group of patients include preserving patency of the IVC and SVC and the distal vessels draining into them, i.e. femoral-iliac veins and innominate-jugular

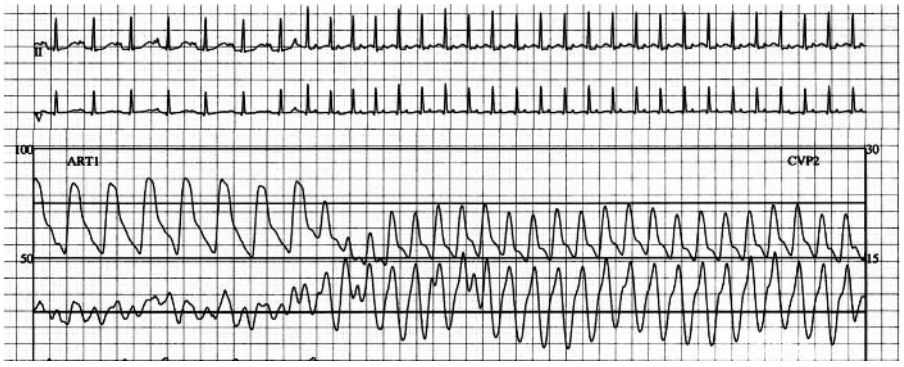


**Fig. 7.9** Electrocardiograph demonstrating normal sinus rhythm the first third of the panel, with onset of supraventricular tachycardia. Note the arterial pressure tracing with a 12–15 torr decrease in systolic pressure, and the loss of the A wave on the central venous pressure tracing, with the appearance of large V waves with a systolic pressure increase from 10 to 16 mmHg.

veins. This is particularly important for single ventricle patients who all will require future catheter and surgical interventions. The risk of vessel occlusion in newborn patients with standard catheters of 3 Fr size or larger is at least 5.8% for a catheter left in 7 days or longer, and thrombosed vessels preclude their use in the future. Thrombosis of the SVC is a life-threatening complication, because future cavopulmonary anastomosis becomes extremely difficult or impossible. Therefore, the SVC catheterization should be avoided in the newborn period unless there is no other alternative.

## Complications of vascular access

### Thrombosis

This is the single most frequent complication, especially among infants. Central venous thrombosis develops in 5.8% of neonatal patients, which is ten times that of older patients, and accounts for 40–50% of central venous thromboses after congenital heart surgery.[78] The frequency significantly decreases in patients over 6 months of age. Factors that contribute to the risk of thrombosis include: (i) large bore catheters in small vessels, i.e. larger than 4 Fr in small infants; (ii) duration of cannulation exceeding 7 days; (iii) venous stasis due to extreme fluid restriction or low cardiac output; (iv) infusion of high osmolarity fluids, i.e. concentrated dextrose in parenteral nutrition fluids; and (v) hypercoagulable states.[79] Immediate consequences of SVC thrombosis include SVC syndrome[80] with increased intracranial pressure, and chylothorax from ineffective drainage of the thoracic duct into the SVC. Inferior vena cava thrombus leads to ascites, renal and intestinal dysfunction, and edema of the lower abdomen and extremities. The patient must be assessed carefully for signs of thrombosis, and suspicion of thrombosis should be evaluated by ultrasound examination. Treatment modalities include removing the catheter, heparinization, thrombolytic agents such as tissue plasminogen activator and urokinase,[81–83] antithrombin III replacement,[84] and surgical thrombectomy. Mortality from SVC thrombosis is reported to be as high as 33% and therefore it is critical to try to prevent this complication, preferably by avoiding SVC catheters in patients under 4 kg. Thrombosis also leads to a higher rate of infection.[85,86] Heparin-bonded catheters decrease the rate of thrombosis and do not increase the risk of bleeding;[85,87] however, it is currently not possible to bond both heparin and antibiotics to the same catheter. In patients with occlusion of central veins from previous catheters, magnetic resonance venography may be useful in identifying patent veins for future interventions.[88]

Thrombosis or dissection of an artery is a serious complication that must be treated immediately. Immediately after arterial catheter placement it is important to inspect the distal extremity, comparing it to the other extremity, and palpate distal pulses. Placement of a pulse oximeter probe distal to the catheter serves as a continuous monitor and early warning of vascular insufficiency. Transient compromise to perfusion immediately after catheter placement due to arterial spasm or during low output states may be observed. However, when extremity perfusion is significantly compromised, treatment by removal of the catheter, surgical consultation, use of vasodilators, warming the extremity, heparin, thrombolytics, surgical thrombectomy, or surgical reconstruction is indicated.[89]

### Malposition/perforation

Central venous catheter tips should not lie in the RA. Adult and pediatric studies have consistently demonstrated a higher rate of heart and great vessel perforation with associated cardiac tamponade when catheter tips are in the atrium.[35,90–94] Perforation is also less common with right-sided lines, e.g. right IJ or subclavian, because the catheter tip is parallel to the vein wall. The catheter tip of left-sided lines are frequently at a 45–90° angle of incidence to the SVC or atrium, and mechanical models demonstrate that this position is more likely to lead to great vessel perforation.[95] Finally, 5–10% of patients with congenital heart disease have a left SVC,[94] which most often drains into the coronary sinus or left atrium, and both of these sites are undesirable locations for a catheter tip.[96] Thus the ideal position of a CVC is in the mid-SVC with the tip parallel to the vein wall

(see Fig. 7.2). Soft polyurethane or silicone catheters are also much less likely to perforate than stiffer polyethylene catheters.[95] Perforation is recognized by inability to consistently aspirate blood, an abnormal waveform, and signs and symptoms of pericardial tamponade or hemothorax. Treatment involves aspiration of all the blood possible through the catheter and establishing alternate access, intravascular volume replacement, and drainage of the pericardial or pleural blood, by needle, tube, or surgical exploration.

Many authorities recommend positioning the tip of the catheter in the superior half of the SVC, above the pericardial reflection. This recommendation is based on the theoretical concept that if there is a perforation, cardiac tamponade will not be produced, and also the catheter tip will be above the SVC bypass cannula and thus yield accurate CVP measurements on bypass.[97] There are several problems with this approach in congenital heart surgery, particularly in small patients. First the SVC is often only 4–5 cm long, leaving little room for error in placement. It is preferable to have the catheter slightly too deep in the SVC, because this will lead to accurate pressure measurements and proper infusions of drugs and fluids. When a multilumen catheter is positioned too cephalad in the SVC, one of the proximal ports may not be inside the jugular vein, leading to extravascular extravasation of important or caustic drugs and fluids.[98] In addition, the pericardium is usually opened in congenital heart surgery and drained postoperatively, rendering placement above the pericardial reflection moot. Many series of catheter placements in children document that the IJ route results in tip placement in the SVC or RA 98–100% of the time, whereas the subclavian route has a 5–15% incidence of catheter malposition, i.e. across the midline in the contralteral brachiocephalic vein, or up the ipsilateral IJ vein.

When IVC catheters are used, accurate CVP measurements are usually obtained whether above or below the diaphragm. Umbilical venous catheters should be above the level of the diaphragm at the IVC–RA junction but not in the RA[99] to ensure passage through the ductus venosus and parallel position to the IVC wall.[100]

A recently described complication from femoral venous catheters is inadvertent placement in the lumbar venous plexus, which may result in paraplegia from epidural hematoma or infusion of vasoconstrictive substances.[101,102] Catheterization of the lumbar venous plexus usually occurs when there is partial or total occlusion of the IVC from previous interventions, and the guidewire passes posteriorly through collateral circulation into the lumbar plexus. This malposition may be suspected during insertion when resistance to catheter passage is encountered, or the catheter will not thread its entire length. An anteroposterior radiograph reveals an abnormal catheter course, often appearing to be more lateral than normal. A lateral radiograph will definitely diagnose such malposition—the catheter passes very posterior and the tip is posterior to the vertebral bodies. The catheter must be removed immediately and the patient assessed for neurologic deficit if this malposition is discovered.

Inadvertent arterial puncture can nearly always be prevented by the use of an ultrasound guidance system for CVC placement (see above). However, if this complication occurs, the following general principles are useful After needle puncture if there is any question about whether the vessel is an artery, remove the needle immediately, elevate the area, and hold firm pressure for 5–10 min. A small bore needle puncture of the carotid or femoral artery, e.g. 20 gauge or smaller, is not usually an indication to cancel surgery. If a larger hole is created in the artery, i.e. a dilator and the catheter have been placed, pressure transduction can be used to confirm location. In this case, a discussion with the surgeon must ensue. Normally, the catheter can be removed, and pressure held without consequences unless a very large catheter was used, e.g. introducer sheath or large-bore CVP catheter, in which case surgical exploration and repair should be undertaken. In most cases of elective cardiac surgery, it is prudent to postpone the case if a large hole has been made in the artery. The case can usually be safely performed 24 hours later if no bleeding has occurred. In emergency or urgent cases that must proceed despite a large hole in the artery, the neck or groin should be prepped into the field for exploration if excessive bleeding or hematoma formation occur.

## Pneumothorax

This complication is most frequent with the subclavian approach, but also may occur with the IJ approach, especially with the low puncture sites, e.g. jugular notch approach. To avoid this complication with the subclavian approach it is important to advance the needle only during expiration. A very shallow approach with the needle directed just posterior to the clavicle and at the sternal notch is also important. For the IJ vein, a higher puncture site and limiting the caudad advancement of the needle to stop above the clavicle will usually prevent this complication.[103]

Continuous aspiration should be performed as the needle is advanced using a saline-filled syringe. If air is aspirated as the needle is advanced, attempts at venipuncture should stop immediately, and careful monitoring for compromise of ventilation and hemodymanics should ensue. A chest radiograph should be obtained to make the diagnosis, and pleural drainage by needle, catheter, or tube should be undertaken if indicated. After sternotomy the pleura can be opened on that side during sternotomy if pneumothorax is diagnosed or suspected.

## Infection

Catheter-related sepsis results in significant morbidity, some mortality, prolongation of ICU stay, and increased expense.

The incidence of arterial catheter-related infection is low. A study of 340 arterial catheters in children revealed a 2.3% incidence of local site infection, and 0.6% catheter sepsis.[104] There is strong evidence that several strategies may be employed to reduce this complication.[105] The first is the use of full barrier precautions, e.g. sterile gown, mask, gloves, and careful septic technique during insertion.[8] Second, chlorhexidine has been shown to be superior to other antiseptic solutions. Finally antibiotic bonding to the resin of the catheter will reduce infection.[106] This can be done in several ways, e.g. antibiotics already embedded in the resin (minocycline/rifampin or chlorhexidine/silver sulfadiazine), or applied at the time of insertion by soaking the outer and inner surfaces of a special catheter in a negatively charged antibiotic at 100 mg/mL concentration (such as vancomycin, cefazolin, or other cephalosporins). Antibiotic is slowly released from the catheter, delaying and reducing colonization, and reducing the incidence of catheter sepsis. The increased cost per catheter is about $20, but one episode of catheter sepsis is estimated to cost $14 000 in 1995 dollars.[106] Central venous catheters indwelling more than 5–7 days have an increased incidence of colonization and sepsis,[107] as well as vessel thrombosis. Suspicion of catheter sepsis should be followed by peripheral blood culture, and blood culture from the central line. The catheter should be removed when possible and the tip cultured. Antibiotic therapy is empirically tailored to the most common institution-specific pathogens, and should provide coverage for *Staphylococcus epidermidis*, which continues to be a common pathogen in catheter-related sepsis.[100]

### Arrhythmias

Other complications associated with vascular access procedures include arrhythmias. Ectopic atrial tachycardia, in particular, has been associated with a catheter tip in the RA.[108,109] Atrial fibrillation has also been associated with CVC placement.[110] More commonly, arrhythmias occur with the passage of the guidewire,[111] and include isolated PACs, supraventricular tachycardia, and if the guidewire is advanced into the right ventricle, premature ventricular contractions and even ventricular tachycardia or fibrillation. Great care must be taken when passing the guidewire to stop advancing it when significant arrhythmias are encountered, and when advancing the catheter over the wire to retract the wire as the catheter is advanced. Patients particularly at risk for significant arrhythmia are those with a known history of arrhythmia, and also those with significant right ventricular hypertrophy.

### Systemic air embolus

Systemic air embolus is a constant threat for patients with central or peripheral venous catheters and intracardiac shunting,[112] particularly two ventricle patients with right-to-left shunting, and single ventricle patients in infancy who have obligate mixing of systemic and pulmonary venous return in the systemic ventricle. Air may lodge in the coronary arteries, especially the right, PA, or brain, leading to potentially serious complications. Observation of the transesophageal echocardiogram, or transcranial Doppler ultrasound as used for neurologic monitoring, reveals rapid passage of any introduced systemic venous air into the aorta and cerebral circulation. For this reason, meticulous attention must be paid to prevent the introduction of air into the systemic venous circulation as much as possible. Precautions include thorough de-airing of all intravenous infusions before connection to the patient, de-airing of continuous flush central venous lines, air filters on continuous infusions, and careful technique when injecting drugs and fluids. The latter involves holding any syringe upright, flushing fluid from the proximal intravenous tubing into it, and aspirating and tapping the syringe first before injecting so that any air is trapped at the superior aspect of the syringe. Constant vigilance of all infusions and the use of TEE as a monitor for intracardiac air and the transcranial Doppler for systemic arterial air may reduce the risk of significant air embolus.

### Other complications

Thoracic duct injury, chylothorax,[113] brachial plexus injury, cervical dural puncture,[114] phrenic nerve injury,[115] vertebral arteriovenous fistula,[116] Horner's syndrome,[4] and tracheal puncture have also been described. These complications can essentially be eliminated with skilled personnel using ultrasound guided techniques to accurately identify the location of the vessel.

Finally, embolization of catheter or guidewire fragments sheared off during difficult insertion procedures occasionally occur.[20] Never withdraw a guidewire or catheter through a needle if any resistance is encountered. If resistance is encountered, the guidewire and needle, or catheter and needle, must be withdrawn completely from the vessel together as a unit.

## Conclusion

Vascular access is a critical issue for every patient undergoing congenital heart surgery. Each team of practitioners develops its own approach to vascular access, and no one approach, e.g. transthoracic vs. percutaneous CVCs, or percutaneous vs. cutdown radial artery access, has been demonstrated to be superior to any other. Complication rates, time for insertion, and expense are significant. Application of the principles of safe insertion, particularly a strategy to preserve access sites in small single-ventricle patients, ultrasound guidance of catheter placement, and the use of antibiotic-impregnated catheters, will improve the outcome of vascular access procedures.

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# 8 Neurologic monitoring and outcome

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## Introduction

The incidence of neurologic complications following heart surgery in children ranges from 6% to 25%.[1,2] A recent retrospective report of a series of 706 children undergoing heart surgery found that 2.3% had acute neurologic complications.[3] Unlike adults, who undergo heart surgery with cardiopulmonary bypass (CPB) where postoperative neurologic sequelae are largely embolic in nature,[4] in children the etiology of this neurologic dysfunction is probably multifactorial.[5,6] Techniques such as deep hypothermic circulatory arrest (DHCA) and low-flow bypass, which have allowed successful correction of complex cardiac defects in neonates and infants may themselves contribute to neurologic damage in this vulnerable population.[7,8] Furthermore, bypass circuitry and the conduct of CPB, the management of arterial blood gas (ABG)—α-stat (not correcting ABG for temperature) vs. pH-stat (correcting ABG for temperature), hematocrit on bypass, rate and extent of cooling, and rewarming are all important contributors to potential brain dysfunction after CPB.[6] In defining the extent of the problem one presupposes that these children are neurologically normal to begin with. However, studies have confirmed central nervous malformations in patients with congenital heart disease (CHD),[5] specifically those with hypoplastic left heart syndrome (HLHS)[9] where brain dysgenesis may approach 30%. In addition children with chromosomal defects, particularly those with microdeletions of chromosome 22, have a higher incidence of central nervous system abnormalities,[10] as do neonates with coarctation of aorta.[11] Hence these developmental brain disturbances add to the acquired brain injury in the perioperative setting.

During CPB, although vital organs other than the brain are routinely monitored, the brain is not monitored. The reason for this glaring omission is seldom a point of contention between the various perioperative teams managing the patient. Any strategy for cerebral rescue from the effects of CPB to the brain must be done by neurologic monitoring systems that allow easy, reliable, reproducible detection of adverse events. Despite the existence of several modalities of monitoring for almost 20 years, in these authors' opinion neurologic monitoring during CPB still remains in its infancy. In this chapter, we review cerebral physiology during cardiac surgery in children; the current modalities for neurologic monitoring; evidence that neurologic monitoring improves neurologic outcome; and finally strategies for improving neurologic outcome.

## Cerebral physiology during cardiac surgery

The experimental basis for understanding neurophysiology in infants and children undergoing cardiac surgery involving CPB with DHCA comes largely from a series of landmark clinical studies undertaken in the late 1980s through mid-1990s by Greeley, Kern, Ungerleider, and colleagues.[12–16] These investigators measured cerebral blood flow by the xenon clearance method in patients during hypothermic CPB and calculated cerebral oxygen extraction by measuring oxygen saturation in the arterial blood (inflow) and in the jugular venous bulb (outflow). Cerebral metabolic rate was calculated for oxygen ($CMRO_2$) in milliliters/minute as $CBF \times (Cao_2 - Cjvo_2)$, where $CBF$ is cerebral blood flow, $Cao_2$ is the oxygen content of arterial blood, and $Cjvo_2$ the oxygen content of jugular venous bulb blood. This method allows instantaneous assessment of the cerebral circulation from rapid changes that occur during CPB. It should be noted that in all of their studies α-stat blood gas management was used. Under deep hypothermic conditions $CBF$ is significantly reduced, but there is an exponentially greater reduction in $CMRO_2$ (Fig. 8.1). A state of luxury perfusion exists with an excess of flow relative to oxygen consumption. The temperature coefficient, or $Q_{10}$, is the ratio of $CMRO_2$ at two temperatures separated by 10°C, and demonstrates the exponential decrease in $CMRO_2$. In neonates, infants, and children, the

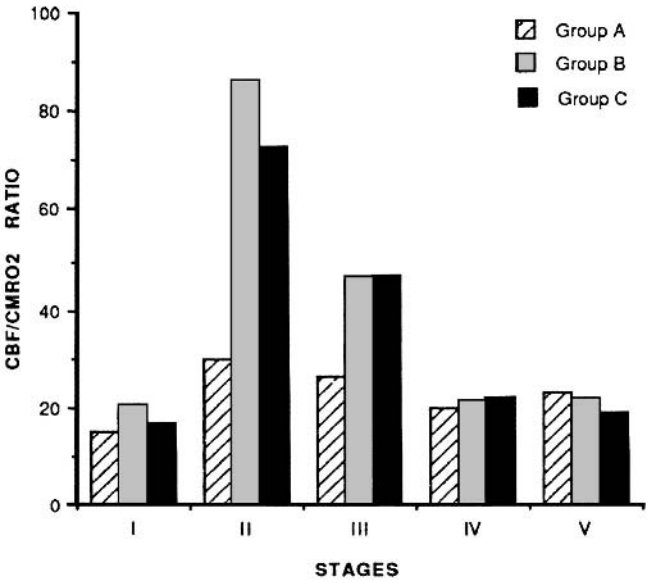


**Fig. 8.1** Cerebral blood flow (*CBF*)/cerebral metabolic rate for oxygen ($CMRO_2$) ratio during cardiac surgery in 46 pediatric patients aged from 1 day to 14 years. Stage I, before cardiopulmonary bypass (CPB); stage II, stable hypothermic conditions at 5 minutes; stage III, stable hypothermic conditions at 25 minutes or just after deep hypothermic circulatory arrest (DHCA); stage IV, rewarmed on CPB; stage V, after CPB. Group A was cooled to 28°C without DHCA, Group B was cooled to 18°C without DHCA, and Group C was cooled to 18°C with DHCA. There is a significant increase in $CBF/CMRO_2$ during deep hypothermic conditions, favoring perfusion over $CMRO_2$; flow/metabolism coupling is present at other times. Reproduced with permission from Greeley WJ, Kern FH, Ungerleider RM. The effect of hypothermic cardiopulmonary bypass and total circulatory arrest on cerebral metabolism in neonates, infants, and children. *J Thorac Cardiovasc Surg* 1991; **101**: 783–94.

$Q_{10}$ is 3.65, meaning $CMRO_2$ decreases by 3.65 times from baseline at 37–27°C, and if cooled to 17°, $CMRO_2$ will decrease 3.65 times from the level found at 27°C. Based on these data the investigators derived a "safe" duration of DHCA at various temperatures. This was estimated to be 11–19 minutes at 28°C, and 39–65 minutes at 18°C. This calculation of a safe duration of circulatory arrest is similar to that seen in a clinical outcome study reviewed later in this chapter.[14] These studies confirm that hypothermia is an important factor for neuroprotection.

In patients undergoing circulatory arrest, both *CBF* and $CMRO_2$ remain decreased after rewarming and following separation from CPB. The decreased *CBF* may be due to higher cerebral vascular resistance.[17] This reduction in *CBF* can be ameliorated with a 10-minute period of cold full-flow reperfusion before rewarming.[18]

The rate and manner of cooling also have significant effects on cerebral oxygenation during CPB.[16] Kern *et al*.[16] exposed infants to two different cooling strategies, aggressive or gradual. The first strategy resulted in a significantly higher $SjvO_2$ (98% vs. 86%), meaning that global cerebral metabolism was more effectively suppressed than with the gradual cooling method. There was considerable patient variability, leading the authors to suggest that more precise monitoring of cerebral hypothermia was warranted. Monitoring the cerebral saturation, either with near-infrared spectroscopy (NIRS) or $SjvO_2$, may provide a more accurate assessment of the state of cerebral metabolism, and CPB can be tailored to the individual. If cerebral saturation is low after the usual cooling period, additional CPB time can ensure higher cerebral saturation before a period of low-flow CPB or DHCA.

Another important factor is the question of pressure–flow autoregulation during hypothermic bypass.[19] Using transcranial Doppler ultrasound (TCD), 25 infants were studied during normothermic (36–37°C), moderate hypothermic (23–25°C), or profound hypothermic (14–20°C) bypass. Cerebral blood flow velocity (*CBFV*) was measured over a wide range of cerebral perfusion pressures (*CPP*s), ranging from 6 to 90 mmHg. Cerebral pressure-flow autoregulation was preserved during normothermic bypass, with *CBF* increasing linearly until a *CPP* of 40 mmHg, then leveling off. In contrast, during both moderate and profound hypothermia, flow became pressure passive, increasing linearly with pressure even at a *CPP* of 60 mmHg.

Even though hypothermia leads to a loss of cerebral autoregulation, the *CBF* response to changes in arterial carbon dioxide tension is preserved in children.[13] Hence blood gas management (α-stat or pH-stat) during CPB significantly affects cerebral physiology and may have an impact on neurological outcome.[20,21] Both *in vivo* and *ex vivo* studies have demonstrated that pH-stat strategy results in greater cerebral blood flow, greater efficiency, and uniformity of brain cooling, and higher brain oxyhemoblobin saturation and less reduced cytochrome $a,a_3$ signifying more oxygen at the mitochondrial level than α-stat blood gas management.[22–24]

Finally, using α-stat management and a xenon washout technique, Kern *et al*.[15] demonstrated that, at moderate and deep hypothermia, reductions of 35–45% from conventional full bypass flow rates (100–110 mL/kg/minute for patients under 25 kg and 2.5 L/minute/$m^2$ for those over 25 kg) resulted in no change in *CBF* and $CMRO_2$ from decreasing CPB flow rates with increasing hypothermia. When flow was reduced by 45–70%, a significant decrease in *CBF* and $CMRO_2$ resulted, associated with an increase in oxygen extraction (i.e. a lower $SjvO_2$). Even at lower flows *CBF* and $CMRO_2$ decreased significantly, but oxygen extraction did not increase, suggesting an excess of flow over metabolic needs. Based on these measurements, the authors derived predicted minimal acceptable pump flow rates at various temperatures for the average pediatric patient (Table 8.1). Their prediction was validated in neonates undergoing the arterial switch operation at 18°C, who required pump flows of 10–20 mL/kg/minute to maintain cerebral blood flow, documented by TCD.[25]

**Table 8.1** Minimal cardiopulmonary bypass flow rates.

| Temperature (°C) | $CMRO_2$ (mL/100 g/min) | Predicted *MPFR* (mL/kg/min) |
|---|---|---|
| 37 | 1.480 | 100 |
| 32 | 0.823 | 56 |
| 30 | 0.654 | 44 |
| 28 | 0.513 | 34 |
| 25 | 0.362 | 24 |
| 20 | 0.201 | 14 |
| 18 | 0.159 | 11 |
| 15 | 0.112 | 8 |

$CMRO_2$, cerebral metabolic rate for oxygen; *MPFR*, minimal predicted flow rate.

Based on the data of, and reproduced with permission from, Kern FH, Ungerleider RM, Reves JG. Effect of altering pump flow rate on cerebral blood flow and metabolism in infants and children. *Ann Thorac Surg* 1993; **56**: 1366–72.

## Neurologic monitoring during congenital heart surgery

### Electroencephalographic technologies

The standard electroencephalogram (EEG) employing between 2 and 16 channels has been utilized in congenital heart surgery.[26] It is a rough guide of anesthetic depth, and can document electrocerebral silence before DHCA.[27] The electro-encephalogram is affected by several factors including anesthetic agents, temperature, and CPB. Impracticalities of the use of an intraoperative EEG include electrical signal interference, complexity of placement, and interpretation. Newer devices using processed EEG technology are more user friendly.

The bispectral index (*BIS*) monitor (Aspect Medical Systems, Newton, MA) is currently used to guide the depth of anesthesia. Bispectral index sensor electrodes are applied to the forehead and temple producing a frontal–temporal montage, which connects to a processing unit. The device is easy to use, electrodes are easy to place, and the monitor requires no calibration or warm up time. Via a proprietary algorithm of Aspect Corporation, *BIS* uses fourier transformation and bispectral analysis of a one-channel processed EEG pattern to compute a single number, the bispectral *BIS* index.[28] This index ranges from zero (isoelectric EEG) to 100 (awake) with mean awake values in the 90–100 range in adults, infants and children.[29] Depth of sedation is difficult to predict using *BIS* scores due to significant individual variability and anesthetic agent.[30] For *BIS* to be effective as a monitor of the depth of anesthesia, one would have to know exact *BIS* values for each anesthetic administered for an individual patient, thus reducing its value.[31] Bispectral index can be used to recognize EEG burst suppression, or electrical silence, which could be useful during DHCA. The monitor displays a real-time EEG waveform, but is subject to motion artifact, EMG activity and radiofrequency interference from electrical equipment in the operating room.

During CPB hemodilution and hypothermia alter pharmacokinetics and pharmacodynamics, which can lead to awareness under anesthesia. The overall incidence of awareness in adults undergoing cardiac surgery varies from 0.3% to 23.0%,[31–33] which is more than in general surgical procedures. Although there are no documented reports of awareness under anesthesia in children undergoing heart surgery, *BIS* monitoring may still be useful to detect a level of awareness. In a cohort of children undergoing open heart surgery with an anesthetic tailored for "fast-tracking," *BIS* scores increased during rewarming, a period considered at risk for awareness under anesthesia.[34] However in this study, and in a similar study in infants less than 1 year of age,[35] *BIS* did not correlate with stress hormone levels, a surrogate for light levels of anesthesia, nor with plasma fentanyl levels. Studies are needed that demonstrate the utility of the *BIS* monitor in infants undergoing DHCA.

### Monitors of cerebral oxygenation

#### Jugular venous bulb oximetry

Jugular venous bulb oximetery ($SjvO_2$) has been utilized in children with CHD since the late 1980s. It is considered the gold standard of global cerebral oxygenation against which all non-invasive measurements are compared. The catheter can be placed by retrograde cannulation of the right internal jugular vein, with or without fluoroscopic confirmation of catheter tip placement.[15] Alternatively, the catheter can be placed by the surgeon after the heart and great vessels are exposed, by cannulating the superior vena cava (SVC) retrograde and advancing it into the jugular venous bulb.[36] $SjvO_2$ can be measured continuously with an oximetric catheter,[37] or intermittent sampling for direct measurement of oxygen saturation. The drawbacks of this method include the invasive and time-consuming nature of retrograde internal jugular vein cannulation rendering it primarily a research tool. Non-invasive monitoring of cerebral oxygen saturation is more practical.

#### Near-infrared spectroscopy

Near-infrared spectroscopy is a non-invasive optical technique used to monitor brain tissue oxygenation. Most devices utilize 2–4 wavelengths of infrared light at 700–1000 nm, where oxygenated and deoxygenated hemoglobin have distinct absorption spectra.[38–40] Commercially available devices measure the concentration of oxy- and de-oxyhemoglobin, and determine cerebral oxygen saturation. The cerebral

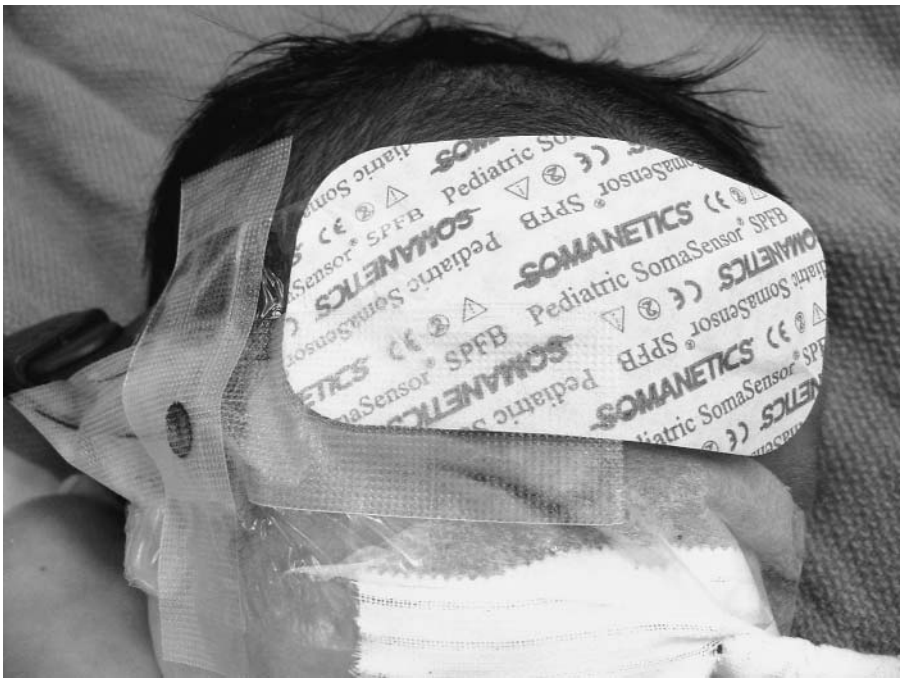


**Fig. 8.2** Near-infrared cerebral oximetry probe on the forehead of a newborn infant. A small disk transcranial Doppler probe is secured over the right temporal area.

oximeter probe is placed on the forehead (Fig. 8.2) below the hairline. A light-emitting diode emits infrared light, which passes through a "banana-shaped" tissue volume in the frontal cerebral cortex, to two or three detectors placed 3–5 cm from the emitter. The proximal detector in the Somanetics INVOS system (Somanetics, Inc., Troy, MI, USA) detects light absorbed by extracranial tissues, and is subtracted from the total signal, leaving only the intracranial contribution. The pediatric model (INVOS 5100) is designed for patients of 4–40 kg and uses a different algorithm that takes into account the thinner skull and extracranial tissues compared to the adult.[41] This device is US Food and Drug Administration (FDA) approved for use in children, is compact, easy to use, and requires little warm up. The INVOS processor displays a numerical value, the measured regional cerebral oxygen saturation index ($rSO_2i$). This index assumes that 75% of the cerebral blood volume in the light path is venous, and 25% is arterial. This 75 : 25 ratio is derived from theoretical anatomical models. Watzman *et al*.[42] attempted to verify this index in children with CHD by measuring jugular venous bulb saturation and arterial saturation, and comparing it to cerebral saturation measured with frequency-domain NIRS. The actual ratio in patients varied widely but averaged 85 : 15. The $rSO_2i$ is reported as a percentage on a scale from 15% to 95%. A cerebral blood volume index (Crbvi) can also be calculated, representing the total hemoglobin in the light path, which may be used as an estimate of cerebral blood volume.

The NIRO 300 (Hamamatsu Photonics, Hamamatsu, Japan) uses spatially resolved spectrophotometry to calculate absolute concentrations of oxygenated and total hemoglobin, rather than as saturations. This device may be more accurate than the INVOS system; however, it is not FDA approved. Prototype cerebral oximeters using frequency-domain technology are under development and have the potential to measure absolute rather than calculated cerebral oxygen saturation.[42]

Direct comparison of the INVOS 4100 and NIRO 300[39] in healthy anesthetized adults during normo-, hypo- and hypercapnia reveals a positive correlation for all data points in both absolute values, and change from baseline values ($r = 0.58$ and 0.85, respectively). However, application of the more sensitive Bland and Altman comparison[43] of the two methods reveals that, although the correlation was good when all 60 values were combined, individual comparison demonstrated possible large differences. The INVOS 5100 pediatric sensor tends to read significantly higher (by 14 ± 8%)[41] than the NIRO 300 4-cm interoptode sensor (pediatric equivalent). Regardless of the device used, it is important to note that all devices measure combined arterial and venous blood oxygen saturation, and cannot be assumed to be identical to $SjvO_2$. A corollary of this issue is that maneuvers to increase arterial oxygen saturation, i.e. increasing $FIO_2$, will increase cerebral oxygenation as measured by these devices, but the $SjvO_2$ may remain unchanged.

In an attempt to validate the non-invasive measurement of cerebral oxygen saturation in children with CHD, $SjvO_2$ and $rSO_2i$ have been compared. In 40 infants and children[44] undergoing congenital heart surgery or cardiac catheterization, the correlation for paired measurements was inconclusive except for infants less than 1 year of age. In 30 patients undergoing cardiac catheterization, an improved correlation ($r = 0.93$) was found.[45] All of these experimental data lead to the

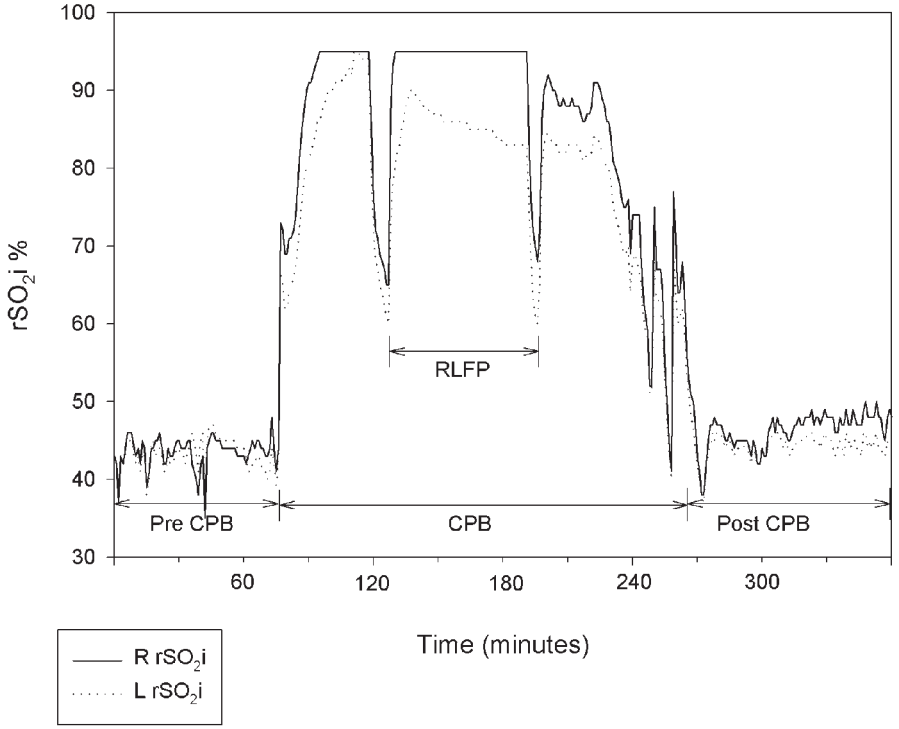


**Fig. 8.3** Typical changes in regional cerebral oxygen saturation index ($rSo_2i$) during cardiac surgery with cardiopulmonary bypass (CPB), regional cerebral low-flow perfusion (RLFP), and deep hypothermic circulatory arrest. R, right; L, left.

appealing idea that NIRS can be used to direct therapy and influence outcome in congenital heart surgery.

***Clinical data in pediatric cardiac surgery***

Changes in cerebral oxygenation have been characterized during CPB in children with or without DHCA (Fig. 8.3).[46] Baseline preoperative cerebral oxygen saturation ($Sco_2$), as measured by a frequency-domain oximeter, varies with cardiac lesion.[40] The baseline cerebral saturation is about 70% in acyanotic patients without large left-to-right intracardiac shunts breathing room air. On room air, $Sco_2$ for cyanotic patients is usually 40–60%; HLHS patients receiving $Fio_2$ 0.17 preoperatively also have lower $Sco_2$, averaging 53%, vs. those receiving $Fio_2$ 0.21 and 3% inspired carbon dioxide, where $Sco_2$ averages 68%.[47] Significant decreases in $Sco_2$ occur during periods of hemodynamic instability or arterial desaturation. Increases occur during cooling and vary with the rate of temperature change. Improvement in cardiac output and oxygen delivery results in an increase in $Sco_2$.

$Sco_2$ predictably decreases during DHCA to a nadir approximately 60–70% below baseline values obtained pre-bypass[46] and the nadir is reached at about 40 minutes, after which there is no further decrease. At this point it appears that the brain does not continue the uptake of oxygen, and interestingly this time period appears to correlate with clinical and experimental studies suggesting that 45 minutes is the safe duration for circulatory arrest.[6] The DHCA initiation at higher temperature results in a faster fall in $Sco_2$ reaching the nadir sooner.[48] Reperfusion immediately results in an increase in $Sco_2$ levels seen at full bypass flow before DHCA.

***Relationships between low cerebral saturation ($Sco_2$) and adverse neurologic outcome***

There is recent clinical evidence suggesting that low cerebral saturations correlate with adverse neurologic outcome. In 26 infants and children undergoing surgery with bypass and DHCA,[49] three with low $Sco_2$ had acute neurologic changes—seizures in one, and prolonged coma in two. In these three patients the increase in $Sco_2$ was much less after the onset of CPB and the duration of cooling before DHCA shorter. In 250 infants and children undergoing cardiac surgery with bypass,[26] relative cerebral oxygen desaturation of more than 20% below pre-bypass baseline was observed in 58%. If left untreated 26% of them had postoperative adverse neurologic events.

There is also evidence from animal models that NIRS can be used as a guide to the safe duration of DHCA. In a study of piglets, the time of the nadir of $Sco_2$ values during DHCA correlated with neurologic outcome: a longer period without apparent oxygen uptake by the brain correlated with a greater chance of adverse neurological outcome. The maximum safe duration without brain oxygen uptake at 17°C was 30 minutes.[24] In another piglet model, NIRS was used to detect cerebral desaturation when the SVC was partially or totally occluded. No other measurement (blood pressure/heart rate on bypass, SVC pressure measurements, or mixed venous oxygen saturation) predicted cerebral desaturation.

This has clinical relevance because cerebral desaturation may develop in small infants undergoing bicaval cannulation, who frequently have SVC obstruction, or patients undergoing cavopulmonary anastomosis, where the SVC is often partially occluded.[50]

It is intuitive to conclude that low cerebral oxygen saturations as measured by NIRS lead to adverse neurologic outcomes and therefore should be monitored and treated. However, additional prospective outcome data in infants and children using this modality is required.

## Transcranial Doppler ultrasound

Transcranial Doppler ultrasound is a sensitive, real-time monitor of *CBFV* and emboli during congenital heart surgery. Currently available instruments utilize pulsed-wave ultrasound at 2 MHz frequency, which is range-gated, emits a power of 100 mW, and has a sample volume length of up to 15 mm. A display of the frequency spectrum of Doppler signals is easily interpreted, and peak systolic and mean flow velocities, in centimeters/second, are displayed, as well as a pulsatility index which is equal to the peak velocity minus the end-diastolic velocity, divided by the mean velocity (Fig. 8.4). The information can be stored digitally and archived to be analyzed off line at a later date. As with cardiac ultrasound, the advantage of pulsed-wave Doppler ultrasound is that a precise sample volume can be selected which insonates only the arteries of interest, without contamination from other sources.

The most consistent and reproducible technique for clinical use in patients of all ages is to monitor the middle cerebral artery (MCA) through the temporal window, which can usually be found just above the zygoma and just anterior to the tragus of the ear (see Fig. 8.2).[51] Several transducer probes are available, ranging from very small disc probes suitable for infants and children, to larger, heavier probes for adolescents and adults. The depth of the sample volume and angle of insonation is adjusted until the bifurcation of the MCA and the anterior cerebral artery (ACA) are detected. This is heralded by a maximal antegrade signal (positive deflection, toward the transducer) from the MCA, accompanied by retrograde flow (negative deflection, away from the transducer) of the same or very similar velocity and waveform, as the MCA flow (Fig. 8.4(b)). The same location should be monitored for an individual patient. Insonation at the MCA–ACA bifurcation also offers the advantage of minimizing interpatient variability. In addition, the MCA supplies the largest volume of tissue of any of the basal cerebral arteries.[52] After obtaining an optimal signal, the probe must be secured, usually by adhesive tape or clear adhesive dressing for the small disc probe, or by adjustments to a padded head ring in larger patients. Care must be taken with the latter system to thoroughly pad all pressure points and to pay particular care to the orbits. For smaller patients, securing the probe by wrapping the head with an elastic bandage is discouraged because pressure sores may develop under the area of the transducer. Also, adjustment to the probe position is often necessary during the case, so access to the transducer is important.

**Table 8.2** Normal transcranial Doppler ultrasound values for infants and children.

| Age | Depth (mm) | Mean velocity (cm/s) | Peak systolic velocity (cm/s) | End-diastolic velocity (cm/s) |
|---|---|---|---|---|
| 0–3 mo | 25 | 24–42 ± 10 | 46–75 ± 15 | 12–24 ± 8 |
| 3–12 mo | 30 | 74 ± 14 | 114 ± 20 | 46 ± 9 |
| 1–3 yr | 35–45 | 85 ± 10 | 124 ± 10 | 65 ± 11 |
| 3–6 yr | 40–45 | 94 ± 10 | 147 ± 17 | 65 ± 9 |
| 6–10 yr | 45–50 | 97 ± 9 | 143 ± 13 | 72 ± 9 |
| 10–18 yr | 45–50 | 81 ± 11 | 129 ± 17 | 60 ± 8 |

In infants, an alternative site for monitoring is through the anterior fontanelle, using a hand-held pencil-type probe, placing the probe over the lateral edge of the fontanelle, and aiming caudally, at a larger depth than for the temporal window, at the internal carotid artery. The depth of measurement and normal-flow velocities for the MCA are listed in Table 8.2.[51] These normal velocities were determined in children without cardiovascular disease. Lesions producing large diastolic runoff, for example large patent ductus arteriosus, will have an effect on diastolic blood flow to the brain. These normal velocities were obtained in awake children under perfect examination conditions. Hemodynamic instability, less than optimal probe positioning, and general anesthesia may reduce these velocities in clinical practice. Often the clinician must accept a stable baseline for the individual patient and use it as the basis for comparison, rather than expect a perfect signal.

Transcranial Doppler ultrasound has been used extensively in pediatric cardiac surgical research to examine cerebral physiology in response to CPB, hypothermia, low-flow bypass, regional low-flow perfusion to the brain, and circulatory arrest. Hillier *et al*.[53] used TCD to study cerebrovascular hemodynamics during hypothermic bypass with DHCA in 10 infants. Cerebral blood flow velocity did not return to baseline levels after DHCA. Calculated cerebral vascular resistance (mean arterial pressure–central venous pressure/*CBFV*) was increased immediately after DHCA, and remained so until the end of bypass. The observed decrease in *CBFV* during cooling was thought to be due to decreased metabolic demand by the brain and thus less blood flow; although α-stat strategy was used. This could be explained by relative cerebral vasoconstriction during cooling in smaller arterioles downstream to the MCA and ACA, since these large arteries do not change their caliber in response to changes in $P_{CO_2}$.[54] Transcranial Doppler ultrasound of the MCA through the temporal window was used to describe the

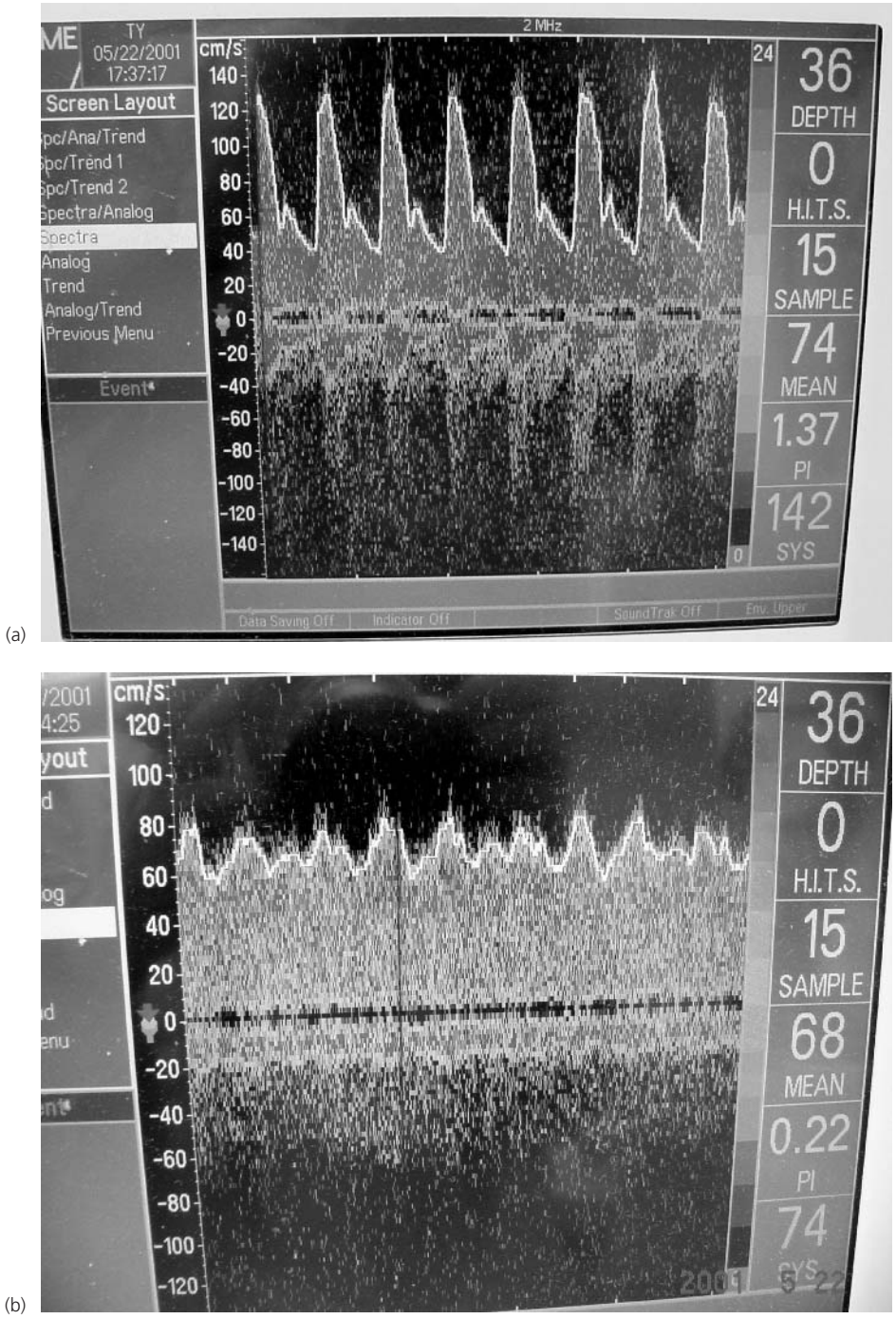


**Fig. 8.4** Transcranial Doppler ultrasound monitor display. A velocity spectrum is displayed with numerical readouts for peak and mean cerebral blood flow velocity (*CBFV*) in centimeters/second and pulsatility index, as well as depth of insonation and sample volume length. (a) Cerebral blood flow velocity spectrum before bypass, (b) on bypass with non-pulsatile flow, and (c) two cerebral emboli can be seen as high intensity signals against the background *CBFV* spectrum.

cerebral pressure–flow velocity relationship during hypothermic bypass in 25 neonates and infants less than 9 months old. Cerebral blood flow velocity was examined over a wide range of *CPP* varying from 6 to 90 mmHg, at three temperatures—normothermia (36–37°C), moderate hypothermia (23–25°C), and profound hypothermia (14–20°C). Cerebral pressure–flow autoregulation was preserved at normothermia, partially affected at moderate hypothermia, and totally lost at profound hypothermia; results that agree with previous research done using xenon to quantitate cerebral blood flow.[12]

Transcranial Doppler ultrasound has also been utilized to determine the threshold of detectable cerebral perfusion during low-flow CPB. Zimmerman *et al*.[25] studied 28 neonates undergoing the arterial switch operation with α-stat pH management. At 14–15°C the pump flow was sequentially reduced to 0 mL/kg/minute. All patients had detectable cerebral blood flow down to 20 mL/kg/minute, while one

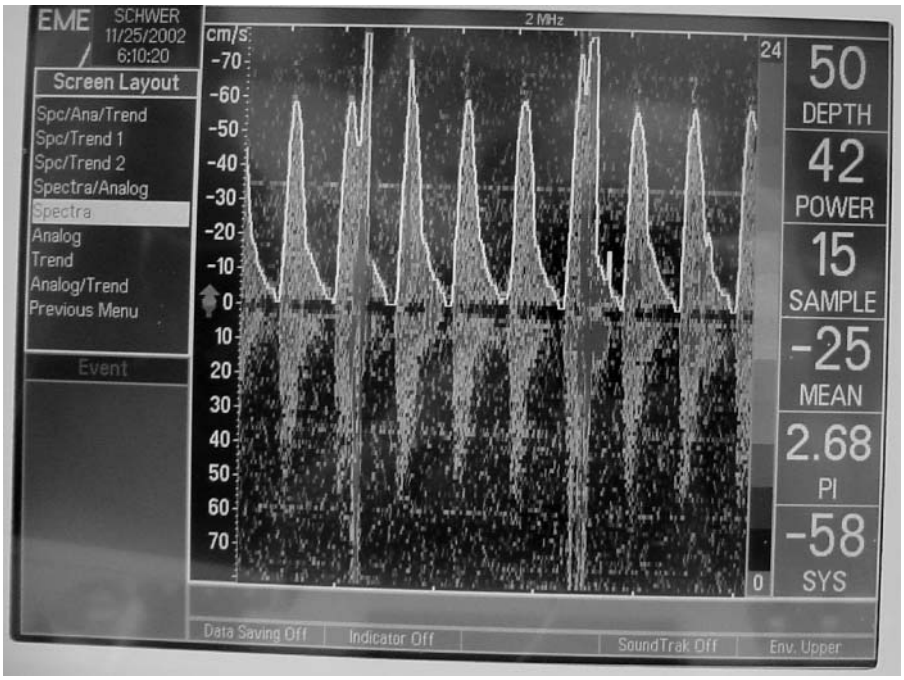


**Fig. 8.4** (cont'd) (c)

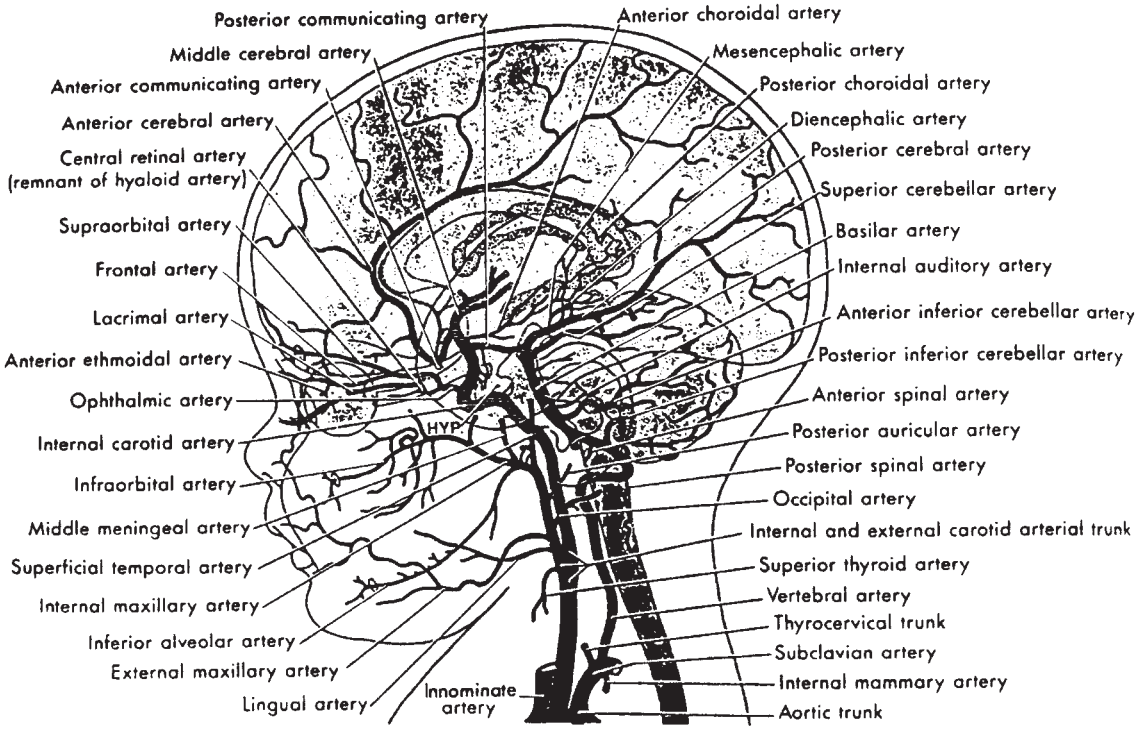


**Fig. 8.5** Arterial supply to the brain in a neonate. Transcranial Doppler ultrasound is used to measure cerebral blood flow velocity in the middle cerebral artery, ideally at its junction with the anterior cerebral artery. Reproduced with permission from Truemper EJ, Fischer AQ. Cerebrovascular developmental anatomy and physiology in the infant and child. In: Bibikian VL, Wechlser LR, eds. *Transcranial Doppler Ultrasonography*, 2nd edn. Oxford: Butterworth–Heineman, 1993: 281–320.

had no perfusion at 20 mL/kg/minute, and eight had none at 10 mL/kg/minute, leading the authors to conclude that 30 mL/kg/minute was the minimum acceptable flow in this population. Finally, Andropoulos *et al*.[55] used TCD of the MCA to determine the level of bypass flow necessary during regional low-flow perfusion for neonatal aortic arch reconstruction. They studied 34 neonates undergoing the Norwood operation or aortic arch advancement and established a baseline mean *CBFV* under full-flow bypass (150 mL/kg/minute) using pH-stat management at 17–22°C : 22 cm/second. They then used TCD to determine the bypass flow necessary to match this value, finding that a mean of 63 mL/kg/minute was necessary. Interestingly, this necessary level of bypass flow did not correlate with mean arterial pressure in the radial artery or cerebral saturation measured by NIRS. The necessary flow as determined by TCD varied widely, leading the authors to conclude that TCD was a valuable monitor to ensure adequate but not excessive cerebral blood flow during this complicated technique.

Cerebral emboli are a frequent threat during open heart surgery in children. Emboli are easily detected by TCD, although this is subject to artifacts such as electrocautery and physical contact with the ultrasound transducer (Fig. 8.4).[56] True emboli have characteristic audio and visual signals and are designated as high intensity transient signals (HITS) which can actually be counted by the TCD software. The filtering criteria must be set to exclude artifacts, and the HITS counter can be an accurate gauge of the number of emboli detected in the artery being monitored. However the number of emboli detected in the carotid artery during pediatric congenital heart surgery did not appear to correlate with acute postoperative neurological deficits.[56] Acute drops in cerebral blood flow detected by TCD can allow for adjustment of aortic cannula, which may avert neurological disaster.

One caveat when utilizing TCD clinically is that this device measures *CBFV*, not blood flow. Cerebral blood flow velocity is dependent on the diameter of the blood vessel whereas cerebral blood flow depends on cerebral vascular resistance, which changes in response to changes in carbon dioxide, temperature, *CPP*, and pump flow. Thus *CBFV* often correlates well with cerebral blood flow in the individual patient, particularly at deep hypothermia when autoregulation is lost and the caliber of the blood vessels is unchanged. However the clinician must always be mindful and estimate the state of the patient's cerebral vascular resistance to translate TCD into meaningful information for clinical decision making.

## Multimodality neurologic monitoring

With combined use of TCD to measure blood flow in the MCA/ACA, and NIRS which measures oxygen saturation of blood in the frontal lobe, it is possible to monitor up to 70% of the blood flow distribution to a cerebral hemisphere.

Simultaneous neurologic monitoring—NIRS, transcranial Doppler, and processed EEG (*BIS*)—may hold the greatest promise in detecting and treating neurologic abnormalities during congenital heart surgery, just as pulse oximetry combined with capnography is more effective at preventing morbidity from ventilation mishaps than either modality alone.[57] A study in infants and children with CHD involving multimodality neurologic monitoring—NIRS, TCD, and four-channel quantitative EEG—showed that 70% (176/250) patients experienced a significant change in one or more parameters. When left untreated, 26% developed adverse neurologic outcomes, compared to 7% that were treated. Interestingly EEG changes were responsible for only 5% of the monitoring abnormalities, with NIRS changes responsible for 58%, and TCD 37%. This study was neither prospective, randomized, nor controlled. The 26% incidence of acute neurologic complications is greater than most other reports of neurologic outcomes after congenital heart surgery. However, to date it represents the best evidence that multimodality neurologic monitoring, particularly NIRS and TCD, in conjunction with a treatment algorithm, reduces neurologic complications following CPB.

Based on these data, and more than 4 years of experience and more than 3000 cases with multimodality neurologic monitoring at Texas Children's Hospital, one possible algorithm for treatment is presented in Table 8.3. In infants under 1 year of age the *BIS* is not used because of space limitations and because of insufficient data confirming its utility in this age group. The anesthesiologist can learn to place and interpret these monitors; however, this algorithm awaits prospective validation of the potential to directly improve outcome.

For the NIRS monitor, a relative decrease of more than 20% from a stable baseline obtained pre-incision is the primary reason for treatment. Other critical values are an r$S_{O_2}$i less than 30%, or greater than 95% accompanied by a significant increase in *CBFV*.

## Temperature monitoring

Cerebral hyperthermia frequently develops after congenital heart surgery with CPB. The metabolic rate and oxygen consumption of neurons is raised during a period when oxygen delivery may be compromised from decreased cardiac output. This places vulnerable watershed areas or partially damaged neurons at risk for permanent cell death.[58] Bissonnette *et al*.[59] measured temperatures in the jugular venous bulb (JBVT), tympanic membrane, lower esophagus, and rectum during and after surgery in 15 infants. The patients were separated from bypass at 35°C rectal, without active warming measures. The mean JBVT was 36.9°C at the end of bypass, and this increased to 39.6°C by 6 hours postoperatively, with one patient reaching 41.4°C. The authors found that the commonly monitored rectal temperature does not reflect

**Table 8.3** Texas Children's Hospital neurologic monitoring treatment algorithm.

| Monitor | Change | Intervention pre/ post bypass | Intervention on bypass | Intervention on DHCA |
|---|---|---|---|---|
| NIRS ($rSo_2i$%) | ↓ ≥ 20% relative to pre-incision baseline | ↑ Cardiac output, ↑hgb, ↑ $Fio_2$, ↑$Paco_2$ | ↑ Pump flow, ↑ $Paco_2$, ↑ *MAP*, ↓ temp., ↑ hgb, √ *CBFV*—adjust cannulae | |
| | DHCA: $rSo_2i$ < 30%, or at nadir > 30 minutes | | | Reperfuse |
| | $rSo_2i$ ≥ 95% | | None; or √ *CBFV*-↓ pump flow or ↓ $Paco_2$ if > 25% above baseline | |
| | $rSo_2i$ < 30% | Rapid institution bypass; aggressive measures to ↑$O_2$ delivery | Aggressive treatment: ↑ Pump flow, ↑ $Paco_2$, ↑ *MAP*, ↓ temp., ↑ hgb, √ *CBFV*—adjust cannulae | Reperfuse |
| TCD (mean *CBFV*, cm/s) | ↓ ≥ 25% from pre-incision baseline | √ Transducer; √ NIRS—if low, ↑ cardiac output, ↑ $Paco_2$, ↑ *MAP* | √ Transducer; √ NIRS—if low: ↑ pump flow, ↑ $Paco_2$, ↑ *MAP*, adjust cannulae | |
| | ↑ ≥ 25% from pre-incision baseline | ↓ $Paco_2$, ↑ anesthetic depth, ↓ *MAP* | ↓ $Paco_2$, ↑ anesthetic depth, ↓ *MAP* | |
| | Emboli: more than isolated HITS | De-air all infusions, Trendelenburg position, stop rapid fluid boluses, search for and treat air entrainment in surgical field, look on TEE for air | De-airing maneuvers, Trendelenburg position, look for air on TEE, slow wean from bypass | |
| *BIS* | ≥ 80 No isoelectric EEG prior to DHCA | ↑ Anesthetic depth | ↑ Anesthetic depth Additional cooling time; lower temperature before DHCA | |
| | < 30 during rewarming on bypass | | Reduce or discontinue volatile agent on pump | |

*BIS*, bispectral index; *CBFV*, cerebral blood flow velocity; DHCA, deep hypothermic circulatory arrest; EEG, electroenchalogram; HITS, high-intensity transient signals; *MAP*, mean arterial pressure; NIRS, near-infrared spectroscopy; $rSo_2i$, regional cerebral oxygen saturation index; hgb, hemoglobin; TCD, transcranial Doppler ultrasound; TEE, transesophageal echocardiogram; √, assess parameter and adjust as necessary. Baseline $rSo_2i$ and *CBFV* refer to pre-incision values during hemodynamically stable period with optimal blood gases. Frequent adjustments of TCD transducer position may be necessary to obtain the optimal signal before making interventions based on abnormally low values.

brain temperature in the perioperative period; the increase in JBVT was postulated to be caused by release of inflammatory mediators in response to CPB. Other investigators also confirm and show that the nasopharyngeal, not tympanic, temperature best reflects brain temperature.

## Improving neurologic outcome in children undergoing open heart surgery

It is clear that neurologic injury in infants and children undergoing congenital heart surgery is multifactorial in origin, and prevention remains the key to avoiding permanent central nervous sytem injury. A multilayer strategy for detection and prevention of neurologic abnormalities in the perioperative period is presented.

### Preoperative care

The principles of maintaining adequate cardiac output and oxygen delivery to the brain are critically important in the immediate preoperative period. Appropriate inotropic support, avoiding hyperthermia, blood transfusion, or prompt balloon atrial septostomy when indicated will stabilize patients and improve oxygen delivery. In some centers, up to 50% of patients presenting for cardiac surgery in the newborn period have their defects diagnosed prenatally. Delivery should occur in a center experienced in the care

of newborns with CHD, and immediate appropriate care instituted.

Neurologic examination, cranial ultrasound, computed tomography scan, and magnetic resonance imaging have detected abnormalities related to preoperative hypoxic-ischemic injury, or malformations, including those associated with chromosomal abnormalities.[60–62]

## Management of cardiopulmonary bypass

### pH-stat vs. α-stat blood gas management

pH-stat management corrects blood gas values for temperature during CPB allowing for greater cerebral blood flow during hypothermia, greater oxygen delivery, and more even distribution of flood flow. The oxyhemoglobin dissociation curve is shifted to the right, facilitating unloading of oxygen.[63] In animal models of DHCA, neurologic outcome is clearly improved when pH-stat is used. In humans (infants) this has been more difficult to demonstrate, although there were trends towards a lower death rate,[20] fewer seizures, and greater hemodynamic stability. However, long-term neurologic follow-up to 4 years of age could not demonstrate a difference if pH- vs. α-stat was used.[21]

## Low-flow bypass vs. deep hypothermic circulatory arrest

Deep hypothermic circulatory arrest, particularly if prolonged over 30–45 minutes, is associated with a higher incidence of neurologic complications. One hundred and eighty patients less than 3 months of age undergoing repair of transposition of the great arteries were randomized to low-flow CPB vs. DHCA in a landmark study at Children's Hospital Boston.[7] There was a higher incidence of seizures and elevated brain creatine kinase in the DHCA group. Seizures became more common after 30 minutes of DHCA. At 1 year follow-up a significant relationship was found between the duration of circulatory arrest and psychomotor development.[64] At 4 years, the DHCA patients fared worse on examination of fine motor function. These studies provide convincing evidence that low-flow bypass is superior to DHCA in the prevention of neurologic injury.

## Regional low-flow cerebral perfusion

Until recently, neonatal aortic reconstruction surgery was believed to require DHCA. The Norwood palliation for HLHS and the aortic arch advancement for repair of the interrupted or severely hypoplastic aortic arch are the most common examples. In recent years, novel perfusion techniques, such as regional low-flow cerebral perfusion,[65] have been developed. Using this technique, the brain is perfused during the aortic reconstruction through a Goretex graft sewn into the base of the innominate artery, or through special small aortic cannulae advanced into the innominate artery (Fig. 8.6). Neurologic monitoring[55] has demonstrated adequate cerebral blood flow and oxygenation using this technique. Utilizing this technique, DHCA to the brain can be limited to less than 10 minutes for the Norwood palliation, or eliminated altogether. This approach has theoretical advantages, and improved neurologic outcome is expected. However, prospective comparison studies have yet to be performed.

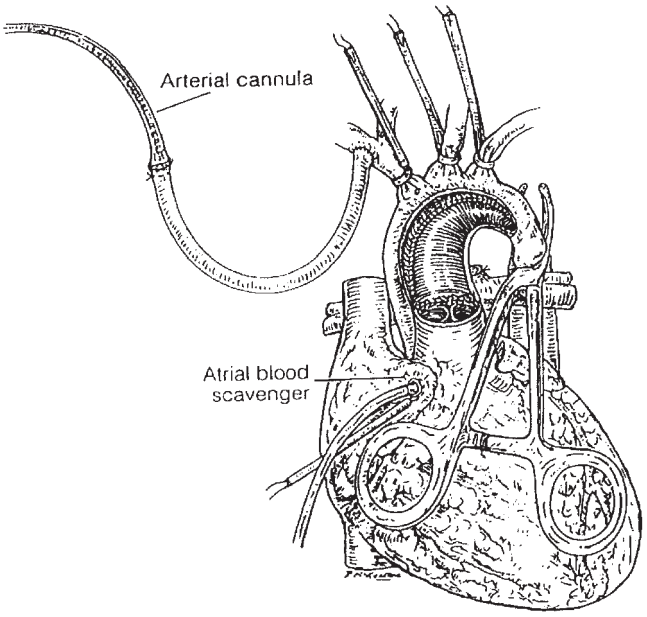


**Fig. 8.6** Regional low-flow cerebral perfusion for the Norwood stage I palliation for hypoplastic left heart syndrome. Arterial inflow for bypass is provided by a small polytetrafluoroethylene graft sewn to the right innominate artery. Instead of deep hypothermic circulatory arrest, flow is provided to the brain at low rates, while the brachiocephalic vessels and descending thoracic aorta are snared, providing a bloodless operating field. Reproduced with permission from Pigula FA, Nemoto EM, Griffiths BP *et al*. Regional low-flow perfusion provides cerebral circulartory support during neonatal aortic arch reconstruction. *J Thorac Cardiovasc Surg* 2000; **119**: 331–9.

## Rate of cooling and rewarming on bypass

There is evidence that brain metabolism is not adequately suppressed during cooling to deep hypothermic levels in some patients. In a study of infants undergoing cooling to 15°C, six of 17 had low jugular venous bulb saturation when this temperature was achieved, suggesting ongoing oxygen consumption that outstripped delivery of oxygen to the brain.[36] Uneven or inefficient cooling of the brain may lead to neurologic deficits. Periods of cooling of less than 20 minutes

were independently associated with lower developmental scores among newborns undergoing the arterial switch operation using DHCA.[66] The risk of developing choreoathetosis is related to shorter periods of cooling.[67] It appears that an insufficient perfusion period during cooling may ineffectively cool watershed areas within the brain leaving them vulnerable to ischemic injury. When low-flow or DHCA is planned the period of cooling should occur over no less than 20 minutes.[16]

### Hemodilution strategy

Classic teaching is that the hematocrit should be reduced to approximately 20 during deep hypothermia, as when blood viscosity increases. Recently, this hypothesis has been challenged with the premise that a higher hematocrit may provide greater oxygen-carrying capacity. A hematocrit of 30 provides slower decay of cerebral oxygenation vs. a hematocrit of 20 in a neonatal pig model with DHCA.[24] In addition neurologic outcome and neuropathologic score was significantly better with higher hematocrit.[58]

### Neuroprotectant agents

At the current time, there is little evidence that any pharmacologic intervention has the potential to improve neurologic outcome in children undergoing congenital heart surgery. Corticosteroids, barbiturates, phenytoin, and aprotinin have been postulated to offer some degree of neuroprotection, but there is no current evidence to support this. One study in newborns has suggested that allopurinol may improve early outcome after congenital heart surgery.[68] Halogenated anesthetic agents used in the bypass circuit, particularly desflurane, show promise in a neonatal pig model.[69]

### Glucose management

In the Boston circulatory arrest study[7] hyperglycemia was not associated with worse neurological outcome and does not appear to be the concern it is in adults; in fact the probability of a perioperative seizure in the newborn is 2–3 times greater with a serum glucose less than 100 mg/dL vs. glucose greater than 200 mg/dL.[70]

### Postoperative management

Besides the basics of maintaining cardiac output and oxygen delivery, measurement of nasopharyngeal temperature and active cooling measures to limit increases in temperature may prevent neurologic injury. Consideration should be given to monitoring of cerebral oxygen saturation in certain high-risk patients. This approach also awaits prospective study of effectiveness in preventing adverse neurologic outcomes.

## Conclusion

As the mortality rate for all congenital heart surgery trends downward toward 1–2% in many large, experienced centers, attention has increasingly turned to other morbidities affecting quality of life, none of which is more important than neurologic outcome. Neurologic morbidity is clearly decreasing as well,[3] but remains a troubling problem. Basic science and clinical outcome studies have been performed in the past 15 years, but more outcome data are required. Despite clinical and experimental evidence that DHCA is detrimental to neurologic outcome, it continues to be in widespread use, and is not restricted to newborn surgery. Comparative studies with novel techniques such as regional low-flow cerebral perfusion, with long-term neurologic follow-up, need to be performed in order to address this question. The non-invasive monitors now available for cerebral oxygenation, blood flow, and EEG—do they improve outcome? Will newer technologies, i.e. frequency-domain spectrophotometers for measurement of cerebral oxygenation, prove to be more accurate? These and many other questions will be important to address as we strive to improve the quality of life for our patients.

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# 9 Intraoperative echocardiography

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## Introduction

The transesophageal approach is recognized as an effective window for imaging intracardiac and vascular structures due to the proximity of the esophagus to the heart and major blood vessels. Initial consideration of using the esophagus as a site of echocardiographic imaging was made in the mid-1970s by Frazin *et al*.[1] who described the use of an esophageal M-mode ultrasonic crystal. The early 1980s marked the introduction of a gastroscope with a two-dimensional transducer. Since the introduction of transesophageal echocardiography (TEE) to the intraoperative setting in the late 1980s,[2] multiple publications have documented the utility of this imaging modality in adult cardiac patients in the evaluation of valvular repair[3–5] and prosthetic valve function,[6,7] and for monitoring of myocardial ischemia[8,9] and left ventricular preload.[10–12] As surgical advances in the care of patients with heart disease rapidly evolve, the contributions of TEE continue to be demonstrated.[13–15] Immediate detection of suboptimal surgical interventions by TEE has been shown to improve surgical outcomes, thereby avoiding subsequent reoperations and reducing morbidity, mortality, and cost.[16] Until the early 1990s, intraoperative evaluation of infants and children undergoing surgery for congenital heart was not feasible via the transesophageal approach due to the fact that probe sizes were not suitable for examination in young children. The subsequent development of miniaturized technology initially generated a number of studies which demonstrated that TEE can be performed safely in the pediatric age group and provides substantial benefit as well.[17–21] This experience has been substantiated over the last decade.

This chapter focuses on the evolution of intraoperative echocardiography for the evaluation and monitoring of pediatric cardiovascular surgery, the benefits of this technology, and the practice of pediatric TEE as it stands today.

## History of pediatric intraoperative epicardial echocardiography

In 1989 Ungerleider *et al*.[22] provided one of the first demonstrations of the use of intraoperative echocardiography in congenital heart surgery. Transducers covered in sterile latex were directly applied to the anterior surface of the heart in order to assess ventricular function before and after cardiopulmonary bypass, and to document the adequacy of the surgical repair. Their findings "directed specific and efficient repair immediately so that all patients left the operating room with documented surgically acceptable results. Comparison of ventricular function between pre- and post-bypass studies enabled appropriate application of pharmacologic agents in the operating room if necessary."[22] These data provided strong support to the notion that intraoperative echocardiography could guide specific surgical or anesthetic adjustments in pediatric cardiac surgery. These observations were supported by additional investigations and underscore the useful role of epicardial echocardiography in the surgical management of congenital heart disease (CHD).[23–26]

Epicardial echocardiography at the present time is reserved for tiny infants in whom the currently available transesophageal probes cannot be used because of size constraints and in patients with contraindications to esophageal instrumentation. Despite its benefits, epicardial echocardiography may have limitations related to transducer size, inadequate windows of interrogation, potential for hemodynamic alterations, and requirement for participation and experience in cardiovascular imaging by the surgeon.

## History of pediatric intraoperative transesophageal echocardiography

Cyran *et al*.[27] described the first experience in pediatric intraoperative TEE in 1989 using an adult-sized probe in children as young as 7.5 years of age. The report noted that this

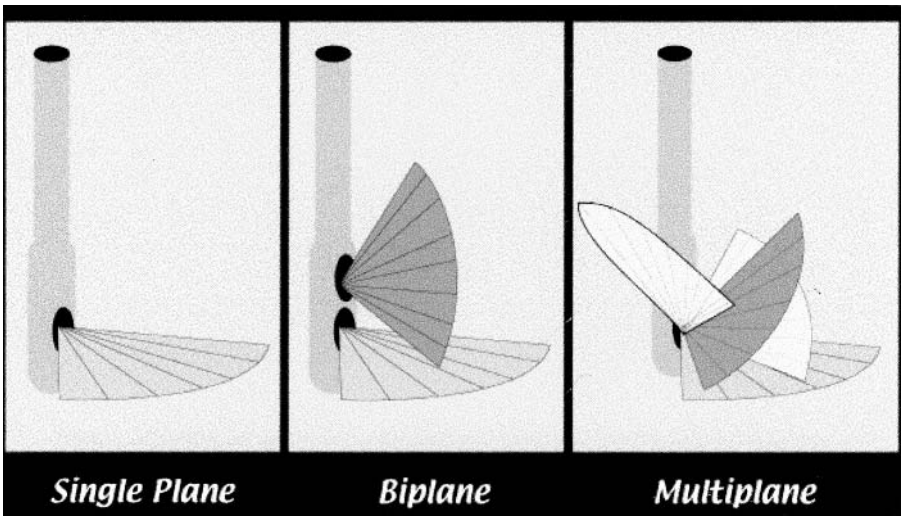



**Fig. 9.1** Types of transesophageal echocardiographic probes. The left panel displays the single plane (monoplane probe) that allows for transverse (horizontal) plane imaging. The middle panel depicts the biplane device that provides for both transverse and longitudinal (vertical) plane interrogation. The right panel depicts the multiplane (omniplane) probe that provides for any number of views from planes acquired in a 0–180° arc.

approach was useful in the evaluation of surgical interventions in CHD. The first probe specifically designed for infants was subsequently designed by Kyo and Omoto with the Aloka/Corometrics Company (Japan).[28,29] This was a single-plane, 5 MHz 26-element phased array probe with a maximum diameter of 6.8 mm. Reports regarding this probe appeared worldwide in the early 1990s documenting the accuracy, immediacy, and feasibility of TEE in the assessment of pediatric cardiac surgery.[17–19,30,31] Initial experience demonstrated that TEE had enhanced diagnostic capabilities in some patients over precordial echocardiography, and the advantage of accuracy equal to that obtained using epicardial imaging.[32–37]

Despite the limitations of TEE, these studies and others suggested that when compared to epicardial echocardiography, TEE did not interrupt surgery, cause potential dysrhythmias or hypotension, or increase the infection risk. Efforts therefore continued into improving the technology of pediatric TEE probes. The principal limitation was the inability to fully evaluate the ventricular outflow tracts, and the poor quality of the resulting images.[38] In 1992 clinical investigations began with the introduction of a new high-resolution single-plane TEE probe with continuous wave Doppler capabilities (5.0 MHz phase array, 48-element) (Fig. 9.1). The images generated with this new probe were superior to those obtained with the previous technology, with resolution sensitive enough to define the coronary arteries and permit visualization of blood flow, even in tiny infants.[39]

Concurrent refinements in spectral and color Doppler modalities allowed for optimal analysis of jet direction and severity of regurgitation, both of which are particularly important in the pediatric surgical setting for baseline assessment and evaluation of residual pathology.

The development of pediatric biplane probes introduced capabilities to examine not only the transverse or horizontal plane (as in the case of single plane devices) but also the longitudinal or vertical plane (Fig. 9.1).[40–43] The additional plane of interrogation allowed for a more complete examination of the ventricular outflow tracts, but the Doppler angle of incidence still did not permit accurate assessment of pressure gradients. Several investigators subsequently demonstrated that advancing the single-plane probe into the fundus of the stomach could provide a view that favorably imaged the outflow tracts, allowing for quantitative assessment of outflow tact obstructions.[44,45] Accordingly, the transgastric views overcame some of the limitations of single and biplane imaging.

Recently multiplane imaging has become available for pediatric patients (Fig. 9.1).[46] A high-resolution minimultiplane TEE probe (5 MHz, 48-element, 9.5–10.0 mm diameter) now allows for the acquisition of images in several planes, which is of particular benefit in the assessment of complex structural heart defects. An even smaller prototype device (micromultiplane TEE probe) with high resolution capabilities (7.5 MHz, 48-element, 8.2 mm diameter), developed by General Electric Corporate Research in association with Odelf Corporation (the Netherlands), has been investigated and proposed as an ideal probe in infants under 2 kg.[47] However, technologic limitations related to the small size of the probe have hindered the further development of this device.

To date, most institutions use a combination of all approaches, transesophageal and transgastric, for comprehensive evaluation of the pediatric heart. Transesophageal echocardiography has been a rapidly evolving field and is considered the standard of care in many cardiac surgical centers for intraoperative evaluation of pediatric patients undergoing surgery for congenital and acquired heart disease.[48,49]

## Indications for transesophageal echocardiography

Transthoracic echocardiography provides excellent definition of cardiovascular anatomy in most infants and young

children. Accordingly TEE should be considered a complimentary imaging modality and not a substitute to the transthoracic exam. Transesophageal echocardiography provides diagnostic-quality images in the majority of congenital cardiac anomalies when transthoracic examination or other studies have not successfully elucidated the necessary clinically relevant information. By overcoming limitations related to poor windows, suboptimal image quality or lung interference, TEE is able to facilitate morphologic and functional assessment of structural cardiac abnormalities. Transesophageal echocardiography might be superior to routine transthoracic echocardiography in the adolescent or adult for the evaluation of malformations such as specific types of atrial septal defects, anomalous pulmonary venous connections, and complex cardiac malformations. This technology is also key in confirming or excluding diagnoses of major clinical relevance in CHD such as atrial baffle pathology (leak or obstruction), Fontan obstruction or related venous thrombus, as well as acquired cardiovascular pathology (valve vegetations, aortic root abscess).[50]

Transesophageal echocardiography also plays an important role in the catheterization laboratory in guiding and monitoring of interventional procedures and evaluating their successes, failures and complications.[51]

Indications for TEE in children have been proposed by various groups. Initial efforts were by the Committee on Standards for Pediatric Transesophageal Echocardiography, Society of Pediatric Echocardiography in 1992.[52] In 1996, task forces of the American Society of Anesthesiologists and the Society of Cardiovascular Anesthesiologists published practice guidelines for perioperative TEE.[53] Shortly thereafter, the American College of Cardiology (ACC)/American Heart Association (AHA) Task Forces, in collaboration with the American Society of Echocardiography (ASE), published recommendations for the clinical application of echocardiography.[54] The ACC/AHA/ASE recently reconvened to update these guidelines.[55] The indications for pediatric intraoperative TEE from the four reports respectfully are summarized as follows:

(a) Intraoperative and post-repair examinations are indicated when operations are performed on cardiac defects in which there are significant residual abnormalities such as outflow tract obstruction, valve regurgitation or stenosis, or intracardiac communications are anticipated or suspected.[52]
(b) Most cardiac defects requiring repair under cardiopulmonary bypass are a category 1 indication for intraoperative TEE, including pre- and post-cardiopulmonary imaging (defined as that being supported by the strongest evidence or expert opinion substantiating that TEE is useful in improving clinical outcomes).[53]
(c) Monitoring and guidance during cardiothoracic procedures associated with the potential for residual shunts, valvular regurgitation, obstruction or myocardial dysfunction is a class I indication (defined as conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective).[54]
(d) Surgical repair of most congenital heart lesions that require cardiopulmonary bypass is a class I indication. The updated guidelines list assessment of residual flow after interruption of a patent ductus arteriosus as a class IIb indication (conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment). Repair of an uncomplicated secundum atrial septal defect is considered a class III indication (defined as conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful/effective and in some cases may be harmful).[55]

In general the recommendations for use of TEE in pediatric heart surgery apply to all cases in which this imaging approach may allow for real-time clinical decision making, hemodynamic monitoring, and immediate assessment of the surgical results.

## Transesophageal echocardiography technique

### Equipment

A number of transesophageal probes are commercially available for use in the pediatric age group. The most commonly used echocardiographic platforms in North America include Philips Medical Systems (former Hewlett Packard, Agilent and ATL Technologies, Andover, MA), Acuson/Siemens (Siemens Ultrasound, Mountain View, CA) and General Electric/Vingmed (General Electric Medical Systems, Milwaukee, WI). Frequently used transesophageal probes and their specifications are listed in Table 9.1. Other TEE probes suitable for pediatric use are marketed by several companies in Europe and Asia.

In general, probes are not interchangeable among echocardiographic platforms. Although there is an increased recognition from companies to allow for probes to be interchangeable between systems in their own platform, in some cases this is not feasible due to differences between older and newer equipment related to advances in technology.

### Probe selection

Although TEE probes can be inserted in tiny neonates, even in those as small as 1.4 kg, the usual weight range for infants and children who can be safely imaged with the current commercially available pediatric probes is over 3 kg.[56] There are minimal differences between the actual transducer dimensions of commercially available pediatric probes, although clinically the biplane probes are sometimes easier to insert

**Table 9.1** Commonly used transesophageal probes in pediatrics.

| Transesophageal probes | Tip dimensions (W × H × L, in mm) | Shaft dimensions (W × L, in mm) | No. of elements | Imaging frequencies (MHz) |
|---|---|---|---|---|
| *Philips (Hewlett Packard/Agilent)* | | | | |
| Pediatric biplane | 9.3 × 8.8 × 27 | 8 × 80 | 64 | 5.5–7.5 |
| Pediatric multiplane | 10.7 × 7.2 × 25.4 | 7.4 × 70 | 48 | 4.0–7.0 |
| Adult multiplane (Omni II) | 14.5 × 11.2 × 42 | 10.5 × 100 | 64 | 4.0–7.0 |
| *Acuson (Siemens)* | | | | |
| Pediatric biplane (V7B) | 9.5 × 8.5 × 31 | 8.5 × 85 | 48 | 5.0–8.0 |
| Pediatric multiplane (V7M) | 10.7 × 8 × 36* | 7 × 70 | 48 | 4.0–8.0 |
| Adult multiplane (V5M) | 14.5 × 11.5 × 45 | 10.5 × 110 | 64 | 3.5–7.0 |
| *General Electric (Vingmed)* | | | | |
| Pediatric multiplane (8T, MPTE) | 10.7 × 7.5 × 37.5* | 7 × 70 | 48 | 3.3–8.0 |
| Adult multiplane (6T/6Tv and 5T/PAMPTE) | 14 × 12.5 × 40 | 10.5 × 110 | 64 | 4.4–8.0 |

Probe specification information provided by respective companies. Imaging frequencies may vary with specific ultrasound system.
*Length of inflexible distal part of the probe.

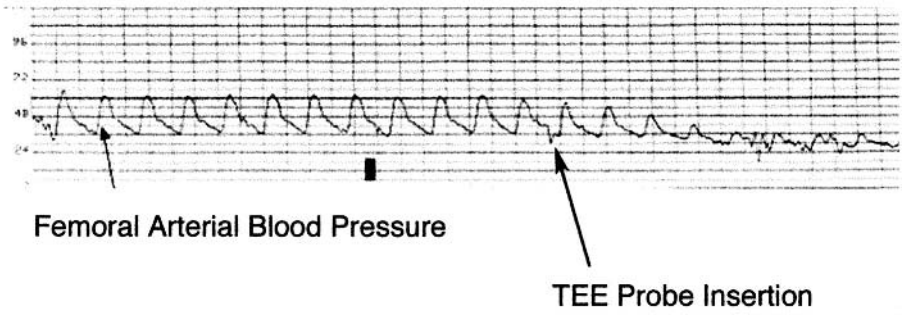



**Fig. 9.2** Hemodynamic alterations in a neonate associated with insertion of a transesophageal echocardiography (TEE) probe. The graphic illustrates dramatic decreases in systemic arterial blood pressure (recorded from a femoral artery catheter) associated with TEE probe insertion in infant with total anomalous pulmonary connection. Hypotension was most likely the result of compression of the pulmonary venous confluence by the probe.

than the multiplane devices. The pediatric multiplane probe is suitable for all ages and may also be considered in small infants, however, the slightly larger and less flexible tip may present a challenge for insertion and potentially a higher risk. In the extremely small neonate, probe insertion and manipulation could be associated with hemodynamic or respiratory compromise and vigilance is imperative. In some cases the arterial blood pressure tracing or pulse oximetry signal may be partially or completely attenuated by probe manipulation (Fig. 9.2). In the event of acute hemodynamic or airway changes the probe should be repositioned or removed immediately.

The superior resolution capabilities of the adult-sized multiplane probes make these devices preferable for children above 15–20 kg. The experience with multiplane probes favors these over biplane transducers, as the ideal positioning of the interrogating plane is feasible and not dictated by the fixed plane of the transducer(s).

A miniaturized 5.5–10.0 MHz single longitudinal plane transducer with a 3.3 mm diameter used for intravascular and intracardiac imaging has been described in pediatric patients for transesophageal applications, four of whom weighed less that 2.5 kg. This probe has the advantage of being extremely small. The single plane may however limit its usefulness.[57]

## Probe insertion

The anesthetic preparation for outpatient TEE includes a careful history, physical examination, and informed consent. The standard safety precautions associated with an endoscopic procedure should be followed. Although serious complications during TEE are rare, it should be considered that this is a semi-invasive/invasive procedure that may result in some degree of patient discomfort and potential risks. In the outpatient setting several options are available for anesthetic management. A combination of oropharyngeal topical anesthesia and intravenous sedation may be suitable for the adolescent or young adult. Younger children, however, will frequently require deep sedation or general anesthesia. Standard cardiorespiratory monitoring should include intermittent blood pressure assessments during the procedure, in addition to electrocardiography, pulse oximetry and capnography. The facilities should be equipped with oxygen and

suction capabilities. In addition, drugs and equipment for emergency therapy or cardiopulmonary resuscitation should be readily available. Patients with CHD may have significant hemodynamic disturbances and be marginally compensated; therefore, the judicious, titrated administration of drugs is warranted. In the case of cyanotic patients, additional considerations apply. These include potential for paradoxical air embolism during the administration of intravenous fluids or drugs, detrimental effects related to the rapid onset of anxiolytics, anticholinergics and sedatives, and decreases in systemic vascular resistance with an associated increase in the magnitude of right-to-left shunting and systemic arterial desaturation.

In the operative setting after the induction of general anesthesia and endotracheal intubation, gastric contents may be suctioned in order to optimize image quality. Some centers prefer nasal over oral endotracheal intubation in view of concerns related to the stability of an oral endotracheal tube during probe manipulation. Regardless of the intubation route, the endotracheal tube should be securely taped to minimize potential for displacement. The lubricated unlocked probe should be advanced gently into the esophagus with the head in midline position. A forward thrust of the mandible frequently assists in the passage of the probe. On occasion direct guidance of the probe with a gloved finger may be helpful. If significant difficulty is encountered and attempts at probe insertion are unsuccessful, direct visualization of the oropharynx with a laryngoscope may assist in esophageal intubation. The probe should never be advanced if resistance is encountered. Once the transducer is positioned behind the heart, the patient's head can be turned to the side to avoid interference with the surgical procedure during manipulation of the probe.

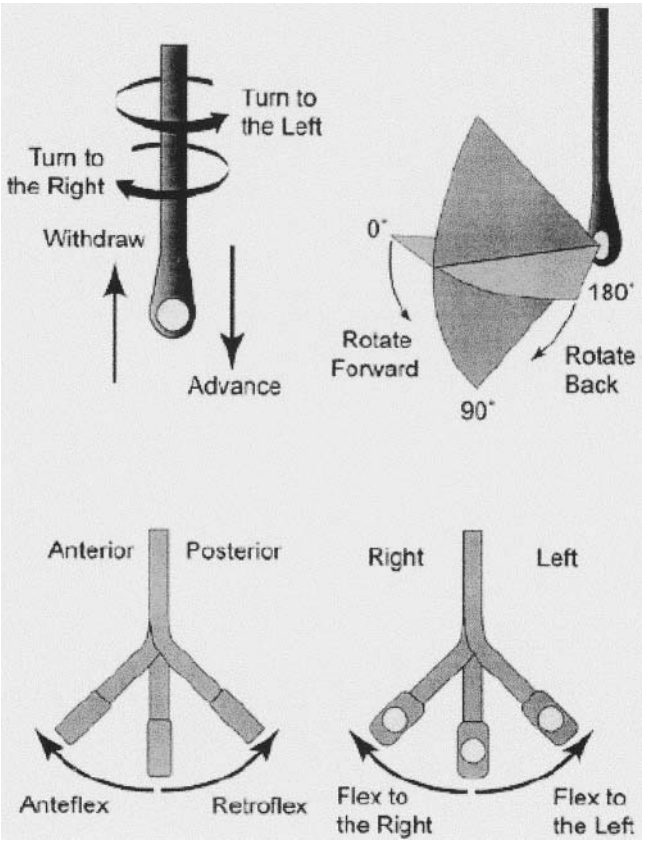



**Fig. 9.3** Terminology used to describe manipulation of the transesophageal echocardiography probe during image acquisition. The general manipulations of the transesophageal echocardiography probe are depicted. Reproduced with permisison from Shanewise JS, Cheung AT, Aronson S *et al*. ASE/SCA Guidelines for performing a comprehensive intraoperative multiplane transesophageal echocardiography examination: Recommendations of the American Society of Echocardiography Council for Intraoperative Echocardiography and the Society of Cardiovascular Anesthesiologists Task Force for Certification in Perioperative Transesophageal Echocardiography. *J Am Soc Echocardiogr* 1999; **12**: 884–900.

## Imaging technique

The TEE probe can be manipulated in three general directions; advanced or withdrawn, anteflexed, or retroflexed, and rotated clockwise or counterclockwise relative to the sagittal plane (Fig. 9.3).[58,59] The multiplane probe obviates some of the manipulations required in single and biplane devices. As general principles of transducer manipulation, anteflexion of the transducer brings structures anterior and toward the base of the heart into view, clockwise rotation allows imaging of rightward structures, and counterclockwise rotation permits viewing of left-sided structures. In the smallest neonates, minimal adjustments in probe position are adequate to change from view to view.

Guidelines have been published for performing a comprehensive intraoperative multiplane echocardiographic examination.[59] Although these recommendations represent a consensus among physicians primarily involved in the care of adults, the guidelines regarding image orientation and nomenclature standards may also be considered applicable to pediatric patients. A systematic and complete exam is emphasized in the document; however, it is recognized that various factors may influence the ability to perform a comprehensive study. In addition to an organized approach for acquisition of the echocardiographic information in patients with CHD, a focused interrogation of the structural cardiac abnormalities in question and their hemodynamic impact is essential.

All examinations should include careful two-dimensional imaging, spectral and color flow Doppler interrogation. To evaluate for small intracardiac shunts contrast injection with agitated saline into a peripheral or central vein may be used as the microbubbles are readily apparent even when a very

small number of these cross an intracardiac defect (right-to-left shunt). Contrast echocardiography may also be useful in the identification of anomalous systemic venous connections as seen in patients with persistent drainage of a left superior vena cava into the coronary sinus.[60,61]

The basic examination described in the sections that follow assumes levocardia (heart in the left thoracic cavity, apex pointing to the left), situs solitus (normal arrangement: stomach to the left, liver to the right, normal systemic and pulmonary venous pathways) and concordant atrioventricular and ventriculoarterial connections. The wide spectrum of structural cardiovascular malformations dictates a modified scheme from the basic examination in many patients. Although a particular sequence for the examination is not emphasized it is extremely helpful for each individual to develop an organized approach in order to perform a comprehensive interrogation in an expeditious manner.

### Transverse plane examination

The short axis views obtained with single or biplane probes consist of cross-sections oriented in an axial plane, and are therefore slightly oblique relative to a true short axis of the heart. This limitation is overcomed by multiplane echocardiography allowing for optimal alignment of the imaging plane with the structures of interest. Manipulation of the probe (advancement or withdrawal) provides images from the base to the apex of the heart. The most cranial short-axis view is obtained at the base of the heart from which the probe is anteflexed slightly to display the aorta, the main pulmonary artery, and its bifurcation. The proximal branched pulmonary arteries can be readily imaged (Fig. 9.4a); however, interposition of the left mainstem bronchus between the esophagus and left pulmonary artery makes imaging of this vessel challenging. Advancement of the probe displays the aortic valve in short axis, the proximal ascending aorta and the origins of the coronary arteries. A 30° retroflexion of the multiplane probe at the level of the base of the heart defines the anatomy of the aortic valve, cusps, commissures, and valve motion throughout the cardiac cycle (Fig. 9.4b). Rotation of the probe in counterclockwise fashion from this position displays the left-sided pulmonary veins; clockwise rotation shows the right-sided pulmonary veins, superior vena cava, and right atrial appendage. Advancement of the probe into the esophagus allows for the four- and five-chamber views to be obtained (Fig. 9.4c,d). This demonstrates the atrial, atrioventricular and ventricular septae, and atrioventricular valves. Further advancement of the probe into the stomach provides for left ventricular short axis images to be obtained seen as multiple cross-sectional views of the left ventricle, mitral valve, and papillary muscles (Fig. 9.4e). Oblique sections of the right ventricle are obtained by slight probe flexion and/or rotation at this level.

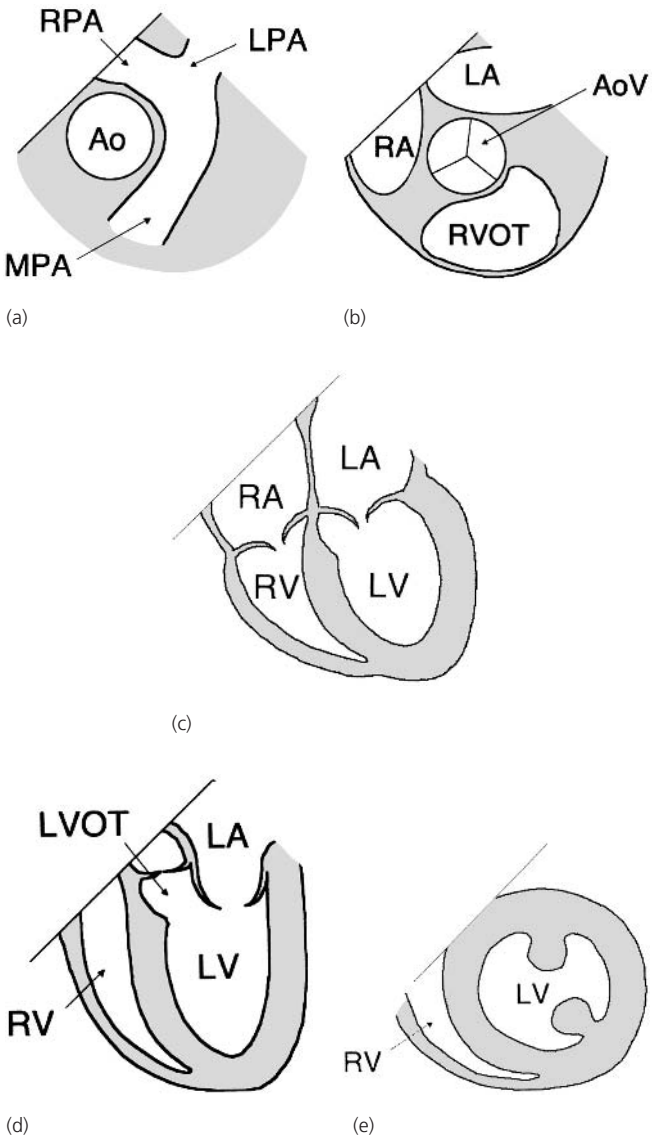



**Fig. 9.4** Transverse plane examination. (a) Pulmonary artery view. The main and branched pulmonary arteries are depicted in this view, obtained at 0° at the base of the heart. (b) Aortic short axis view. The aortic valve cusps are well seen in this short axis view obtained with 30–40° of angulation at the base of the heart. (c) Four-chamber view. This view demonstrates the atrial and ventricular chambers and septal structures. This view is obtained at 0° in the mid-esophagus. (d) Five-chamber view. The structures demonstrated in this view include the right and left atria, right and left ventricles, and left ventricular outflow tract/aorta. (e) Left ventricular mid-papillary short axis view. This view provides for short axis sections of the left ventricle and portions of the right ventricle (obtained at 0–20°). The left ventricular papillary muscles are well demonstrated in this view. This is a frequently used view in the evaluation of left ventricular systolic function (global and segmental) and assessment of preload. Ao, aorta; AoV, aortic valve; LA, left atrium; LPA, left pulmonary artery; LV, left ventricle; LVOT, left ventricular outflow tract; MPA, main pulmonary artery; RA, right atrium; RPA, right pulmonary artery; RV, right ventricle; RVOT, right ventricular outflow tract.

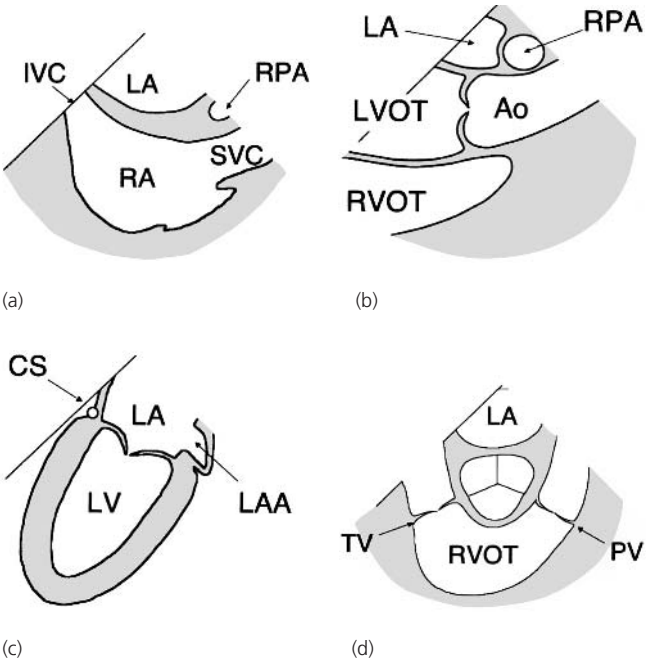



**Fig. 9.5** Longitudinal plane examination. (a) Bicaval view. The superior and inferior vena cavae are seen as they enter the right atrium. This view (90°) allows for evaluation of the atrial septum in the longitudinal axis. The left atrium is also displayed. The pulmonary veins can be interrogated by minimally rotating the transducer from this reference point. The right pulmonary artery is frequently seen in its short axis. (b) Aortic long axis view. Interrogation from the mid-esophageal window at 110° allows for visualization of the left ventricular outflow tract and aorta in the long axis. (c) Two-chamber view. Rotation of the transducer to the left at a 90° angle of interrogation displays the left atrium and left ventricle. The coronary sinus and left atrial appendage are easily identified. (d) Right ventricular inflow–outflow view. This view, obtained by deflection of the probe to a 60° angle, provides for images of the tricuspid valve, right ventricular inlet and outlet portions, pulmonary valve, and main pulmonary artery. Ao, aorta; CS, coronary sinus; IVC, inferior vena cava; LA, left atrium; LAA, left atrial appendage; LV, left ventricle; LVOT, left ventricular outflow tract; PV, pulmonary valve; RA, right atrium; RPA, right pulmonary artery; RVOT, right ventricular outflow tract; SVC, superior vena cava; TV, tricuspid valve.

### Longitudinal plane examination

The TEE long axis examination is feasible with biplane and multiplane probes.[43,62–65] Long axis views of the atrium and large systemic veins (bicaval view), right and left ventricular outflow tracts, and left ventricle can be obtained. With the longitudinal transducer of the biplane probe, clockwise rotation displays the interatrial septum and entrance of the superior and inferior vena cava (Fig. 9.5a). Counterclockwise rotation of the probe provides visualization of the left ventricular outflow tract and ascending aorta (Fig. 9.5b). Further counterclockwise rotation shows portions of the right ventricular outflow tract and main pulmonary artery. The two-chamber view (left atrium and left ventricle) can be obtained with additional counterclockwise probe rotation (Fig. 9.5c). The multiplane probe allows for the bicaval view to be obtained at 90° with the probe rotated rightward, for the two-chamber view at 90° with the probe rotated leftward, a "true" left ventricular outflow tract view at 120°, and a right ventricular inflow and outflow view at 60° (Fig. 9.5d).[66]

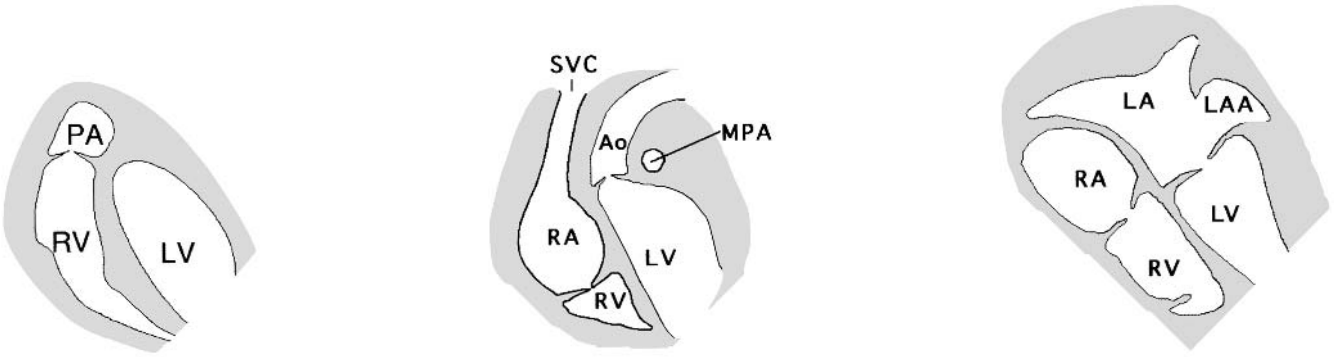
### Transgastric examination

Transgastric examination allows for additional two-dimensional and Doppler information to be obtained. This helps refine the data obtained from the transesophageal windows, and in some cases additional diagnostic details are added that would not be possible otherwise. This is of particular utility when only a single-plane probe is available.

The suggested approach to the transgastric exam is as follows: the probe is advanced into the stomach, anteflexed maximally and positioned anterior to the fundus. When the patient's abdomen is exposed during this maneuver, it is frequently possible to observe the tip of the probe outpouching the abdominal wall. If there is difficulty in achieving the views, the probe is relaxed and withdrawn, then re-advanced and withdrawn with maximal anteflexion to ensure adequate probe contact. Anteflexion should not be performed if resistance is encountered. From this position, rotation of the probe to the left with moderate deflexion provides images of the right ventricular outflow tract and the proximal pulmonary trunk as it courses anteriorly across the surface of the heart (Fig. 9.6a); clockwise rotation and slight flexion from this position permits similar evaluation of the left ventricular outflow tract (Fig. 9.6b). The flexion of the probe is then increased slightly to define the inlet and outlet components of the ventricular septum as well as the atria and atrioventricular valves (Fig. 9.6c). The entrance of the pulmonary veins into the left atrium is demonstrated from this plane, and with rotation of the probe to the right the venous connections to the right atrium can also be seen. Because the probe is some distance from the heart with a portion of the liver interposed, small movements of the transducer subtend large imaging arcs, permitting examination of the heart from the posterior atrial wall to near the anterior surface of the right ventricle. Once imaging of the outflow tracts is completed, pulsed-, continuous-wave Doppler and color flow mapping are performed. The transgastric approach allows for favorable alignment of the Doppler angle of interrogation with the direction of flow in the outflow tracts optimizing spectral Doppler signals.

### Segmental morphologic analysis

The variety of cardiac malformations, wide spectrum of anatomic arrangements and complexity of the defects present




(a) (b) (c)

**Fig. 9.6** Transgastric exam. (a) Right ventricular outflow tract view. Advancement of the probe into the stomach (at 0°) displays sections of the right ventricular apex and outflow, and proximal aspect of the main pulmonary artery. (b) Left ventricular outflow tract view. Probe flexion from the transgastric window reveals the left ventricular tract from a vantage point favorable for spectral Doppler. (c) Four-chamber view. All cardiac chambers can be displayed from this window, in addition to the interatrial and interventricular septae. The pulmonary veins are frequently seen as they enter the posterior aspect of the left atrium. Ao, aorta; LA, left atrium; LAA, left atrial appendage; LV, left ventricle; MPA, main pulmonary artery; PA, pulmonary artery; RA, right atrium; RV, right ventricle; SVC, superior vena cava.

significant challenges in the echocardiographic evaluation of CHD, even to the specialists. A segmental approach is indispensable in the transthoracic assessment and should also extend to the transesophageal examination. The suggested practice includes the assessment of atrial arrangement or situs, and connections of the various cardiac segments (venoatrial, atrioventricular, and ventriculoarterial connections), evaluation of inflows, outflows, septal and valvar structures, and the interrogation of flows with Doppler echocardiography.

## Recognition of common lesions

Echocardiographic information of interest in the pre-bypass evaluation of the most common congenital cardiac defects is noted in Table 9.2. Representative images of some of these anomalies are provided in Figs 9.7–9.9.

A number of excellent textbooks in pediatric echocardiography provide in-depth information on imaging and hemodynamic assessment in CHD.[67–70] These sources are suggested as a reference.

## Assessment of residual pathology

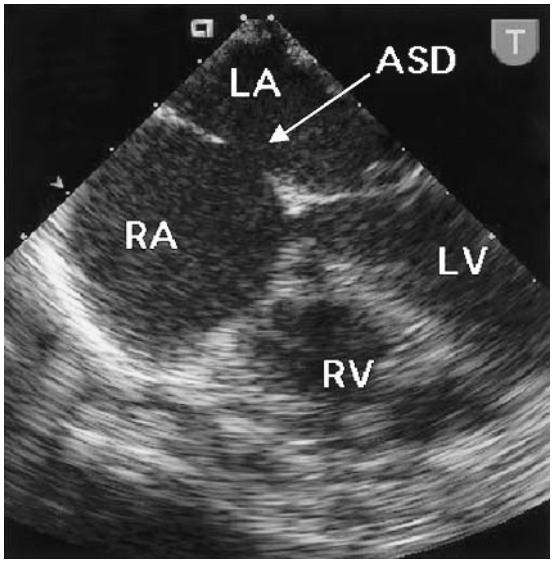
The post-bypass echocardiographic examination requires focus on the specific pathology in question. Guidelines for the postoperative evaluation of common lesions/interventions are suggested in Table 9.3. Among problems that require return to bypass for surgical revision, residual intracardiac shunts, outflow tract obstructions, and valvular regurgitation are most common.

## Assessment of pressure gradients

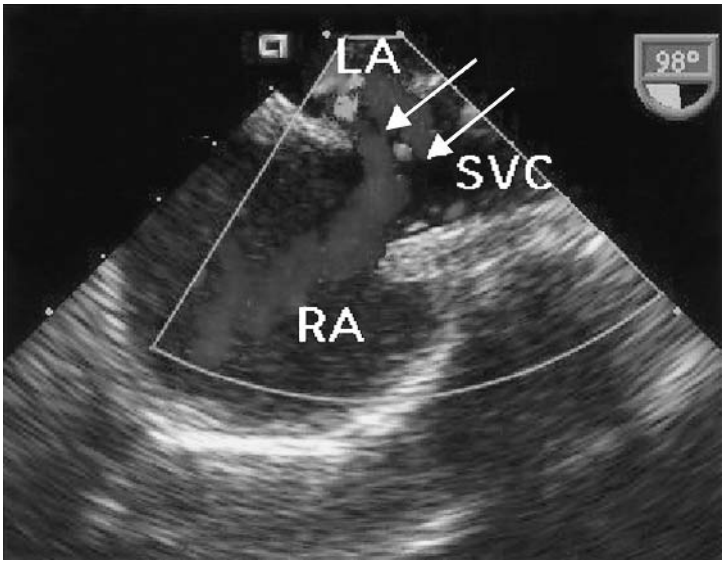
The transgastric approach provides for axial alignment of the Doppler cursor for estimates of pressure gradients across outflow tracts. Doppler predictions are performed using the modified Bernoulli equation (peak pressure difference = $4(V)^2$) (Fig. 9.10). Good correlation has been documented between Doppler estimates of pressure gradients and direct pressure measurements.[45,71,72] It is important to note that preoperative determination of pressure gradients obtained when patients are awake or lightly sedated may differ from those obtained in the operating room under general anesthesia.

## Assessment of ventricular filling and function

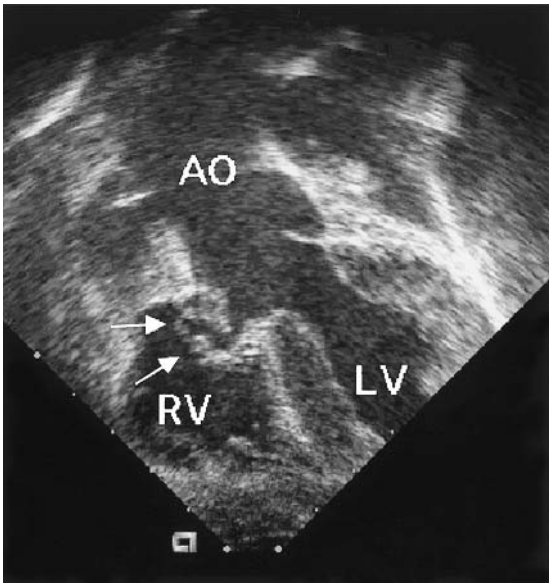
Transesophageal echocardiography is extremely useful in the evaluation of factors that directly affect cardiac output such as preload, contractility, and afterload. This technology has been shown to be a reliable monitor of left ventricular filling changes in pediatric patients. In a study designed to evaluate whether TEE would identify changes in cardiac filling resulting from manipulations of blood volume in children, blood was withdrawn until the systolic blood pressure decreased by 5 and 10 mmHg.[73] Experienced anesthesiologists–echocardiographers blinded to study events were able to identify with high sensitivity and specificity these mild reductions in blood volume by TEE changes in left ventricular end-diastolic area.


LA
ASD
RA
LV
RV

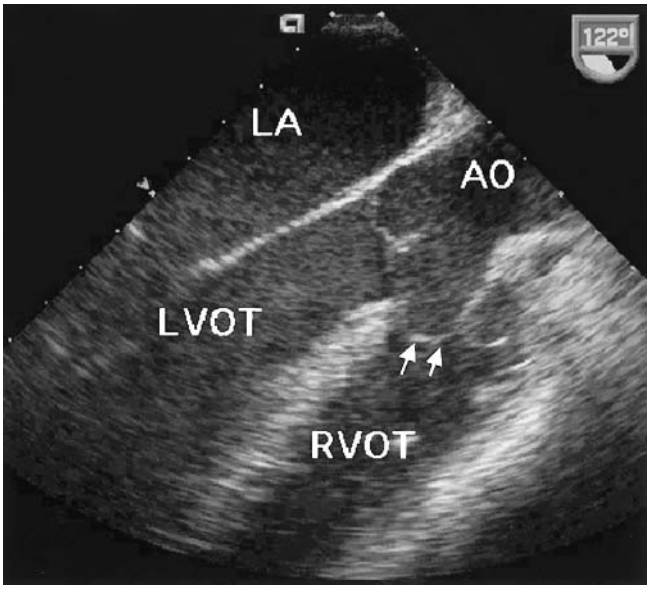
(a)


LA
98°
SVC
RA

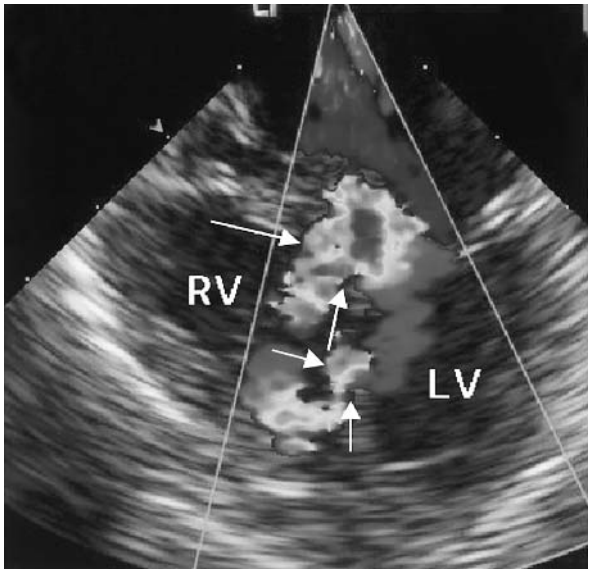
(b)


AO
RV
LV

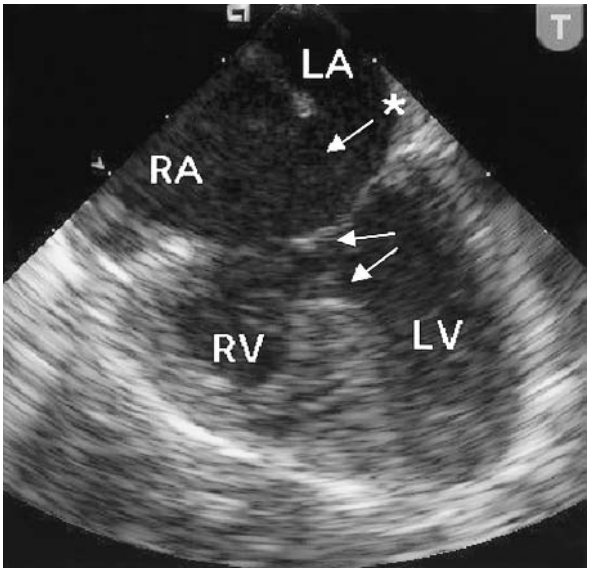
(c)


122°
LA
AO
LVOT
RVOT

(d)


RV
LV

(e)


LA
*
RA
RV
LV

(f)

Several investigations have also documented the utility of TEE in the evaluation of ejection fraction. Transesophageal echocardiography estimation of ejection fraction reached a good correlation ($r = 0.98$) when compared to measures of ejection fraction by transthoracic echocardiography.[74] A comparison made between transthoracic and transesophageal echocardiography for assessment of ventricular function in pediatric patients showed poor correlation likely due to technical limitations.[75]

Transesophageal echocardiography is frequently used to monitor myocardial ischemia in adults, and it has also been suggested that segmental wall motion abnormalities as detected in pediatric patients may be a surrogate of compromised myocardial blood flow.[76] This is particularly applicable to patients undergoing procedures that involve coronary artery manipulations.

## Influences of intraoperative transesophageal echocardiography on anesthetic and surgical management

The overall incidence of change in surgical management with the aid of intraoperative TEE has been reported to be in the range of 3–15%,[39,77–79] and does not differ significantly from that previously described for epicardial echocardiography.[22,24,26] Various studies have suggested that preoperative diagnoses can be changed in 3–5% and the return to bypass rate as directed by TEE to be in the 3% range. A recent report on intraoperative TEE during congenital heart surgery in a wide range of patients (2 days to 85 years) described a major impact in 13.8% of cases.[79] This was more frequent during reoperations and in patients undergoing valve repairs and complex outflow tract reconstructions.

Several reports have also documented the many contributions of TEE to anesthetic management.[80,81] Two large studies that included a large number of congenital cardiac cases undergoing surgery demonstrated changes in inotropic strategy and volume replacement to be frequent interventions as a direct result of TEE.[81,82]

Additional benefits of TEE in pediatric heart surgery include ensuring adequacy of cardiac de-airing, a significant concern in this patient population where interventions frequently require a cardiotomy, and guidance during placement of intravascular and intracardiac catheters.[83]

## Outcome and effectiveness of pediatric intraoperative echocardiography

There is limited information regarding improvement in clinical outcomes based on intraoperative TEE. However, despite the lack of rigorous scientific scrutiny the data regarding the contributions of TEE has been so compelling that the technology has been incorporated into clinical practice in many centers. A prospective study designed to evaluate the efficacy of intraoperative epicardial color flow mapping to predict outcome after surgical repair noted that if patients left the operating room with residual pathology, there was a high rate of reoperation and of early death.[84] Alterations in ventricular function after bypass also resulted in a higher incidence of early death. Patients with acceptable surgical results as documented by epicardial echocardiography had a greater than 90% likelihood of long-term acceptable outcome.

In one series of 230 patients in which the issue of outcome was addressed, if a residual abnormality was detected by TEE and revised, the outcome was excellent in 76% (13/17) of patients.[85] Twelve patients were identified that had suboptimal outcomes; 16% (2/12) had residual defects that may have been amenable to further surgery and 84% (10) had final outcomes that were believed to be unrelated to a problem identifiable by TEE. Thus if immediate revision of a repair was performed, the outcome was improved; if the patient was left with a residual defect, the outcome was suboptimal.

## Transesophageal echocardiography in the catheterization laboratory

Cardiac catheterization is used selectively in the anatomic

**Fig. 9.7** (opposite) Echocardiographic images of septal defects. (a) Secundum atrial septal defect. Four-chamber view demonstrates the typical appearance of a secundum type atrial septal defect located in the central region of the interatrial septum (arrow). (b) Sinus venosus atrial septal defect. Color Doppler exam a of superior vena cava-type sinus venosus atrial septal defect in the bicaval view. Left-to-right shunting across the defect is noted in the superior aspect of the interatrial septum (arrows). Also reproduced in color, facing p. 146. (c) Perimembranous ventricular septal defect. Transgastric left ventricular outflow tract view displays tricuspid valve aneurysmal tissue (arrows) partially occluding a defect in the region of the membranous ventricular septum. (d) Subarterial (supracristal) ventricular septal defect. Long axis view demonstrates herniation of aortic valve cusp through subpulmonary ventricular septal defect (arrows). The proximity of the defect to the semilunar valves is shown. (e) Muscular ventricular septal defects. Color Doppler interrogation of the muscular septum in the four-chamber view documents multiple levels of ventricular shunting. Also reproduced in color, facing p. 146. (f) Complete atrioventricular septal (canal) defect. Two-dimensional mid-esophageal four-chamber view of complete atrioventricular septal defect illustrates a defect in the inferior portion of the interatrial septum known as ostium primum atrial septal defect (noted as arrow with asterisk) and inlet type of ventricular septal defect located in the superior-posterior aspect of the ventricular septum (arrows). AO, aorta; ASD, atrial septal defect; LA, left atrium; LV, left ventricle; LVOT, left ventricular outflow tract; RA, right atrium; RV, right ventricle; RVOT, right ventricular outflow tract; SVC, superior vena cava.

**Table 9.2** Pre-bypass echocardiographic data by type of congenital heart defect.

| Cardiac pathology | Presurgical echocardiographic information of interest |
|---|---|
| Atrial septal defect | Define location and size of defect<br>Evaluate pulmonary venous drainage<br>Assessment of atrioventricular valve regurgitation<br>Baseline determination of ventricular function |
| Ventricular septal defect | Define location and size of defect<br>Evaluate for additional intracardiac shunts<br>Investigate for associated pathology (aortic valve herniation/prolapse, aortic regurgitation, subaortic membrane, pulmonary valve stenosis, double chamber right ventricle, atrioventricular valve regurgitation)<br>Baseline determination of ventricular function |
| Atrioventricular septal defect | Define location, size and type of defects<br>Evaluate for additional septal defects<br>Assessment of atrioventricular valve (Rastelli type, atrioventricular valve regurgitation, relation of valvar structures to ventricles, balanced vs. dominant type, valvar support apparatus)<br>Interrogation of ventricular outflows (for obstruction)<br>Baseline determination of ventricular function |
| Aortic stenosis | Evaluate location and severity of obstruction (subvalvar, valvar, supravalvar)<br>Define aortic valve anatomy<br>Evaluate for aortic regurgitation<br>Assess for ventricular hypertrophy and function |
| Pulmonic stenosis | Evaluate location and severity of obstruction (subvalvar, valvar, supravalvar)<br>Define pulmonary valve anatomy<br>Determine size of pulmonary arteries<br>Evaluate for intracardiac shunts<br>Assess for ventricular hypertrophy and function |
| Pulmonary/conduit regurgitation | Evaluate severity of regurgitation and possible obstruction<br>Interrogate atrial and ventricular septum for shunts<br>Assess ventricular sizes and function |
| Tetralogy of Fallot | Define size and location of septal defects<br>Evaluate right ventricular outflow tract (subvalvar, valvar and supravalvar regions)<br>Define morphology, obstruction, gradients<br>Determine size of pulmonary arteries<br>Evaluate aortic valve competence/aortic override<br>Evaluate origin and course of coronary arteries<br>Baseline determination of ventricular function |
| d-Transposition of the great arteries | Evaluate ventriculoarterial relationships and intracardiac shunts (location, size, flow direction, relation to outflows)<br>Assessment of outflow tract obstruction<br>Evaluate atrioventricular and semilunar valves<br>Evaluate origin and course of coronary arteries<br>Assessment of septal geometry (as an indicator of ventricular pressures)<br>Evaluate ventricular sizes and function |
| Double outlet right ventricle | Evaluate septal defects (size, shunt direction, location, relation of ventricular septal defect to great arteries)<br>Assess physiology based on anatomic findings (i.e. ventricular septal defect, transposition or Taussig–Bing, tetralogy type)<br>Evaluate great artery relationship (normal, malposed, side by side)<br>Evaluate for outflow obstruction<br>Assess ventricular sizes and function |
| Truncus arteriosus | Evaluate septal defects (size, location)<br>Evaluate truncal valve (for stenosis/regurgitation)<br>Assess origin of the pulmonary arteries (type of truncus), pulmonary blood flow<br>Assess ventricular function |
| Single ventricle | Evaluate morphologic type<br>Assess atrioventricular and semilunar valves, inflows and outflows<br>Interrogate for adequacy of interatrial communication if indicated<br>Evaluate prior surgical interventions<br>Assess ventricular function |

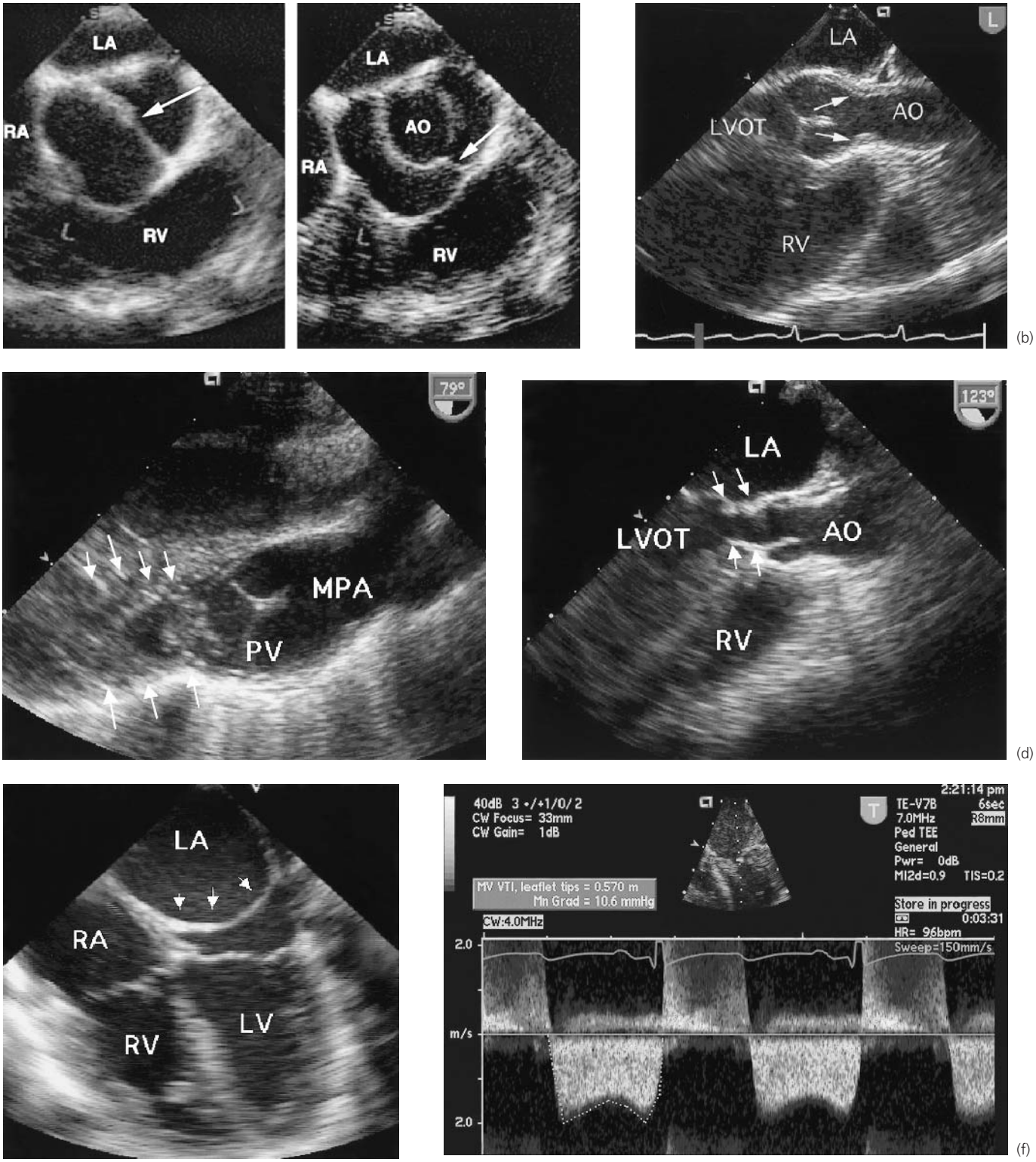



**Fig. 9.8** Echocardiographic images of obstructive lesions. (a) Bicuspid (bicommissural) aortic valve. Left panel showing diastolic frame of bicuspid aortic valve in the short axis view (arrow points to the coaptation site). Right panel depicting typical "fish mouth" appearance of bicuspid aortic valve in systolic frame. The region of commissural fusion is noted by the arrow. (b) Supravalvar aortic stenosis. Aortic long axis view demonstrating the typical hourglass deformity that accounts for narrowing of the sinotubular region (arrows) in a patient with supravalvar aortic stenosis. (c) Double chamber right ventricle. Long axis view of pulmonary outflow tract in a patient with right ventricular obstruction displaying severe hypertrophy of muscle bundles located below the level of the pulmonary valve. (d) Subaortic stenosis. Two-dimensional echocardiographic appearance of complex subaortic obstruction. A fibromuscular narrow tunnel (arrows) is noted accounting for the left ventricular outflow tract obstruction. (e) Cor triatriatum. The classic membrane (arrows) that partitions the atrium into separate compartments in the cor triatriatum is highlighted in this mid-esophageal four-chamber view. (f) Mitral stenosis. Spectral Doppler interrogation in a patient with moderate to severe mitral valve obstruction demonstrating an estimated mean transmitral gradient of 10.8 mmHg by continuous wave Doppler. Also reproduced in color, facing p. 146. AO, aorta; LA, left atrium; LV, left ventricle; LVOT, left ventricular outflow tract; MPA, main pulmonary artery; PV, pulmonary valve; RA, right atrium; RV, right ventricle.

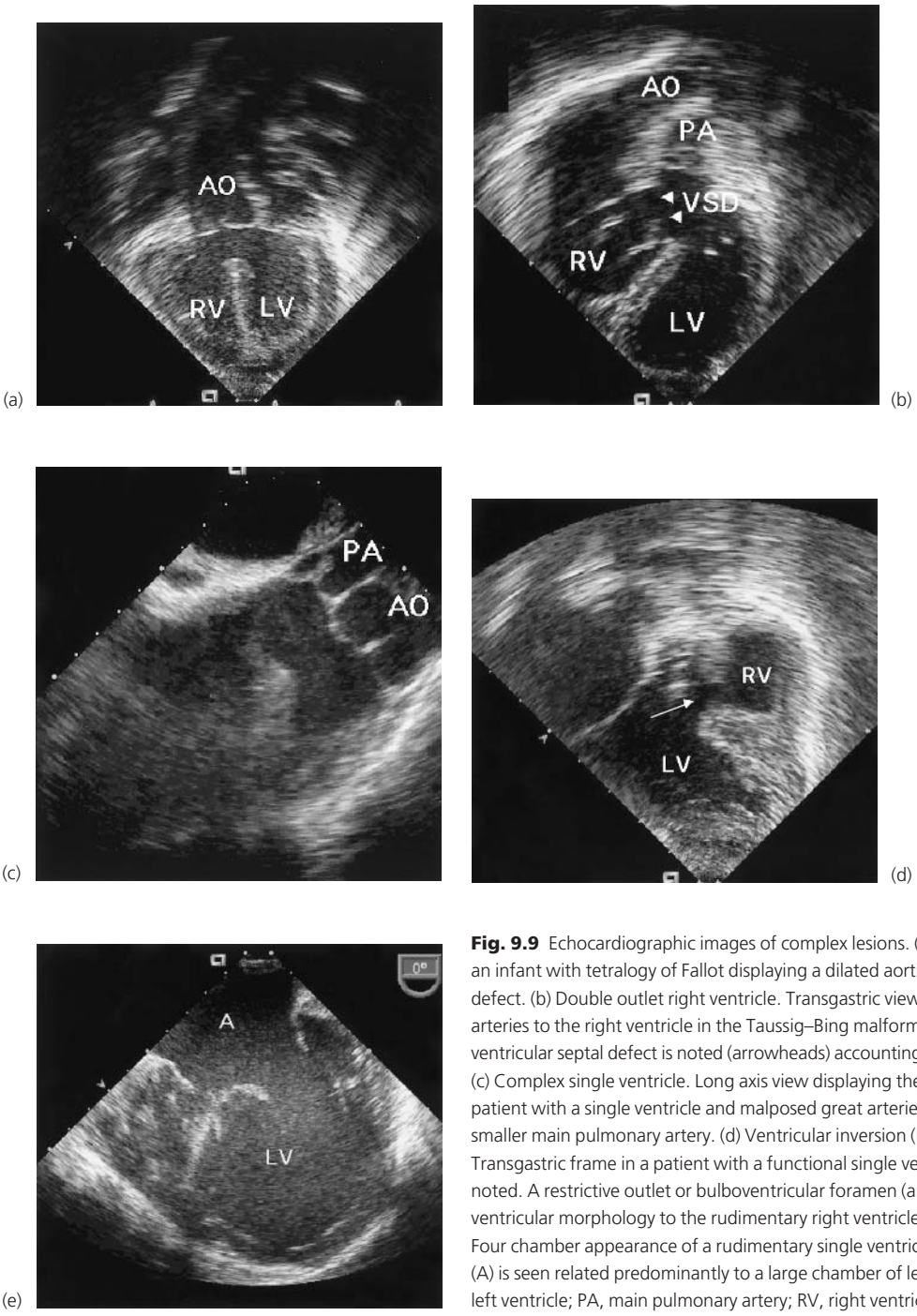



**Fig. 9.9** Echocardiographic images of complex lesions. (a) Tetralogy of Fallot. Transgastric view of an infant with tetralogy of Fallot displaying a dilated aortic root overriding a large ventricular septal defect. (b) Double outlet right ventricle. Transgastric view demonstrating the relationship of the great arteries to the right ventricle in the Taussig–Bing malformation. The subpulmonary location of the ventricular septal defect is noted (arrowheads) accounting for physiology similar to that of transposition. (c) Complex single ventricle. Long axis view displaying the parallel relationship of the great arteries in a patient with a single ventricle and malposed great arteries. The aorta is positioned anteriorly to the smaller main pulmonary artery. (d) Ventricular inversion (l-transposition of the great arteries). Transgastric frame in a patient with a functional single ventricle. The discrepant ventricular sizes are noted. A restrictive outlet or bulboventricular foramen (arrow) communicates the larger ventricle of left ventricular morphology to the rudimentary right ventricle or subaortic chamber. (e) Single ventricle. Four chamber appearance of a rudimentary single ventricle (univentricular heart). A common atrium (A) is seen related predominantly to a large chamber of left ventricular morphology. AO, aorta; LV, left ventricle; PA, main pulmonary artery; RV, right ventricle; VSD, ventricular septal defect.

and functional evaluation of CHD. Over the last two decades, interventional procedures have become increasingly employed in the non-surgical management of congenital cardiac anomalies. Transesophageal echocardiography allows for a safer and more effective application of catheter-based approaches and may reduce fluoroscopic exposure, amount of contrast material administered, and duration of the interventional procedure.[86,87] Studies addressing the role of this imaging modality confirm major contributions. These include: (i) acquisition of detailed anatomic and hemodynamic data prior to and during the procedure; (ii) real time evaluation of catheter placement across valves and vessels; (iii) immediate assessment of the results; and (iv) monitoring of complications associated with interventions. The refinement in interventional cardiac catheterization techniques coupled with advances in TEE now allow for the high

**Table 9.3** Post-bypass echocardiographic data by type of congenital heart defect repair or surgical procedure.

| Cardiac pathology | Evaluate for the following in the post-surgical echocardiographic exam |
|---|---|
| *Atrial septal defect* | |
| Secundum | Residual shunt<br>Atrioventricular valve regurgitation<br>Ventricular function |
| Sinus venosus | Residual shunt<br>Superior vena cava obstruction<br>Pulmonary venous obstruction (if associated anomalous pulmonary venous return)<br>Ventricular function |
| *Ventricular septal defect* | |
| Perimembranous | Residual shunt (tiny leaks may be acceptable at the edges of the patch)<br>Atrioventricular valve regurgitation, aortic insufficiency<br>Right ventricular pressure can be calculated by using the tricuspid regurgitant jet or residual ventricular septal defect peak velocity<br>Ventricular function |
| Supracristal, subarterial (doubly committed) | Residual shunt (as above)<br>Residual or new aortic/pulmonary insufficiency compared to pre-bypass exam<br>Ventricular function |
| Muscular or inlet | Residual shunt (as above, tiny/small residual muscular ventricular septal defect may be acceptable)<br>Atrioventricular valve regurgitation<br>Ventricular function |
| *Atrioventricular septal defect (ASD)* | |
| Partial or ostium primum ASD/cleft mitral valve | Residual shunts<br>Residual/new atrioventricular valve regurgitation (mild regurgitation may be acceptable)<br>Mitral inflow obstruction (if mitral cleft closed)<br>Ventricular function |
| Complete atrioventricular septal defect | Residual atrial or ventricular level shunts<br>Atrioventricular valve stenosis (particularly if annuloplasty or left-sided cleft closure performed)<br>Atrioventricular valve regurgitation<br>Left ventricular outflow tract obstruction<br>Ventricular function |
| Aortic stenosis (subvalvar, valvar, supravalvar) | Residual outflow obstruction or aortic insufficiency<br>New ventricular septal defect<br>Mitral regurgitation<br>Ventricular function |
| Ross procedure | Aortic stenosis or insufficiency<br>Right ventricular outflow tract conduit (for stenosis/regurgitation)<br>Global and segmental left ventricular function |
| Tetralogy of Fallot | Residual ventricular septal defect or unmasked defects<br>Residual right ventricular outflow tract obstruction<br>Pulmonary regurgitation<br>Right ventricular systolic pressure can be assessed by using the tricuspid regurgitant jet<br>Right and left ventricular function |
| Right ventricular conduit operation | Conduit stenosis or insufficiency<br>Atrioventricular valve competence<br>Ventricular function |
| Arterial switch operation (Jatene procedure) | Neo-aortic and pulmonic anastomoses (for stenosis)<br>Semilunar valve competence<br>Outflow tracts (for obstruction) |

*Continued p. 150*

**Table 9.3** (cont'd)

| Cardiac pathology | Evaluate for the following in the post-surgical echocardiographic exam |
|---|---|
| | Atrioventricular valve regurgitation<br>Residual intracardiac shunts<br>Coronary flow<br>Global and segmental left ventricular function |
| Double outlet right ventricle | Residual intracardiac shunts<br>Outflow tract obstruction<br>Atrioventricular/semilunar valve regurgitation<br>Right ventricular to pulmonary artery conduit function (if applicable)<br>Ventricular function |
| Truncus arteriosus | Truncal valve (aortic) stenosis and insufficiency<br>Right ventricular to pulmonary conduit (for stenosis or insufficiency)<br>Atrioventricular valve regurgitation<br>Residual ventricular level shunt<br>Estimate right ventricular/pulmonary artery pressures<br>Ventricular function |
| Fontan or Glenn procedure | Flow in Fontan/Glenn connections<br>Evaluate Fontan fenestration if performed<br>Atrioventricular valve regurgitation<br>Atrial septum for evidence of obstruction (if stenosis/atresia of atrioventricular valve)<br>Ventricular function |
| Total anomalous pulmonary venous return | Adequacy of pulmonary venous anastomosis<br>Residual atrial level shunt<br>Atrioventricular valve regurgitation<br>Right ventricular/pulmonary artery pressure (can be estimated from tricuspid or pulmonary regurgitant jets)<br>Right and left ventricular function |

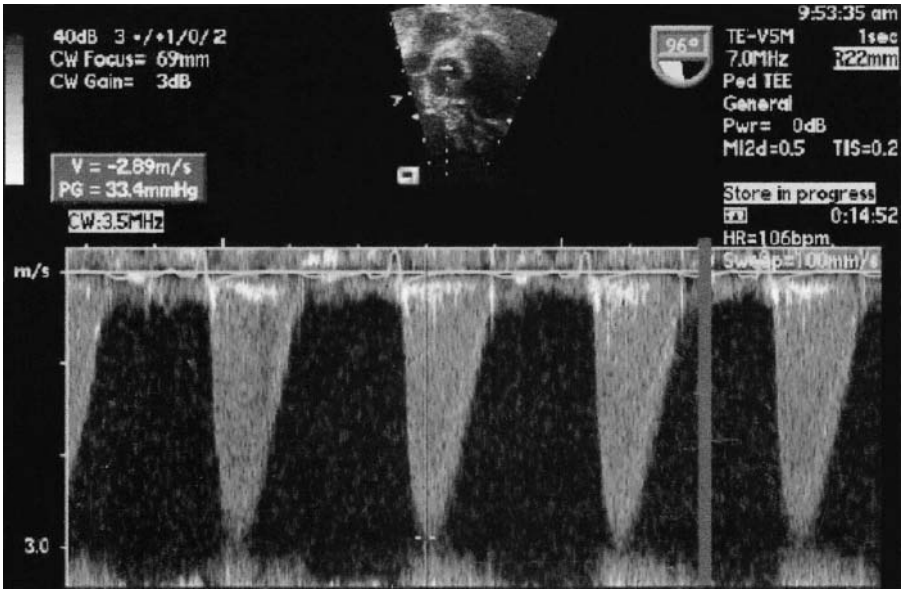



**Fig. 9.10** Continuous wave Doppler interrogation of left ventricular outflow tract in patient with subaortic obstruction demonstrating gradient estimation peak velocity across outflow measures 2.89 m/second, predicting a peak gradient of 33.4 mmHg (obtained by application of the modified Bernoulli equation or $4(V)^2$). Also reproduced in color, facing p. 146.

success rate of these procedures and their low incidence of complications.

## Training and certification in pediatric transesophageal echocardiography

Guidelines for physician training in TEE were published by the ASE Committee for Physician Training in 1992.[88] Regarding pediatric TEE, recommendations were as follows:

> One should have a thorough knowledge of cardiac disease, and the hemodynamic alterations associated with acquired and congenital disorders, understanding of ultrasonic image formation and Doppler assessment of intracardiac blood flow, the range of normal structural findings and echocardiographic manifestations of a large number of cardiac disorders. Physicians performing and interpreting diagnostic TEE studies should first develop experience with general echocardiographic techniques consistent with at least level II training in echocardiography. This training involves the performance and primary interpretation (with supervision) of approximately 300 general echocardiographic studies over a period of 6 months or achievement of the equivalent level of experience. Training in the TEE examination needs to include development of cognitive and technical skills. Recommended practical experience includes introduction of the TEE probe and manipulation, optimization of instrument controls, and interpretation of the findings.[88]

Training and certification in intraoperative echocardiography has received considerable attention in recent years. Most guidelines, however, have focused on the adult with little emphasis on pediatric TEE or congenital pathology. Prior recommendations by the Committee on Standards for Pediatric Transesophageal Echocardiography have suggested that the guidelines for training of non-pediatric cardiologists in pediatric TEE be consistent with those required for pediatric cardiology trainees, and should be individualized to include the existing level of familiarity a physician may have with children and their heart disease. It is strongly recommended that a pediatric cardiologist knowledgeable in TEE participate in the performance and interpretation in studies in infants and young children and those with complex heart disease.

A pediatric task force appointed by the Pediatric Echocardiography Council of American Society of Echocardiography is currently addressing revised practice guidelines for TEE in children.

A joined task force of the ASE and Society of Cardiovascular Anesthesiologists has recently published revised guidelines for training in perioperative echocardiography.[89] Echocardiographic evaluation of CHD is included under the section on advanced training. The task force recommends that for those seeking advanced training in perioperative echocardiography cognitive skills should include:

1. Knowledge of CHD (if congenital practice is planned then this knowledge must be detailed).
2. Detailed knowledge of all other diseases of the heart and great vessels that is relevant in the perioperative period (if pediatric practice is planned then this knowledge may be more general than detailed).
3. Detailed knowledge of the techniques, advantages, disadvantages, and potential complications of commonly used cardiac surgical procedures for treatment of acquired and CHD.

The guidelines propose that skills should include knowledge of CHD and of the techniques, advantages, disadvantages, and potential complications of commonly used procedures in congenital heart surgery.

Given these recommendations and training requirements, it has been asked how one should proceed as an anesthesiologist interested in pediatric TEE. With increasing experience by those involved in pediatric intraoperative TEE, the issue has also been raised of who is responsible for the intraoperative interpretation of TEE and the role of the anesthesiologist. Recent publications indicate that properly trained cardiac anesthesiologists are able to utilize this technology competently resulting in changes in medical and surgical management in a significant number of patients.[80,81] We believe that one should follow the general guidelines established by the American Society of Anesthesiologists and the Society of Cardiovascular Anesthesiologists: "Anesthesiologists with advanced training in perioperative TEE should be able to exploit the full diagnostic potential of TEE in the perioperative period." [89] Because it is essential in many intraoperative applications to obtain a definitive interpretation of the TEE examination at the time of surgery, the task force strongly recommends that anesthesiologists actively pursue collaboration with surgeons, cardiologists, or other physicians involved in a patient's care as a team approach. This would propose a core of interested individuals (anesthesiologists, pediatric cardiologists, and cardiothoracic surgeons) who collaborate as the guidelines have suggested.

In 1996 the Society of Cardiovascular Anesthesiologists appointed a task force to develop a certification process to recognize knowledge and proficiency in the interpretation of perioperative TEE.[90] The inaugural formal examination was given in 1998.[91] This examination is currently administered by the National Board of Echocardiography. The test focuses on adult heart disease with a small component of CHD in the adult; pediatric TEE has not been formally addressed.

## Quality assurance

All quality assurance programs for echocardiography should include the following elements: indications for the study,

technical aspects of performing and recording the examination, application of examination findings to physiologic conditions, documentation, equipment, care of equipment, professional communication, education, and billing.[89]

At most institutions, the pediatric TEE examinations are viewed and interpreted immediately and reports for the pre- and post-bypass examinations are generated. In consideration of the educational value, some centers highly encourage the retrospective review of the echocardiographic data when significant discrepancies are identified between these and the intraoperative surgical findings.

## Limitations

The literature extensively documents the utility of TEE in congenital heart surgery and in the detection of residual abnormalities that may require immediate revision. Despite the significant contributions of TEE to intraoperative care some limitations are recognized. Thus, decisions regarding return to bypass to address residual pathology should consider that a variety of factors (the level of inotropic support, high catecholamine state during the immediate bypass period, loading conditions, and functional state of the myocardium) may influence the echocardiographic findings and may under- or overestimate the hemodynamic severity of the condition in question. This implies that the optimal setting for hemodynamic assessment in most patients requires conditions that reflect the patient's baseline steady state, a potential challenge in the operating room. Decisions regarding return to bypass to address suboptimal repairs require assessment of the overall risk–benefit ratio, and in many instances this is a clinical judgment not exclusively based on the echocardiographic information but also influenced by numerous other factors.

## Contraindications

Conditions associated with increased risk of complications such as esophageal pathology, recent esophageal surgery, severe respiratory decompensation, or inadequate control of the airway are generally considered contraindications to TEE. Additional clinical scenarios that require assessment of the risk–benefit ratio for TEE include cervical spine injury or deformity and severe coagulopathy. In the presence of a gastrostomy feeding tube the TEE examination is still feasible; however, we defer the transgastric examination. In patients with a known aberrant (retroesophageal) subclavian artery we suggest placement of the catheter for arterial blood pressure monitoring in an extremity not being supplied by the anomalous vessel, since loss of the arterial pressure tracing may be seen upon esophageal intubation or probe manipulation.[92,93] Pulse oximetry monitoring in the extremity supplied by the aberrant vessel may be useful as an indicator of adequate distal bed perfusion. Surgical interventions to address isolated vascular anomalies, such as vascular rings, generally do not benefit significantly from TEE. In these cases, TEE probe insertion can lead to respiratory compromise as the trachea and esophagus are restricted to a confined space by the surrounding vascular structures. In infants with anomalous pulmonary venous connections, consideration should be given to potential compression of the posterior pulmonary venous confluence by the transesophageal probe resulting in detrimental hemodynamic effects (see Fig. 9.2).[94] Potential alternatives in this clinical scenario are the introduction of the probe after sternotomy or during the bypass period.

## Complications

Serious complications during pediatric TEE are rare.[95] Most children, including infants, tolerate transesophageal examination well; however, hemodynamics and respiratory parameters must be closely monitored. Blood pressure generally remains stable but can drop precipitously if probe flexion compresses the aorta. Accordingly, placement of the TEE probe is recommended following arterial line placement. Changes in blood pressure resulting from aortic compression during probe manipulation may or may not be evident depending on the location of the arterial catheter or pulse-oximeter sampling probe. A recent case report also noted life-threatening hemodynamic deterioration as a result of acute decreases in pulmonary blood flow presumably related to compression of the pulmonary artery and related structures.[96] Respiratory compromise can occur in association with probe manipulation, peak inspiratory pressures can increase, and systemic arterial desaturation can be seen. In addition, movement of the endotracheal tube may occur during the examination, resulting in displacement into the mainstem bronchi or tracheal extubation. Capnography may be particularly helpful in the recognition of these complications. If desaturation acutely occurs correct position of the endotracheal tube must be confirmed and occasionally the TEE probe must be immediately withdrawn. For all of the above reasons, we recommend frequent monitoring of the peak inspiratory pressures throughout the TEE examinations. While the probe is being withdrawn the endotracheal tube should be firmly held to prevent inadvertent extubation. Although hemodynamic or respiratory alterations can occur in small infants, these are relatively infrequent and fear of compromise should not prevent use of intraoperative TEE in patients when otherwise indicated.[97,98]

Esophageal injury can occur related to intraoperative TEE. A study where flexible esophagoscopy was performed following TEE in infants and children demonstrated frequent mild mucosal injury.[99] A recent study has documented an 18% incidence of dysphagia among pediatric patients under-

going cardiac operations where TEE was used. Although the lack of a control group did not allow for the assessment of the direct effects of TEE, the study suggested that the presence of the probe was a risk factor in this cohort of patients.[100] A case report of an unrecognized esophageal perforation in a small infant during intraoperative TEE underscores the fact that meticulous care must be exercised in the insertion and manipulation of these probes in all patients, in particular in the critically ill neonate.[101] This report raises the concern that this occurrence may be higher than previously suspected and recommends that clinicians keep this diagnosis in mind in the presence of crepitus in the neck, subcutaneous emphysema, pneumomediastinum, or retropharyngeal gas.

## Endocarditis prophylaxis

Endocarditis after TEE examination has been reported in the literature but is considered an unlikely event.[102] The most recent guidelines of the AHA have stated that endocarditis prophylaxis is not routinely recommended for TEE but should be considered optional in high-risk patients.[103]

## Conclusion

In many centers TEE is considered the standard of care for intraoperative assessment of most congenital heart repairs prior to removal of the bypass hardware and closure of the sternotomy.[49,104] This technology has become a valuable adjunct to surgical and anesthetic management. The literature documents the significant perioperative benefits of TEE in the care of infants/children undergoing surgical interventions for congenital/acquired heart disese and the impact in clinical decision-making. Diagnoses can be confirmed or altered preoperatively, the surgical plan can be modified, and the operative procedures can be immediately evaluated and revised if necessary. Contributions to anesthetic care include real time monitoring of ventricular filling, cardiac function, ensuring adequate cardiac de-airing, in addition to optimization of hemodynamic management strategies. Furthermore, the intraoperative transesophageal findings assist in the formulation of plans for postoperative care. Although the data thus far regarding the contributions of TEE to pediatric cardiac surgery is quite compelling, further studies are needed to address the impact of this technology on clinical outcomes.

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# 10 Bleeding and coagulation: Monitoring and management

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## Introduction

Manipulations of the coagulation system before, during, and after cardiopulmonary bypass (CPB) are an integral part of the management of patients undergoing cardiac surgery. As the field of pediatric cardiac surgery has progressed toward total corrective or major palliative procedures in younger children with more complex congenital defects, it has become apparent that post-CPB coagulopathies and bleeding are disproportionately greater in these smaller children compared to adolescents or adults[1] and require aggressive intervention to correct. Therefore, in children, management of coagulation during cardiac surgery takes on a magnified importance. The ability to restore hemostasis after CPB in children must begin with a knowledge of their baseline coagulation parameters and an understanding of the coagulation changes associated with CPB. Patient and surgical factors that are associated with post-CPB bleeding as well as coagulation tests that are predictive of this bleeding should be identified. Finally, an appreciation of the consequences of ongoing post-CPB bleeding and an awareness of the transfusion and pharmacologic strategies available to attenuate this bleeding are essential to successfully restore balance to the coagulation system in children after CPB.

## Baseline coagulation parameters

The baseline coagulation status of neonates and infants is greatly influenced by maturational factors and by pathophysiologic disturbances that accompany congenital heart defects.

### Maturational factors

At birth, the coagulation system is immature and continues in a state of maturation throughout the first year of life. Significant deficiencies in levels of the vitamin K-dependent factors (II, VII, IX, and X) and the contact factors (XI, XII, prekallikrein, and high-molecular-weight kininogen [HMWK]) exist at birth. Hepatic immaturity with decreased factor synthesis and accelerated clearance of factors by increased basal metabolic rates in children are cited as causes of these deficiencies.[2,3] Most of these procoagulant factor levels at birth are only 40% to 50% of those found in adults and do not reach adult levels until later than 6 months of age (Fig. 10.1). Essentially all of the inhibitors of coagulation are also present in low levels during the first year of life. At birth, protein S and C levels are less than 40%, heparin cofactor II levels are 45%, and antithrombin III (ATIII) levels are 60% of adult values and, again, do not attain adult levels until after 6 months of age. Only platelet counts and levels of fibrinogen, factors V, VIII, von Willebrand factor, and XIII are at adult ranges at birth.[2] However, evidence exists that platelet aggregation is impaired[4] and that fibrinogen exists in a dysfunctional "fetal" form in newborns[2] even though these factors are not quantitatively deficient. Thus, qualitative immaturities add further to the precariousness of a newborn's coagulation system.

In light of these quantitative and qualitative deficiencies, the functional integrity of the coagulation system in young infants could be questioned. Fortunately, however, the results of most coagulation tests, including prothrombin time (PT) and thrombin clotting time, are within normal adult ranges within a few days after birth.[2] Only the activated partial thromboplastin time (aPTT) is prolonged for a substantial time before falling to adult ranges at about 3 months of age. The dependence of the aPTT on the actions of several of the deficient vitamin K-dependent and contact factors may explain its initial prolongation. The maintenance of normal coagulation tests in early infancy may result from a relative balance achieved by the simultaneous immaturities of both the coagulation factors and their inhibitors during this period. If anything, the process tends towards increased coagulability. Thromboelastography (TEG) actually has shown that neonates and infants clot faster and have increased clot strength compared to adults.[5] Despite the maintenance of the functional integrity of the coagulation system in infants,

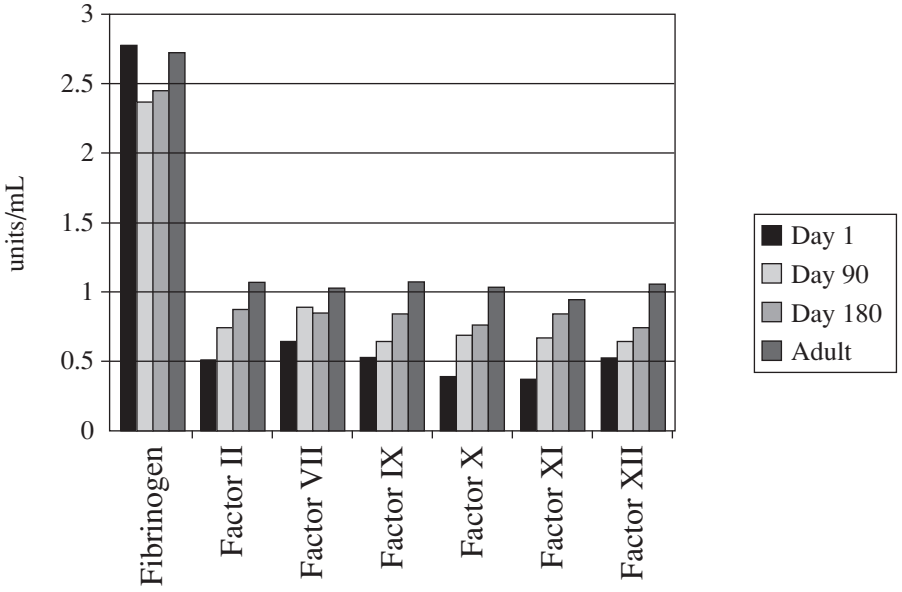


**Fig. 10.1** Coagulation factor levels during infancy and adulthood. Adapted with permission from Andrew M, Paes B, Johnston M. Development of the hemostatic system in the neonate and young infant. *Am J Pediatr Hematol Oncol* 1990; **12**: 95–104.

the effect of the maturational deficiencies in their coagulation systems is such that these children have little margin of safety once they encounter the further alterations in hemostasis produced by exposure to CPB.

### Influence of congenital cardiac pathophysiology

Other disturbances of the coagulation systems of children can be created by the pathophysiology of their congenital heart defects. Baseline coagulation defects have been demonstrated in children with both non-cyanotic and cyanotic defects, although a consistent association of specific cardiac defects with certain hemostatic abnormalities is not evident. Coagulation abnormalities have been reported in 58% of children with non-cyanotic defects. Decreased fibrinogen levels and platelet counts, prolonged bleeding times, and fibrinolytic activity were noted, especially in infants. Children with cyanotic defects have been shown to have a 71% incidence of coagulation abnormalities.[6] Cyanotic patients with hematocrits greater than 50% have been shown to have prolonged PT and aPTT, decreased levels of fibrinogen and factors V and VIII, and thrombocytopenia.[7] Decreased levels of factors II, VII, IX, and X, defective platelet function, and accelerated fibrinolysis have also been demonstrated in patients with cyanotic defects.[8–10] The number of hemostatic abnormalities present preoperatively correlates with the severity of polycythemia, and a relationship between the presence of preoperative hemostatic defects in cyanotic children and the severity of postoperative bleeding has been noted.[8] The etiologies of these abnormalities are not completely understood. Children with preoperative coagulation abnormalities often have poor cardiac function.[11] Hepatic dysfunction from subsequent hypoperfusion or from perfusion of the liver with hypoxemic and hyperviscous blood could impair synthesis of coagulation factors.[9] Finally, it should be remembered that drugs with platelet inhibiting properties, such as prostaglandin $E_1$ ($PGE_1$) and aspirin, are not uncommonly administered to children with cyanotic heart defects and may further impair their coagulation systems.

Interestingly, young children with cyanotic heart defects appear to develop a hypercoagulable state prior to the onset of polycythemia. Evidence for this is seen in the trend for increased levels of platelets, fibrinogen, and factors V and VIII in these children, and could help explain findings in the early literature of pulmonary thrombi in infants with cyanotic defects who died before the onset of polycythemia.[7] Therefore, children with cyanotic heart defects are subject to the opposite extremes of coagulation problems depending on the progression of their pathophysiology.

## Coagulation changes associated with cardiopulmonary bypass

The use of CPB introduces variables that can significantly alter the coagulation status of all patients. The hemodilution encountered upon commencement of CPB can be extreme and can critically modify the delicate hemostatic equilibrium that exists in young children. Furthermore, the extra-corporeal circuit exposes the patient's blood to a large nonphysiologic surface with the consequent activation of inflammatory and coagulation cascades and the production of further coagulation abnormalities. Therefore, quantitative and qualitative hemostatic alterations accompany the use of CPB.

### Hemodilution

The hemodilution associated with CPB produces profound

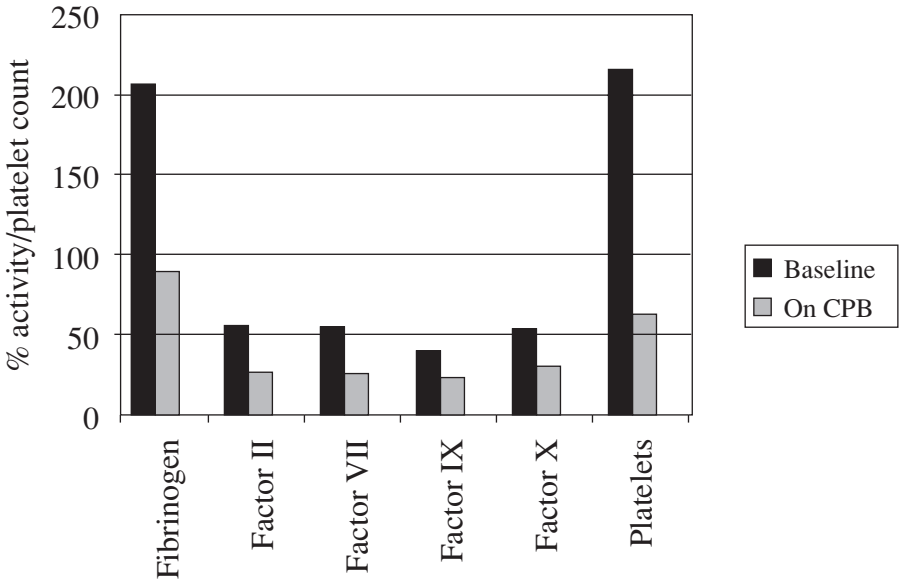


**Fig. 10.2** Coagulation factor dilution in neonates upon initiation of cardiopulmonary bypass. Adapted from Kern FH, Morana NJ, Sears JJ *et al*. Coagulation defects in neonates during cardiopulmonary bypass. *Ann Thorac Surg* 1992; **54**: 541–6, with permission from the Society of Thoracic Surgeons.

quantitative hemostatic changes and may be a principal culprit of the complex coagulation defects that occur after CPB in small children. The priming volume of the CPB circuit can be two to four times the blood volume of this population of patients. With the initiation of CPB, coagulation factor levels have been shown to decrease by 50% and platelet counts by 70% in neonates, despite the use of whole blood in the priming solution (Fig. 10.2).[3] During the course of CPB these factor levels remain relatively constant but then increase somewhat at the end of CPB due to hemoconcentration and/or their increased production as acute phase reactants.[3,12] However, at the termination of CPB and after the administration of protamine in children under 8 kg, mean fibrinogen levels of 62 mg/dL (29% of baseline level) and mean platelet counts of 64 000/μL (16.5% of baseline) have been reported.[13] This hemodilution-induced reduction of coagulation factor levels combined with the decreased baseline levels in children under 6 months of age creates a situation where factor levels at the conclusion of CPB approach the minimum concentration required for adequate hemostasis (15% for factor V, 30% for all other factors).[14]

## Qualitative coagulation changes

The extracorporeal circuit provides a huge negatively charged surface that allows for massive activation of the contact factors (XII, XI, prekallikrein, and HMWK) as CPB commences. Contact activation results in the production of factor XIIa, kallikrein, bradykinin, and plasmin. Consequently, the intrinsic coagulation cascade, the fibrinolytic system, and the body's inflammatory response are all massively activated upon the initiation of CPB and all produce significant qualitative coagulation changes that contribute to the coagulopathy associated with CPB (Fig. 10.3).[15]

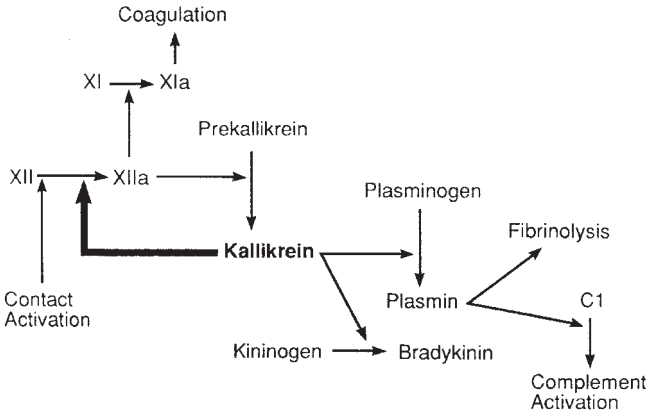


**Fig. 10.3** The contact activation cascade. The coagulation system, the fibrinolytic system, and the body's inflammatory response are thus activated. Reproduced from Levy JH, ed. *Anaphylactic Reactions in Anesthesia and Intensive Care*. Stoneham, MA: Butterworth–Heinemann, 1992: 51–62, with permission from the author.

## Thrombin generation

Upon initiation of CPB, thrombin can be generated via several mechanisms. Activation of the intrinsic coagulation cascade through the contact factors is one path of thrombin production. Stimulation of the inflammatory response causes the expression of tissue factor on monocytes and endothelial cells,[16] thus allowing thrombin generation via the extrinsic (tissue factor) cascade as well. Aspiration of blood from the surgical field through the CPB circuit exposes more tissue factor on cell membranes. Heparin is routinely administered prior to CPB in an attempt to attenuate thrombin generation. If anticoagulation were omitted, catastrophic clotting of the

extracorporeal circuit and the patient would occur. Despite the administration of adequate doses of heparin to maintain an acceptable activated clotting time (ACT) and the absence of visible blood clot, thrombin is still generated during CPB.[17] This thrombin goes on to play a significant role in the production of post-CPB coagulopathies.

## Fibrinolysis

The fibrinolytic system may be activated by several mechanisms that work in tandem during the process of cardiac surgery. Endothelial cells can be stimulated to release tissue plasminogen activator (tPA) by thrombin,[18] by bradykinin generated through the contact activation system, and by the stimuli of skin incision and sternotomy.[19] Tissue plasminogen activator stimulates the conversion of plasminogen to its active form plasmin. Plasmin then causes fibrinolysis by breaking arginine and lysine peptide bonds in fibrinogen and fibrin.[20] Plasmin also can be generated by the direct actions of factor XIIa and kallikrein on plasminogen.[15] Potentiating these mechanisms that activate the fibrinolytic system is a decrease in the levels of the inhibitors of plasmin during CPB.[21] This combination of enhanced activation and decreased inhibition of plasmin sets the stage for fibrinolytic activity during CPB. Indeed, measurements of fibrin split products and clot lysis activity[22,23] as well as modified thromboelastograms[24–26] have demonstrated the occurrence of fibrinolysis during CPB in both adults and children. This fibrinolytic activity usually resolves without intervention within 90 minutes of the termination of CPB,[22] possibly because of significant and persistent increases of plasminogen and plasmin inhibitors during this time.[27] The contribution of fibrinolysis to post-CPB bleeding is not clear since several studies have found no correlation between postoperative blood loss and the intraoperative occurrence of fibrinolysis.[14,22,25,26] However, the products of the fibrinolytic system, plasmin and fibrin split products, may play a role in the creation of other qualitative coagulation defects during CPB.

## Platelet dysfunction

Platelet function abnormalities are deemed to be the most common etiology for excessive postoperative bleeding in adult cardiac surgical patients.[14] Exposure to the CPB circuit alters the ability of platelets both to adhere to exposed subendothelial surfaces and other platelets and to aggregate with each other. Platelet adhesiveness is achieved through the glycoprotein Ib (von Willebrand) receptor. Plasmin generated by activation of the fibrinolytic system during CPB and the turbulence and shear stresses imposed by CPB have both been shown to destroy this important platelet adhesive receptor.[28,29] Platelet aggregation after CPB is impaired after the platelets are "activated" during CPB. Activation of platelets leads to a depletion of their granules and a reduction of their ability to "stick" to each other afterward.[14] Thrombin generated during CPB,[30] fibrin degradation products resulting from plasmin's action on fibrin during CPB,[31] and plasmin itself [32] may all be responsible for this platelet activation during CPB. The subsequent impairment of the platelets' abilities to adhere and aggregate results in severe platelet dysfunction after CPB (Fig. 10.4).

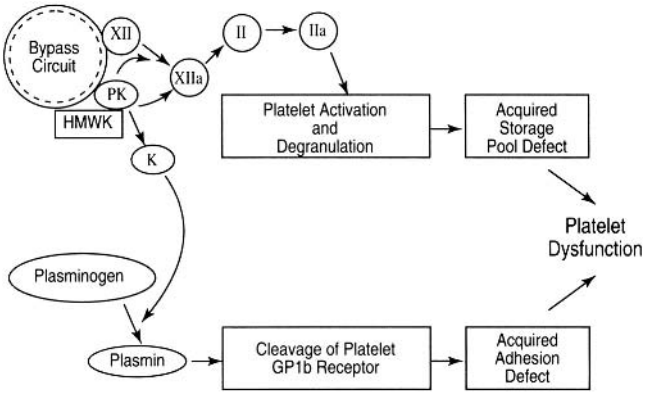


**Fig. 10.4** Proposed mechanism for the development of platelet dysfunction during cardiopulmonary bypass. II, factor II; XII, factor XII; HMWK, high-molecular-weight kininogen; K, kallikrein; PK, prekallikrein. Reproduced with permission from Carr ME. Control of perioperative bleeding: Pharmacologic agents. In: Wechsler AS, ed. *Pharmacologic Management of Perioperative Bleeding*. Southampton, NY: CME Network, 1996: 29.

## Anticoagulation

Anticoagulation is a coagulation change mandated, rather than produced, by CPB in order to attenuate thrombin generation with subsequent clotting and promotion of qualitative coagulation defects. Because of its instant action and ease of neutralization, heparin is used to achieve this anticoagulation. Heparin exerts its anticoagulant effect by combining with ATIII and consequently greatly accelerating ATIII's inhibition of thrombin and other activated coagulation factors. In adults and older children, the response to heparin is proportional to ATIII levels. However, this relationship is complicated in infants because, despite their lower ATIII levels, their response to heparin is not diminished.[33] Fortunately, an initial dose of heparin standardized to body weight usually achieves acceptable levels of anticoagulation not only in adults and older children but also in infants.

A significant variability in heparin's anticoagulant effect has been noted in adults[34] and found to be even more pronounced in young children.[1] Furthermore, heparin's half life is considerably shorter in children than adults.[35] Because of these variations, the degree of heparin-induced anticoagulation must be assessed continually during and immediately after CPB. This can be accomplished by measuring heparin

levels or by measuring its anticoagulant effect. Arguments exist as to which of these methods is more appropriate because measurement of heparin levels does not take into account the tremendous variability in individual patients' responses to heparin, whereas measurement of the ACT to assess heparin's anticoagulant effect is influenced by factors other than heparin. While heparin levels decline upon the commencement of CPB in all patients, these levels are significantly lower during CPB in children than adults even in the presence of acceptable ACT levels.[35,36] These lower heparin levels may be the result of a higher blood volume to body weight ratio in children thus effectively allowing heparin dosing calculations based on body weight to underestimate the needed dose for children. On the other hand, ACT values may remain high despite lower heparin levels because of the interplay of other factors that influence ACT values. Hypothermia and hemodilution synergistically prolong the ACT after heparin administration.[37] The complexity of the surgical procedures performed on young children often necessitates much lower temperatures than are routinely used in adult patients. Additionally, hemodilution upon the commencement of CPB in small children can be profound, as previously discussed. Therefore, it is not surprising that despite the maintenance of acceptably prolonged ACT values during CPB, the coagulation system is not totally inhibited as evidenced by the occurrence of thrombin generation and fibrinolysis.[17,25] However, data defining required heparin levels for complete inhibition of the coagulation system during CPB in children are lacking. In clinical practice, the ACT is most often used to document what is felt to be adequate levels of anticoagulation during CPB. As can be predicted, ACT measurements are usually significantly prolonged during the hypothermic period of CPB and require no further heparin administration during this time for maintenance of acceptable measurements. However, during the period of rewarming, the ACT values may fall rapidly thus necessitating their constant monitoring and the not infrequent administration of additional heparin prior to terminating CPB.

With the termination of CPB, the ACT becomes a very useful test in confirming the adequacy of heparin neutralization with protamine. At this point, however, ACT values continue to be influenced by factors other than heparin and its reversal with protamine. Even after adequate protamine dosing, the ACT can remain prolonged because of abnormally low coagulation factor levels, especially low levels of fibrinogen and factors VIII and XII.[38,39] On the other hand, normal ACT values can exist in the presence of platelet abnormalities or factor VII deficiency and continued bleeding.[38] Therefore, while return of the ACT to baseline levels is a very good indication that heparin has been completely neutralized,[39] the ACT is not a sensitive test for predicting the presence of post-CPB coagulopathies and the likelihood of continued bleeding.

**Table 10.1** Consequences of ongoing bleeding.

| |
|---|
| Hemodynamic instability |
| Cardiac tamponade |
| Massive transfusion |
| Hypothermia |
| Hyperkalemia |
| Hypocalcemia |
| Metabolic alkalosis |
| Dilutional coagulopathy |
| Cytokine infusion |
| Respiratory insufficiency |
| Increased blood donor exposures |
| Infectious agents |
| Transfusion reactions |
| Immunomodulation |
| Increased morbidity and mortality |

## Managing coagulopathies associated with cardiopulmonary bypass

Managing the coagulopathies associated with CPB is critical in order to minimize the consequences of ongoing bleeding (Table 10.1). Identification of risk factors associated with post-CPB bleeding in children allows the anticipation of bleeding as CPB is concluded and thus permits adequate preparation for its management. Knowledge of which coagulation tests can help predict those children who will experience ongoing bleeding after CPB and establishment of an institutional infrastructure that allows the rapid acquisition of these tests is important. A blood bank service that is able to provide a variety of products ranging from whole blood and packed red blood cells to pheresed platelet units, individual platelet units, fresh frozen plasma (FFP), and cryoprecipitate as well as concentrated individual coagulation factors is an absolute necessity. The ability to concentrate, wash, leukoreduce, and irradiate blood products should also be available. The blood bank should be staffed with personnel who have a thorough knowledge of transfusion medicine and can provide timely advice to clinicians. Preoperative communication with this staff is mandatory in order to insure the availability of necessary blood products prior to any surgery. Pharmacologic agents known to attenuate or help treat post-CPB coagulopathies should be available as should equipment used in blood conservation techniques such as cell salvage and ultrafiltration. Finally, the potential for late postoperative thrombotic complications should be appreciated in certain subsets of children.

### Risk factors

Associations have been found between several patient, laboratory, or surgical characteristics and post-CPB blood

loss and transfusion requirements in children. Patient age appears to be the variable with the most significant association. Post-CPB blood loss and blood product administration varies inversely with age, with children younger than 1 month being at greatest risk.[40] Since age is a continuous variable, further work has found 12 months to be the age below which greater blood loss should be anticipated.[41] Body weight has also been found to be a predictor of post-CPB bleeding. Children weighing less than 8 kg have been found to have significantly more bleeding and transfusion requirements than larger children.[13] Therefore, children less than 1 year of age or 8 kg body weight should be considered at high risk for significant post-CPB coagulation problems.

Batteries of preoperative laboratory tests have also been examined to determine their abilities to predict excessive post-CPB bleeding. Preoperative hematocrit level, aPTT, and certain TEG parameters (α and shear modulus) have been found to be associated with 12-hour chest tube drainage in one study of 482 children.[42] This study found no association between preoperative ACT, PT, platelet count, fibrinogen level, or other TEG parameters (*R*, *K*, and *MA*, see p. 163) and postoperative chest tube drainage. Based on their findings, these authors proposed that children may be at increased risk for postoperative bleeding if any of the following preoperative laboratory values are found: hematocrit > 45%, aPTT greater than or equal to 49 s, or TEG α less than or equal to 34°. Another investigation, however, found no preoperative coagulation test, including all of those noted above, to be predictive of or to correlate with 24-hour chest tube drainage in a study of 75 children.[13] Despite the differences in these findings, the conclusions of the one study justify obtaining coagulation tests preoperatively in children scheduled for cardiac surgery. Values that lie outside of the guidelines previously mentioned should alert one to the upcoming possibility of excessive bleeding after CPB.

Several factors associated with surgical technique also show correlations with post-CPB blood loss and transfusion requirements. In children less than 1 year of age, the degree of hypothermia during CPB and the use of deep hypothermic circulatory arrest are significant factors; whereas, in children older than 1 year, the duration of CPB, the complexity of the surgical procedure, and repeat sternotomy are significant factors. The surgeon performing the procedure has also been found to be a correlating variable. Finally, the presence of either preoperative congestive heart failure or polycythemia is associated with higher post-CPB blood loss, and children who bleed significantly after chest closure in the operating room are at risk to continue this excessive bleeding in the postoperative period.[41]

## Coagulation tests

While the presence of a significant coagulopathy in infants at the conclusion of CPB is almost always abundantly clear from the appearance of the surgical field, an elusive task after CPB in older children is the determination of the significance of any ongoing bleeding and the specific etiologies of the coagulopathy involved. Multiple coagulation tests obtained during and after CPB have been examined in attempts to identify a test that can be deemed the "gold standard" for delineating significant coagulopathies and children who will bleed excessively after CPB.

During CPB, platelet counts and TEG *MA* values have been found to be associated with postoperative chest tube drainage in children.[42] The platelet count during CPB yielded the best association to allow one to distinguish those children who will bleed excessively. Values less than or equal to 108 000/μL provided a sensitivity of 83% and a specificity of 58% in distinguishing these children. The TEG *MA* value, on the other hand, was the only coagulation test significantly associated with total blood products transfused during the first 24-hours postoperatively. Both platelet count and fibrinogen level were found to correlate with the TEG *MA* value during CPB in this study.

After CPB and heparin neutralization with protamine, platelet counts, fibrinogen levels, and TEG α and *MA* values have been found to correlate independently with postoperative chest tube drainage in pediatric patients.[13] Platelet count and fibrinogen level correlated with the TEG α and *MA* values as well. As was noted during CPB, the platelet count and the TEG *MA* value after CPB were again the tests that were most consistently associated with postoperative bleeding. Another investigation also found post-CPB TEG *MA* as well as *K* values to be associated with 24-hour chest tube drainage in children.[43] The post-CPB TEG was 100% accurate and 73% specific in its ability to predict increased postoperative bleeding in this study. It seems, therefore, that platelet counts, fibrinogen levels, and TEG parameters provide useful data to help define coagulopathies after CPB in children.

In adults, algorithms have been established to guide the management of post-CPB coagulopathies and have been based on ACT values, PT, aPTT, platelet counts, fibrinogen levels, and TEG values. Use of these algorithms has resulted in a decrease in postoperative chest tube drainage and blood product usage when compared to therapeutic interventions based solely on clinical judgements of the appearance of the operative field.[44–46] Constructing and testing comparable algorithms for children remains to be accomplished. Pediatric algorithms should probably be built around platelet counts, fibrinogen levels, and TEG parameters. Transfusion thresholds for each of these parameters will need to be established. The influence of many factors independent of the coagulation system, however, must always be considered when managing post-CPB coagulopathies in children. Patient demographics, CPB techniques, and extensive extracardiac suture lines will all contribute to postoperative bleeding in pediatric patients independent of any coagulopathy that may or may not simultaneously exist.

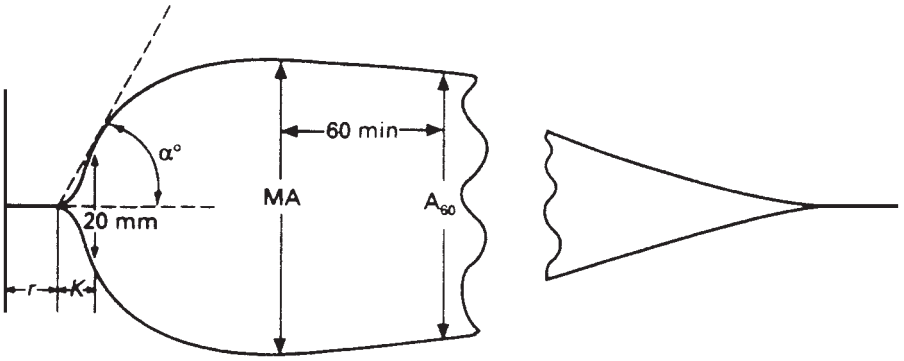


**Fig. 10.5** Quantification of thromboelastography variables. See text for definitions. Reproduced with permission from Mallett SV, Cox DJ. Thromboelastography. *Br J Anaesth* 1992; **69**: 307–13. ©The Board of Management and Trustees of the British Journal of Anaesthesia. Reproduced by permission of Oxford University Press/British Journal of Anaesthesia.

In order to use an algorithm to guide the management of post-CPB coagulopathies, the results of coagulation tests must be rapidly available to clinicians. Technology currently exists to allow on-site measurements of whole blood PT, aPTT, and platelet counts in the operating room.[44,46] The use of TEG for this purpose has also been growing. Thromboelastography is a unique test in that it allows assessment of the global coagulation picture from the initiation of clot formation to clot lysis or retraction. Five parameters are measured from a TEG tracing and other parameters can then be calculated from these measurements. (Fig. 10.5) The reaction time, or *R* value, is measured from the beginning of the tracing until an amplitude of 2 mm is reached and is expressed either in millimeters of chart distance or in minutes. The *R* value is similar to whole blood clotting time and reflects the function of the intrinsic coagulation pathway. Coagulation factor deficiencies and the presence of heparin result in prolongation of the *R* value. The coagulation time, or *K* value, is the interval from the end of the *R* value (2 mm amplitude) until the tracing reaches an amplitude of 20 mm and is also measured in millimeters or minutes. The angle (α) is measured as the slope of the outside divergence of the TEG tracing from the point of the end of the *R* value. The *K* and α values assess the rate of clot formation. Thrombocytopenia, platelet dysfunction, and hypofibrinogenemia will prolong the *K* value and reduce the α value. The maximum amplitude (*MA*) is the width of the TEG tracing (in millimeters) at its widest point. The *MA* is a reflection of the maximum strength of the clot and is influenced most importantly by fibrinogen levels, platelet counts, and platelet function as well as by factors VIII and XIII. Abnormalities of any of these will diminish *MA* values. The A-60 value is the amplitude of the TEG tracing 60 minutes after the *MA* value has been reached. This value is useful in measuring clot retraction or destruction by comparing it to the *MA* value. An A-60 : *MA* ratio (whole blood clot lysis index) of less than 0.85 has been used to define fibrinolysis. The elastic shear modulus (*G*) is calculated from the *MA* value by the equation:

$$G = (5000\,MA)/(100 - MA).$$

The shear modulus is reported in dynes/cm$^2$ and is affected by platelet counts and fibrinogen levels.[47] Analysis of a TEG tracing permits an assessment of the entire coagulation process at a given time and gives an overview of the interplay of all the components of coagulation as they work together to form and maintain a clot. Delay in clot initiation, slow build-up of the clot, weakness of the formed clot, and fibrinolysis can all be detected by TEG.

The TEG can be modified to become a rapid point-of-care test. Activation of blood with either celite or tissue factor in children allows *MA* values to become evident within 6–15 minutes of starting the test. These *MA* values are 30% greater than unactivated values; however, platelet counts and fibrinogen levels continue to correlate with these activated values.[26] Adding heparinase or protamine to blood samples neutralizes circulating heparin and allows TEG data to be obtained during CPB.[25,26] After CPB, heparinase-modified TEGs can also be helpful in discerning the contribution of residual circulating heparin to persistently prolonged ACT values after initial protamine administration.[24] Therefore, TEG is poised to become a very useful coagulation monitor in children should algorithms be built to help manage their post-CPB coagulopathies.

## Blood product therapy

Since infants will have an obvious coagulopathy at the conclusion of CPB, the first point to be considered in blood product therapy is the use of whole blood vs. individual coagulation products. Whole blood less than 48 hours old has been shown to better limit post-CPB blood loss in children under 2 years of age and, more specifically, in patients of this age undergoing complex surgical procedures (arterial switch, Glenn, Fontan, truncus arteriosus repair, stage I palliation for hypoplastic left heart syndrome [HLHS]) when compared to the use of a reconstituted product composed of 1 U each of packed red blood cells, platelets, and FFP.[48] This improvement in hemostasis was felt to be secondary to the presence of better functioning platelets in the whole blood as assessed by platelet aggregation tests. Children older than 2 years and

those of any age undergoing less complex procedures did not show this benefit. Despite this hemostatic benefit of fresh whole blood and its advantage of reducing donor exposures, its use must be supplemented at times with the transfusion of individual coagulation products to optimally control post-CPB blood loss, especially in younger patients. One study of 30 neonates found that despite the use of fresh whole blood, 70% of the neonates also received platelet transfusions, 37% received cryoprecipitate, and 17% received FFP as second-line treatments for inadequate clot formation and excessive transfusion requirements.[3] Additionally, whole blood less than 48 hours old is not readily available at all pediatric cardiac surgical centers and, when it is, it usually has been stored at 4°C, a factor which significantly depresses platelet function compared to storage for similar lengths of time at room temperature.[49] Therefore, the transfusion of separate component products plays a primary role in treating post-CPB coagulopathies in children in many institutions.

The effects of different coagulation products in correcting abnormalities of TEG parameters, platelet counts, and fibrinogen levels after protamine administration in children have also been investigated.[13] Since abundant evidence that qualitative platelet dysfunction[14,28,31,44,50] as well as severe quantitative platelet deficiencies[3,12] exist after CPB, initial treatment of ongoing bleeding after adequate heparin neutralization was with platelet transfusions. Platelet administration substantially improved the TEG parameters in addition to the platelet count. Approximately 40% of children were found to need only platelet transfusions to adequately control bleeding and, in these patients, TEG parameters were returned to baseline values by the platelet transfusion alone. The use of cryoprecipitate or FFP to manage continued bleeding and abnormal TEG values after adequate platelet transfusion was then compared. Cryoprecipitate administration raised fibrinogen levels to normal and significantly further improved TEG parameters, whereas FFP not only failed to increase fibrinogen levels but also worsened all TEG parameters. Patients given platelets followed by FFP had substantially more 24-hour chest tube drainage than those receiving cryoprecipitate. Additionally, patients receiving FFP required more coagulation product administration in the intensive care unit (ICU) than did those receiving cryoprecipitate. Therefore, it was advocated that when using component therapy to treat post-CPB coagulopathies in children, platelet transfusion followed by cryoprecipitate, if needed, seems the better approach to restore hemostasis, and it was noted that smaller children required this additional administration of cryoprecipitate more often to adequately control their post-CPB coagulopathies.[13]

## Pharmacologic strategies

An even more effective method of combating post-CPB coagulopathies would be their prevention. While priming volumes of extracorporeal circuits are continually being adjusted to minimize the quantitative defects caused by hemodilution, many investigators have attempted to attenuate the qualitative defects with pharmacologic therapies. Desmopressin acetate, antifibrinolytics (ε-aminocaproic acid and tranexamic acid), and aprotinin have been evaluated for their abilities to accomplish this during CPB.

### Desmopressin acetate

Desmopressin acetate (1-deamino-8-D-arginine vasopressin [DDAVP]) is a synthetic analogue of the posterior pituitary hormone, vasopressin. Administration of DDAVP has been shown to increase plasma levels of the procoagulant factor VIII:C and of the von Willebrand factor.[50,51] Importantly, the plasma level of the larger, more hemostatically active, multimers of von Willebrand factor have been shown to increase after DDAVP.[52] The von Willebrand factor plays a major role in mediating platelet adhesion to exposed subendothelium by binding to adhesive glycoprotein Ib receptors on the platelet membrane and to the exposed subendothelial collagen.[50] DDAVP may also improve hemostasis by a direct effect on blood vessel walls to increase platelet adhesiveness and promote platelet spreading at sites of vessel injury.[52] Since DDAVP seems to improve hemostasis by enhancing platelet function and since platelet dysfunction has been incriminated as a cause of post-CPB bleeding, DDAVP has been used in an attempt to curb blood loss after cardiac surgery.

Studies involving the routine prophylactic administration of DDAVP (0.3 μg/kg) to adults undergoing primary coronary artery bypass grafting have shown no reduction in post-CPB blood loss or transfusion requirements.[53,54] When given to adults undergoing more complex procedures, such as valve replacements or repeat sternotomies, DDAVP has been shown to decrease blood loss during the first 24 postoperative hours.[51] Additionally, when DDAVP has been given to adult patients with documented platelet function abnormalities (prolonged bleeding times and decreased TEG *MA* values) and continued bleeding after CPB, the bleeding and the amount of blood products transfused have been significantly reduced compared to patients not receiving DDAVP.[50,55] Two studies have investigated the prophylactic administration of DDAVP (again, 0.3 μg/kg) to children after cardiac surgery, in many cases after complex procedures, and neither has shown a reduction in blood loss or transfusion requirements with this therapy.[56,57]

Potential complications following the use of DDAVP could relate to its endocrine functions; however, no evidence of vasoconstriction (smooth muscle effects) or of alterations in water balance (antidiuretic hormone effects) have been noted.[50,51,53,55,57] Although tPA is released by DDAVP, no fibrinolysis has been demonstrated with its use.[52,54] No evidence of an increased risk of thrombosis has been found after the use of DDAVP.[50,53]

The routine prophylactic use of DDAVP after CPB in children and adults does not seem to improve hemostasis. Administration of DDAVP to select patients with documented platelet function abnormalities (prolonged bleeding times or decreased TEG *MA* values) in the face of ongoing bleeding may prove beneficial.

### Antifibrinolytics

Epsilon-aminocaproic acid (EACA) and tranexamic acid (TA) are the two clinically available antifibrinolytic drugs. The antifibrinolytic actions of EACA were discovered in 1959 and the subsequent research for more potent drugs with similar actions found TA in 1962. Epsilon-aminocaproic acid is a synthetic monoaminocarboxylic acid whose structure is closely related to the amino acid lysine. Tranexamic acid is the trans isomer of 4-aminoethylcyclohexane carboxylic acid. Both exert their antifibrinolytic effect most importantly by competitively binding with the lysine binding sites of plasminogen, thus altering plasminogen's conformation and thereby preventing plasminogen activators from converting the plasminogen to its active form, plasmin. At significantly higher concentrations, these drugs bind directly to plasmin that has already formed, thus directly inhibiting the plasmin's activity. Both drugs are fairly rapidly excreted by the kidneys, although TA has a longer half-life. Tranexamic acid is six to 10 times more potent than EACA.[20,58]

Both EACA and TA have been shown to inhibit fibrinolytic activity when used prophylactically during CPB.[19,59] Although some postulate that fibrinolysis is not a major contributor to post-CPB bleeding,[14,22,25,26] a reduction in post-CPB blood loss and transfusion requirements has been demonstrated with the prophylactic use of these drugs in adults.[54,58–60] The contribution of the products of fibrinolysis to the generation of post-CPB platelet dysfunction no doubt plays a role. Indeed, studies with TA have shown not only that TA preserves platelet function after CPB but also that the amount of postoperative bleeding correlates with the post-CPB platelet function and not with the occurrence of fibrinolysis.[32,61] Other adult studies, however, have failed to show any beneficial hemostatic effect with the use of these antifibrinolytic agents.[62,63] Several investigations focusing only on children have revealed no reduction in bleeding or blood product transfusions during the first 24 hours after CPB with the prophylactic use of either EACA or TA.[64–66] However, when the children with cyanosis were analyzed separately in these studies, both EACA and TA significantly reduced postoperative blood loss and transfusion requirements.[64,65] Additionally, another study has indicated a significant reduction in 24-hour blood loss and transfusion requirements in children undergoing repeat sternotomies who were prophylactically given TA.[67] Therefore, the prophylactic use of antifibrinolytic agents to attenuate post-CPB bleeding may be efficacious in children with cyanotic heart defects and in those undergoing repeat sternotomies.

Multiple dosing regimens have been reported for each of these antifibrinolytics in adult patients and then have been extrapolated to the pediatric population. For EACA, a plasma level of 130 μg/mL is needed to inhibit fibrinolysis.[68] Since EACA that is administered intravenously is rapidly excreted by the kidneys, successful dosing protocols have used a loading dose followed by a continuous infusion. Published schedules for intravenous administration of EACA to adults include a loading dose of 100 mg/kg followed by an infusion of 1 g/hour,[20] a loading dose of 150 mg/kg followed by an infusion of 30 mg/kg/hour,[69] and a loading dose of 50 mg/kg loading dose followed by an infusion of 25 mg/kg/hour.[70] All of these doses achieve plasma levels of at least 130 μg/mL. Published pediatric dosing regimens include a loading dose of 75 mg/kg followed by an infusion of 15 mg/kg/hour[64] and a loading dose of 150 mg/kg followed by an infusion of 30 mg/kg/hour.[66] The higher of these doses was felt by the investigators to be appropriate to achieve the desired plasma levels of 130 μg/mL after comparison to adult protocols.[66] A recent pharmocokinetic study in children undergoing repair of congenital heart defects with bypass used a best-fit two-compartment model, and recommended a loading dose of 75 mg/kg, 75 mg/kg into the bypass circuit, and an infusion of 75 mg/kg/hour in the pre- and post-bypass periods, in order to achieve predicted plasma levels of 260 μg/mL in 95% of patients.[67]

Dosing regimens for TA have been analyzed more on a pharmacodynamic basis. Again, most regimens employ a loading dose followed by a continuous infusion because of rapid renal elimination of TA. Although lower doses of TA have been shown to attenuate the fibrinolysis associated with CPB in adults, a loading dose of 10 mg/kg followed by an infusion of 1 mg/kg/hour is needed to reduce post-CPB blood loss. Higher doses (double and quadruple this amount) have been found not to further reduce postoperative blood loss in adults.[61] A dosing protocol using a loading dose of 100 mg/kg after induction followed by another 100 mg/kg dose in the pump prime and an infusion of 10 mg/kg/hour has proven beneficial in pediatric patients.[68] It has been emphasized with both antifibrinolytics that since the initiation of fibrinolysis begins with skin incision and continues with sternotomy, pericardiotomy, and the initiation of CPB, administration of these drugs starting prior to skin incision results in significantly more reduction of fibrinolysis, platelet dysfunction, and blood loss than administration after CPB and protamine infusion.[32,71]

Much concern has been voiced about potential thrombotic complications after the use of antifibrinolytics, although none of the previously cited reports found any significant increase in thrombotic or embolic problems in either adults or children. These complications are of more concern when antifibrinolytics are used incorrectly during a hypercoagulable

state with compensatory fibrinolysis (disseminated intravascular coagulation [DIC]) rather than during the primary fibrinolysis that may occur after CPB.[72]

### Aprotinin

Aprotinin is a serine protease inhibitor isolated from bovine lung. Its ability to inhibit trypsin, plasmin, and kallikrein has been known since the 1930s, with its clinical use first reported in 1953 for the treatment of acute pancreatitis.[73,74] High doses of aprotinin were found in 1987 to be useful in reducing blood loss and transfusion requirements in adults undergoing repeat cardiac surgery as well as primary coronary artery bypass graft (CABG).[75,76] Since then, multiple investigations have explored the use of aprotinin in a variety of patient populations requiring CPB.

Aprotinin's antagonism of kallikrein and plasmin leads to its beneficial hemostatic effects after CPB.[73] Kallikrein is the central component of the contact activation cascades and thus stimulates thrombin formation via the intrinsic coagulation pathway, generates bradykinin from HMWK, and cleaves plasminogen to form plasmin.[15] Thrombin, bradykinin, and plasmin are all involved in the initiation of fibrinolysis and the production of platelet dysfunction associated with CPB: thrombin stimulates tPA release and "activates" platelets thus diminishing their future ability to aggregate,[14] bradykinin stimulates tPA release, and plasmin not only lyses fibrinogen and fibrin but also cleaves the adhesive glycoprotein Ib receptor from platelet surfaces thus decreasing the platelets' ability to adhere to exposed subendothelial surfaces. Plasmin also interferes with the subsequent binding of fibrinogen to the aggregatory glycoprotein IIb-IIIa platelet receptors.[28,76] Plasmin, kallikrein, and thrombin are all also involved in perpetuating the inflammatory response that accompanies CPB by activating the complement cascade, neutrophils, and endothelial cells. Aprotinin is able to inhibit plasmin at plasma levels of only 50 KIU/mL and does so by rapidly forming an almost irreversible complex with it. At much higher plasma levels (200 KIU/mL), aprotinin also inhibits kallikrein formation thus attenuating its central role in the production of post-CPB coagulopathies and the activation of the inflammatory response.[77]

Abundant evidence exists documenting aprotinin's ability to decrease blood loss and transfusion requirements ater CPB in adults undergoing CABG or valve surgery both as primary or redo procedures.[73,75,76,78] These beneficial effects seem even greater in adults considered at high risk for post-CPB bleeding such as those undergoing repeat sternotomies, those with acute bacterial endocarditis, and those with recent aspirin ingestion.[74,79] Conflicting reports have been published concerning aprotinin's effects on blood loss and transfusion requirements after CPB in children. Several factors probably combine to create the dichotomy in these studies. The children included in most investigations were very heterogenous in their ages and sizes as well as in their cardiac defects and the subsequent surgical procedures they underwent. Furthermore, a vast array of aprotinin dose regimens were used as were a variety of heparin and protamine protocols, CPB circuit primes, and transfusion triggers. However, almost all currently available data indicate that in children undergoing primary sternotomies, the administration of aprotinin does not decrease blood loss or transfusion requirements.[80,81] Blood loss 6 hours postoperatively was found in one study to be significantly reduced in children undergoing primary sternotomies who received a "high dose" of aprotinin, but even in these children the 24-hour blood loss and the transfusion requirements were not reduced by aprotinin.[23] However, reproducible evidence exists that aprotinin is beneficial in children undergoing repeat sternotomies. Reductions in transfusion requirements and attenuation of post-CPB TEG abnormalities have been demonstrated with the use of aprotinin in studies comprised exclusively of this subset of children.[82,83] In addition, the time required for chest closure in the operating room and the durations of postoperative mechanical ventilation, ICU stay, and total hospitalization were reduced in these children, possibly reflecting the attenuation of the inflammatory response to CPB by aprotinin. Despite the significant cost of aprotinin, savings of several thousand dollars were realized in the hospital charges for each of these children thus proving aprotinin to be cost effective as well as hemostatically efficacious. These beneficial effects of aprotinin were dose dependent with greater hemostatic and economic advantages found with the use of higher doses.

Another homogenous group of children that has been found to benefit from the use of aprotinin is neonates undergoing arterial switch procedures. An early study found a significant reduction in the time required for chest closure in the operating room when aprotinin was administered to these patients.[84] Subsequently, an investigation that included a group of 56 neonates undergoing arterial switch procedures found reductions in 24-hour chest tube drainage and transfusion requirements, again in a dose dependent fashion.[81]

A wide range of dosing regimens have been used when administering aprotinin to children, and, as indicated, the beneficial effects of aprotinin are greater with higher doses. The adult literature indicates that achieving aprotinin plasma levels of 200 KIU/mL is of paramount importance since this level is necessary for the inhibition of kallikrein and the subsequent blockade of kallikrein's activation of the coagulation, fibrinolytic, and inflammatory systems.[73] This blockade of kallikrein is deemed the pivotal difference between aprotinin and the antifibrinolytic agents. The only pediatric study to measure plasma aprotinin levels found maximum levels of 99 ± 25 KIU/mL 30 minutes after the initiation of CPB in children receiving a 30 000 KIU/kg loading dose of aprotinin after the induction of anesthesia with another 30 000 KIU/kg placed in the pump prime. No infusion of aprotinin was

used.[23] Other pediatric studies have used higher aprotinin doses in children but have not measured plasma levels.[80–83] Doses in these studies have been based either on body weight or body surface area. Weight based regimens have originated as extrapolations from adult dosing protocols and have included a loading dose and pump prime dose of 35 000–50 000 KIU/kg accompanied by an infusion of 10 000–20 000 KIU/kg/hour. Body surface area based regimens apparently evolved from discussions with the manufacturers of aprotinin and have used a loading and a pump prime dose of 240 mg/m$^2$ with an infusion of 56 mg/m$^2$/hour.[84] However, no pediatric dosing recommendations are included in the manufacturer's product insert. Dosing calculations based on body surface area result in the administration of much larger amounts of aprotinin than those based on body weight. Studies to determine the plasma level of aprotinin reached with each of these various doses are needed before a definitive pediatric dosing protocol can be advocated.

Several potential problems have been reported in adults receiving aprotinin, but pediatric studies have not conclusively related any adverse events with the administration of aprotinin. Concern about renal impairment following the use of aprotinin in adults exposed to periods of deep hypothermic circulatory arrest has not borne out in children.[23,83] Reports of dysrhythmias,[82] neurologic events,[82] and thrombotic problems[81] either have been found not to differ significantly between control groups and those children receiving aprotinin or have been felt to be multifactorial in origin. Since aprotinin is derived from bovine lung, it represents a foreign protein and, therefore, carries a risk for allergic reactions on repeat exposures. The incidence of this occurring has been found to be 2.5–2.8%[85,86] and is significantly related to the length of time between exposures to aprotinin. Patients with a re-exposure interval of less than 200 days have demonstrated a 4.5% incidence of adverse reactions whereas the incidence falls to 1.5% in those with a longer interval.[85] Those manifesting these adverse reactions have been found to possess very high antiaprotinin immunoglobulin G (IgG) antibody concentrations. Unfortunately, the occurrence of high antiaprotinin IgG antibody levels is only 60% predictive of adverse reactions upon repeat exposures; however, no adverse reactions have occurred when these IgG levels were low or undetectable preoperatively. Interestingly, skin prick tests to assess immunoglobulin E (IgE) antibody-mediated hypersensitivity have not been found to be predictive of subsequent adverse reactions to re-exposure to aprotinin.[86] Based on this knowledge, the following recommendations have been made for situations when a repeat exposure to aprotinin is being contemplated: (i) re-exposure should be avoided within 6 months of a previous exposure; (ii) a test dose of 1 mL (10 000 KIU) of aprotinin should be administered prior to the loading dose; (iii) test and loading doses should be delayed until conditions for rapid commencement of CPB are present; (iv) the addition of aprotinin to the pump prime should be delayed until after the loading dose has been safely given; (v) $H_1$ and $H_2$ blockers as well as standard treatments for hypersensitivity–allergic reactions (epinephrine, corticosteroids) should be readily available. Should an exceptional situation arise where the clinical benefit of readministering aprotinin within 6 months of a previous exposure is felt to outweigh the risk of an allergic reaction, preoperative testing for antiaprotinin IgG antibodies should be performed and the use of aprotinin should proceed only in the absence of these antibodies and still with utmost caution.[85,86]

Finally, care must be taken to insure a safe level of anticoagulation when aprotinin is used. Through its inhibition of kallikrein and the subsequent activation of factor XII, aprotinin inhibits the intrinsic coagulation cascade. This inhibition acts synergistically with that produced by heparin to augment the prolongation of celite ACTs.[87] Although some feel this synergy is helpful in preventing thrombin generation, others feel that celite ACT measurements can not be depended upon to reflect adequate anticoagulation in the presence of aprotinin. On the other hand, kaolin, a negatively charged molecule, binds aprotinin, a positively charged molecule, thus preventing aprotinin from inhibiting intrinsic coagulation. Kaolin ACTs, therefore, are not influenced by the presence of aprotinin.[88] To insure adequate anticoagulation when aprotinin is being used, it is suggested that celite ACTs be maintained greater than 750 s, kaolin ACTs be maintained over 480 s, heparin levels be monitored, or supplemental heparin be administered at a routine interval (usually hourly) during CPB even in the presence of adequate ACT measurements.[89,90]

## Blood conservation

Measures to conserve autologous blood during pediatric open heart surgery are worthwhile because of the severity of post-CPB coagulopathies and the resultant blood loss. Several blood conservation options are possible and success is likely to be enhanced if multiple measures are employed. The efficacy of some blood conservation techniques varies with the child's age (Table 10.2). Preoperatively, the patient's likelihood of bleeding should be assessed and a blood conservation strategy chosen that has a favorable ratio between potential benefit and risk. Techniques of proven value in children that are not discussed elsewhere in the chapter will be emphasized.

### Preoperative considerations

Preoperative autologous donation (PAD) is the collection and anticoagulation of whole blood from a patient for anticipated perioperative transfusion. It eliminates the risk of bloodborne infections and incompatibility issues, including graft-vs.-host disease, and diminishes immune modulation.

**Table 10.2** Blood conservation techniques. Possible means for reducing allogenic blood transfusions during pediatric cardiac surgery.

| Management strategy | Neonate | Teenager |
|---|---|---|
| *Preoperative* | | |
| Autologous blood donation | — | + |
| Erythropoietin, iron | — | + |
| Plateletpheresis | — | — |
| *Surgery* | | |
| Limit hypothermia | + | + |
| Limit duration of CPB | + | + |
| Avoid circulatory arrest | + | + |
| Meticulous hemostasis | + | + |
| Topical sealants | ? | + |
| *Anesthesia* | | |
| Normothermia after CPB | + | + |
| Transfusion algorithm | + | + |
| Antifibrinolytic agents | + | + |
| Acute normovolemic hemodilution | — | ? |
| Anesthetic technique and agents | ? | ? |
| Antithrombin III | ? | ? |
| DDAVP | — | — |
| *Cardiopulmonary bypass* | | |
| Limit prime volume | + | + |
| Nonsanguinous prime | — | + |
| Defined target hematocrit during bypass | + | + |
| Ultrafiltration | + | + |
| Cell salvage | + | + |
| Heparin/protamine titration | + | + |
| Heparin concentration monitored | ? | + |
| Heparin coated circuit | ? | ? |
| Blood substitutes | ? | ? |
| Centrifugal pump | — | ? |
| Reinfuse circuit residual fluid | — | — |
| *Postoperative* | | |
| Transfusion algorithm | + | + |
| Reinfuse shed blood | — | ? |

+ = Strategy useful in children. ? = Strategy possibly useful but benefit unproven in children. — = Strategy not useful in children.
CPB, cardiopulmonary bypass; DDAVP, 1-deamino-8-D-arginine vasopressin.

The amount of blood collected from a single donation is typically limited to 10% of the child's total blood volume. Most pediatric patients selected for PAD are more than 7 years old or weigh more than 40 kg. The rate of donation reactions is 2–5% and increases with decreasing age and weight. Limited venous access is an additional concern. The use of PAD for cardiac surgery remains controversial because of safety concerns and the risk of delaying surgery. Adults with unstable coronary artery disease, aortic stenosis, or congestive heart failure are generally excluded from PAD. Suitability of PAD in children with congenital heart disease depends on the anticipated consequences upon a patient's cardiac pathophysiology. Although PAD has been safely performed in children weighing less than 20 kg with simple cardiac anomalies,[91] the technique is usually limited to teenagers and is performed infrequently.

Recombinant human erythropoietin α (EPO), the primary growth factor for red blood cells, is approved in the USA, Canada, Japan, and Europe for use in patients donating autologous blood before surgery. Treatment with EPO (100 U/kg subcutaneously three times a week for 3 weeks and intravenously on the day of surgery) increased the amount of autologous blood that could be collected and minimized allogenic blood exposure in children (age range 2–14 years) undergoing repair of atrial or ventricular septal defects.[92] The combined use of EPO and PAD for pediatric cardiac surgery is new and has potential. However, it is expensive, invasive, and probably will be limited to children undergoing elective non-complex cardiac surgery. Platelet count increases with EPO therapy. While this may be an advantage in some cases, it would be a concern in prothrombotic patients, including those with single ventricle physiology.

## Intraoperative considerations

The influences of differing anesthesia techniques or agents on bleeding during pediatric cardiac surgery are poorly known. Basic principles would suggest avoidance of high blood pressure and venous congestion. Of interest, patients undergoing unifocalization of aortopulmonary collaterals may be at greater risk for hemorrhage from postoperative liver dysfunction. Intraoperative measures to preserve hepatic blood flow could be worthy of consideration.

Acute normovolemic hemodilution (ANH) is the removal before CPB of whole blood from the patient while maintaining isovolemia by crystalloid or colloid infusion. The patient's blood is reinfused after CPB. Although safe, the technique is seldom indicated during pediatric cardiac surgery because children undergo substantial hemodilution during CPB and consequently have less red cell mass available for ANH. Additionally, the platelets in ANH blood are often insufficient to correct post-CPB deficits in platelet number and function. Indeed, the efficacy of ANH even in adult cardiac surgery is questioned.

Platelet-rich plasma can be obtained by plateletpheresis after induction of anesthesia and transfused after CPB. Recent reviews conclude that the current technology is clinically ineffective and plateletpheresis should not be considered for routine use.

Fibrin glue has been used in children undergoing repair of congenital heart defects and is most efficacious in controlling low pressure venous bleeding. Exposure to topical sealants that contain aprotinin results in an antibody response similar to that observed after intravenous aprotinin administration. When exposed to fibrin glue of bovine origin, patients may develop antibodies against bovine factor V or X. These

antibodies can then cross-react to inhibit the patient's own factor V or X.

## Perfusion considerations

Unfortunately, the degree of hemodilution incurred by small infants during CPB is extreme. Although perfusionists have devised methods of limiting hemodilution, almost all neonates require a blood-containing prime. The optimum hematocrit during CPB remains undefined and probably is influenced by factors such as blood flow, degree of hypothermia, and the type of cardiac anomaly.

Ultrafiltration has been repeatedly demonstrated to be useful during pediatric open heart surgery. This technique uses convection transport across a semipermeable membrane under a hydrostatic gradient to remove water and low molecular weight solutes from blood. Effects include hemoconcentration of the patient, removal of inflammatory mediators, and an ability to manipulate plasma electrolytes and colloid osmotic pressure. Ultrafiltration reduces the requirement for allogenic blood products by increasing the patient's hematocrit, concentrating coagulation plasma proteins, and modulating the systemic inflammatory response to CPB.[93] Heparin blood concentration increases because it is highly protein bound and hence not filtered.[94] There are several methods of ultrafiltration. A blood-containing CPB prime can be ultrafiltered prior to initiation of CPB; conventional ultrafiltration is performed during CPB; modified ultrafiltration (either arteriovenous or venovenous) occurs after separation from CPB. The amount of ultrafiltrate obtained can be increased by adding fluid to the CPB circuit to maintain isovolemia. It is unclear which of the ultrafiltration variants provides maximal clinical benefit.

Blood shed intraoperatively can be collected into an automated centrifuge-based blood salvage instrument that produces a suspension of washed, concentrated red blood cells containing little or no heparin. Likewise, red cells present in the CPB circuit after separation of the patient from CPB can be salvaged. Red cell salvage has been found to be a useful blood conservation technique during pediatric cardiac surgery.[95] Washed red cells lack plasma proteins and will lead to coagulation factor depletion if transfused in large volumes.

Unprocessed residual CPB fluid can be returned to the patient. However, this is not optimal because the fluid has a low hematocrit and contains heparin, fibrinolysis byproducts, and cellular debris. Mediastinal and pleural shed blood can be collected postoperatively and reinfused but the technique is seldom used in pediatric cardiac surgery. There is concern that reinfused shed blood promotes a coagulopathic state because shed blood not only contains decreased amounts of coagulation factors and increased levels of fibrin degradation products but also stimulates tPA. Additionally, the hematocrit of shed blood is usually less than 20%.

## Postoperative thrombosis

Children, especially neonates, can become hypercoagulable postoperatively as a consequence of the coagulation changes associated with CPB and the treatment of post-CPB coagulopathies. After CPB, there is ongoing thrombin generation, but fibrinolysis is reduced because of increased plasminogen activator inhibition. Furthermore, anticoagulant capacity is diminished with decreased protein S, protein C, and ATIII activities. Additionally, factors predisposing to clotting are present, including low blood flow, exposure to foreign materials, and the presence of central venous catheters. Children who have undergone a Glenn anastomosis or a Fontan procedure are at an increased risk for venous thrombosis, probably because of the simultaneous presence of many of these factors. Other procoagulant concerns postoperatively include the relatively common prevalence of activated protein C resistance from the factor V Leiden mutation[96] and the infrequent occurrence of heparin-induced thrombocytopenia.

It is important to monitor the postoperative pro and anticoagulant status of children at high risk for venous thrombosis and to remove central venous lines as soon as possible after surgery. Mortality rates of 33–50% after postoperative clinical venous thrombosis are reported.[97] Neonates have a 10-fold risk compared to older children. Correction of factor deficiencies, anticoagulant therapy with heparin and/or warfarin, thrombectomy, and thrombolysis may be necessary in preventing or managing postoperative hypercoagulable states.

## Summary

Ongoing bleeding after cardiac surgery in children produces significant morbidity and thus demands that clinicians caring for these children be knowledgeable about the etiologies and management of post-CPB coagulopathies. Risk factors and coagulation tests have been identified that permit one to anticipate and then treat bleeding after CPB. Pediatric investigations have defined the utility of specific blood products in restoring hemostasis and the appropriate use of pharmacologic therapies for attenuating postoperative blood loss. However, much work remains to be done in children in this arena. Continued manipulations of extracorporeal circuits to minimize quantitative and qualitative hemostatic derangements, development of pharmacologic agents to inhibit the inflammatory response to CPB and to provide better anticoagulation during CPB, and development of blood substitutes and more targeted coagulation products remain a few of the goals that will further enhance our ability to safely care for these children. Meanwhile, recognition of the significance of this aspect of pediatric cardiac surgery will allow clinicians to minimize one source of morbidity associated with these procedures.

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# 3 Preoperative considerations

# 11 Preoperative evaluation and preparation: A physiologic approach

Lydia Cassorla

## Introduction

Assessment of the patient with congenital heart disease (CHD) is a unique challenge for the anesthesiologist due to a wide range of anatomic lesions and the need for in-depth understanding of each patient's physiologic abnormalities. An interdisciplinary approach is recommended to optimize the contributions of all members of the perioperative team. Regular pre-surgical meetings attended by representatives from pediatric cardiac surgery, pediatric cardiology, pediatric cardiac anesthesiology, radiology, and pediatric intensive care facilitate patient assessment and provide a forum to review each case and view diagnostic studies prior to elective surgeries. Most patients have already undergone extensive anatomic evaluation; however, each specialist contributes a unique perspective to the comprehensive plan for perioperative care and ensures that major concerns are communicated. An effective system to organize and exchange patient information is a key element of success, as in many cases the primary preoperative challenge the anesthesiologist faces is the integration of a great deal of data. The anesthesiologist must correlate the information, optimize the preoperative condition of the patient, and prepare for anticipated intraoperative challenges.

It is assumed that the reader is familiar with general principles of pre-anesthetic assessment for both pediatric and adult patients. The focus of this chapter is upon: What is special about the assessment of a patient who has CHD? The goal is to formulate a rational, customized anesthetic plan. Given the wide variety of lesions, important keys lie in understanding CHD terminology, and in a method to classify patients based upon their physiology. These tools are discussed below as the first and second goals of the preoperative assessment.

## Impact of current trends on the preoperative assessment

Current trends in congenital heart surgery further reinforce the need for a careful methodology for preoperative assessment. Specific factors include an increase in the number of patients with CHD undergoing surgery, diagnostic advances, a trend toward corrective procedures performed on small, potentially unstable infants, and the frequency of surgery performed on the day of hospital admission.

### Demographics

Due to improved diagnosis and outcome, the population of patients with CHD undergoing surgery in the USA is growing (see Chapter 1). Increasingly, patients survive to adulthood following corrective or palliative surgery, including those with complex structural lesions.[1,2] Anesthesia for non-cardiac surgery in patients with CHD is therefore becoming more common in all surgical venues, including outpatient surgery centers and labor and delivery suites (see Chapters 13 & 26). In addition, new mothers with CHD are much more likely to have offspring with cardiac defects than the population at large. A 16% incidence of CHD is reported in the children of women with CHD, irrespective of whether the mother's lesion was unoperated, palliated, or corrected.[3] This contrasts with an overall incidence of CHD of 0.5–1.2% of live births.[4,5] Immigration brings older children and adults with uncorrected CHD to US medical centers as well.

### Diagnostic tools

Diagnostic tools are continually evolving and provide a broad range of preoperative information for assessment. Echocardiography, computerized tomography (CT), and nuclear cardiology now create stunningly detailed images. Fetal diagnosis of CHD is commonplace and has facilitated the coordination of resources at congenital heart surgery centers and improved outcomes.[6] The anesthesiologist must be able to utilize the information derived from each major diagnostic modality. The potential utility of intraoperative transesophageal echocardiography (see Chapter 9) may also be identified, as small sized probes permit intraoperative assessment of nearly all pediatric patients.

### Surgical and non-invasive approach

Rapid and ongoing evolution of surgery for CHD has had a huge impact on the preoperative preparation required for the pediatric cardiac anesthesiologist. Improved surgical outcomes and a focus upon structural correction in the neonatal period has tremendously increased the number of major procedures performed in the first days and weeks of life (see Chapters 1 & 12). The development of non-surgical techniques has widened the therapeutic arena to include the interventional cardiac catheterization laboratory as well. Examples include device closure of septal defects, balloon dilation of stenotic valves and vessels, and placement of coils and stents (see Chapter 25).

### Preoperative stabilization of the neonate

In nearly all cases the neonate can be stabilized to permit thorough preoperative assessment and preparation of the surgical team. Important therapies include administration of prostaglandin $E_1$ ($PGE_1$) to maintain patency of the ductus arteriosus, balloon atrial septostomy to enhance mixing of pulmonary and systemic venous return, and red blood cell transfusion to optimize hemoglobin levels for patients with marginal oxygen transport. Pulmonary vascular resistance (*PVR*) may be manipulated with alterations of inspired oxygen concentration, carbon dioxide level, and nitric oxide therapy. Inotropic and/or vasodilator support may enhance the ability of the neonatal heart to meet cardiac output (*CO*) demands (see Chapters 14 & 27). In nearly all cases, therefore, the anesthesiologist has time to perform a careful review of the available data and surgical plan.

### Surgery on the day of hospital admission

Most elective surgeries and interventional procedures are currently performed on the day of hospital admission for economic reasons. The logistics of the preoperative evaluation of this most challenging group of patients must be carefully coordinated to avoid suboptimal patient assessment or last minute cancellations.

## Preoperative goal no. 1: Understand congenital heart disease terminology

### Terminology and segmental approach to anatomy

In order to understand and communicate information regarding CHD, the anesthesiologist must first make sense of the terminology. The first modern attempt to classify CHD was published in 1936 by Dr Maude E. Abbott.[7] Since that time additional nomenclature published by multiple authors has led to more than one term for many similar conditions and structures. Among others Lev, Van Praagh, Anderson *et al.*, and de la Cruz and Nadal-Ginard[8–12] have made important contributions in this field. While there is currently no consensus opinion from national or international organizations regarding anatomic terms for CHD there is a movement to do so. A summary of commonly used terms is presented in Table 11.1.

### Segmental approach

For practical purposes it is useful to consider the heart as composed of three types of segments—atria, ventricles, and great arteries.[10,13–15] During normal development they divide into right- and left-sided structures, each side having characteristic morphologic features. Segments may be described as right- or left-sided to define their location relative to other cardiac structures, or morphologically right or left to describe their anatomic features. Normal anatomy is the standard for defining morphologic features. Therefore a morphologically right structure is normally right-sided, but may be left-sided, and vice versa.[16] Basic morphologic characteristics of each normal segment are described in Table 11.2.

### Atrial sidedness or situs

Situs describes the laterality of asymmetric structures within the cardiovascular, respiratory, and gastrointestinal systems. From a cardiac standpoint it is based upon the location of the atria. The usual arrangement, situs solitus, is one of a right-sided, morphologically right atrium, and a left-sided, morphologically left atrium. Note that the venous connections are not definitive, as there can be anomalous drainage of the systemic or pulmonary veins.

Conditions of abnormal situs include situs inversus, isomerism, and indeterminate situs—situs ambiguous. These are some of the most complex of congenital abnormalities and are discussed in Chapter 22. Situs inversus exists when morphologically right- and left-sided structures lie in a mirror image of the normal arrangement. Isomerism is present when both the right- and left-sided atria are mirror images of the same morphological type. Right isomerism exists when the right-sided and left-sided atria are mirror images of a morphologically right atrium, and left isomerism exists when both atria are mirror images of a morphologically left atrium. Bronchi, pulmonary segments, abdominal great vessels, and abdominal organs show characteristics of the atrial situs.[17] Right isomerism is usually associated with absence of the spleen and therefore is often called asplenia. Left isomerism is termed polysplenia due to the potential for multiple spleens. When isomerism is present, the heart and stomach are often on opposite sides (visceroatrial heterotaxy). Heterotaxy is therefore often used as a synonym for isomerism although is not strictly equal. Both isomerism and indeterminate situs are also called situs ambiguous.[14,16–18]

**Table 11.1** Commonly used anatomic terms for congenital heart disease.

| | |
|---|---|
| ASD | Atrial septal defect |
| Asplenia | Right isomerism, bilateral right sidedness |
| AVSD | Atrioventricular septal defect, "AV canal," an endocardial cushion defect. Characterized by a single atrioventricular ring, with both a primum ASD and a VSD in complete defects |
| Balanced ventricles | A pair of ventricles of nearly equal size. Often used to describe the ventricles of a patient with AVSD. Balanced ventricles are more easily separated during surgery to achieve a two-ventricle repair |
| Bulb | A ventricular structure that gives rise to a great vessel but that has no inlet valve. The orifice connecting it to the other ventricle is a *bulbo-ventricular-foramen* |
| Concordance | Connection of two structures of identical morphologic sidedness, e.g. morphologically right-to-right, or left-to-left. Used to describe atrioventricular or ventriculoarterial connections. Does not describe position of structures within the body or position with respect to other cardiac structures |
| Dextrocardia | A right-sided heart, or a heart with a rightward base–apex axis |
| Discordance | Connection of a morphologically right-sided structure to a morphologically left-sided structure at the atrioventricular or ventriculoarterial level. *See concordance* |
| d-loop ventricles | Looping describes the internal organization of the ventricles. First described by Van Praagh in 1964, "right-handed" or d-loop is the result of normal looping of the heart in formation. Consistent with the illustration of an *imaginary right hand* placed with its *palm against the septal surface of the right ventricle*, the thumb extending back through the atrioventricular valve toward the atrium, and the fingers extending toward the right ventricular outflow tract and pulmonary valve. With d-looping the left hand would be similarly positioned only for the left ventricle |
| Dominant ventricle | A ventricle that is much larger than its companion, often a double inlet, or double outlet ventricle, or part of an unbalanced atrioventricular septal defect. *See unbalanced ventricles* |
| Double inlet ventricle | A ventricle into which both atrioventricular valves flow |
| Double outlet ventricle | A ventricle which gives rise to both great vessels. This term is usually applied when at least half of the second outlet valve lies over the ventricle |
| d-related great vessels | Aortic valve to the right of the pulmonary valve. The normal arrangement is a right-posterior aorta with respect to the pulmonary trunk. (Previously thought to represent ventricular looping, however this is an unreliable marker. Many references have used the term d-transposition, for example, as synonymous for complete transposition with d-looped ventricles and l-transposition as synonymous with corrected transposition with l-looped ventricles. This is now generally considered incorrect usage of the term) |
| Hemitruncus | Right or left pulmonary artery arising directly from the aorta |
| Heterotaxy | An abnormality in left–right arrangement. Includes isomerism syndromes, discordance, and imbalance of morphologically left- and right-sided structures |
| Levocardia | A left-sided heart, or a heart with a leftward base–apex axis |
| l-loop ventricles | Abnormal, "left-handed" ventricular looping. Consistent with the illustration of an imaginary *left hand* placed with its *palm against the septal surface of the morphologic right ventricle*, the thumb extending back through the atrioventricular valve toward the atrium, and the fingers extending toward the right ventricular outflow tract and pulmonary valve. With l-looping the right hand would be similarly positioned only for the morphologic left ventricle. *See d-loop ventricles* |
| l-related great vessels | Aortic valve to the left of the pulmonary valve. (Previously thought to represent l-looped ventricles, however now known to be an unreliable marker. *See d-related great vessels*) |
| Malalignment | A malposition of the atrial or ventricular septum that results in an overriding valve. The malposition may be lateral, rotational or both |
| Mesocardia | A centrally located heart, or a heart with an inferior base–apex axis |
| Overriding valve | Biventricular emptying of an atrioventricular valve or biventricular emptying of a semilunar valve. Associated with malalignment VSD |
| Polysplenia | Left isomerism, bilateral left sidedness |
| Semilunar valve | Ventriculoarterial outlet valve |

*Continued p. 178*

**Table 11.1** (cont'd)

| | |
|---|---|
| Single outlet | Single great vessel arising from the heart. Diagnoses include aortic atresia, pulmonary atresia, common arterial trunk (truncus arteriosus), or a solitary arterial trunk (without evidence of pulmonary or aortic atresia) |
| Single ventricle | Technically, the presence of only one anatomic ventricle. Term usually applied to patients with one functional ventricle and often to those with *single ventricle physiology*—complete mixing of the systemic and pulmonary venous return. May be associated with one or two great vessels |
| Situs ambiguous | Indeterminate sidedness. Includes isomerism |
| Situs inversus | Mirror image sidedness with respect to normal with a morphologically right atrium on the left side and a morphologically left atrium on the right side |
| Situs solitus | Normal sidedness |
| Straddling valve | Anomalous insertion of atrioventricular valve cords into both sides of the interventricular septum. Severe straddling may preclude a two-ventricular repair |
| TGA or TGV | Transposition of the great arteries (vessels). Ventriculoarterial discordance |
| Truncus arteriosus | A single semilunar valve and annulus that gives rise to a single common arterial vessel from which both the systemic and the pulmonary circulations branch. May be associated with a truncal valve of more than three, and rarely two, cusps. Always associated with a VSD just below the truncal valve |
| Unbalanced ventricles | A pair of ventricles of unequal size. Often used to describe the ventricles of a patient with AVSD. When significantly unbalanced, the ability of the smaller ventricle to perform adequately if separated from its companion is called into question. *See balanced ventricles* |
| Univentricular atrioventricular connection | Both atria are connected to one ventricle via two valves (double inlet ventricle) or absence of the right or left atrioventricular connection (single atrioventricular connection) |
| VSD | Ventricular septal defect |

**Table 11.2** Characteristic morphologic features of major cardiac structures.

| | |
|---|---|
| Right atrium | The most consistent morphologic features are its broad-based appendage, presence of pectinate muscles in the vestibule, and a well-defined crista terminalis. Normal venous connections include the superior and inferior vena cavae and the coronary sinus; however, it is the morphology of the appendage that is the arbiter of atrial morphology |
| Left atrium | A narrow-based appendage is characteristic. Pectinate muscles are limited to the appendage. There is no crista terminalis. Normal venous connections include the four pulmonary veins; however, their drainage may be anomalous |
| Right ventricle | Coarse trabeculations in the apical portion of the ventricular are the most characteristic feature in malformed hearts. Association with a tricuspid atrioventricular valve is present in hearts with two ventricles and two atrioventricular valves. *See tricuspid valve* |
| Left ventricle | The apex of the ventricle has finer trabeculations than the morphologically right ventricle. Associated with a morphologic mitral atrioventricular valve in hearts with two ventricles and two atrioventricular valves. The septal surface is "bald," meaning without septal cordal attachments to the atrioventricular valve. *See mitral valve* |
| Tricuspid valve | Features include three leaflets (septal, inferior or mural, and anterior) and multiple cordal attachments to the ventricular septal surface |
| Mitral valve | Features include two leaflets with two papillary muscles. Each papillary muscle supports adjacent parts of both leaflets. Fibrous continuity of the septal (anterior) leaflet with the leaflets of the aortic valve is present, and there is absence of cordal attachments to the ventricular septum |
| Pulmonary artery | Branches soon after its origin into the right and left pulmonary arteries. Anomalous origin of individual pulmonary arteries from the aorta is sometimes seen |
| Aorta | Normally gives rise to the coronary arteries and the systemic arterial tree. Anomalous origin of individual coronary arteries is sometimes seen. The first vessel after the coronaries, the innominate artery, branches to the side contralateral to the aortic arch |

When working with patients with isomerism, it is especially important for the anesthesiologist to keep in mind the relationship of the pulmonary and bronchial anatomy to atrial situs. A patient with right isomerism will have bilateral, mirror-imaged "right" lungs. Each lung will have right-sided morphology, including three lobes, a short mainstem bronchus and an upper lobe bronchus that separates before the pulmonary artery crosses (eparterial branching pattern).[18] When left isomerism is present both lungs will have mirrored left-sided morphology.

### Connections

There are two series of connections. Atria are connected to ventricles by atrioventricular (AV) valves, which "go with the ventricle." That is to say an AV valve generally has right morphological characteristics when opening into a morphologically right ventricle and left morphological characteristics when opening into a morphologically left ventricle. The ventriculoarterial (VA) connections are semilunar valves. Concordance or discordance is described at both the AV and the VA level. Connections are concordant when the morphologic characteristics of the segments they connect are both either right or left. Connections are discordant when a morphologically right structure is connected to a morphologically left structure or vice versa.[10,11,16,18] Two variations of transposition of the great arteries (TGA) illustrates these principles:

Transposition of the great arteries = ventriculoarterial discordance:

- TGA with AV concordance = "complete transposition." Pulmonary venous blood passes from the left atrium to left ventricle and enters the pulmonary artery. The patient is cyanotic and requires stabilization and surgery in the neonatal period as oxygen transport is dependent upon bidirectional shunting at the atrial and ductal levels.
- TGA with AV discordance = "corrected transposition." Pulmonary venous blood passes from the left atrium to right ventricle and enters the aorta. In this situation the two discordant connections balance or "correct" the circulatory abnormality. There is no oxygen desaturation or need for urgent surgery, although the anatomic right ventricle is prone to failure in later life as it is charged with pumping to the systemic circulation.

### Position of the heart

Two issues are pertinent regarding the position of the heart—the orientation of the base to apex axis, and the location of the heart within the chest. The terms levocardia, dextrocardia, and mesocardia are used to describe both, resulting in some confusion; however, they most often refer to the direction of the apex. It is best to communicate a clear description of the relation of the heart within the thorax independently from the base to apex axis. The normal arrangement is levocardia (apex leftward) with a left-sided heart. Mesocardia (apex caudad) is associated with isomerisim. Dextrocardia (apex rightward) may or may not be associated with situs inversus. Note that a heart may displaced toward the right chest and still demonstrate levocardia.[18]

### Right and left

The usage of "right" and "left" to denote morphologic structures as well as sidedness and relation has been reviewed above. A third usage of these terms relates to shunting. When describing a shunt, conventional rules apply and the "right" circulation is that which consists of systemic venous blood, either in the veins, heart, or pulmonary arterial tree. "Left" circulation describes blood draining from the lungs in the pulmonary veins, heart, or systemic arterial tree. Therefore a right-to-left shunt is systemic venous admixture into the systemic arterial circulation and not necessarily shunting of blood from a right-sided or morphologically right structure to a "left" structure. A fourth use of "right" and "left" refers to right- and left-handed ventricular looping[19] and is described under d-loop and l-loop in Table 11.1.

## Preoperative goal no. 2: Understand the cardiac pathology and physiology

Once familiar with basic anatomic terminology and the segmental approach, one is ready to classify the cardiac pathology. Congenital heart disease can be classified from an embryologic, anatomic, and a physiologic perspective.[20] The pediatric cardiologist may prefer an approach that begins with clinical findings at presentation and assists in the diagnosis of the lesion, or one that follows along anatomic lines. Even after hundreds of cases, however, unfamiliar variations of anatomy may be encountered. In most cases anesthetic management and risks follow from the patient's physiologic state rather than their specific anatomy. In other words, a diverse number of anatomic lesions may lead to a similar physiologic condition and therefore merit similar anesthetic management strategies.

It is more pragmatic, therefore, for the anesthesiologist to group patients based upon the physiologic consequences of their anatomy.[21] This step, which represents the most unique aspect of the preoperative assessment of CHD patients, allows the anesthesiologist to devise a rational anesthetic plan and predict potential intraoperative problems. One criticism of this approach is the fact that the physiologic state of an individual patient may change. For example an "acyanotic" patient may demonstrate cyanosis if conditions such as *PVR* or blood pressure change. However it is precisely the ability of the anesthesiologist to recognize that the physiologic situation has changed, understand the implications in the context of the patient's disease, and respond in a dynamic

**Table 11.3** Physiologic classification of congenital heart disease.

| |
|---|
| *I Acyanotic congenital heart disease* |
| A With left-to-right shunt |
| 1 ASD |
| 2 VSD |
| 3 PDA |
| 4 AVSD (may also be cyanotic) |
| 5 Tetralogy of Fallot (may also be cyanotic) |
| 6 Partial anomalous pulmonary venous return |
| B Without left-to-right shunt |
| 1 Valvular heart disease |
| 2 Subvalvular or supravalvular obstruction |
| 3 Cor triatriatum |
| 4 Double chambered right ventricle |
| 5 Cardiomyopathies |
| *II Cyanotic congenital heart disease* |
| A Pulmonary blood flow dependent upon the ductus arteriosus |
| 1 Tetralogy of Fallot, with severe right ventricular outflow obstruction |
| 2 Pulmonary atresia or severe stenosis |
| 3 Tricuspid atresia with pulmonary stenosis |
| 4 Ebstein's anomaly, severe |
| B Systemic blood flow dependent upon the ductus arteriosus |
| 1 Hypoplastic left heart syndrome |
| 2 Severe coarctation or interruption of the aorta |
| C Mixing lesions without duct-dependent circulation |
| 1 Large ASD or VSD |
| 2 AVSD with large communication |
| 3 Double inlet ventricle |
| 4 Double outlet ventricle |
| 5 Truncus arteriosus |
| 6 Tricuspid atresia without pulmonary stenosis |
| 7 Total anomalous pulmonary venous return |
| 8 Transposition of the great arteries (may be dependent upon the ductus for mixing and oxygen transport) |

ASD, atrial septal defect; AVSD, atrioventricular septal defect; PDA, patent ductus arteriosus; VSD, ventricular septal defect.

setting that are the hallmarks of appropriate care. The following pathophysiologic classification is outlined in Table 11.3.

## Acyanotic congenital heart disease

### With left-to-right shunt

#### *Etiologies*

Atrial septal defect (ASD), ventricular septal defect (VSD), selected patients with atrioventricular septal defect (AVSD or "AV canal"), and partial anomalous pulmonary venous return are examples of acyanotic CHD with left-to-right shunt. At both the atrial and ventricular level pressure on the left side of the heart normally exceeds that on the right side over the great majority of the cardiac cycle. In the presence of a relatively small intracardiac communication, therefore, the predominant flow abnormality is the passage of blood from the left to right. Some degree of right-to-left shunting is usually detectable. (Large communications permit varying degrees of bidirectional shunting, or mixing.) A patent ductus arteriosus (PDA) will result in an acyanotic patient when pulmonary arterial pressure remains below systemic arterial pressure throughout the cardiorespiratory cycle.

#### *Physiologic abnormalities and risks*

The primary physiologic abnormalities that may result from lesions that permit left-to-right shunting are increased volume loading of one or more of the cardiac chambers, decreased systemic *CO*, and increased intracardiac and/or pulmonary vascular pressures. Congestive heart failure (CHF) may result if the work of the heart exceeds compensatory mechanisms and reserve. Deterioration in gas exchange may result from pulmonary congestion.

Patients with substantial left-to-right shunting often demonstrate pulmonary hypertension. It is desirable to determine whether elevated pulmonary pressures are present, and whether they are due to augmented flow, resistance, or both. While echocardiography may be helpful to estimate pulmonary pressure and relative pulmonary to systemic flow, it is not possible to determine the resistance in the pulmonary arterial circulation without cardiac catheterization.

Decreased systemic blood flow in the presence of left-to-right shunt is often due to excess flow to the pulmonary bed, often called pulmonary "over circulation". In this setting left atrial pressure (*LAP*) is usually elevated as a result of augmented pulmonary venous return. Diastolic blood pressure may be compromised if systemic *CO* is reduced or there is a low-resistance vascular bed, such as a large anomalous pulmonary vessel or ductus arteriosus, branching from the proximal aorta. Coronary ischemia without coronary disease or anomalies may result from the combination of high *CO*, elevated *LAP* and low diastolic blood pressure.

When a large systemic-to-pulmonary shunt is present at the ventricular or arterial level the systolic pressure in the pulmonary artery will equal that in the aorta because they are in parallel with the same head of pressure. A large VSD or PDA are examples. One rule of thumb is to anticipate equalization of pressures when the diameter of the communication exceeds 75% of a normal aortic annulus diameter. If the pulmonary and systemic beds are exposed to equivalent pressure, the pulmonary to systemic flow ratio ($\dot{Q}$p : $\dot{Q}$s) is inversely related to the relative vascular resistances. Ohm's law can be transformed to its cardiovascular equivalent to understand a simplified relationship between pressure, flow, and resistance.

$I = \frac{E}{R}$ Ohm's Law

$I$ = current flow (amperes)

$E$ = electromotive force (volts)

$R$ = resistance (Ohms)

$\dot{Q} = \frac{P}{R}$ cardiovascular equivalent

$\dot{Q}$ = flow

$P$ = pressure

$R$ = vascular resistance

***Compensatory mechanisms***

Excess pulmonary blood flow returns to the left atrium and must again be ejected by the heart. The primary compensatory mechanisms to maintain an elevated *CO* include tachycardia, eccentric ventricular hypertrophy, and enlargement of all chambers receiving excess flow. If systemic blood flow is compromised, systemic vascular resistance (*SVR*) may increase to maintain blood pressure.

***Signs of limited reserve***

Pulmonary congestion may result in increased work of breathing. Patients may tire easily while feeding, and demonstrate dyspnea, diaphoresis, and lengthy feeding. Failure to thrive with poor weight gain is often an indication of inadequate systemic flow. Signs include poor growth, tachycardia, hypotension, decreased capillary refill, acidosis, and organ hypoperfusion. Systemic congestion may also be present. Toward the end of the first month of life the elevated *PVR* of the neonatal period decreases toward normal. If a large communication is present between the pulmonary and systemic circulations, a patient with CHF may deteriorate at this time as the decline in *PVR* further augments pulmonary blood flow. Ventilation–perfusion mismatch, hypoxemia, and frank pulmonary edema may result.

***Stabilizing therapies***

Stabilizing therapies include digoxin and diuretics for patients with systemic or pulmonary congestion, supplemental oxygen and ventilatory support for patients with pulmonary dysfunction, and afterload reduction for those with poor systemic perfusion. Inotropes may be useful to stabilize patients with severe congestive failure. If oxygen transport to the tissues is marginal due to low *CO*, blood transfusion to increase arterial oxygen content may also be a useful preoperative therapy.

A word of caution about oxygen and ventilatory therapy is in order. It is critical for the anesthesiologist to identify patients who may be at risk for deterioration if supplemental oxygen or controlled ventilation is instituted. Due to the pulmonary vasodilating effects of increased $P_{AO_2}$ and/or decreased $P_{ACO_2}$, patients with large left-to-right shunts at the ventricular or great vessel level may experience a sudden increase in pulmonary blood flow if alveolar oxygen concentration or ventilation is increased. Systemic hypotension often accompanies reduced resistance of the pulmonary vascular bed in this setting. The combination of high left-atrial filling from excess pulmonary blood flow and systemic hypotension may precipitate a rapid downward spiral due to low coronary perfusion pressure and myocardial ischemia. Cardiac failure or even cardiac arrest may soon follow. Patients with a significant pulmonary shunt at the level of the great vessels (such as a large PDA) are most vulnerable to coronary ischemia due to ongoing pulmonary runoff during the diastolic phase of the cardiac cycle and the potential for particularly low diastolic blood pressure. It is therefore useful to ensure that monitoring devices display diastolic blood pressure prominently, rather than a mean value.

### Without left-to-right shunt

***Etiologies***

Acyanotic lesions without left-to-right shunt consist primarily of valvular heart disease or cardiomyopathy. Subvalvular or supravalvular obstruction, cor triatriatum, and double-chambered right ventricle are also in this category.

***Physiologic abnormalities and risks***

The primary potential physiologic consequences are decreased systemic *CO*, and excess pressure and/or volume in one or more of the cardiac chambers. Obstructive lesions limit *CO* by mechanically interfering with forward flow. Regurgitant lesions limit forward flow by introducing pump inefficiency. Cardiomyopathies result in pump failure or obstruction due to hypertrophy. Elevated intracardiac pressures, congestive failure, and pulmonary hypertension may occur. Patients with substantial obstruction to left-sided flow, such as those with severe mitral stenosis, aortic stenosis, or subaortic stenosis are at particular risk for induction of anesthesia and may not tolerate an inhalation technique (see Chapter 19). They should be identified preoperatively and scheduled with care as prolonged fasting may further compromise their reserve. In selected cases preoperative intravenous fluids may add to the safety of fasting.

***Compensatory mechanisms***

If the obstruction is at the ventricular outlet, concentric hypertrophy results, with a salient effect on ventricular wall stress. An undesirable side effect of ventricular hypertrophy, however, is diastolic dysfunction. A high end-diastolic filling pressure is often present long before systolic dysfunction and pump failure occurs. In pediatric patients, subvalvular stenosis is a common variant, with the potential for a dynamic component to outflow obstruction. In these patients tachycardia, hypovolemia, and positive inotropes may be deleterious.

Regurgitant lesions result in excess volume work for the ventricle involved. With chronic regurgitation, chamber enlargement results. Eccentric hypertrophy mitigates the elevated wall stress associated with ventricular dilation. Additional compensatory mechanisms include tachycardia and elevated filling pressures. Diastolic dysfunction precedes systolic pump failure in this situation as well.

***Signs of limited reserve***

Patients may demonstrate signs of inadequate systemic output due to low *CO*. Poor feeding and growth, tachycardia, hypotension, decreased capillary refill, acidosis, organ hypoperfusion, and signs of right- or left-sided congestive failure

may occur depending upon the site of obstruction, regurgitation, or myocardial failure.

***Stabilizing therapies***

Stabilizing therapies are similar to those for patients with left-to-right shunts, and include digoxin and diuretics for patients with systemic or pulmonary congestion, supplemental oxygen or positive pressure ventilation for patients with pulmonary dysfunction, and afterload reduction for patients with poor systemic perfusion due to valvular insufficiency or dilated cardiomyopathy. Inotropes may be useful to stabilize patients with severe congestive failure. If oxygen transport to the tissues is marginal due to low *CO*, blood transfusion to optimize hemoglobin and arterial oxygen content may also be a useful preoperative therapy.

## Cyanotic heart disease

### Physiology of cyanotic heart disease

Arterial desaturation and cyanosis are the result of venous admixture to the systemic circulation, called right-to-left shunting. With normal cardiac anatomy this occurs most often in the lungs due to alveolar collapse or vascular shunts. In the context of structural heart disease right-to-left shunting is usually accompanied by some element of left-to-right shunting, however whenever significant arterial oxygen desaturation is present the patient is considered to have cyanotic heart disease. As noted above, when describing a shunt the systemic venous blood is "right" and pulmonary venous blood is "left," regardless of the location or morphologic characteristics of the structures involved.

When venous admixture is significant, the relative volume and saturation of systemic venous and pulmonary venous blood determine arterial saturation. Therefore, systemic arterial saturation will depend to some extent upon factors that determine systemic venous oxygen saturation in addition to the normal determinants of pulmonary venous oxygen saturation. These are outlined in Table 11.4. Arterial saturation will fluctuate with changes in pulmonary function and shunt fraction, but also with changes in hemoglobin, temperature, and *CO*. If the systemic circulation supplies an important source of pulmonary blood flow, arterial saturation will vary with systemic blood pressure as well. Examples of this situation include PDA, aortopulmonary collateral vessels, and any prosthetic shunt from the aorta or its branches to the pulmonary artery.

***Importance of $\dot{Q}p : \dot{Q}s$***

While all patients with cyanotic heart disease have venous admixture, they do not all have decreased pulmonary blood flow. Many are at risk for excess pulmonary blood flow. An important goal of the preoperative assessment is to interpret the patient's arterial saturation in terms of the individual physiology and to estimate a desired value for $SpO_2$. Optimal saturation for patients with complete mixing of pulmonary and systemic venous return, for example, is not the maximum achievable value. A 1 : 1 relationship between pulmonary and systemic flow is generally considered optimal, and usually results in arterial oxygen saturation between 75% and 85%. When pulmonary blood flow is limited, incremental increases in the ratio have a relatively large positive effect on arterial saturation. However when the ratio exceeds 1 : 1 further increases in pulmonary blood flow have a diminishing effect upon saturation.[22] The benefits of an increased arterial saturation are more than outweighed by the cost of overcirculation to the pulmonary bed. Another way of looking at this problem is that the risk of high output cardiac failure increases while the incremental gains in oxygen content of the blood diminish. This relationship is illustrated in Fig. 11.1.

**Table 11.4** Factors determining arterial oxygen saturation ($SaO_2$) with right-to-left shunt.

| |
|---|
| 1 Determinants of pulmonary venous oxygen saturation |
| (a) $P_{AO_2}$ |
| (b) Gas exchange |
| (c) Alveolar ventilation |
| 2 Determinants of systemic venous oxygen saturation* |
| (a) $\dot{V}O_2$ |
| (b) Hemoglobin |
| (c) Cardiac output |
| (d) Factors affecting the oxyhemoglobin dissociation curve |
| 3 Pulmonary to systemic blood flow ratio ($\dot{Q}p : \dot{Q}s$)* |

*Normally, these factors do not play a significant role in determining $SaO_2$.
$P_{AO_2}$, pulmonary alveolar oxygen tension; $\dot{Q}p : \dot{Q}s$, pulmonary to systemic blood flow ratio; $\dot{V}O_2$, oxygen consumption

## Classification of cyanotic heart disease

Cyanotic patients may be divided into three broad physiologic categories based upon the role of the ductus arteriosus. Each is discussed separately below.

### Cyanotic heart disease with duct-dependent pulmonary blood flow

***Etiologies***

Ductus-dependent pulmonary blood flow is primarily associated with obstruction to right ventricular inflow or outflow. Examples include pulmonary stenosis or atresia, tetralogy of Fallot with severe right ventricular outflow obstruction, tricuspid atresia, and Ebstein's anomaly.

***Physiologic abnormalities and risks***

Patients are primarily at risk for decreased pulmonary blood

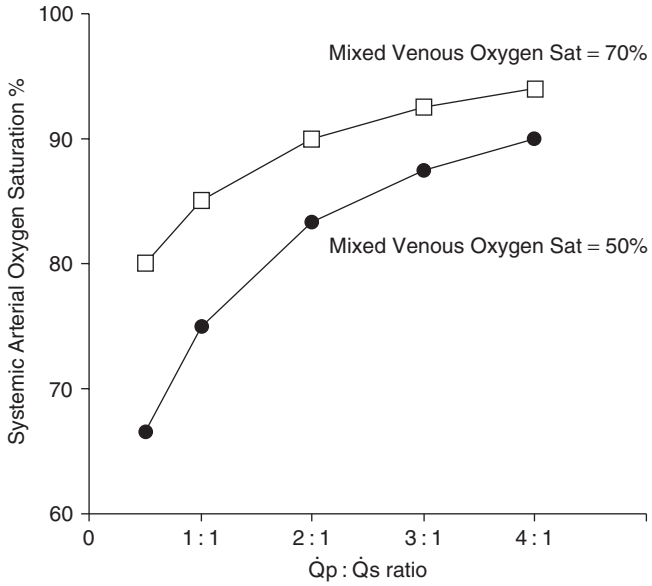



**Fig. 11.1** The effect of variable $\dot{Q}p : \dot{Q}s$ ratio on expected arterial oxygen saturation when systemic and pulmonary venous blood are completely mixed. A pulmonary venous oxygen saturation of 100% is assumed. Note that the incremental increase improvement in systemic arterial saturation diminishes at high $\dot{Q}p : \dot{Q}s$ ratios. Two mixed venous saturations are illustrated, 50% and 70%. Mixed venous oxygen saturation will vary with hemoglobin concentration, cardiac output, and oxygen consumption.[22]

flow and cyanosis. Most require surgery to provide a stable supply of blood to the lungs. With an important component of pulmonary blood flow provided via the aorta and ductus arteriosus, flow to the lungs depends upon the systemic blood pressure, resistance in the ductus, and *PVR*. Systemic blood pressure, in turn, depends upon *CO* and *SVR*.

***Compensatory mechanisms***

Systemic vascular resistance is a key determinant of the perfusion pressure to the duct, and therefore must be maintained. Increased hemoglobin also augments the oxygen-carrying capacity of the pulmonary blood flow and improves oxygen transport. Acidosis, if present, results in an augmented respiratory drive and a chronic respiratory alkalosis, augmenting the alveolar $P_{O_2}$.

***Signs of limited reserve***

Until patients undergo surgical intervention they are critically dependent upon the ductus arteriosus for pulmonary blood flow and oxygen transport. Severe hypoxemia may be demonstrated if ductal flow is marginal. Acidosis may be severe due to combined respiratory and metabolic components. If compensatory mechanisms and stabilizing measures are exhausted patients may develop myocardial dysfunction leading to further decreases in *CO* and blood pressure. Pulmonary blood flow is pressure dependent (via the ductus) therefore hypotension will result in a tandem downward spiral of arterial saturation and cardiac function.

***Stabilizing therapies***

Prostaglandin $E_1$ is usually effective to maintain a low resistance in the ductus. Potential complications of $PGE_1$ include tachycardia, hypotension, apnea, hyperpyrexia, and seizures. Additional therapies to reduce *PVR* such as supplemental oxygen, respiratory and/or metabolic alkalosis, phosphodiesterase inhibitors, and nitrate or nitric oxide therapy may be helpful. Systemic blood pressure and *CO* must be maintained to provide adequate perfusion pressure to the ductus. If pulmonary blood flow remains critically low, blood transfusion to a hemoglobin level of approximately 17 g/dL may augment the oxygen content of the pulmonary venous blood and enhance oxygen transport. Inotropic support may be helpful. Sedation must be used with caution and carefully assessed for its potential effect on *SVR* and blood pressure.

## Cyanotic heart disease with duct-dependent systemic blood flow

***Etiologies***

Obstructions or limitations to flow through the aortic valve or proximal aorta are associated with duct-dependent systemic blood flow. Examples include hypoplastic left heart syndrome, interrupted aortic arch, and severe coarctation of the aorta with persistent flow through the ductus arteriosus.

***Physiologic abnormalities and risks***

This group of patients is at risk for increased pulmonary blood flow and decreased systemic perfusion. Surgical goals are to stabilize the blood flow to the body and limit blood flow to the lungs, as pulmonary blood flow is usually above normal when systemic blood flow is dependent upon the ductus arteriosus. Arterial oxygen saturation is usually adequate; however, patients remain at risk for decreased oxygen delivery due to anatomic obstruction to systemic flow rather than diminished oxygen content of the blood. Saturation in the descending aorta may be lower than that in the ascending aorta due to differential perfusion from the right and left hearts.

***Compensatory mechanisms***

Because the pulmonary vasculature is usually receiving more than normal flow, the heart receives excess pulmonary venous return. Tachycardia is necessary to maintain an elevated *CO* in the volume-loaded neonatal heart as the ability to augment stroke volume is limited. Systemic vascular resistance is often elevated in response to decreased systemic perfusion.

***Signs of limited reserve***

Patients may demonstrate acidosis due to inadequate systemic perfusion. Excess pulmonary flow may result in undesirable effects such as pulmonary congestion or edema. Reduced coronary perfusion pressure and myocardial dysfunction may occur, particularly if diastolic blood pressure is

low in the setting of elevated *LAP*, as described above in the section on acyanotic disease with left-to-right shunt.

***Stabilizing therapies***

As for patients with duct-dependent pulmonary blood flow, ductal patency must be maintained with $PGE_1$. In this circumstance, however, the goal is to ensure systemic blood flow. Additional strategies are aimed at increasing *PVR* to limit pulmonary congestion and improve systemic blood flow. Pulmonary vascular resistance may be increased with an $F_{IO_2}$ of less than 0.21, and/or intentional respiratory acidosis via permissive alveolar hypercapnia or inspired carbon dioxide. Because flow to the periphery is compromised, attention to hemoglobin concentration is warranted to optimize systemic oxygen transport. Inotropic support may assist in maintaining *CO* in the face of excess pulmonary venous return.

### Cyanosis due to mixing lesions

***Etiologies***

The third group of cyanotic patients includes those with intracardiac right-to-left or bidirectional shunting without duct-dependent pulmonary or systemic flow. Examples in this category include large VSD, AVSD, and double inlet or outlet ventricle, single AV valve, total anomalous pulmonary venous return, and truncus arteriosus. Truncus arteriosus may be considered in this grouping as ductal patency is very rare unless interruption of the aorta is also present. Before surgery, TGA may be considered a mixing lesion with the potential for inadequate mixing. When feasible, surgical goals include the separation of the pulmonary and systemic circulations and correction of any obstructions to systemic or pulmonary blood flow.

***Physiologic abnormalities and risks***

Pure right-to-left shunt is rare and is associated with right ventricular inflow or outflow obstruction that is mild enough to permit survival without the duct. "Mixing" or bidirectional shunting of blood is usually present. Pulmonary blood flow may be low, normal, or high. Therefore, signs of either inadequate systemic or inadequate pulmonary flow may be present. In some conditions complete mixing of all pulmonary and systemic venous blood is obligatory. Examples include double inlet or double outlet ventricle or conditions with single AV valves. In this situation arterial saturation is a helpful guide to the relative pulmonary and systemic flow. With normal hemoglobin and oxygen consumption an arterial oxygen saturation of 75–85% generally indicates well balanced pulmonary and systemic flow. In many cases, however, the degree of mixing or streaming of blood is unknown unless cardiac catheterization is performed.

***Compensatory mechanisms***

Given time, hemoglobin concentrations will increase due to the effect of arterial desaturation on hemopoietin and red blood cell production. If pulmonary blood flow is elevated, additional pulmonary venous return may create additional volume work for the heart. Tachycardia and increased *SVR* may occur to maintain *CO* and blood pressure.

***Signs of limited reserve***

Depending upon whether the systemic or pulmonary circulation is more tenuous, patients may demonstrate signs of limited pulmonary or systemic blood flow. Patients with evidence of pulmonary congestion due to pulmonary overcirculation are among the most difficult to manage during transport to the operating room and during the pre-bypass period. Supplemental oxygen and hyperventilation may cause a detrimental increase pulmonary blood flow and CHF. On the other hand, if pulmonary congestion is already present hypoventilation and decreases in $F_{IO_2}$ may be equally intolerable as intrapulmonary shunting and hypoxemia may rapidly occur.

***Stabilizing therapies***

Therapy must be individualized depending upon the specific physiology. If, for example, dynamic pulmonary stenosis is present, β-blockers may improve pulmonary flow. If systemic flow is compromised due to excess pulmonary blood flow, strategies to increase *PVR* and maintain coronary perfusion pressure, as outlined above, may be useful.

## Summary—physiologic classification

To facilitate the preoperative evaluation, patients may be grouped into acyanotic and cyanotic categories. Acyanotic patients may or may not have left-to-right shunting with augmented pulmonary blood flow. Cyanotic patients have some degree of right-to-left shunt, however not all have decreased pulmonary blood flow. They may be physiologically grouped according to the role of the ductus arteriosus. If either the pulmonary or systemic circulation is dependent upon the ductus, $PGE_1$ therapy is initiated until surgery is performed. Patients with ductal dependence of the pulmonary blood flow usually have reduced pulmonary blood flow. Those with ductal dependent systemic blood flow usually have increased pulmonary blood flow and may have limited systemic perfusion. Patients with intracardiac shunting without dependence upon the ductus have variable pulmonary and systemic blood flow and varying degrees of bidirectional shunting. Those with large left-to-right shunts are at risk for acute pulmonary congestion, poor systemic perfusion and sudden deterioration if interventions such as supplemental oxygen or increased ventilation cause *PVR* to decline. It is important to identify this category of patients preoperatively as they must be managed very carefully upon transport to the operating room and before cardiopulmonary bypass (CPB).

Initial questions for physiologic classification:

- Is the patient cyanotic?
- Is there a left-to-right, right-to-left, or mixed shunt?
- Is either the pulmonary or systemic circulation dependent upon the ductus?
- Is there a pressure or volume overload on any of the cardiac chambers?
- What compensatory mechanisms or stabilizing therapies are in place?
- What is the current degree of cardiopulmonary reserve?
- Is there a risk of deterioration if $F_{IO_2}$ or ventilation is increased?

## Preoperative goal no. 3: Review additional history, physical exam, and studies

### History and physical examination

A complete medical history and a focused physical examination are performed.

Most patients have undergone evaluation by pediatric, pediatric cardiology, and pediatric cardiac surgery specialists before surgery is scheduled. The anesthesiologist's assessment adds important information in two areas. First, conditions apart from the surgical diagnosis that are of particular interest to anesthetic management may be detected. These include airway abnormalities, bronchospasm, gastroesophageal reflux, and issues pertaining to vascular access. Second, meeting the patient preoperatively provides an opportunity for the anesthesiologist to become familiar with specific details of the physical examination and to form a first-hand impression of the patient's condition and state of reserve. The physical examination should include the measurement of $S_{PO_2}$, blood pressure, and assessment of pulses in all extremities. Previous anesthetic records and operative reports are particularly valuable to answer questions. The side of previous modified Blalock–Taussig shunts should be known prior to induction of anesthesia as arterial pressure may be unreliable in the ipsilateral arm.

Congenital heart disease is often accompanied by additional defects, many of which are genetic.[5,23–25] In the Baltimore–Washington Infant Heart Study of 1981–1989, nearly 28% of patients had associated anomalies or syndromes.[26] The most common is Down's syndrome (9%), however a large number of defects are represented. With the growth of genetic science, specific chromosomal etiologies are defined with increasing frequency.

Patients with conotruncal abnormalities, including pulmonary atresia, truncus arteriosus, and interrupted aortic arch are at an increased risk for chromosome 22q11 deletion, known as velocardiofacial syndrome or diGeorge's syndrome.[27] Hypocalcemia and an absent thymus are often demonstrated in this condition. Due to immunologic depression, banked blood products are irradiated to prevent graft-vs.-host disease for patients known to have DiGeorge syndrome and for patients in high risk groups mentioned above. Complete transposition, on the other hand, is usually an isolated cardiac defect without associated anomalies. Vascular anomalies, especially abnormal origin of the subclavian artery, are important to the anesthesiologist, as they may impact the site of optimal monitoring and vascular access. The anesthesiologist must be aware of associated anomalies in CHD patients and assess their pertinence to anesthetic management on a case-by-case basis.

### Growth and development

A relationship between CHD and growth impairment has been documented for decades.[28–30] Infants with more complex lesions are significantly smaller than normal while those with isolated defects such as ASD and VSD are generally normal in weight. It is therefore important to assess growth, functional, neurologic, and cognitive milestones, and note whether they are at or below par. While cyanosis appears to be a factor in growth impairment and developmental delay, there is not a direct correlation with degree of hypoxemia. Patients who remain cyanotic after surgery, however, continue to make slower progress.[30–32] Poor growth after birth often results from fatigue during feeding. Other causes of feeding difficulties may also be present. Previous aortic arch surgery (repair of interrupted arch or Norwood reconstruction) may result in esophageal dysfunction. Patients with associated neurologic conditions or cleft lip or palate may not feed normally.[28] The anesthesiologist should be especially aware of developmental abnormalities and note any areas that may overlap with potential anesthetic complications.

### Congestive heart failure

Congestive heart failure (CHF) is classically defined as the inability of the heart to meet systemic needs for *CO* and oxygen transport. In the setting of CHD where primary pump failure is rare, it is usually due to a structural lesion that results in either volume or pressure overload of a ventricle, or both.[33,34] The term congestive heart failure is also used to describe excess pulmonary blood flow without gross inadequacies of systemic flow. This ambiguity sometimes leads to confusion regarding the nature of a problem described as "congestive heart failure."

Causes of CHF in infants include volume overload due to large shunts or severe valvular regurgitation, obstructive conditions and cardiac muscle diseases such as endocardial fibroelastosis, and CHF secondary to non-cardiac conditions.[33] Patients with systemic right ventricles are particularly at risk. Patients with large shunts typically do not

develop heart failure until the *PVR* falls in the third or fourth week of life, at which time the pulmonary circulation receives a disproportionately high share of blood flow. Rarely, tachy- or bradyarrhythmias may lead to heart failure.[35]

Difficulty feeding, excessive perspiration, and poor growth are the most common symptoms of CHF in infants. Findings include cardiomegaly (cardiothoracic ratio > 0.5), tachycardia, tachypnea, and pulmonary congestion. Hepatomegaly, a gallop rhythm, pulmonary edema and vascular collapse may be seen. Respiratory rates of greater than 45 and heart rate greater than 150 are suggestive. Mottling and slow capillary refill in the extremities are severe signs. Pharmacologic therapy for CHF includes digoxin, diuretics, afterload reduction, and inotropes for critically ill patients. Supplemental oxygen or respiratory support may be necessary if pulmonary congestion or pulmonary edema is severe.[33,34]

## Pulmonary hypertension

The pulmonary circulation is thick-walled and has a high resistance in the fetus. Beginning with the first minutes of life *PVR* drops dramatically in response to distension of the vessels with aeration of the lungs, increased $P_{AO_2}$, and multiple endogenous vasodilating factors. The majority of the decrease in *PVR* is completed by the first 3 weeks of life. Larger pulmonary vessels continue to regress over several months.[22] In patients with CHD the pressure and resistance of the pulmonary circulation often do not decline normally. Structural disease, depressed pulmonary venous saturation, and excess flow are all potential factors.[36]

Systolic pulmonary artery pressures (*PAP*s) are often estimated by Doppler echocardiography and are measured at cardiac catheterization if anatomically possible. The term "pulmonary hypertension" is ambiguous with regard to etiology. The anesthesiologist must correlate knowledge about pulmonary vascular flow to interpret whether pulmonary hypertension, if present, is due to elevated flow, elevated resistance, or both. If pressure is elevated in proportion to excess flow one may anticipate a rapid decline in pulmonary pressure when the source of shunt is repaired. Once structural pulmonary vascular changes develop, however, elevations in *PVR* may be irreversible.[37] Many patients have reactive pulmonary hypertension and demonstrate reduced *PVR* when exposed to elevated alveolar oxygen concentrations, alkalosis,[38] or nitric oxide.[37] For patients scheduled for bidirectional Glenn or Fontan surgeries the assessment of *PVR* is a key determinant of eligibility for the procedure, as the pulmonary blood flow will be dependent on passive flow through the pulmonary circulation.[39,40] Whenever pulmonary hypertension is present, special attention to the function of the pulmonary ventricle and its valves is merited as well, as secondary changes may have diminished reserve or resulted in cor pulmonale.

## Patients with pacemakers

Cardiac pacemakers sense bradycardia, tachycardia, or both. Bradycardia sensing pacemakers are usually placed for sinus node dysfunction or high grade AV conduction defects and respond by pacing the selected chambers (see Chapter 15) Most tachycardia sensing devices today are implantable cardioverter defibrillators (ICDs) and respond by delivering electrical energy aimed at cardioversion. Newer ICDs have bradycardia sensing and pacing capabilities as well. Others may also have the capability to terminate some tachydysrhythmias with rapid pacing, a function that was previously available without ICD capability.[41]

Whenever a patient has a permanent pacemaker in place, the indications for pacing, underlying rhythm, device type and its functional status must be researched preoperatively. This may present a significant challenge, especially with expanding indications for pacing, mobility of patients, and the development of many new and sophisticated devices. In all cases, a preoperative electrocardiogram (ECG) is indicated. If atrial or ventricular pacing is continuous the underlying rhythm may be unknown without previous medical records. If no pacing is demonstrated, current pacer function may be in question. Consultation with specialists in electrophysiology may be indicated if information is lacking. Electronic interrogation of device settings and reprogramming may be required; however, one must first know the manufacturer of the device.

During surgery, electrocautery may inhibit bradycardia detection and lead to asystole if bradyarrhythmia or conduction block is present. Continuous application of an external magnet over bradycardia sensing pacemakers usually reverts function to a fixed rate, asynchronous pacing mode. A decision to reprogram the pacemaker during the perioperative period should be made on a case-by-case basis. It is essential to know if tachycardia sensing is part of the pacemaker capabilities to determine appropriate perioperative management.

All tachycardia sensing capabilities should be disabled prior to surgery, as electrocautery or supraventricular tachyarrhythmias may trigger defibrillation.[42,43] This may be performed by reprogramming the device or with external application of a magnet. Unfortunately, the action and duration of magnet application to switch off tachycardia sensing differs among major device manufacturers. Regardless of manufacturer, however, an externally applied magnet will not convert bradycardia sensing devices to an asynchronous pacing mode if the device has tachycardia sensing capability. The anesthesiologist must therefore carefully assess the need for intraoperative pacing for any patient with a device that has both pacing and ICD capabilities. If the patient relies upon the pacemaker for ventricular pacing it is prudent to reprogram the device to an asynchronous mode prior to surgery as electrocautery is likely to inhibit sensing of bradycardia and a

magnet will have no therapeutic effect. Intraoperative application of external pacing/defibrillator pads is appropriate for all patients with cardiac pacemaker devices.

## Preoperative studies

### Laboratory studies

Appropriate laboratory studies include complete blood count (CBC), blood urea nitrogen (BUN), creatinine, electrolytes, coagulation studies, a screen for antibodies, and a crossmatch for appropriate blood products. Unless blood loss or transfusion has recently occurred, an elevated hemoglobin level is a valuable indicator of chronic cyanosis. Diuretic therapy may result in dehydration, hypochloremic metabolic alkalosis, or hypokalemia. Although polycythemic patients may have abnormal coagulation,[44,45] they may also have abnormal coagulation study results if the laboratory is unaware of their hematocrit, as fractional serum volume is reduced and distorts test results. Patients with extremely elevated hemoglobin concentrations (hematocrit > 65%) may have poor capillary flow due to hyperviscosity, which can reduce oxygen transport and lead to intravascular coagulation.[46,47] Additional studies include serum glucose in infants and critically ill patients, and ionized calcium in infants and in patients suspected or known to have diGeorge's syndrome. Blood type and antibody screen is performed in all patients and blood is crossmatched as indicated by patient age, condition, and proposed procedure.

### Electrocardiogram

The ECG should be reviewed for signs of abnormal rhythm, conduction, chamber hypertrophy, and as a baseline for postoperative comparison. Its interpretation is complicated by the abnormal position of many structures. ST-segment and T-wave abnormalities may indicate ventricular strain or ischemia. Dysrhythmias are discussed in Chapter 15.

### Chest radiograph

The clinical relevance of the preoperative chest radiograph to the anesthesiologist is primarily the lung fields and tracheobroncheal tree. Determination of situs may also be assisted by identifying the laterality of the stomach, liver, and their relation to the position of the heart within the thorax. Historically, the chest radiograph has played an important role in the differential diagnosis of many congenital heart lesions. The ability to discern pulmonary vascularity, cardiac size, position, shape, and associated vascular, bronchial and skeletal anomalies are all helpful, however echocardiography has proven a more powerful and convenient preoperative diagnostic tool.[48]

The degree of pulmonary vascular markings and lung water are of principal importance as they may indicate increased pulmonary vascular pressures or congestion. The highest risk category for CHF includes non-cyanotic patients with left-to-right shunt, patients with duct-dependent systemic blood flow, and those with mixing lesions and unrestricted pulmonary blood flow. In cyanotic patients, therefore, the pulmonary vasculature will be normal or decreased unless a coexisting left-to-right shunt is present. Cardiomegaly as evidenced by a cardiothoracic ratio greater than 0.5 is a useful sign of CHF or pericardial effusion in spite of structural lesions and cardiac malposition. Cardiomegaly is usually proportionate to pulmonary arterial vascularity unless coarctation of the aorta or myocardial disease is present.[49]

Regional lung disease may also result from CHD. Compression of one or more pulmonary veins, or bronchi may result in lobar congestion or hyperinflation. Patients with tetralogy of Fallot with absent pulmonary valve are particularly at risk due to an enlarged pulmonary artery. The anesthesiologist should specifically look at the image of the tracheobronchial tree on the preoperative chest film. Anomalies of situs will include mirror imaging (isomerism) of normal tracheobronchial structures, which may be important if endotracheal intubation is planned. If pulmonary problems occur intraoperatively, advance knowledge of the bronchial anatomy is key to proper interpretation of bronchoscopy findings.

Inspection of the lateral chest film for evidence of reduced space between the sternum and the heart is important for patients undergoing repeat sternotomy. When the retrosternal space is reduced an increased risk of inadvertent disruption of anterior cardiac or prosthetic structures during surgical dissection through scarred tissue is present. Most commonly the right heart, pulmonary artery, or prosthetic right ventricular outflow conduit is involved. The anesthesia team may wish to tailor their plans regarding intravenous access and blood availability prior to CPB in view of this heightened risk. The surgical and perfusion teams will need to prepare for alternative cannulation sites and the potential for urgent institution of CPB. In selected cases the surgeon may elect to dissect or cannulate the femoral vessels prior to dissection and sternotomy.

For older patients with coarctation of the aorta, rib notching may be present. This indicates well-developed collateral arterial flow and a reduced risk of ischemia to organs distal to the coarctation site if the aorta is cross-clamped.

### Echocardiography

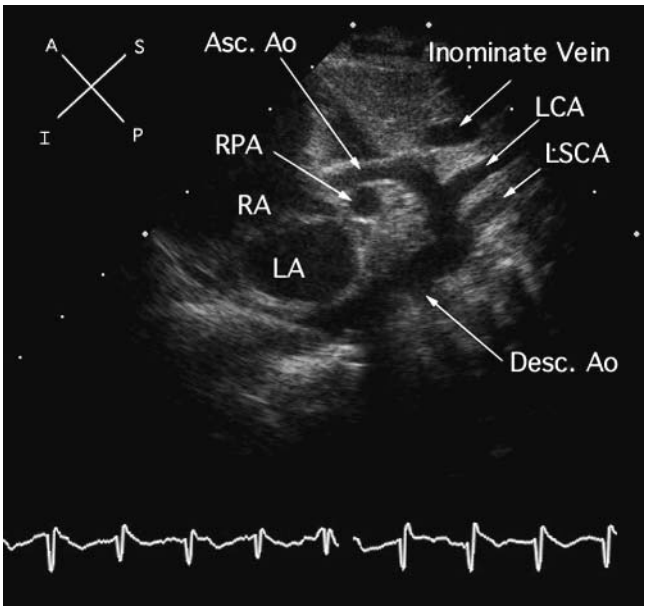
Currently, the anatomic pathology for which congenital heart surgery is scheduled is most often defined by echocardiography. It has proved such a powerful tool that pediatric cardiologists express concern that their auscultatory skill

is diminishing due to lack of use! Prior to 1988 nearly all congenital heart surgery patients underwent preoperative cardiac catheterization. Today cardiac catheterization is most often performed to answer remaining physiologic questions following an echocardiographic diagnosis or to further define structures with angiography that are difficult to image with echo. Many patients undergo complete repair of major congenital heart defects without cardiac catheterization.[50] Advantages of echocardiography include its non-invasive nature, relative lack of biologic effects, ample acoustic windows in infants (due to the paucity of bony structures), and the ability to use high frequency, high-resolution transducers in small patients due to the proximity of cardiac structures to the body surface. Technologic advances now permit stunningly clear images that may be transmitted digitally without loss of detail (Fig. 11.2). Disadvantages of echocardiography include the inability to obtain absolute rather than relative hemodynamic data, and the high degree of technical skill required to obtain optimal studies and a certain degree of subjective interpretation of spatial relations.

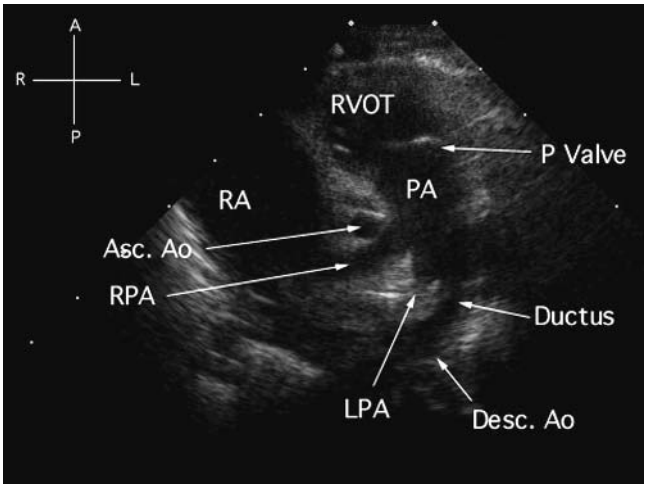
The vast majority of preoperative echocardiographic studies are pre-cordial (transthoracic) rather than transesophageal due to the greater number of available acoustic windows, and the need for general anesthesia in infants and children to facilitate transesophageal studies. It is therefore important for the pediatric cardiac anesthesiologist to become familiar with pre-cordial views and the range of information that can be derived. Normal acoustic windows for pre-cordial echo in infants include suprasternal, parasternal, apical, and subcostal approaches. The plane of the transducer may be oriented in line with the three orthogonal planes of the body: sagittal, coronal, and transverse. More commonly it is to be oriented along the planes of the heart in short axis, or in long axis in the "four chamber" or "two chamber" cross sections. The short and long axis of the heart is normally not in line with the orthogonal planes of the body, however, as the apex is situated to the left and anterior to the base.[51,52] Examples of parasternal short axis and the "ductus cut" views are illustrated in Fig. 11.2.

The preoperative assessment of congenital heart surgery patients usually consists of a complete echocardiographic examination including two-dimensional imaging, spectral (pulse and continuous wave) and color Doppler interrogation of cardiac inflow and outflow, as well as imaging of pathologic flow, and associated structures of interest. Imaging information is obtained regarding cardiac and great vessel anatomy, as well as myocardial and valvular function. Quantitative echocardiography is useful to calculate shunts, estimate intracardiac pressures and to evaluate the severity of myocardial or valvular dysfunction. If tricuspid regurgitation is present, pulmonary arterial systolic pressure can usually be estimated.

Ideally, the anesthesiologist should review the preoperative echo study images for optimal understanding and




(a)




(b)

**Fig. 11.2** (a) Hypoplastic left heart syndrome—aortic arch. "Ductus cut" view. This view is achieved via the suprasternal notch and is useful for imaging the ductus arteriosus, coarctation of the aorta, and other aortic arch anomalies. Note the small ascending aorta compared to the descending component. The innominate artery is not seen as it lies outside the plane of the transducer. The left common carotid and subclavian arteries are clearly visualized as well as the large difference in diameter of the ascending and descending aortic arch components. Note that the size of the right pulmonary artery exceeds that of the ascending aorta. (b) Hypoplastic left heart syndrome—pulmonary artery. Parasternal short axis view. The pulmonary trunk and branch pulmonary arteries are usually easily visualized with pre-cordial echocardiography. This image demonstrates the large size discrepancy between the ascending aorta and the pulmonary artery as well as a clear view of the ductus connecting to the descending aorta. The right pulmonary artery is better visualized than the left pulmonary artery in this view. Asc. Ao, ascending aorta; Desc. Ao, descending aorta; LA, left atrium; LCA, left coronary artery; LPA, left pulmonary artery; LSCA, left subclavian artery; PA, pulmonary artery; RA, right atrium; RPA, right pulmonary artery; RVOT, right ventricular outflow tract. All images are courtesy of the Pediatric Echocardiography Laboratory at the University of California, San Francisco.

potential comparison with intraoperative and postoperative echocardiography. As a minimum, all preoperative echocardiogram reports should be available for review and a pediatric echocardiographer should review any studies from outside hospitals to determine the adequacy of the study and interpretation of the pathology.[53] Preoperative echocardiographic assessment should be completed before admission to the operating room and not rely upon an intraoperative transesophageal examination, as the acoustic windows are more limited and physiologic conditions may be significantly altered by general anesthesia and positive pressure ventilation.

### Cardiac catheterization

While the indications for cardiac catheterization have decreased in tandem with the rise of other diagnostic modalities, whenever preoperative cardiac catheterization has been performed the anesthesiologist should review the report. It will include measurements of pressure and oxygen saturation from some or all of the cardiac chambers. From these data pressure gradients, systemic and *PVR*s, and shunts may be quantified. Systemic and pulmonary flow may be calculated as absolute quantities or as a relative ratio, the $\dot{Q}p : \dot{Q}s$. A ratio of greater than 1 indicates left-to-right shunting while a ratio of less than 1 indicates right-to-left shunting. Note that a ratio of close to 1 : 1 does not by itself rule out bidirectional shunt. The Fick method is used for quantification of pulmonary and systemic flow, using oxygen consumption as the "indicator." While actual oxygen consumption can be measured, it is often estimated from tabled data. Angiography is usually performed to further define any anatomic structures in question.[54,55]

Interpretation of data from patients with structural heart disease is a challenge for the beginner; however, the basic principles for measurement and calculation are readily understood. It is useful to follow the sequence of pressures and saturations in a flow-directed pathway to detect evidence of obstruction or shunt. Normal values for newborns and older children are presented in Chapter 25 (see Table 25.1, p. 411). Note that oxygen saturation is normally stable from the right ventricle to the pulmonary artery, and from the left atrium to the aorta. Deviations indicate intracardiac shunting. Pressures are normally equal on both sides of the AV valves at the end of diastole. Peak ventricular systolic pressure normally equals the peak systolic pressure in the corresponding great vessel. Pressure gradients indicate obstruction at or near the valves. Pulmonary venous desaturation may indicate intrapulmonary shunt from lung disease, pulmonary arteriovenous malformation, or may result from hypoventilation due to sedation for the procedure. Arterial desaturation indicates right-to-left shunt in the heart, lungs or the great vessels. Formulae used to calculate flows, shunts, and resistances are presented in Chapter 25 (see Table 25.2, p. 412).

Many patients undergo cardiac catheterization to assess the anatomy and resistance of the pulmonary vasculature. If patients have left-to-right shunting and pulmonary hypertension, interventions in the cardiac catheterization laboratory may be undertaken to assess the reactivity of the pulmonary vasculature. Typically 100% oxygen or vasodilator therapy including nitric oxide response is utilized while intracardiac and great vessel pressure and saturation measurements are repeated. If the *PVR* does not decline, the patient may have fixed pulmonary vascular obstructive disease and not benefit from surgical correction.

Pressure and saturation information from cardiac catheterization may be codified in a graphic form for preliminary or final reports. An example is illustrated in Fig. 11.3. The anesthesiologist should be familiar with the format used for displaying preliminary information at their institution, as formal reports may not be available preoperatively if surgery follows soon after cardiac catheterization.

### Magnetic resonance imaging

Improved technology in magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) has followed the tremendous advances of echocardiography in the diagnosis and assessment of CHD. Application thus far has been predominately for lesions that are difficult to evaluate by echocardiography, such as coarctation of the aorta, branch pulmonary arterial stenosis, pulmonary venous connections, vascular rings, and complex three-dimensional relationships. However increasingly refined techniques and the ability to perform functional assessment of ejection fraction and regurgitant volumes position MRI for continued expansion in its role regarding preoperative assessment of CHD patients. Technologic advances including fast imaging have enhanced image detail and permitted quantification of shunts, valvular regurgitation, and relative flow to the right and left pulmonary arteries.[56–61]

Advantages of MRI over other imaging techniques include the absence of ionizing radiation or contrast agents. The effectiveness of echocardiography also decreases as children grow due to more limited acoustic windows. Therefore MRI may be an alternative as well as a complementary technique in older children and adults with CHD.[62] Magnetic resonance imaging is particularly successful for evaluation of some areas that traditionally difficult to assess with echocardiography, such as right ventricular function and pulmonary flow.[56,58,60,61,63] Future perioperative applications include an augmented role in determining the desirability and timing of surgery. For example the ability to assess right ventricular function may assist in the difficult question of timing for pulmonary valve replacement following initial correction of tetralogy of Fallot.[64,65] Patients considered for the Fontan operation also benefit from assessment of the dimensions of the right and left pulmonary arteries, which is facilitated with

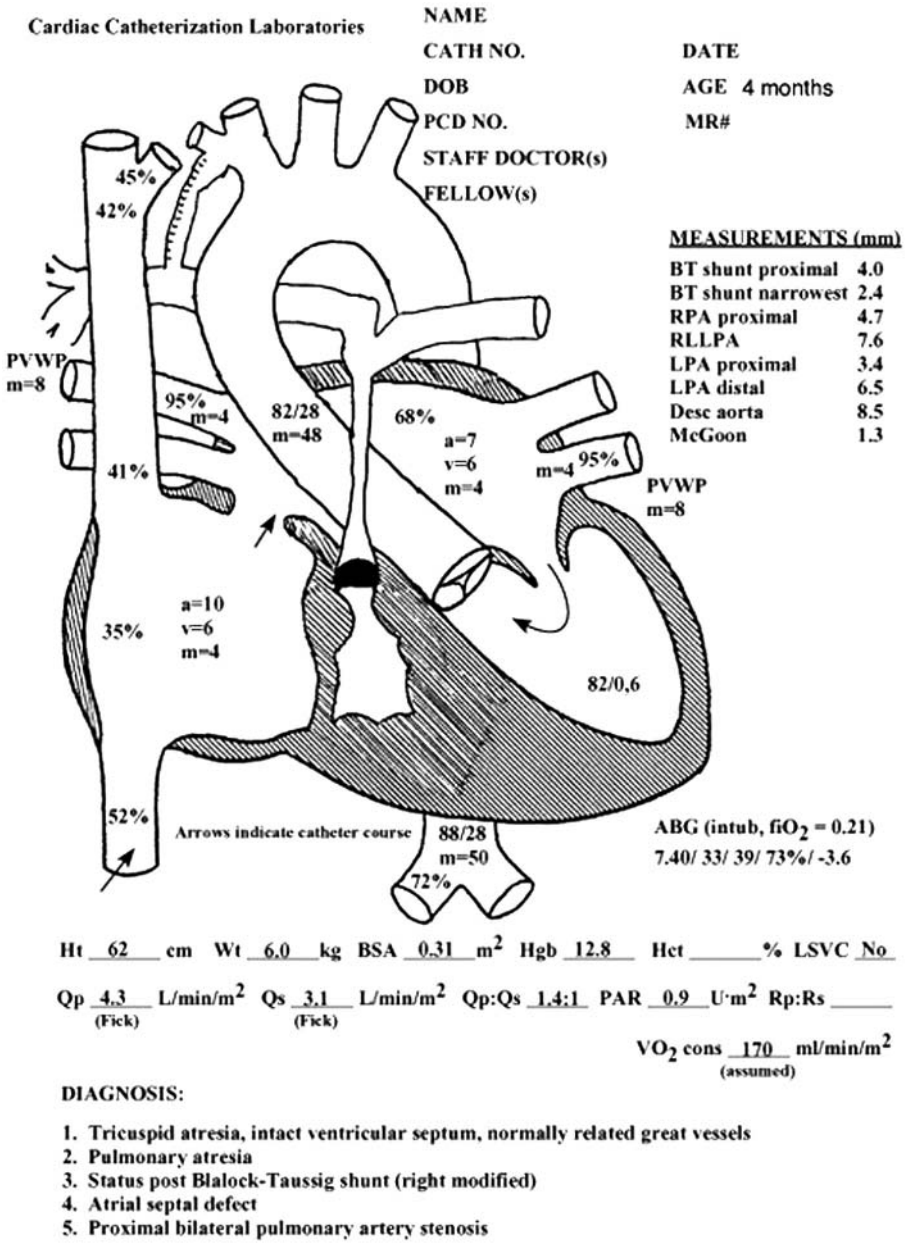



**Fig. 11.3** Cardiac catheterization diagram. Data from a 4-month-old patient with tricuspid and pulmonary atresia are shown. This is a concise, convenient, one-page summary of the patient's anatomy, history, physiology, and catheterization data. It can be stored in paper or digital format and easily projected for surgical case conference. Numbers followed by percentages are measured oxygen saturations; plain numbers are pressure values. a, atrial a-wave pressure; ABG, arterial blood gas; *BSA*, body surface area; BT, Blalock–Taussig; LPA, left pulmonary artery; LSVC, presence of a left superior vena cava; *m*, mean pressure; McGoon, McGoon ratio of pulmonary artery to aorta size; *PAR*, pulmonary artery vascular resistance; *PVWP*, pulmonary venous wedge pressure; *Q*p, pulmonary blood flow; *Q*s, systemic blood flow; RLLPA, right lower lobe pulmonary artery; RPA, right pulmonary artery; *R*p : *R*s, ratio of pulmonary to systemic vascular resistance; *v*, atrial v-wave pressure; $V_{O_2}$ cons, oxygen consumption.

MRI.[66,67] Unlike echocardiography, it is rarely performed to establish the primary cardiac diagnosis.

The MRI technique used to generate morphologic images is primarily sliced spin-echo images through the heart and thorax. Imaging slices typically have a thickness of 5 mm with a 1 mm gap between slices. Thinner slices and increased excitation may be used for areas of interest. Compensation for cardiac and respiratory motion is achieved by synchro-

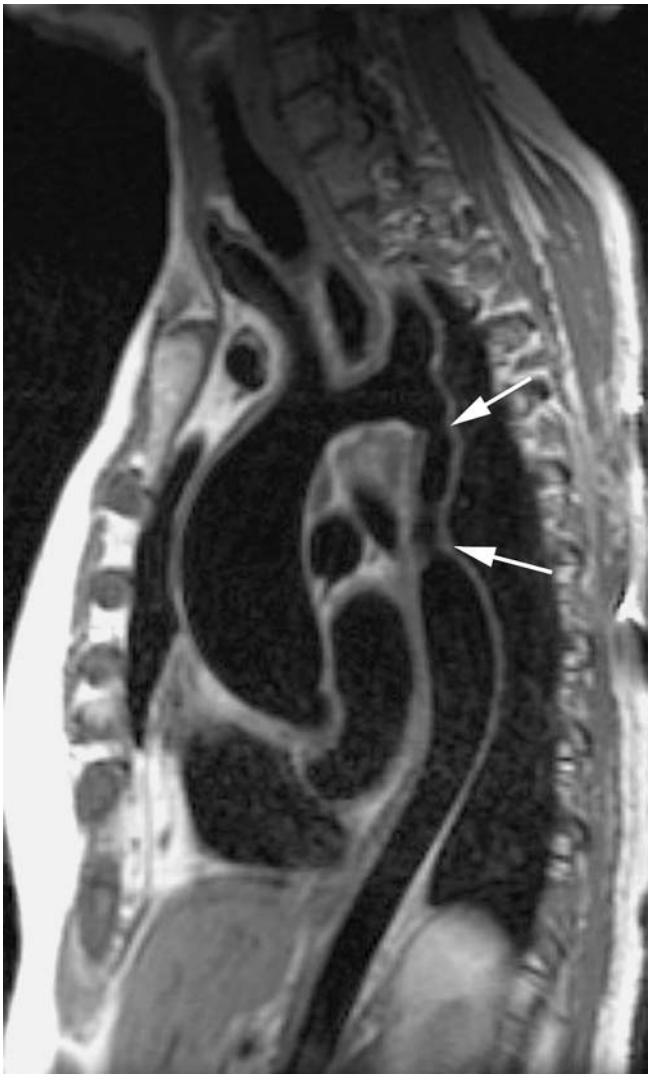


**Fig. 11.4** Oblique sagittal T1-weighted magnetic resonance image of the thorax in a 13-year-old boy showing moderate to severe aortic coarctation (arrows). Dilation of the ascending aorta is also present.

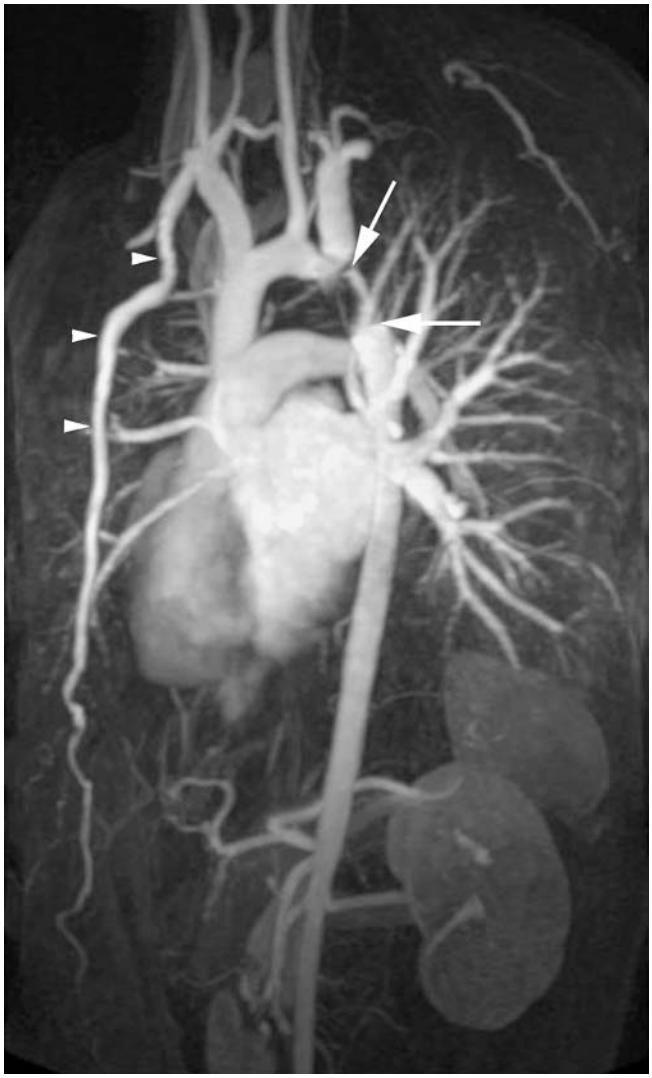


**Fig. 11.5** Oblique sagittal volume rendered image from a contrast enhanced magnetic resonance angiography in a 15-year-old boy showing severe aortic coarctation (arrows) just distal to the origin of the left subclavian artery. Large collateral vessels are seen on the posterior superior aspect of the thorax. Enlarged internal mammary arteries are also present (arrowheads).

nization with the ECG signal and a sensor on the patient's abdomen. As multiple cardiac cycles are required to complete the image of each slice, the time to complete a study is somewhat dependent upon heart rate. When possible, breath holding or apnea is employed to eliminate respiratory motion. For increased spatial resolution of vascular structures gadolinium-enhanced MRA is performed. Three-dimensional reconstruction can also be performed using this technology, creating striking images (Figs 11.4 & 11.5). Physiologic information is derived from additional techniques including gated fast gradient-echo sequences and velocity-encoded cine MRI. Blood flow can be calculated from velocity and cross-sectional measurements.[56,68] As experience and technology grow, the role of MRI and MRA in the management of CHD patients is very likely to expand.[59,69]

### Computerized tomography

While utilized less frequently than MRI, the use of contrast-enhanced conventional or spiral CT imaging has a distinct role in the assessment of CHD patients, particularly those with vascular rings, aortic abnormalities, and pericardial disease.[70] Ultra-fast CT scanning and electron-beam tomography acquire images more quickly than MRI and can be ECG triggered to eliminate motion artifact. Therefore, some pediatric patients may tolerate ultra-fast CT scanning without the sedation that is normally required for more lengthy MRI examinations. When contrast is added to ECG-triggered electron beam tomographic images, fine resolution permits

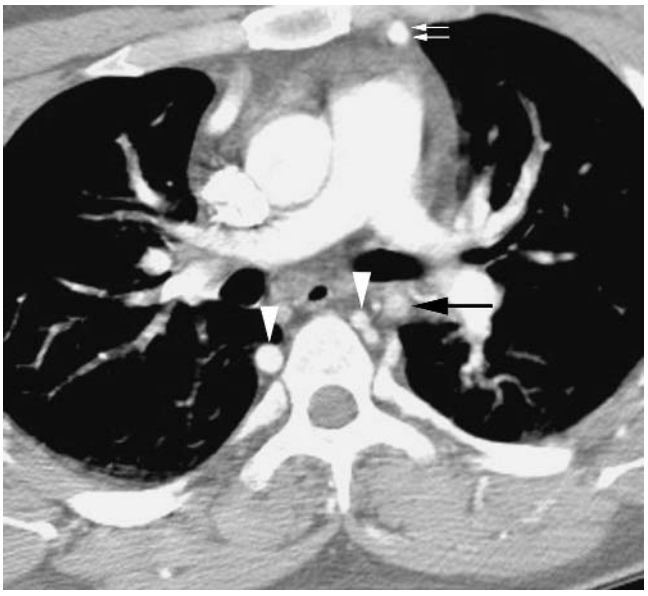


**Fig. 11.6** Severe aortic coarctation in a 19-year-old man diagnosed with aortic coarctation using narrow collimation contrast enhanced multislice computed tomography. The axial computed tomography image shows severe aortic coarctation. The main pulmonary artery is seen branching into the right and left pulmonary arteries. The ascending aorta is imaged in cross section alongside the pulmonary artery. In comparison, the black arrow indicates the severely narrowed proximal descending thoracic aorta. Enlarged internal mammary arteries (double white arrows) and numerous enlarged collateral vessels (arrowheads) are also present.

diagnosis of intracardiac defects, pulmonary vascular anomalies, cardiac muscle mass and motion.[71,72] However, the use of ionizing radiation and intravenous contrast remain (Fig. 11.6).

## Preoperative goal no. 4: Determine if the patient information is adequate

During a busy day caring for critically ill patients, the temptation to accept available preoperative information as complete must be questioned continually. A critical approach is advocated, with an eye open for key information that is not evident. Are the anatomic pathology and the proposed procedure clarified? The indication for surgery, impetus for its timing, and expected outcome for the individual patient must be understood. How does the proposed surgery fit into the long-term plan? Is the upcoming surgery palliative, corrective, or part of a staged series of procedures? Is it urgent or elective? Only when these questions have been answered can the anesthesiologist determine if the available information is adequate.

Generally, a recent ECG, echocardiogram, chest radiograph, and laboratory examination as outlined above are performed. A summary of information expected in the preoperative assessment is found in Table 11.5. As mentioned, cardiac catheterization is performed less often than in the past due to advances in echocardiography and MRI.[50,56,72] Because many CHD patients are evaluated in outside medical centers prior to surgery, it is particularly helpful to review available information regarding elective cases several days in advance. This provides time to obtain valuable data, reduces unnecessary repetition of tests, and allows for preparation of the patient and the perioperative team.

**Table 11.5** Preoperative assessment.

| | All cases | As indicated |
|---|---|---|
| History and physical exam | X | |
| Pulse oximetry | X | |
| Chest radiograph | X | |
| ECG | X | |
| CBC, electrolytes, BUN, creatinine | X | |
| Glucose, calcium | | X |
| Coagulation studies | X | |
| Blood type and antibody screen | X | |
| Blood crossmatch | | X |
| Echocardiogram: complete two-dimensional, spectral, and color Doppler study | X | |
| Cardiac catheterization | | X |
| MRI/MRA | | X |
| Computerized tomography | | X |

BUN, blood urea nitrogen; CBC, complete blood count; ECG, electrocardiogram; MRA, magnetic resonance angiography; MRI, magnetic resonance imaging.

## Preoperative goal no. 5: Prepare the patient and family

### Patient and family education, and informed consent

A detailed discussion of the role of the anesthesiologist in the upcoming surgery is required, incorporating informed consent guidelines. The plans for premedication, monitoring, induction and maintenance of anesthesia, blood transfusion, and postoperative care are discussed. If the patient is old enough to understand, he or she should be included in appropriate sections of this discussion, reassured, and told what to expect. Particular emphasis should be placed on specific instructions. Patients and their families receive a great deal of new information prior to congenital heart surgery. It is a natural time of apprehension for all concerned. For patients being admitted on the day of surgery, instructions regarding eating and drinking, specific medications, and logistics must be communicated clearly and given to the patient and their family in writing whenever possible.

## Fasting, premedication, and preoperative orders

### Preoperative fasting

Guidelines for fasting do not differ from other surgeries. Clear liquids are generally considered safe for small children and older patients up to 2 hours prior to surgery. Patients with swallowing difficulties, gastroesophageal reflux, abnormal gastric motility, or neurologic disease may merit longer fasting times. Special attention is warranted to avoid dehydration in children scheduled for surgery later in the day, particularly those with cyanotic heart disease. If a patient is polycythemic, taking diuretics, or has significant systemic outflow obstruction, consideration should be given to administering intravenous fluid preoperatively as the potential risk of dehydration is increased and the time of surgery may be unpredictable.

### Medications

General principles apply regarding administration of regular medications on the day of surgery, and most medications are given. It is especially important to continue inhalers for patients with bronchospasm. Exceptions include diuretics in selected patients, and insulin in diabetic patients. Some experienced clinicians withhold digoxin therapy for 1 day prior to surgery with CPB as it is felt to represent a risk factor for malignant ventricular arrhythmias associated with potassium fluctuations following bypass.[34]

## Antibiotic prophylaxis for bacterial endocarditis

Prophylactic antibiotics for dental, oral, respiratory tract, gastrointestinal, and genitourinary procedures are indicated in patients with cardiac defects for prevention of endocarditis. Patients who have had congenital heart repairs should also receive antibiotic prophylaxis with the exception of those who have had closure of a secundum ASD, VSD or PDA more than 6 months previously. Patients with residual leaks should be treated. The risk of postoperative endocarditis appears to be greatest in patients with prosthetic valves, conduits, and grafts as well as those with tetralogy of Fallot and aortic stenosis. The regimens recommended by the American Heart Association for antibiotic dosage are listed in Chapter 26.[73]

### Premedication

The time of separation of the patient from his or her family is particularly stressful for all concerned. Generous premedication is usually helpful to reduce patient anxiety and facilitate separation. If the structural facilities permit induction with the family present, this may also be helpful. Cyanosis from cardiac disease is not a general contraindication to premedication.[74,75] Desaturation due to intracardiac shunt will not be worsened by premedication unless pulmonary blood flow or lung function is affected. The anesthesiologist is generally present during and after premedication. Pulse oximetry may be employed to monitor the effect on saturation with administration, and supplemental oxygen should be immediately available. Judicious dosing is warranted in sicker patients, however, as transient decreases in saturation may occur[76] and pulse oximetry is less accurate in lower ranges of saturation.[77] Most patients are admitted on the day of surgery and do not have an intravenous line in place. A variety of medications have been used with success for sedation and anxiolysis in congenital heart surgery patients. General guides are that patients under 1 year of age rarely require premedication, oral medication is preferred to nasal, and injections are universally disliked.

Oral midazolam 0.5–1.0 mg/kg is usually an effective anxiolytic. Generally, no more than 20 mg of midazolam is administered orally. If patients will not take an oral medication, nasal midazolam 0.3 mg/kg can be rapidly injected using a short intravenous catheter or slip-tip syringe. A concentration of 5 mg/mL is recommended to minimize volume, although it is irritating to the nasal mucosa. Rarely, a child or developmentally delayed adult presents a particular challenge with regard to premedication. In such cases ketamine, 4–5 mg/kg with glycopyrrolate 10–20 μg/kg and midazolam 0.1 mg/kg can be injected intramuscularly. This may also be the agent of choice for induction patients in whom an inhalation induction is deemed risky. Oral ketamine may also be employed in doses of 2–10 mg/kg in combination with midazolam 0.5–1.0 mg/kg.[75,78] Rectal administration of benzodiazepines and barbiturates is also reasonable for patients 1–3 years of age.

## Preoperative intravenous placement

Older children may express a preference for an intravenous induction of anesthesia. Many have had ample experience with intravenous lines and phlebotomy. Premedication and placement of a topical anesthetic cream is usually helpful; however, bravery often falters as anxiety mounts on the day of surgery.

## Communicate essential findings and plan

Both written and verbal communication are important components of the preparation for surgery. Because a great deal of information is often available for congenital heart surgery patients, an appropriate summary focused upon the pathophysiology and issues pertinent to the anesthetic plan is appropriate. Anatomic findings that impact potential vascular access or monitoring, such as occluded vessels or anomalous origin of the subclavian artery, are valuable parts of this summary. Use of acronyms and names of rare syndromes should be minimized in favor of clear, descriptive terminology. Any

important findings in the history or condition of the patient that are not evident in the surgical assessment must be communicated to the surgical team as early as possible, especially if they may impact the readiness of the patient for surgery as planned. When working with such complex patients, it is particularly helpful to speak with the surgical team preoperatively when questions about the anatomic implications, therapeutic approach, or surgical plan remain.

## Summary

The preoperative evaluation of patients prior to congenital heart surgery is a special challenge because of the wide range of potential anatomic and physiologic abnormalities. An interdisciplinary approach to assessment and review of diagnostic studies is optimal for the preparation of the patient and the perioperative team. The pediatric cardiac anesthesiologist requires a working knowledge of pediatric cardiology terminology and commonly used diagnostic modalities to interpret the large amount of patient information that is accumulated for most cases. With these tools the physiologic consequences of the malformed heart may be appreciated along with the remaining degree of cardiopulmonary reserve.

A system for physiologic classification utilizing noncyanotic and cyanotic categories with an emphasis on the role of the ductus arteriosus is recommended. Anesthetic strategy follows from the physiologic category and condition of the patient rather than their specific anatomy in most cases. Attention should be paid to compensatory mechanisms and existing therapies as they must be maintained during the preparation for anesthesia and the pre-bypass period.

Patients at particular risk for deterioration at the outset of anesthetic care include those with left-sided obstructive lesions, such as aortic stenosis, and those with excess pulmonary blood flow for whom supplemental oxygen and mechanical ventilation may present new dangers. These individuals must be identified preoperatively and managed accordingly. For most children over 1 year of age, including those with cyanosis, routine premedication is appropriate and safe with pulse oximetry and supplemental oxygen available.

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# 12 Approach to the premature and full-term infant

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## Introduction

Advances in pediatric cardiology and cardiac surgery over the past 20 years have resulted in a substantial decrease in morbidity and mortality associated with congenital heart disease (CHD). Most congenital heart lesions are now amenable to either anatomical or physiological repair early in infancy. Opinion regarding the optimal timing of corrective surgery for infants with symptomatic CHD regardless of age or weight has undergone radical changes over the last two decades. Rather than the previous strategy of initial palliation followed by correction in early childhood, the current approach in most centers is complete repair within days to weeks of birth if feasible. Advances in diagnostic and interventional cardiology, the evolution of surgical techniques and conduct of cardiopulmonary bypass (CPB), and refinements in postoperative management have all contributed to the successful strategy of early corrective two-ventricle repair. A further advance in recent years has been the extension of this approach to the premature and low-birth-weight neonate (LBWN). However, the low mortality achieved with two-ventricle repairs has not been the experience in LBWN undergoing palliation for single ventricle defects, such as hypoplastic left heart syndrome (HLHS).

Cardiac surgery in the premature and very-low-birth-weight infants imposes additional challenges for the anesthesiologist. As for any pediatric cardiac procedure, a thorough understanding of the pathophysiology of various defects, the planned surgical procedure, and anticipation of specific postoperative problems are essential. There are additional considerations, however, when providing anesthesia to the premature neonate and LBWN. These include immaturity of the airway, lungs, cardiovascular system, liver, kidney, and central nervous system, making these infants more susceptible not only to surgical complications but also to anesthetic complications. Finally, as the limits for managing newborns with CHD continue to be extended, the next challenge on the horizon appears to be fetal cardiac surgery.

This chapter will describe general principles relevant to anesthesia for the newborn, including the premature and the very LBWN with CHD. The impact of sequela related to prematurity, the outcome of cardiac surgery in the premature and full-term neonate, and possible new directions as fetal cardiac surgery will be discussed.

## Approach to treatment in the neonate

### Early palliation

Ten to 20 years ago it was common for low-birth-weight and premature neonates to undergo initial palliation or medical management of congenital cardiac defects with the aim to achieve a certain size prior to repair. This was primarily because of the technical limitations for various surgical repairs and the risks associated with CPB. However the actual "target" size or weight that a neonate should achieve to tolerate successful repair was never well documented.

The aim of palliative procedures is to control pulmonary blood flow sufficiently to allow for growth but without excessive flow or volume overload to the pulmonary circulation and the systemic ventricle. Nevertheless palliation with a pulmonary artery (PA) band or a modified systemic-to-PA shunt such as Blalock–Taussig (BT) shunt can be difficult procedures in neonates, and complications even more problematic in LBWN (Table 12.1). For example, the size of a systemic-to-pulmonary shunt can be very difficult to determine and the geometry of the shunt is critical. A relatively large shunt may lead to excessive pulmonary blood flow, congestive heart failure (CHF) and possible pulmonary vascular obstructive disease (PVOD). Conversely, a small shunt leads to inadequate pulmonary blood flow, lower arterial oxygen saturation ($Sao_2$), possible shunt thrombosis, and distortion or stenosis of pulmonary arteries making further repair even more difficult. Assuming a normal cardiac output, hematocrit and absence of pulmonary venous desaturation, an ideal $Sao_2$ between 80% and 85% indicates a relatively balanced

**Table 12.1** Complications of palliative surgery.

| |
|---|
| *Complications of systemic-to-pulmonary shunts* |
| Early complications: |
| Excessive pulmonary blood flow → CHF |
| Inadequate pulmonary blood flow → cyanosis |
| Kinking of the shunt |
| Thrombosis |
| Late complications: |
| Distortion of pulmonary arteries |
| Asymmetrical growth of the pulmonary arteries |
| Pulmonary vascular occlusive disease |
| *Complications of pulmonary artery banding* |
| Early complications: |
| Band too loose → excessive pulmonary blood flow → CHF |
| Band too tight → inadequate pulmonary blood flow → cyanosis |
| Late complications: |
| Complications at band site: |
| Dislocation of the band |
| Erosion of the pulmonary artery |
| Residual stenosis after repair |
| Aneurysm |
| Complications proximal to band site: |
| Right ventricular hypertrophy |
| Subaortic stenosis |
| Pulmonary valve stenosis |
| Complications distal to the band: |
| Pulmonary artery stenosis |

CHF, congestive heart failure.

circulation with a pulmonary to systemic blood flow ratio ($Qp : Qs$) close to 1 : 1. In our experience, a modified BT shunt of 3.5 mm is the optimal size to use in a neonate. If a 3.0 mm shunt is used, the risk for sudden thrombosis and acute obstruction in the early postoperative period is increased, even in low birth weight newborns. A further problem of a small shunt is the likelihood of outgrowing the shunt size causing progressive cyanosis and leading to earlier surgical intervention. Alternatively, if a larger shunt size (i.e. 4.0 mm) is used in a newborn, the excessive pulmonary blood flow may compromise systemic perfusion, cause ventricular volume overload, heart failure, and prolonged postoperative recovery.

Banding of the PA to reduce pulmonary blood flow is also a difficult palliative procedure. If the band is too tight severe cyanosis may occur, and if the band is too loose the increase in pulmonary blood flow will contribute to CHF and possible PVOD. Distortion, stenosis and migration of the band may complicate later surgery, cause right ventricular hypertrophy, subaortic stenosis, and pulmonary valve stenosis. Determining the correct size of a band at the time of surgery is difficult. There are no accurate formulas for band size, and the hemodynamic changes at the time of band placement must be closely observed. Ideally, the banded PA will result in an increase in systemic systolic blood pressure of approximately 20%, and depending on the underlying pathology a fall in $Sao_2$ to around 85% breathing room air. The pressure gradient across the band can also be directly measured; usually a fall in pressure of approximately 50% proximal to distal across the band is sufficient. Because hemodynamic changes are essential to monitor at the time of PA band placement, it is important to avoid anesthetic techniques that could decrease ventricular function or cardiac output. Therefore, an opioid technique is most often necessary, and extubation delayed until the hemodynamic effect of the band is determined as the patient emerges from anesthesia and starts to wean from mechanical ventilation.

## Early repair

As noted previously, whenever possible, early repair of two ventricle congenital cardiac defect is preferable. This limits the consequences of excessive pressure and volume overload to the ventricles and pulmonary circulation, and the potential detrimental effect of chronic hypoxia. The underlying premise is that early repair allows for more normal growth and development.

This approach has become the preferred management strategy in most centers in recent years. Prior to this, concerns over the potential increased morbidity and mortality of newborns and young infants undergoing early bypass and surgical repair, meant that pediatric cardiologists often tried to delay surgery whenever possible and attempted to control their patients' symptoms medically. However, trying to control pulmonary blood flow and volume overload on an immature myocardium with medical management alone is often extremely difficult.

Further, the problems associated with pulmonary overcirculation, chronic volume, and/or pressure load on the ventricles and cyanosis may substantially affect development and lead to myocardial and pulmonary injury, which will affect the outcome from subsequent repairs.[1] It is also likely that the imbalance between pulmonary and systemic blood flow will increase in newborns with a large left-to-right shunt as pulmonary vascular resistance (*PVR*) falls in the first few weeks of life and the physiologic nadir in hematocrit is reached. The clinical manifestations of an infant with CHF are shown in Table 12.2. The increased work of breathing and tachypnea secondary to an increase in pulmonary blood flow and total lung water results in an increase in metabolic demand and an increase in the percentage of the total cardiac output directed towards respiratory muscle work (most notably the diaphragm). This essentially diverts cardiac output from other metabolically active functions, in particular from the splanchnic circulation and absorption of food. The abnormal circulatory physiology is unable to meet metabolic needs and patients fail to thrive.

For these reasons it is prudent to correct the pathophysiology early to promote normal growth and development, and

**Table 12.2** Symptoms and signs of congestive heart failure and cardiac failure in a neonate and infant.

| |
|---|
| *Low cardiac output:* |
| Tachycardia |
| Poor extremity perfusion |
| Cardiomegaly |
| Hepatomegaly |
| Gallop rhythm |
| *Increased respiratory work:* |
| Tachypnea |
| Grunting |
| Flaring of alaenasi |
| Chest wall retraction |
| *Increased metabolic work:* |
| Failure to thrive |
| Poor weight gain |

primary correction rather than palliation of congenital heart lesions is the goal even in premature infants or infants with very low birth weight. Nevertheless, the risk for cardiac surgery and CPB for neonates compared to infants and older children is increased, particularly at lower body weight.[2,3] The causes are multifactorial, and include technical issues related to small cardiac structures and cannulation for CPB, the immaturity of organ systems (especially the lungs, myocardium and germinal matrix), increased risk of bleeding from coagulopathy after CPB, and an immature stress response that may increase the risk for infection and promote a catabolic state in newborns with limited nutritional reserves. This directly contributes to a longer duration of mechanical ventilation and longer intensive care and hospital stay. Our better understanding of the stress responses and cardiovascular physiology in the full-term neonate has contributed to the dramatic success that is currently achieved with neonatal reconstructive cardiovascular surgery. In spite of these successes, there remains some hesitancy to performing similarly complex reconstructive operations when heart defects occur in premature and LBWNs.

## Outcome

Although the risk for early mortality in neonates undergoing cardiac surgery and CPB may be increased, randomized and prospective studies comparing the morbidity that may occur in neonates with critical lesions who are treated medically in the hope of weight gain, compared to surgical morbidity and mortality, have not been performed. Such has been the nature for many of the advances in CHD management.

For example, infants with an increased pulmonary blood flow who undergo delayed surgical intervention often fail to thrive and are at risk for recurrent respiratory infections. Their work of breathing and energy expenditure is significantly increased, and infants are not only tachypneic, but often have wheezing throughout their lung field on auscultation, and cardiomegaly with hyperinflated lung fields on chest radiograph. Cardiac surgery and CPB may be delayed because of concern for intercurrent infection and the risk for exacerbation or reactivation of inflammatory lung processes, which in turn may cause intrapulmonary shunting and severe hypoxemia, pulmonary hypertension, and prolonged mechanical ventilation. The early repair or palliation of defects to limit pulmonary overcirculation and volume load on the systemic ventricle will often avoid these complications.

Although the management of neonates in the immediate postoperative period after a two-ventricle repair can be a challenge, the current successful outcomes are such that mortality is no longer a reliable index against which to measure or compare new or alternative treatments in this group of patients. In contrast, this has not been the case for palliative procedures in patients with complex single-ventricle defects, although there has been a steady improvement in survival and longer-term outcome in neonates with single-ventricle disease in recent years.

# Limited physiologic reserve

Care of the critically ill neonate requires an appreciation of the special structural and functional features of immature organs. The neonate appears to respond more quickly and extremely to physiologically stressful circumstances; this may be expressed in terms of rapid changes in, for example, pH, lactic acid, glucose, and temperature.[4]

The physiology of the preterm and full-term neonate is characterized by a high metabolic rate and oxygen demand (two to threefold increase compared to adults) which may be compromised at times of stress because of limited cardiac and respiratory reserve. The myocardium in the neonate is immature with only 30% of the myocardial mass comprising contractile tissue, compared to 60% in mature myocardium. In addition, neonates have a lower velocity of shortening, a diminished length–tension relationship, and a reduced ability to respond to afterload stress.[5,6] Because the compliance of the myocardium is reduced, the stroke volume is relatively fixed and cardiac output is heart-rate dependent, therefore the Frank–Starling relationship is functional only within a narrow range of left ventricular end-diastolic pressure. The cytoplasmic reticulum and T-tubular system are underdeveloped and the neonatal heart is dependent on the transsarcolemmal flux of extracellular calcium both to initiate and sustain contraction (see Chapter 3). It is important to note that much of this information is derived from animal data. It is not known to what extent prematurity causes an additional detriment in functional myocardial reserve.

Cardio–respiratory interactions are important in neonates and infants. In simple terms, ventricular interdependence refers to a relative increase in ventricular end-diastolic volume and pressure causing a shift of the ventricular septum and diminished diastolic compliance of the opposing ventricle.[7] This effect is particularly prominent in the immature myocardium. Therefore, a volume load from an intracardiac shunt or valve regurgitation, and a pressure load from ventricular outflow obstruction or increased vascular resistance, may lead to biventricular dysfunction. For example, in neonates with tetralogy of Fallot and severe outflow obstruction, hypertrophy of the ventricular septum may contribute to diastolic dysfunction of the left ventricle and an increase in end-diastolic pressure. This does not improve immediately after repair in the neonate, as it takes some weeks to months for the myocardium to remodel. Therefore an elevated left atrial pressure is not an unexpected finding after neonatal tetralogy repair. This circumstance may be further exacerbated if there is a persistent volume load to the left ventricle following surgery, such as from residual ventricle septal defects (VSDs).

The mechanical disadvantage of an increased chest wall compliance and reliance on the diaphragm as the main muscle of respiration limits ventilatory capacity in the neonate. The diaphragm and intercostal muscles have fewer type I muscle fibers, i.e. slow contracting, high oxidative fibers for sustained activity, and this contributes to early fatigue when the work of breathing is increased. In the newborn, only 25% of fibers in the diaphragm are type I, reaching a mature proportion of 55% by 8–9 months of age.[8,9] Diaphragmatic function may be significantly compromised by raised intra-abdominal pressure, such as from gastric distension, hepatic congestion, and ascites.

The tidal volume of full-term neonates is between 6 and 8 mL/kg and, because of the above mechanical limitations, minute ventilation is respiratory rate dependent. The resting respiratory rate of the newborn infant is between 30 and 40 breaths/minute, which provides the optimal alveolar ventilation to overcome the work of breathing and match the compliance and resistance of the respiratory system. When the work of breathing increases, such as with parenchymal lung disease, airway obstruction, cardiac failure, or increased pulmonary blood flow, a larger proportion of total energy expenditure is required to maintain adequate ventilation. Infants therefore fatigue readily and fail to thrive.

The neonate has a reduced functional residual capacity (*FRC*) secondary to an increased chest wall compliance (*FRC* being determined by the balance between chest wall and lung compliance). Closing capacity is also increased in newborns, with airway closure occurring during normal tidal ventilation.[10] Oxygen reserve is therefore reduced, and in conjunction with the increased basal metabolic rate and oxygen consumption two to three times adult levels, neonates and infants are at risk for hypoxemia. However, atelectasis and hypoxemia does not occur in the normal neonate because *FRC* is maintained by dynamic factors including tachypnea, breath stacking (early inspiration), expiratory breaking (expiratory flow interrupted before zero flow occurs) and from laryngeal breaking (auto positive end-expiratory pressure).

Organ immaturity of the liver and kidney may be associated with reduced protein synthesis and glomerular filtration, such that drug metabolism is altered and synthetic function is reduced. These problems may be compounded by the normal increased total body water of the neonate compared with the older patient, along with the propensity of the neonatal capillary system to leak fluid out of the intravascular space.[11] This is especially pronounced in the neonatal lung, in which the pulmonary vascular bed is almost fully recruited at rest and the lymphatic recruitment required to handle increased mean capillary pressures associated with increases in pulmonary blood flow may be unavailable.[12]

The glomerular filtration rate (*GFR*) is very low at birth but will rapidly normalize regardless of post-conceptional age. However, urinary sodium excretion increases slowly during the first 2 years of life. The inability of immature kidneys to concentrate urine and to excrete acute water and sodium loads makes fluid management in neonates and especially preterm infants difficult. Urinary acidification capability is limited in neonates and the bicarbonate threshold reduced. Thus premature infants have decreased serum bicarbonate levels and lower serum pH (a non-anion gap acidosis). Neonates tolerate fluid restriction poorly, so fasting should be kept to a minimum and intravenous fluid started early; however excessive fluid administration (as after CPB) is also tolerated poorly. In order to induce diuresis in neonates larger doses of furosemide compared to adults are needed. The dosing of drugs, which largely depend on renal excretion, will have to be reduced and, if possible, the plasma concentration should be closely checked in order to avoid accumulation and side effects.

The caloric requirement for neonates and especially preterm neonates is high (100–150 kcal/kg/24 hours) because of metabolic demand. The task of supplying nutrition for growth becomes even more difficult when necessary limits are placed on the total amount of fluid that may be administrated either parentally or by the enteral route in preterm neonates with CHD. Hyperosmolar feedings have been associated with an increased risk of necrotizing enterocolitis (NEC) in the preterm neonate, or to the neonate born at term who has decreased splanchnic blood flow of any cause (e.g. left-sided obstructive lesions).[13]

## Systemic inflammatory response to cardiopulmonary bypass

It is well recognized that the exposure of blood elements to the non-endothelial surfaces of the CPB circuit, along with

ischemic/reperfusion injury, induces a systemic inflammatory response syndrome (SIRS), which includes activation of numerous signaling cascades including complement, fibrinolytic, proinflammatory cytokine, and oxygen radical pathways. The effects of the interactions of blood components with the extracorporeal circuit is magnified in neonates due to the large bypass circuit surface area and priming volume relative to patient blood volume.

The inflammatory response is therefore more pronounced in very-low-birth-weight and premature newborns, and along with this, so are the clinical manifestations. The immaturity of the stress response, low receptor density, and low vascular tone may be additional factors that magnify the clinical features of the SIRS in these patients. The clinical consequences include increased interstitial fluid and generalized capillary leak, and potential multiorgan dysfunction. Total lung water is increased with an associated decrease in lung compliance and increase in $A–aO_2$ gradient. Myocardial edema results in impaired ventricular systolic and diastolic function. A secondary fall in cardiac output by 20–30% is common in neonates in the first 6–12 hours following surgery, contributing to decreased renal function and oliguria.[14] Sternal closure may need to be delayed due to mediastinal edema and associated cardiorespiratory compromise when closure is attempted. Ascites, hepatic ingestion, and bowel edema may affect mechanical ventilation, cause a prolonged ileus and delay feeding. A coagulopathy post-CPB may contribute to delayed hemostasis.

Over recent years, numerous strategies have evolved to limit the effect of the endothelial injury resulting from the SIRS. Understanding the triggers, timing, and pattern of the complex cascades related to the SIRS is essential to modify or attenuate this response. A variety of anti-inflammatory treatment modalities have been studied including leukocyte depletion, neutrophil adhesion blockade, and heparin-coating of the CPB circuit to reduce complement and leukocyte activation. To date, no single treatment has been proven to attenuate the endothelial reaction and clinical response following CPB in neonates and infants, which highlights the multifactorial nature of the inflammatory response.

The most important strategy remains limiting both the time spent on bypass and use of deep hypothermic circulatory arrest (DHCA). This is clearly dependent, however, upon surgical expertise, experience, and patient size. For the LBWN, DHCA is necessary to effect surgical repair. Hypothermia, steroids, and aprotinin (a serine protease inhibitor) are important pre-bypass measures to limit activation of the inflammatory response. Attenuating the stress response, the use of antioxidants such as mannitol and anti-inflammatory agents such as glucocorticoids, altering prime composition to maintain hematocrit and oncotic pressure, and ultrafiltration during rewarming or immediately after bypass are also used to limit the clinical consequences of the inflammatory response.

Hemofiltration has become a technique commonly used to hemoconcentrate, and possibly remove, inflammatory mediators; for example, complement, endotoxin, and cytokines during or after CPB.[15–17] Hemofiltration techniques include modified ultrafiltration (MUF) whereby the patient's blood volume is filtered after completion of bypass, conventional hemofiltration whereby both the patient and circuit are filtered during rewarming on bypass, and zero-balance ultrafiltration in which high volume ultrafiltration essentially washes the patient and circuit blood volumes during the rewarming process.[17]

Early clinical experience reported improved systolic and diastolic pressures during filtration, and improved pulmonary function has also been noted with reduction in *PVR* and total lung water.[18,19] While MUF post-bypass has proven to improve early hemodynamic and pulmonary function, the improvement in pulmonary compliance may not be sustained beyond the immediate post-ultrafiltration period.[20] While these techniques are useful to hemoconcentrate and remove total body water, they do not prevent the inflammatory response. And while it is perhaps modified, this response is nevertheless idiosyncratic; despite all the above maneuvers, some neonates and infants will still manifest significant clinical signs of the SIRS and delayed postoperative recovery.[20] The development of drugs that will prevent the adhesion molecule/endothelial interaction, which is pivotal in the inflammatory response, continues to be pursued in both laboratory and clinical studies.

Peritoneal dialysis has been recommended as a means to treat total body fluid overload, particularly during low output states following cardiac surgery. Recent studies have reported successful treatment of fluid overload with continuous peritoneal dialysis, without significant morbidity and hemodynamic effects.[21,22] In addition to decompressing the abdomen, which may in turn improve respiratory mechanics and requirements for mechanical ventilation, peritoneal dialysis also assists with postoperative fluid balance, and may have the potential benefit of removal of proinflammatory cytokines.[23]

## Neurological injury

Deep hypothermia (< 18°C) with either low-flow CPB or circulatory arrest (CA) is necessary for many neonates undergoing cardiac surgery either because of size limitations for cannulation or to facilitate the surgical procedure. The conduct of deep hypothermic CPB is critical for optimal myocardial and neurologic protection.

In many centers, the practice has shifted away from the use of DHCA for periods beyond 30–40 minutes if the repair can be satisfactorily accomplished with low-flow techniques.[24,25] While there may be no optimal "safe" duration of DHCA, the accepted limit has declined over recent years from

approximately 60 minutes to the 40 minutes range at temperatures less than 20°C.[24] With improvements in neurologic protection over recent years, the incidence of overt injury, i.e. postoperative seizures, has declined substantially. While long-term neurodevelopmental outcome after DHCA in children is still being clarified, this has nevertheless become an important outcome variable when evaluating neurologic protection strategies.[26]

Neurologic injury is an inherent risk for any patient undergoing cardiac surgery and CPB. Early in the development of bypass strategies, postoperative seizures were a relatively common occurrence. They were generally self-limiting and did not imply longer-term seizure activity. However, it is now clear that seizures are a manifestation of neurologic injury, consistent with the release of excitatory neurotransmitters which produce neuronal injury by *N*-methyl-D-aspartate (NMDA) receptor-gated calcium channels.[27] Adverse neurological sequelae are multifactorial post-bypass and may be secondary to the duration of CPB,[28,29] rate and depth of cooling,[30–32] perfusion flow rate,[33] duration of CA, pH management on bypass,[34,35] hematocrit,[36,37] and embolic events. Strategies to optimize cerebral protection during deep hypothermic bypass, with or without CA, include a longer duration of cooling (over 20 minutes), the use of pH-stat strategy of blood gas management during cooling (i.e. addition carbon dioxide to the oxygenator), and maintaining a higher hematocrit (> 25%).

## Stress response

In general terms the "stress response" is a systemic reaction to injury, with hemodynamic, endocrinologic, and immunologic effects (Table 12.3). Stress and adverse postoperative outcome have been linked closely in critically ill newborns and infants. This is not surprising given their precarious balance of limited metabolic reserve and increased resting metabolic rate. Metabolic derangements such as altered glucose homeostasis, metabolic acidosis, salt and water retention, and a catabolic state contributing to protein breakdown and lipolysis, are commonly seen following major stress in sick neonates and infants.[38] This complex of maladaptive processes may be associated with prolonged mechanical ventilation courses and intensive care unit (ICU) stay, as well as increased morbidity and mortality.

The neuroendocrine stress response is activated by afferent neuronal impulses from the site of injury, traveling via sensory nerves through the dorsal root of the spinal cord to the medulla and hypothalamus. Anesthesia can therefore have a substantial modulating effect on the neuroendocrine pathways of the stress response by virtue of providing analgesia and loss of consciousness. Outcomes after major surgery in neonates and infants may be improved when the stress response is attenuated. This was initially reported in two controlled, randomized trials comparing $N_2O/O_2$/curare anesthesia with or without fentanyl in neonates undergoing patent ductus arteriosus ligation[4], and with or without halothane in neonates undergoing general surgery.[39] Fentanyl doses as low as 10 μg/kg may be sufficient for effective baseline anesthesia in neonates, although larger doses are necessary for prolonged anesthesia. A bolus dose of 10–15 μg/kg has been demonstrated to effectively ameliorate the hemodynamic response to tracheal intubation in neonates.[40]

It is important to distinguish between suppression of the endocrine response and attenuation of hemodynamic responses to stress. Because of their direct effects on the myocardium and vascular tone, anesthetic agents can readily suppress the hemodynamic side effects of the endocrine stress response. The same is true when inotropic and vasoactive agents are administered during anesthesia. However, the postoperative consequences of the endocrine stress response, in particular fluid retention and increased catabolism, remain unabated. Relying on hemodynamic variables to assess the level of "stress" is therefore often inaccurate. Metabolic indices such as hyperglycemia and hyperlactatemia are also indirect markers of "stress," particularly as they are influenced

**Table 12.3** Systemic response to injury.

| |
|---|
| *Autonomic nervous system activation:* |
| Catecholamine release |
| Hypertension, tachycardia, vasoconstriction |
| |
| *Endocrine response:* |
| Anterior pituitary: |
| ↑ ACTH, GH |
| Posterior pituitary: |
| ↑ Vasopressin |
| Adrenal cortex: |
| ↑ Cortisol, aldosterone |
| Pancreas: |
| ↑ Glucagon |
| Insulin resistance |
| Thyroid: |
| Decreased conversion of $T_4$ to $T_3$ |
| |
| *Metabolic response:* |
| Protein catabolism |
| Lipolysis |
| Glycogenolysis / gluconeogenesis |
| Hyperglycemia |
| Salt and water retention |
| |
| *Immunologic responses:* |
| Cytokine production |
| Acute phase reaction |
| Granulocytosis |

ACTH, adrenocorticotropic hormone; GH, growth hormone; $T_4$, thyroxine; $T_3$, triiodo thyronine.

by other factors such as fluid administration and cardiac output.

The effect of surgical stress has been particularly evaluated in neonates and infants undergoing cardiac surgery. Wood *et al*.[41] first demonstrated a substantial increase in epinephrine and norepinephrine levels in response to profound hypothermia and CA in infants undergoing cardiac surgery. The hormonal and metabolic response was further characterized by Anand *et al*.[42] and noted to be more extreme and distinct from that seen in adults. In addition to an increase in catechol, glucagon, endorphin, and insulin levels, hypoglycemia and lactic acidemia persisted into the postoperative period. In an important subsequent study, Anand and Hickey[43] compared a high dose sufentanil technique with a combined halothane–morphine anesthetic technique in 45 neonates undergoing cardiac surgery and deep hypothermic CPB. They reported a significant attenuation of hormonal and metabolic responses to surgery and bypass in the sufentanil group, with less postoperative morbidity and mortality. A conclusion from these studies supported the notion that reducing the stress response with large dose opioid anesthesia, and extending this into the immediate postoperative period, was important to reduce the morbidity and mortality associated with congenital heart surgery in neonates.

These studies were performed over a decade ago. During the intervening period, there have been substantial changes in the perioperative management of children with heart disease as well as the management of CPB in general; along with these changes outcomes have considerably improved. Further, it has been well demonstrated that high dose opioid anesthetic techniques do not consistently block the endocrine stress response to cardiac surgery. To evaluate this further, however, it is necessary to separate pre-bypass and bypass responses.

*Pre-bypass*: The dose of sufentanil used by Anand and Hickey[43] was extremely high and difficult to translate to the more common practice of fentanyl-based anesthesia. Two recent studies in neonates, infants and older children undergoing cardiac surgery have demonstrated attenuation of the pre-bypass endocrine and hemodynamic response to surgical stimulation with a variety of anesthetic techniques. These have included high dose fentanyl (50 μg/kg) either by bolus or infusion,[44,45] and high dose bolus fentanyl (25–150 μg/kg) with or without low dose isoflurane.[46] Based upon the lack of significant stress responses reported in these studies, it is reasonable to conclude that there was appropriate neuraxial inhibition in these patients and that they were adequately anesthetized during this pre-bypass phase of surgery. There were no significant postoperative complications (from hemodynamic and pulmonary complications through to awareness) reported in the studies. It is not possible to conclude, however, that one technique is superior to another. No specific dose response between opioid plasma level and level of hormone or metabolic stress response has been established, nor a specific benefit for the method or route of opioid administration, i.e. bolus or continuous infusion.

*Bypass*: The initiation of the endocrine stress response may be from a myriad of causes and the relative contributions are speculative. Besides the surgical stimulus, additional factors include the effects of CPB, i.e. hypothermia, contact activation, hemodilution, and non-pulsatile flow.[47–49] Distinct to the effect of anesthesia in the pre-bypass phase, anesthesia techniques have not been demonstrated to consistently obtund the responses to bypass.[43,45,50] This is primarily because CPB initiates a second mechanism for establishing the stress response independent of surgical stimulation, namely the acute phase response and inflammatory cytokine release.

Cytokines are produced from activated leukocytes, fibroblasts, and endothelial cells as an early response to tissue injury, and have a major role in mediating immunity and inflammation. Cytokine production reflects the degree of tissue trauma or injury. They stimulate the production of acute phase proteins in the liver (i.e. C-reactive protein, fibrinogen, $\beta_2$-macroglobulin and other antiproteinases), stimulate the adhesion molecule cascade, increase protein catabolism and augment release of adrenocorticotropic hormone (ACTH) from the anterior pituitary.[51,52] In addition to direct tissue injury, exposure of blood to foreign surfaces and the systemic inflammatory response as previously mentioned is also a potent stimulus for cytokine production and, with this, the stress response.

## High dose opioid anesthesia

In the early experience with bypass in neonates and infants, the use of high dose opioid anesthesia to modulate the stress response was perceived to be one of the few clinical strategies available that was associated with the demonstrable improvement in morbidity and mortality.[43] More recently, it has been demonstrated that opioids do not in fact modify the endocrine or metabolic stress response initiated by CPB; despite this, mortality and morbidity continues to remain low. Gruber *et al*.[44] demonstrated a significant increase in stress hormone levels in infants during CPB compared to pre-bypass levels although there was no change in plasma fentanyl concentrations.

Whereas the neonate may be more labile to changes in intravascular pressures, *PVR*, and cardiac output than older children, in fact the neonate is quite capable of coping with the acute phase of surgical stress. It is less common today to see neonates in the immediate post-bypass period with extensive peripheral edema or anasarca and, along with that, impaired ventricular function, reactive pulmonary hypertension, and substantial alterations in lung compliance and airway resistance. An example of this is the incidence of postoperative pulmonary hypertensive events. Pulmonary hypertensive crisis were more common a decade or more ago

in infants who had been exposed to weeks or months of high pulmonary pressure and flow, such as truncus arteriosis, complete atrioventricular canal defects, and transposition of the great arteries with ventricular septal defects. High dose opioids were an important component of management for patients at risk for pulmonary hypertensive crises; however, this now occurs much less frequently because patients are often operated upon at an earlier age and are therefore less likely to have significant or irreversible changes in the pulmonary vascular bed. Therefore, changes in surgical practice, and in particular the timing of surgery have meant that the longer-term pathophysiologic consequences of various defects are less apparent than they were 10–20 years ago. A strategy of large dose opioid anesthesia to blunt the stress response may therefore be a less critical determinant of outcome.

This is not to say, of course, that the high dose synthetic opioids are not necessary for neonatal cardiac surgery. Synthetic opioids are potent analgesics and provide hemodynamic stability because of their lack of negative inotropic or vasoactive properties. Because of the limited physiologic reserve, the pathophysiology of underlying cardiac defects and the clinical consequences of the systemic inflammatory response to bypass in the neonates, using an anesthetic technique that has minimal hemodynamic side effects is clearly desirable.

It remains to be determined what the optimal opioid dose should be to ensure an adequate depth of anesthesia. In a retrospective, pharmacodynamic study of fentanyl, Hansen and Hickey[53] demonstrated that 50 μg/kg of fentanyl was necessary to reduce the potential for sudden ventricular fibrillation (VF) in neonates with HLHS prior to CPB. The risk of sudden VF is increased in neonates with HLHS prior to CPB and in response to surgical stimulation because of the limited coronary blood flow. In these patients coronary perfusion is dependent upon retrograde flow around the hypoplastic aortic arch, which may be inadequate to meet the demand of an increase in myocardial work, related to tachycardia and increased wall stress from a light level of anesthesia. A similar circumstance is also seen in patients with truncus arteriosus, although in this case coronary perfusion is limited by the low truncal root pressure from excessive runoff into the pulmonary circulation.

There are many preferences and techniques for opioid-based anesthesia for cardiac surgery. Our common practice for neonates undergoing cardiac surgery and deep hypothermic CPB is to administer up to 50 μg/kg of fentanyl prior to sternotomy, and to supplement with low dose isoflurane titrated to hemodynamic response. During rewarming on CPB, a further 25 μg/kg of fentanyl is administered, and up to an additional 25 μg/kg fentanyl post-CPB according to hemodynamic stability and prior to transport to the ICU. The main aim is to provide an anesthetic that maintains hemodynamic stability and allows the anesthesia team to concentrate on all other aspects of the surgery, bypass, and post-CPB care. Sudden changes in hemodynamics before and after bypass may develop secondary to myocardial dysfunction, residual anatomic lesions, loss of sinus rhythm, changes in preload state, variable *PVR*, and alterations in mechanical ventilation to mention a few; using a high dose opioid anesthesia technique allows the anesthesiologist to focus on an evolving hemodynamic picture without the distraction of side effects from anesthetic drugs.

## Premature infants and low-birth-weight neonates

Although the technical aspects of CPB in small neonates are challenging, surgical advances now allow routine corrective repair of complex heart disease in neonates weighing less than 2 kg (LBWNs). In our experience, neither gestational age nor patient size precludes successful complete repair of lesions such as tetralogy of Fallot, truncus arteriosus, and transposition of the great arteries, and survival for corrective surgery in neonates weighing less than 2 kg may now approach 90%.[2,54]

While the successful outcomes of term-newborns undergoing cardiac surgery and CPB is now well established and a standard of care, the continued improved survival of preterm and LBWNs has added a new dimension to management of CHD. In addition to the physiologic limitations previously described for any newborn, compounded by the effects of the underlying cardiac disease and surgical interventions, the complications of prematurity are further considerations. The management of respiratory distress syndrome (RDS), fluid balance, NEC, and intraventricular hemorrhage may be even more difficult in a premature newborn who has CHD. Conversely the early repair of specific cardiac defects may be prevented by complications of prematurity. Further, while a technically successful repair maybe possible, the longer-term development and hazard function for reintervention in premature and LBWNs undergoing cardiac surgery has not been established.

### Pulmonary function

The immature airway and lungs of the premature and very LBWN predispose to obstruction, hypoxia, and ventilation difficulties. Lung compliance is reduced because the alveoli are primarily composed of thick-walled saccular spaces. The very compliant chest wall results in a significant mechanical disadvantage with lower *FRC* and oxygen reservoir, lower minute ventilation, and early respiratory muscle fatigue. Dead space ventilation as a proportion of tidal volume is increased, which promotes further risk for respiratory failure. Production of surfactant begins between 23 and 24 weeks of gestation, and may be inadequate until 36 weeks of gestation.[55] Respiratory distress syndrome from surfactant

deficiency results in low lung volumes and poor compliance, and increased intrapulmonary shunt and ventilation/perfusion ($V/Q$) mismatch leading to severe hypoxia. Lung injury associated with inflammatory mediator release related to mechanical ventilation or high concentration of inspired oxygen may contribute to prolonged weaning and chronic lung disease or bronchopulmonary dysplasia (BPD).

Persistent cardiac failure or excessive pulmonary flow from certain cardiac defects will increase total lung water and prevent or delay weaning from mechanical ventilation in the LBWN or premature newborn. Although RDS with increased *PVR* will limit pulmonary blood flow initially, as the lung injury resolves and the *PVR* decreases, pulmonary blood flow will substantially increase. For premature infants without RDS, pulmonary vascular tone is usually very low, and pulmonary blood flow may therefore be very high in the circumstance of a cardiac defect with a large left-to-right shunt, such as truncus arteriosus. Medical management with mechanical ventilation, diuretics, inotropes, and vasodilators is often ineffective in such cases. A low cardiac output state often persists with significant runoff to the pulmonary circulation. Continuing with medical management while waiting for an appropriate weight gain is frequently ineffective and the only alternative is surgical intervention. Palliation with a PA band to limit pulmonary blood flow is difficult to judge in a LBWN or premature infant because of technical considerations, and subsequent distortion of the pulmonary arteries may severely limit later surgical procedures. Therefore, complete surgical repair early in the course of management may be indicated to provide the optimal conditions for growth and development.

A similar problem arises in LBWN or premature infants who are cyanosed at birth from pulmonary outflow obstruction and ductus-dependent pulmonary blood flow. A longer-term infusion of prostaglandin $E_1$ ($PGE_1$) may be considered; however the side effects of apnea and gastric mucosal hyperplasia are limitations. Further, the run off across a large ductus is difficult to control and systemic hypoperfusion may develop. Palliation with modified BT shunt is possible, but may be limited by the size of the pulmonary arteries and geometry of the shunt. In addition to distortion of the pulmonary arteries, flow across the shunt could be excessive and result in systemic hypoperfusion and cardiac failure from volume overload. Therefore the side effects of palliation may not allow for subsequent growth and development, and the best alternative may be early surgical repair. This is the case for patients with tetralogy of Fallot, with or without pulmonary atresia, and successful repair in LBWN and premature infants has been reported. Nevertheless, the postoperative course of these patients is often prolonged and characterized by restrictive right ventricular physiology. However, if complete repair has been successful without significant residual lesion, this approach with anatomic correction of the circulation provides the best option for growth.

Premature and LBWN infants with single ventricle physiology or a parallel circulation are difficult to manage, and an adequate balance between the ductus-dependent pulmonary or systemic flow may not be achieved. Prolonged mechanical ventilation using a low inspired oxygen concentration or added carbon dioxide to the fresh gas flow may be necessary to raise *PVR*. Systemic hypoperfusion, NEC, renal hypoperfusion, and feeding intolerance are common problems. Excessive pulmonary blood flow and cardiac failure means that prolonged mechanical ventilation is necessary. As previously mentioned a prolonged $PGE_1$ infusion is also not desirable and although low concentrations maybe used, a dose–response relationship between ductal size and $PGE_1$ dose has not be demonstrated. Early palliative surgery with a shunt or band in single ventricle defects is usually necessary, however once again size restrictions are a limiting factor.

The potential for RDS is another important consideration for premature infants undergoing CPB. Lung injury post-cardiac surgery is initiated by shear forces and from contact of blood with the non-endothelial surfaces of the extracorporeal circuit resulting in activation of a systemic inflammatory response.[56] However surfactant depletion may also occur,[57] and when combined with endothelial injury, may contribute to pulmonary hypertension and altered lung compliance in the immediate postoperative period. However there are no data to support prophylactic use of surfactant, pre- or post-CPB, and in our experience significant morbidity and lung injury secondary to RDS from surfactant depletion post-CPB is uncommon. Nonetheless, we have tended to use surfactant both intraoperatively and during the early postoperative period in premature infants (< 36 weeks gestation) if there is evidence of RDS or altered lung compliance.

## Necrotizing enterocolitis

Congenital heart disease may be an important predisposing factor to developing NEC. Using a case-controlled study of neonates admitted to a cardiac ICU over a 4-year period, McElhinney *et al*.[58] reported that cardiac defects with the potential for significant run off from the systemic to pulmonary circulation, specifically HLHS, aortopulmonary window, truncus arteriosis, and patients who had episodes of poor systemic perfusion, were more likely to develop NEC. This supports the notion that one of the principal underlying mechanisms of NEC in patients with CHD is mesenteric ischemia. Of note, the feeding history or the type of feed, the use of indwelling umbilical catheters, and cardiac catheterization did not correlate with the incidence of NEC.

Although most of the cases of NEC were successfully managed medically without surgical intervention, the duration of hospitalization was significantly prolonged in those with NEC. The incidence of NEC reported by McElhinney *et al*.[58] was 3.3%, which was similar to an incidence of 3.5% reported by Cheng *et al*.[59] In this study, surgical intervention in

neonates with symptomatic congenital disease who develop NEC was retrospectively evaluated. Patients with CHD and diagnosis of NEC had a high mortality of 57%. However, those patients with proven NEC (without perforation) who underwent early cardiac surgery had a higher survival than in those managed medically and had delayed surgery (75% vs. 44%).

Clinical signs of NEC include abdominal distention, feeding intolerance, temperature and glucose instability, heme-positive or frank blood in the stool, abdominal guarding, and tenderness. Abdominal radiographs may demonstrate distention or an abnormal gas pattern, pneumatosis, portal air, or intraperitoneal air consistent with perforation. Thrombocytopenia and leukocytoses are usually evident on blood examination. If NEC results in perforation or severe bowl ischemia, the neonate may develop sepsis syndrome with hypotension, third space fluid loss, poor perfusion, and edema. On most occasions, patients can be treated medically with fluid restriction, antibiotics, and vasoactive support; less frequently, laparotomy may be necessary. The key to management, however, is to improve perfusion and oxygen delivery to the gut. Therefore, once hemodynamically stable without clinical signs of sepsis syndrome, early cardiac surgical intervention to improve splanchnic perfusion is preferable.

## Intraventicular hemorrhage

The risk for intraventricular hemorrhage (IVH) decreases with increasing gestational age (risk at 23 weeks varies from 10% to 83%; at 25 weeks the incidence has decreased to 10–22%).[55] Intraventricular hemorrhage in the newborn infant is determined largely by cerebral immaturity and hemodynamic disturbances, thus even in the term infants with complex CHD there may be an increased incidence of IVH related to fluctuation in perfusion pressure, cerebral "steal" phenomena from excessive diastolic run off, acidosis, and hypoxia. The diagnosis of IVH before surgery is important, because of the potential for extension of the hemorrhage during CPB related to anticoagulation, increased fibrinolytic activity, and changes in perfusion pressure.

There are no prospective data suggesting an increased risk for IVH in low birth weight infants if they undergo early repair and CPB.[2,60] There are also no data to suggest an increased incidence of neurologic injury manifested by clinical or electroencephalograph (EEG) seizure activity. Longer-term neurodevelopmental outcomes are also unknown for this group of patients.

As a baseline, we routinely perform a cranial ultrasound in all premature (< 35 weeks gestation) neonates prior to cardiac surgery. There are no clear guidelines as to how to manage neonates who have an IVH detected by ultrasound prior to surgery. Delaying surgery as long as possible is prudent to lower the risk for extension and further neurologic injury. This may not be possible for some defects; however, in general our practice is to wait approximately 7–10 days before undergoing surgery and CPB.

## Outcome

Several studies have evaluated the overall outcome of preterm and very-low-birth-weight infants undergoing congenital heart surgery.[2,54,61–64] One of the earliest studies addressing patient size and outcome was by Pawade *et al*.[65] They reported a hospital mortality of 16.5% for patients less than 2.5 kg, with risk factors including univentricular cardiac defects and duration of CPB. Chang *et al*.[54] reported a 70% survival rate in 100 patients with birth weight <2.5 kg with congenital heart lesions. Patients were divided into three groups: Group 1 (n = 62) had early surgical intervention with a survival rate for palliation of 78% and for primary repair of 82%. Group 2 (n = 26) had late surgical intervention (at a mean age 4.3 months) after being managed medically prior to corrective surgery; 23% (6/26) died during medical management, and of the 20 out of 26 undergoing surgery, 90% survived. In group 3 (n = 12), no intervention was undertaken (lethal prognosis) and all died. The conclusion from this paper was that prolonged efforts to achieve medical stability and promote weight gain may not yield superior result compared to early surgical intervention. Rossi *et al*.[1] reported their experience of 30 patients less than 2 kg with CHD, citing a hospital survival of 83% and no difference in mortality rates based on age, weight, or type of surgical procedure, although premature infants tended to have an increased risk for hospital mortality. Reddy *et al*.[2] reported 102 patients who underwent complete surgical repair for CHD (mean weight of 2.1 kg and 66 premature < 36 weeks). Preoperative morbidity was more common among patients referred late for surgical correction. There were 10 early deaths and the survival at 1 year was 82%. Regression analysis revealed no correlation between weight or gestational age with survival, but the factors that did correlate included longer bypass time, complex anomalies, and diagnosis of truncus arteriosus. No patients suffered post-bypass intracerebral hemorrhage.

These initial reports concentrated particularly on neonates less than 2.5–3.0 kg. However, the size limits have been decreased even further with recent reports of successful surgery in the very LBWN. Dees *et al*.[66] reported their retrospective experience of premature low birth weight infants undergoing cardiac surgery. The median gestational age of their patients was 33 weeks and mean birth weight 1.85 kg. They noted an increased risk for NEC by a factor of 1.7, and an overall mortality twice that of patients in the neonatal ICU of similar age and size who did not have CHD. In our experience at Children's Hospital, Boston, evaluating 116 neonates weighing <2 kg at birth with CHD, early age at diagnosis, need for cardiopulmonary resuscitation before surgery, presence of multiple congenital anomalies, and more complex

cardiac disease characterized the neonates with highest risk for death regardless of gestational age and birth weight. Finally, Reddy and Hanley[61] reported the outcomes of 20 infants less than 1.5 kg who underwent complete repair of congenital heart defects. Modification of neonatal CPB techniques were necessary; however, there were only two early deaths unrelated to the surgical procedure. No patient had evidence of intracranial hemorrhage post-bypass and at 14 months follow-up there was only one late death. Repeat surgical and catheter reinventions were necessary in four patients. There were no neurological sequelae attributable to surgery. A conclusion from these studies further supports the notion that low birth weight and prematurity do not appear to be limitations to successful repair of complex two-ventricle defects, although long-term follow-up is necessary to determine growth and development patterns.

Conversely, low birth weight and prematurity continue to be reported as significant risk factors for early mortality in patients with complex single-ventricle disease, in particular HLHS. Forbess *et al*.[67] evaluated anatomic subtypes and preoperative physiologic variables associated with early mortality after stage I Norwood procedure and noted that aortic atresia, mitral atresia, a small ascending aorta, metabolic acidosis, and weight less than 3 kg, all increased risk for early mortality. Mahle *et al*.,[68] in a retrospective review of 840 patients who underwent stage I surgery for HLHS, reported that surgical experience had a significant impact on outcome, with patients operated in the later surgical era having improved survival. In addition, weight less than 2.5 kg was associated with higher mortality in this study.[68] In a retrospective review by Weinstein *et al*.[69] of 67 LBWN patients with HLHS undergoing stage I Norwood palliation (14 patients < 2 kg and two patients < 1.5 kg), early mortality, defined as death within 30 days or before hospital discharge, was 51% (34/67). Although they were unable to identify patient, procedural, or time-related variables that correlated with increased mortality, the mortality rate in this group of patients remains higher than that reported for patients of larger size who undergo stage I palliation.

## Fetal cardiac intervention and surgery

Advances in fetal echocardiography have improved accuracy in the diagnosis and evaluation of congenital heart lesions and functional pathology, which has in turn lead to improved perinatal management and counseling. Studies have shown that, specifically for HLHS and transposition of the great arteries among other lesions,[70,71] prenatal diagnosis does result in an improved preoperative condition with decreased mortality. Fetal cardiac surgery is not currently a realistic therapeutic option for critical CHD; it is nevertheless a future direction for management. The progress and future potential of in *utero* cardiac repair may enable salvage of a life-threatening *in utero* condition and optimize long-term outcome by altering *in utero* cardiac development. The rationale for fetal cardiac intervention is that altered blood flow and pressure patterns in the developing heart cause hypoplasia and inadequate development of major cardiac structures, including ventricular chambers, arborization of great vessels, and pulmonary vasculature.

The various anatomic and physiologic limitations to fetal cardiac surgery has resulted in interest directed towards fetal intervention using catheterization techniques, involving a percutaneous transuterine approach. To date, there has been limited experience in human fetal cardiac intervention and efforts have been restricted to attempts at dilating severely stenotic aortic and pulmonary outflow tracts and treatment of congenital heart block.[72] The results from these procedures have been guarded; however, important information regarding technical details and the fetal response to catheter intervention has been obtained.

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# 13 Approach to the teenaged and adult patient

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## Introduction

Advances in cardiac surgery and perioperative care in the past several decades have meant that over 85% of infants born with congenital heart disease (CHD) are now expected to reach adulthood. There are, in fact, relatively few conditions for which the surgical repair is completely and uniformly totally curative for the entire population.[1] Cure requires that normal cardiovascular function be achieved and maintained, life expectancy is normal, and further medical evaluation for CHD is not required. It is estimated that there are currently over 500 000 adults in the USA with CHD, 55% of whom remain at moderate to high risk, and over 115 000 of whom have truly complex disease.[2] Put another way, "the number of adults with CHD now equals the number of children with CHD."[3]

These patients bring with them problems related to complex postoperative anatomy and physiology which will not be familiar to physicians used to caring for adults, and also medical problems that accrue with aging, which will not be familiar to physicians used to caring for children. This problem has resulted in two American College of Cardiology sponsored Bethesda Conferences in the past several years, most recently in 2001.[3] These panels have recommended the establishment of regionalized adult congenital heart centers which consist of a full coterie of professionals educated and experienced in the care of the adult with CHD. A specific recommendation was that non-cardiac surgery on CHD patients with moderate to complex disease be performed at an adult CHD center with the consultation of an anesthesiologist experienced with CHD.[3,4]

This chapter reviews the organ system sequelae of longstanding CHD, both non-cardiac and cardiac; and the anatomy, pathophysiology, and surgical approach to the common lesions. Finally, perioperative and anesthetic outcomes are reviewed, and specific recommendations made for the anesthetic approach to adults with CHD.

## Non-cardiac sequelae of longstanding congenital heart disease

### Pulmonary sequelae

Lesions resulting in increased pulmonary blood flow or in obstruction to free pulmonary venous drainage can both cause increased interstitial fluid with decreased pulmonary compliance[5] and increased work of breathing. Patients with cyanotic disease and chronic hypoxemia have increased minute ventilation with normal $PaCO_2$.[6] Cyanotic patients appear to have a normal ventilatory response to hypercarbia but a blunted response to hypoxemia[7,8] which resolves after surgical correction.[9] End-tidal $PCO_2$ underestimates $PaCO_2$ in cyanotic patients with decreased, normal, or increased pulmonary blood flow.[10]

Although enlarged, hypertensive pulmonary arteries or an enlarged left atrium can on occasion entrap the pulmonary arterial tree causing atelectasis, pneumonia, or focal emphysema in children; this is rare in adults. Hemoptysis is a finding of late stage Eisenmenger physiology, and thrombosis of upper lobe pulmonary arteries can occur in patients with Eisenmenger physiology and erythrocytosis.[11] Prior thoracic surgery may have resulted in phrenic nerve damage.

The incidence of scoliosis in CHD patients is as high as 19%, is more common in children with cyanotic CHD, and may develop in adolescence, years after surgical correction of cyanosis.[12] The interaction of cyanosis and early lateral thoracotomy in the development of scoliosis remains unclear. Although rare, scoliosis can be severe enough to impact pulmonary function.

The most serious complication of longstanding pulmonary hyperemia is the development of Eisenmenger physiology (see below). The age at which this develops depends on the underlying physiology (earlier at high altitude, for example), and also the level of the shunt. Patients with atrial level

shunts may not develop evidence of pulmonary vascular disease until late middle age.

## Hematologic sequelae

Hematologic sequelae are predominantly a consequence of longstanding cyanotic CHD and include abnormalities of both red cell regulation and hemostasis. Chronic hypoxemia results in increased renal erythropoietin production. The relationship among oxygen saturation, 2,3-diphosphoglycerate, and red cell mass is relatively poor.[13] The oxygen–hemoglobin dissociation curve is usually normal or minimally right-shifted. Most patients establish an equilibrium state. They have a stable hematocrit and are iron replete. Some patients, however, develop excessive hematocrits and are iron deficient, resulting in a hyperviscous state. Symptoms of hyperviscosity are rare at hematocrits less than 65% if the patient is not iron deficient (Table 13.1). Iron deficient red cells are less deformable than iron replete red cells, and will cause increased viscosity for the same hematocrit. Iron deficiency can be related to inappropriate, repeated phlebotomies in an attempt to reduce hematocrit. The blood cells will be microcytic and hypochromic in the face of erythrocytosis. Treatment with oral iron should be undertaken with care, as rapid increases in hematocrit can ensue.

Erythrocytosis and hyperviscosity are associated with the development of cerebral venous thrombosis in children less than 4 years old, but not in adults with cyanotic CHD, regardless of hematocrit.[11]

Therapy is recommended for temporary relief of *symptomatic* hyperviscosity only (not due to dehydration). Symptoms usually regress within 24 h of a partial isovolumic exchange transfusion. It is rare for adult patients to require removal of more than 1 U of blood. Phlebotomy should only be undertaken in symptomatic patients, and not to treat asymptomatic high hematocrits. Phlebotomized blood can be banked for autologous perioperative transfusion if needed. Prolonged preoperative fasting should be specifically avoided in these patients, as rapid increases in hematocrit can accompany dehydration. Each volume of erythrocytotic blood contains less plasma than normal blood (Fig. 13.1).

A variety of hemostatic abnormalities have been described in cyanotic patients. Bleeding diatheses are uncommon at hematocrits less than 65%, although surgical bleeding can occur. Generally the degree of the bleeding diathesis mirrors the hematocrit. Platelet counts are typically low normal, and are occasionally low, but bleeding is not related to the thrombocytopenia. When corrected for the decreased plasma volume in each blood sample, total plasma platelet count is closer to normal (Fig. 13.1). Abnormalities of platelet function have also been reported.[14] Patients with synthetic vascular anastamoses or low-pressure conduits are often maintained on chronic antiplatelet therapy.

Abnormalities of both the intrinsic and extrinsic coagulation pathways with abnormalities of a variety of specific clotting factors have been inconsistently described in cyanotic patients. Fibrinolytic pathways are normal.[15] On occasion patients with both cyanotic and acyanotic CHD have been described with deficiencies of the largest von Willebrand factor multimers, which have corrected following corrective cardiac surgery.[16]

The decreased plasma volume in erythrocytotic blood may cause spurious results of the prothrombin and partial thromboplastin times. The fixed amount of anticoagulant in the sample tube presumes a normal plasma volume and may be excessive for an erythrocytotic sample (Fig. 13.1). If informed of the patient's hematocrit, the clinical laboratory can provide an appropriate tube. Correcting to an idealized hematocrit of 45%, the appropriate amount of citrate can be added to the tube as follows:

$$\text{Milliliter citrate} = (0.1 \times \text{blood volume collected}) \times [(100 - \text{patient's hematocrit})/55].$$

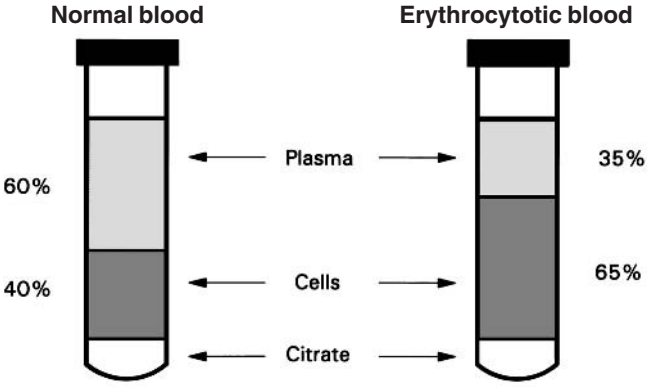


**Fig. 13.1** The effect of a fixed amount of citrate anticoagulant in tubes of blood with normal and increased hematocrit. The fixed anticoagulant volume combined with decreased plasma volume in the erythrocytotic blood results in artifactual elevation of the prothrombin and partial thromboplastin times. Similarly, although the concentrations of platelets are identical in both samples of plasma, the platelet count per milliliter of whole blood (which is reported by the laboratory) will be lower in erythrocytotic blood. Reproduced with permission from Baum VC. The adult with congenital heart disease. *J Cardiothorac Vasc Anesth* 1996; **10**: 261–82.

**Table 13.1** Signs and symptoms of hyperviscosity syndrome.

| |
|---|
| Headache |
| Faintness, dizziness, light headedness |
| Blurred or double vision |
| Fatigue |
| Myalgias, muscle weakness |
| Paresthesias of fingers, toes, or lips |
| Depressed mentation, a feeling of dissociation |

Due to the excessive hemoglobin turnover in cyanotic CHD, adult patients with cyanotic CHD have an increased incidence of calcium bilirubinate gallstones, and biliary colic can develop years after cardiac surgery has resolved the cyanosis.[11]

Factors besides intrinsic hemostatic defects can increase the risk of excessive perioperative bleeding in patients with cyanotic CHD, particularly during thoracic surgery. These include increased tissue vascularity, elevated systemic venous pressure, and abnormal aortopulmonary and transpleural collateral vessels. In addition, many patients will have had prior intrathoracic surgery.

### Renal sequelae

Abnormal renal histopathology with chronic cyanotic CHD includes hypercellular glomeruli with basement membrane thickening, focal interstitial fibrosis, tubular atrophy, and hyalinization of afferent and efferent arterioles.[17] High plasma uric acid levels can be found in adults with cyanotic CHD. Although one might presume that this is from increased urate production, it is rather due to inappropriately low fractional uric acid excretion.[18] This enhanced urate reabsorption is believed due to renal hypoperfusion with a high filtration fraction. Urate stones and urate nephropathy are, however, rare.[19] Arthralgias are common, but gouty arthritis is less frequent than would be expected from the degree of hyperuricemia.[18]

### Neurologic sequelae

Adults with unmodified or persistent intracardiac shunts remain at risk for paradoxical emboli. Even patients with a predominant left-to-right shunt are at some risk. Although it has been said that unlike children, adults with cyanotic CHD are not at risk for the development of cerebral thrombosis no matter the level of hematocrit,[11,20] that conclusion has been challenged.[21] In any event, adults do remain at risk for the development of brain abscesses. A healed childhood brain abscess can serve as a nidus for seizures throughout adulthood.

Prior thoracic surgery can have caused iatrogenic peripheral nerve damage. Surgery at the apices of the lung, such as Blalock–Taussig shunts, patent ductus arteriosus (PDA) ligation, pulmonary arterial band, and coarctation repair in particular, are associated with injury to the recurrent laryngeal nerve, the phrenic nerve, and the sympathetic chain. Resultant injuries can be permanent.

## Vascular access considerations

Both congenital abnormalities and alterations due to cardiac catheterization or surgery can affect the suitability of a variety of vessels for cannulation by the anesthesiologist. These are summarized in Table 13.2.

## Pregnancy

As more children grow into adulthood with CHD, so will more of them become pregnant. The physiologic changes of pregnancy, labor, and delivery can significantly alter the physiologic status of these patients. Readers are referred to more specialized books for a more complete discussion of the pregnant woman with CHD.[22] Pregnancy considerations are included under specific defects listed below.

Pregnancy can be carried successfully to term with vaginal delivery for women with most congenital cardiac lesions. Pulmonary hypertension, depressed ventricular function, and cyanosis are predictors of maternal and fetal complications. Patients with Eisenmenger physiology are at particularly high risk. Up to 47% of cyanotic women will develop deterioration of functional capacity during pregnancy.[23]

**Table 13.2** Vascular access considerations.

| Vessel | Potential problem |
|---|---|
| Femoral vein(s) | In older patients may have been ligated if cardiac catheterization done by cutdown. In younger patients may be thrombosed after use of larger therapeutic catheters |
| Inferior vena cava | Some lesions (particularly asplenia) associated with discontinuity of the inferior vena cava. Will not be able to pass a catheter from the groin to the right atrium |
| Left subclavian and pedal arteries | Blood pressure will be low in the presence of coarctation of the aorta or following subclavian flap repair (subclavian artery only), and variably so if postoperative recoarctation |
| Subclavian artery | Blood pressure low with classic Blalock–Taussig shunt on that side, and variably so with modified Blalock–Taussig |
| Right subclavian artery | Blood pressure artifactually high with supravalvar aortic stenosis (Coanda effect) |
| Superior vena cava | Risk of catheter-related thrombosis with Glenn operation |

Anticoagulation is recommended for cyanotic women and women with Eisenmenger physiology during the third trimester and the first postpartum month. The decrease in systemic vascular resistance that accompanies pregnancy is better tolerated in patients with regurgitant lesions.

Bacterial endocarditis prophylaxis is not currently recommended for uncomplicated deliveries, although it is probably common clinical practice. Episiotomies would be an indication for prophylaxis.

## Psychosocial issues

Adolescents often have psychological peculiarities well known to pediatricians, and teenagers with CHD are no different. Issues of denial, sense of immortality, and desire for risk taking can all impact on optimally caring for these adolescents as they transition into adulthood. Body conscious adolescents may struggle with bodies that are scarred due to prior surgery and may have physical limitations. Although most adolescents and adults with CHD function quite well, adults with CHD are less likely to be married or cohabiting, and are more likely to be living with their parents.[24]

Adult CHD patients may have difficulty in obtaining life and health insurance after they are no longer covered under their parents' policies.[25] Life insurance is somewhat more readily available than in the past, but policies vary widely among insurers.[26]

## Cardiac sequelae

The hemodynamic effects of an anatomical cardiac defect can be compounded by time, and modified by imposed chronic cyanosis or pulmonary vascular disease. Myocardial dysfunction can be inherent to the CHD, but can also be due to surgical injury, including inadequate intraoperative myocardial protection.[27,28] This is particularly true of now middle-aged adults who had surgical repairs several decades ago. Although the basic pathophysiology might be well understood by those caring for children with CHD, the natural history of these lesions may be unexpected. Some patients with dysmorphic syndromes will develop heart disease in adult life. For example 46% of a young adult Down's syndrome population without CHD developed mitral valve prolapse, and a small number developed aortic insufficiency.[29] The large number of cardiac lesions and subtypes, compounded with an array of surgical palliative and corrective procedures, make a complete cataloging of all defects and modifications impossible in this context. This chapter is primarily devoted to the more common and physiologically important defects. Both short-term and long-term surgical results from older series may not reflect current results.

## Acyanotic lesions

### Atrial septal defect and partial anomalous pulmonary venous connection

Both the natural history and the outcome after surgery for partial anomalous pulmonary venous return are similar to that of the physiologically similar secundum atrial septal defect (ASD).[30–32] Because patients with otherwise uncomplicated ASDs often remain asymptomatic until adulthood, ASDs account for about one-third of CHD discovered in adults. Survival of unrepaired defects into adulthood is routine, but complications developing in adulthood provide the rationale for routine childhood correction. There is a mortality of 6%/year over 40 years of age,[30–32] and essentially all patients over 60 years of age are symptomatic. Patients with large, unrepaired defects often die of right ventricular failure or atrial tachyarrhythmias in their thirties or forties.[33] In addition to atrial tachyarrhythmias and paradoxical emboli, left-to-right shunting through the defect can increase with aging. Systemic hypertension and/or ischemic coronary disease can occur with aging, and both decrease left ventricular diastolic compliance, which increases the left-to-right shunt. After the age of 40 years, patients can develop pulmonary vascular disease, now pressure loading the chronically volume loaded right ventricle. Mitral insufficiency can develop in adulthood and is significant in about 15% of adult patients.[34]

Incomplete resolution of right ventricular dilation has been reported with surgical closure after 5 years of age.[35] Left ventricular dysfunction has been reported by some in patients having surgical closure in adulthood.[36] Postoperative survival in patients without pulmonary vascular disease is similar if operated on before 24 years of age, but survival is worse if surgery is done between 25 and 41 years of age, and worse yet after 41 years of age.[37]

Pregnancy is uncomplicated in the vast majority but, with the hypervolemia of pregnancy, heart failure can develop during pregnancy with larger defects. Peripheral venous thrombosis carries with it the risk of paradoxical embolization.

### Ventricular septal defect

The long-term natural history of ventricular septal defect (VSD) has been reviewed in detail.[38] More than 75% of small and even moderate-sized VSDs close spontaneously during childhood by a gradual ingrowth of surrounding septum. Over 90% of those defects that will close spontaneously will have closed by 10 years of age. Other mechanisms of natural closure include closure by tricuspid valve tissue, prolapsed aortic valve tissue, and endocarditis. There is an incidence of aortic insufficiency in adults with VSD from prolapse into the defect.[39] Otherwise, a small VSD in the adult is of no hemodynamic import, other than the continuing risk of endocarditis.

Pulmonary vascular disease can progress if closure of a large VSD is delayed.

Several studies have shown possible ventricular dysfunction years after surgical closure.[40–42] However, most of these patients had surgery late, by current standards. It appears that the changes of chronic volume overload resolve if surgical correction is undertaken by 5 years of age.

Pregnancy is well tolerated in the absence of pulmonary hypertension or pre-existing heart failure. Pregnancy with a spontaneously or surgically closed defect carries no additional risk, in the absence of additional cardiac problems.

## Patent ductus arteriosus

Patent ductus arteriosus rarely close spontaneously after the neonatal period. In addition to the consequences of chronic left-to-right shunting, in the adult the PDA may become calcified or aneurysmally dilated with the risk of rupture. This increases the risk of surgery, which will rarely require the use of cardiopulmonary bypass.[43] Unrepaired, one-third of patients die of heart failure, pulmonary arterial hypertension or endocarditis by 40 years of age, and two-thirds by the age of 60 years.[44] Small PDAs do not carry a hemodynamic risk for pregnancy.

## Coarctation of the aorta

There is a significant morbidity and mortality from unoperated coarctation of the aorta in the adult. There is a 25% mortality by 20 years of age, 50% by 30 years of age, 75% by 50 years of age, and 90% by 60 years of age.[45–48] Causes of death include left ventricular failure, rupture of cerebral aneurysms, and dissection of a post-coarctation aneurysm. Left ventricular failure can develop in unrepaired adults over 40 years of age. Unless repair is undertaken early in life, there is an incremental risk for the development of premature coronary atherosclerotic disease. Even with operation, coronary artery disease is the leading cause of death 11–25 years after operation.[49] Bicuspid aortic valve is a common coexisting lesion, and often does not become stenotic until middle age or older, although it is always an endocarditis risk. Coarctation can also be associated with functionally significant mitral valve abnormalities. Patients who have had coarctation repairs in childhood may develop aneurysms at the site of the repair, or restentosis of the repaired area in adolescence or adulthood. Half of patients operated on after 40 years of age have persistent hypertension, and many of the remainder will have abnormal hypertensive responses to exercise. Long-term survival after surgery is worse the older the patient at the time of surgery, with a 15-year survival of only 50% in patients having surgery at over 40 years of age.

Hypertension can be exacerbated during pregnancy in women with unoperated coarctation, with the risks of aortic dissection or rupture, heart failure, angina, and rupture of a circle of Willis aneurysm. Blood pressure control is of great importance during pregnancy. Most aortic ruptures during pregnancy occur prior to labor and delivery. Epidural analgesia would help minimize hypertension during delivery.

## Aortic stenosis

Most adult patients with aortic stenosis have a bicuspid aortic valve. Although endocarditis risk is lifelong, symptoms often do not develop until late middle age or later. Once symptoms develop (angina, syncope or near syncope, heart failure) survival is markedly shortened: median survival is 5 years after the development of angina, 3 years after syncope, and 2 years after heart failure.[50]

Most mothers with aortic stenosis can have safe pregnancies with vaginal deliveries. Severe aortic stenosis (valve area $< 1.0\ cm^2$) may cause maternal clinical deterioration and significant maternal and fetal mortality. Hemodynamic monitoring during delivery is critical with maintenance of preload and avoidance of vasodilation and hypotension. When required, percutaneous balloon valvuloplasty appears to carry lower risk than open valvotomy during pregnancy.

## Pulmonary valve stenosis

Apart from neonates with critical pulmonic stenosis, long-term asymptomatic survival is routine.[38] Mild pulmonic stenosis in the adult does not require surgical correction; there is a 94% survival 20 years after diagnosis.[51] However with aging, right ventricular fibrosis and right ventricular failure can develop, which is the most common cause of death, occurring usually in the fourth decade. Essentially all patients who have relief of stenosis surgically or by balloon valvuloplasty have normal postoperative right ventricular function, but abnormal ventricular function may not completely normalize after late correction. Isolated pulmonary stenosis even of a severe degree, is usually well tolerated during pregnancy, despite the volume overload.

## Congenitally corrected transposition of the great vessels (l-transposition, ventricular inversion)

Most patients whose anatomic right ventricle is the systemic ventricle as an isolated defect will have normal biventricular function through early adulthood, but can develop right ventricular failure with increasing age.[52] Second or third degree heart block occurs with an incidence of about 2%/year, and more than 75% of patients have some degree of heart block, although the intrinsic pacemaker remains above the bundle of His with a narrow QRS. l-Transposition is associated with an Ebstein-like deformity of the tricuspid valve (in the systemic ventricle). There is a significant incidence of tricuspid insufficiency (physiologically analogous to mitral insufficiency in the normal heart) even in patients without this

Ebstein-like malformation, and the incidence is higher still in patients with this valve deformity.[53]

### Ebstein's anomaly of the tricuspid valve

Following tricuspid valve replacement (the current approach is repair if possible) up to 25% of patients will have high-grade atrioventricular block. There is often associated a right-sided bypass tract resulting in Wolff–Parkinson–White accelerated conduction, allowing rapid ventricular rates and possible development of ventricular fibrillation. This is a particular concern as 25–30% of patients will develop supraventricular tachyarrhythmias in addition to the fraction that will develop atrial fibrillation as a consequence of aging.

In the absence of marked cyanosis, pregnancy and delivery are generally well tolerated, but with an increased incidence of prematurity and fetal loss.

## Cyanotic lesions

### Tetralogy of Fallot

Tetralogy of Fallot is the most common cyanotic lesion encountered in adults. Unoperated, approximately 25% of patients will survive to adolescence, following which the mortality is 6.6%/year. Only 3% will survive to the age of 40 years.[54] Unlike children, adolescents and adults with tetralogy do not develop hypercyanotic "tet spells." The outcome in patients surgically corrected as adults is worse compared to surgical correction in childhood.[55]

Although the VSD component is currently approached through the right atrium, adult patients may have had repair via a right ventriculotomy. Right ventricular function in these patients can have an abnormal response to exercise. Repair at an earlier age (< 12 years of age) results in better long-term right ventricular function. In the (now uncommon) unrepaired adult patient, the development of systemic hypertension in adult life will impose an additional load on both ventricles, not just the left ventricle. The increased systemic resistance can decrease the right-to-left shunt and improve cyanosis, but at the expense of right- or biventricular failure.

Up to 5.5% of postoperative patients may have sudden death or require treatment for ventricular tachycardia, often years after surgical correction.[56] The foci for these arrhythmias are typically in the right ventricular outflow tract and can be ablated. However, premature ventricular contractions and even non-sustained ventricular tachycardia are not uncommon but may not be associated with sudden death,[57] making it difficult to know which patients to treat. Additional long-term complications include chronic pulmonary insufficiency and aneurysm formation at a right ventricular outflow tract patch.

Women who have had a good surgical correction without residual defects should tolerate pregnancy and delivery well. Women with uncorrected tetralogy of Fallot, particularly those with significant cyanosis, have a high incidence of fetal loss (80% with hematocrit > 65%). The fall in systemic resistance with pregnancy and delivery can worsen cyanosis, and the physiologic volume load can exaggerate failure of both ventricles.

### Transposition of the great arteries (d-transposition)

With a 1-year mortality of approximately 100%, all adults with d-transposition will have had some type of surgical correction. Many adults will have had atrial type repairs, of either the Mustard or Senning type. Some teenagers will be young enough to have had repair by an arterial switch operation. Some adults will have had repair of d-transposition and VSD with a Rastelli type repair.

Atrial repairs result in a systemic right ventricle. Patients who have had an atrial type repair have consistently abnormal right ventricular function, with a right ventricular ejection fraction of about 40%. It has been suggested that the earlier the surgery the better the right ventricular function, although it remains abnormal.[58] Right ventricular dysfunction can be progressive.[59]

There is a significant incidence of late electrophysiologic sequelae after atrial repair, including sinus node dysfunction (bradycardia), junctional escape rhythms, atrioventricular block, and supraventricular tachyarrhythmias. These atrial arrhythmias can result in sudden death, presumably from 1 : 1 conduction causing ventricular fibrillation.[60] The frequency of tachyarrhythmias increases after the tenth postoperative year.

It is still too premature to know the very long-term outcome after the arterial switch operation. Many of these children have abnormal resting myocardial perfusion, and the implication for the development of coronary artery disease in adulthood remains unknown.

Pregnancy and delivery are generally well tolerated after an atrial or Rastelli repair, however right ventricular failure and worsening functional capacity can occur. There is an increased incidence of prematurity and small infants in the offspring of these women.

### Single ventricle anatomy

This large rubric includes such lesions as tricuspid atresia and more complex anatomy with a single ventricle, and thus long-term survival depends on the type and degree of coexisting cardiac malformations. Both pulmonary stenosis (protecting the pulmonary vasculature from excessive flow) and a competent atrioventricular valve improve long-term survival. A single ventricle of left ventricular morphology

allows for better ventricular function than does one of the right ventricular type.[61] Palliation with an aortopulmonary shunt is associated with volume loading of the single ventricle and decreasing function with age.

Pregnancies have been reported in women with single ventricles. There is a high incidence of fetal loss, premature delivery, and small infants. Stable patients, however, can have vaginal delivery. The risk of pregnancy increases significantly with increasing degrees of cyanosis.

## Fontan physiology

The Fontan operation has undergone many iterations and modifications since its original report in 1971. There is evidence that despite early improvement in function, these patients, at least those done early in the experience with this operation, have continued decline in function with continued long-term mortality.[62]

## Truncus arteriosus

Essentially all patients who survive to adolescence will have had surgical repair. Although conduits placed in early childhood will be outgrown, valved conduits placed in late childhood should suffice for adult size. There can be ongoing problems with incompetence or stenosis of both the truncal valve, now analogous to the aortic valve, and the valved right ventricle to pulmonary artery conduit. Because the conduit often lies immediately behind and in close proximity to the sternum, it can be at very high risk of accidental incision during later sternotomy.

## Eisenmenger's syndrome

Eisenmenger physiology is compatible with survival into adulthood.[63] Survival is 80% 10 years after diagnosis, and 42% at 25 years.[64] Significant mortality occurs with noncardiac surgery and pregnancy.[65] The onset of irreversible pulmonary vascular disease depends on the degree of shear rate, and for atrial level shunts such as ASDs it may not develop until mid-life. Patients with pulmonary vascular disease face significant potential perioperative risks and constitute a major proportion of adults referred for anesthetic evaluation prior to non-cardiac surgery. Findings are summarized in Table 13.3.

**Table 13.3** Signs, symptoms, and findings with Eisenmenger's syndrome.

- Physical examination: Loud pulmonic component of the second heart sound, single or narrowly split second heart sound, Graham-Steell murmur of pulmonary insufficiency, pulmonic ejection sound ("click")
- Chest radiography: Decreased peripheral pulmonary arterial markings with prominent central pulmonary vessels ("pruning")
- Electrocardiogram: Right ventricular hypertrophy
- Impaired exercise tolerance
- Exertional dyspnea
- Palpitations (often due to atrial fibrillation or flutter)
- Complications from erythrocytosis/hyperviscosity (see text)
- Hemoptysis from pulmonary infarction or rupture of pulmonary vessels or aortopulmonary collateral vessels
- Complications from paradoxical embolization
- Syncope from inadequate cardiac output or arrhythmias
- Heart failure (usually end-stage)

Fixed pulmonary vascular resistance precludes rapid adaptation to intraoperative hemodynamic changes. Changes in systemic vascular resistance are mirrored by changes in the degree of right-to-left shunting. Systemic vasodilators, including regional anesthesia, must be used with caution, and close assessment of intravascular volume is important. Epidural anesthesia has been used successfully in these patients, but the local anesthetic should be delivered in small increments.[66] Postoperative postural hypotension can increase the degree of right-to-left shunting, and these patients should be cautioned to change position slowly.

Placement of pulmonary artery catheters is problematic and not without potential complication in patients with pulmonary vascular disease, who can also have hemostatic defects associated with erythrocytosis.[67] Pulmonary hypertension is a risk factor for pulmonary artery rupture. Right-to-left intracardiac shunting and abnormal cardiac anatomy may make passage to the pulmonary artery difficult without fluoroscopy. Given that the relative resistances of the systemic and pulmonary beds will be reflected in systemic oxygen saturation, which is readily measured by pulse oximetry, and measurements of thermodilution output will not accurately reflect systemic output, the value of a pulmonary artery catheter in these patients is minimal at best and they are essentially never indicated. One possible exception is the patient with pulmonary vascular disease and an ASD who is at risk to develop right ventricular failure if suprasystemic right ventricular pressures develop.[68]

Fixed pulmonary vascular resistance is by definition unresponsive to pharmacologic manipulation. Nevertheless it would seem prudent to avoid those factors known to exacerbate pulmonary resistance including hypothermia, hypercarbia, acidosis, hypoxia, and α-adrenergic agonists. Although the last of those is commonly listed, it has seemed that in the context of pulmonary vascular disease due to a shunt lesion, systemic vasoconstrictive effect predominates and systemic oxygen saturation will increase.

Appropriate nerve blocks offer an attractive alternative to general anesthesia. If patients undergo general anesthesia, consideration should be given to returning them to an intensive care unit for gradual emergence and close observation. Because of the increased perioperative risk, patients should be observed at least overnight in an intensive care type of unit, particularly if they have not had any recent surgery or

anesthesia and their response will be unknown. Ambulatory surgery is possible, however, for patients having had uncomplicated minor surgical procedures with sedation or nerve block.

Pregnancy carries with it a very high mortality risk—30% of all pregnancies end in maternal death, and a successful first pregnancy does not preclude maternal death during a subsequent pregnancy.[69] The changes in hemodynamics of both pregnancy and delivery increase maternal risk. Pulmonary embolism (macro and micro) has caused peripartum deaths, and death can occur days after delivery. Women should be carefully monitored, with arterial catheters, during delivery. Epidural analgesia, delivered slowly and carefully, can mitigate many of the deleterious hemodynamic changes of active labor. There is a high incidence of premature deliveries. Pulmonary hypertension and pregnancy has been reviewed in detail.[70,71]

## Perioperative and anesthetic outcome

In a recent retrospective review from Texas Children's Hospital (TCH),[72] the anesthetic management and immediate outcome of adult and teenaged patients undergoing surgery for CHD were compared to lesion-matched control patients under 6 years of age. The primary outcome variable was death within 30 days of surgery, and secondary outcomes were major neurological morbidity, mechanical ventilation beyond 24 h postoperatively, and length of ICU and hospital stay.

Perioperative and outcome data from this review are presented in Table 13.4. All patients who experienced major neurological morbidity or perioperative mortality were in the older patient group, and all of those were undergoing repeat operations. Four patients died within 30 days of surgery, none in the operating room. No deaths or other major intraoperative events occurred in any patient undergoing a first-time operation, whether in the younger or older patient group.

The anesthetic agents used for both younger and older patients were very similar. Etomidate was used more frequently for induction of anesthesia in older patients, and sevoflurane was used more commonly in younger patients. All patients received a narcotic-based technique using fentanyl. Also there was no difference between groups regarding the use of single or multiple inotropic agents.

Fifty-nine percent of the older patients vs. 15% of younger patients required antiarrhythmic treatment, and greater numbers of older patients received lidocaine, amiodarone, and magnesium sulfate. Temporary cardiac pacing was used, and defibrillation performed more frequently in the older patients. Of the arrhythmias requiring treatment, 58% were ventricular in the adults compared to 24% in the control patients.

The only other published study regarding perioperative outcome of adults with CHD is from the Royal Brompton Hospital (RBH).[73] These authors report a slightly greater overall mortality, 6.8% compared to 4.7% in the TCH study. They also found reoperation to be a significant risk factor for early postoperative mortality, and that the number of previous operations correlated with increased mortality. Cyanosis and increasing age were also correlated with increased mortality. Compared to the TCH study, patients in the RBH study were significantly older, with a mean age of 31 years, and one-third of the non-survivors in the RBH study were over 50 years of age.

From these retrospective reviews, there appears to be an increased incidence of perioperative morbidity among older patients with CHD undergoing cardiac surgery, and certain groups of patients have the greatest risk, particularly the single ventricle patient. Because there is improved outcome from the Fontan procedure, the number of these patients requiring surgery in adulthood will increase in the future. In these patients, the transition from spontaneous to positive pressure ventilation will decrease pulmonary blood flow and cardiac output. Cardiac output is also significantly compromised by non-sinus rhythm, hypovolemia, or myocardial depressant anesthetics. The only patient requiring epinephrine after the induction of anesthesia in the TCH review was scheduled for a Fontan revision.

Another group of patients with greater risk of mortality or major morbidity are those with cyanosis, especially those requiring repeat sternotomy. These two factors were the best predictors of early mortality in the RBH study, and all deaths and major complications occurred among these patients in the TCH study. There are several reasons for this observation. First, longstanding cyanosis leads to increased risk for coagulopathy and organ dysfunction. Second, most of these patients had ventricular dysfunction, which renders the myocardium more vulnerable to the ischemic insult from cardiopulmonary bypass and aortic cross-clamping, thereby increasing the possibility of postoperative ventricular failure and arrhythmias.

## Anesthetic management

Based on the above data and our experience, we recommend the following management for adult patients undergoing congenital heart surgery:

*Preoperative preparations*:

1 Patient data should be presented to a multidisciplinary group consisting of cardiologists, surgeons, and anesthesiologists. Data analysis includes: laboratory results, cardiac catheterization, echocardiography, Holter monitor results, chest radiograph, and magnetic resonance imaging. Among this group of specialists a consensus can be developed regarding the timing of surgery and surgical options, which may include cardiac transplantation.

**Table 13.4** Perioperative patient data and outcome.

| | | Older patients | Control patients | *P*-value |
|---|---|---|---|---|
| Patient data | Number | 85 | 170 | |
| | Age (yrs) (mean ± SD) | 21.2 ± 10 | 2.0 ± 1.5 | < 0.001* |
| | Age range (yrs) | 13–71 | 0–5 | |
| | Weight (kg) (mean ± SD) | 61.6 ± 22 | 10.7 ± 4.6 | < 0.001* |
| | Reoperation (no. (%)) | 49 (58) | 51 (30) | < 0.001* |
| | Cyanosis (no. (%)) | 19 (22) | 90 (53) | < 0.001* |
| Surgery | Fontan or revision (no. (%)) | 14 (16) | 35 (21) | 0.536 |
| | Conduit change or placement (no. (%)) | 9 (11) | 15 (9) | 0.820 |
| | Valve repair/replacement (no. (%)) | 10 (12) | 18 (11) | 0.944 |
| | ASD/VSD repair (no. (%)) | 18 (21) | 34 (20) | 0.956 |
| | Complex repair (no. (%)) | 28 (33) | 63 (37) | 0.611 |
| | Other (no. (%)) | 6 (7) | 5 (3) | 0.321 |
| Intraoperative data (min) | Anesthesia time (mean ± SD) | 451 ± 149 | 383 ± 95 | < 0.001* |
| | Surgical time (mean ± SD) | 349 ± 139 | 290 ± 91 | < 0.001* |
| | CPB time (mean ± SD) | 159 ± 85 | 140 ± 63 | 0.065 |
| | Aortic cross-clamp time (mean ± SD) | 91 ± 51 | 84 ± 45 | 0.315 |
| Temperature outcome | Lowest temp on bypass (°C) (mean ± SD) | 27.9 ± 4.2 | 27.1 ± 3.8 | 0.135 |
| | Bleeding requiring transfusion (no. (%)) | 41 (48) | 90 (53) | 0.565 |
| | Dysrhythmia requiring treatment (no. (%)) | 43 (51) | 26 (15) | < 0.001* |
| | Inotropes (no. (%)) | 69 (81) | 149 (88) | 0.232 |
| | Vascular access problems (no. (%)) | 10 (12) | 53 (31) | 0.001 |
| | CPR (no. (%)) | 2 (2) | 0 | 0.210 |
| | ↓BP on induction requiring epinephrine (no. (%)) | 1 (1) | 0 | 0.420 |
| | Femoral bypass (no. (%)) | 2 (2) | 0 | 0.210 |
| | Massive hemorrhage (no. (%)) | 4 (5) | 0 | 0.021* |
| | IABP/VAD/ECMO (no. (%)) | 0 | 0 | 1.000 |
| | Postoperative ventilation > 24 h (no. (%)) | 17 (20) | 54 (32) | 0.068 |
| | Neurologic complication (no. (%)) | 3 (4) | 0 | 0.065 |
| | Intraoperative death (no. (%)) | 0 | 0 | 1.000 |
| | Postoperative death (no. (%)) | 4 (5) | 0 | 0.021* |
| Length of stay | ICU LOS (days) (mean ± SD) | 3.0 ± 3.0 | 4.0 ± 3.2 | 0.016* |
| | Hospital LOS (days) (mean ± SD) | 9.3 ± 25.2 | 9.2 ± 8.7 | 0.966 |

*$P < 0.05$ by *t*-test or chi-square. ASD, atrial septal defect; ↓BP, decreased blood pressure; CPB, cardiopulmonary bypass; CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; ICU, intensive care unit; LOS, length of stay; SD, standard deviation; VAD, ventricular assist device; VSD, ventricular septal defect. Reproduced with permission from Andropoulos DB, Stayer SA, Skjonsby BS *et al*. Anesthetic and perioperative outcome of teenagers and adults with congenital heart disease. *J Cardiothorac Vasc Anesth* 2002; **16**: 731–6.

2 The patient's cardiac rhythm should be assessed, particularly the functioning of pacemakers and underlying cardiac rhythm in case of pacemaker failure.
3 An anesthetic plan with the patient's unique pathophysiology and anticipated response to anesthetic interventions should be developed. This is particularly important for the single ventricle patient with poor ventricular function, who may be intolerant to myocardial depressants, positive pressure ventilation, or loss of sinus rhythm.

*General operating room care:*

1 Establish large bore intravenous access and provisions for rapid infusion of volume. A pressurized rapid infusion system capable of delivering at least 500 mL/min of warmed fluid or blood is recommended. In the case of massive bleeding, rapid infusion can be established utilizing the bypass machine. Tubing from the venous reservoir is passed through a roller pump head and connected to large bore venous access. The patient is heparinized, and large volumes can be transfused while preparations are made to rapidly institute bypass via the femoral route.
2 Multifunction external pacing, defibrillating, and cardioversion pads should be applied and antiarrhythmic drugs

immediately available. In pacemaker-dependent patients who have very slow or non-existent underlying ventricular escape rhythms, a preoperative transvenous pacemaker should be considered.

3 A preoperative discussion between the surgeon, anesthesiologists, and perfusionist should include plans for emergency femoral bypass if necessary.

4 Preparations should be made to treat postoperative hemorrhage. Tranexamic acid, ε-aminocaproic acid, and aprotinin are effective in reducing bleeding in these patients. Adequate blood products, including platelets, fresh frozen plasma, and cryoprecitipate should be available. Cell salvage, with reinfusion of washed autologous red blood cells, is appropriate.[74] Thromboelastography[75] during bypass, with heparinase and celite added to neutralize heparin and speed results, may be particularly useful to predict the need for blood products post-bypass, particularly in patients with baseline coagulopathy of cyanosis.

5 Transesophageal echocardiography is indicated for congenital heart surgery in infants and children; these guidelines are also applicable to adult congenital heart surgery.[76–78]

6 Neurologic monitoring with transcranial Doppler ultrasound (to assist in detecting and limiting cerebral emboli), bispectral index, and near-infrared spectroscopy may be helpful in minimizing neurological complications.[79]

## Conclusion

As the number of operations for adult CHD increases, these surgeries will be performed in a variety of institutions and systems. The optimal environment for performing congenital heart surgery on adult patients may be lacking in many situations. In our opinion, this type of surgery is best accomplished in a system designed for adults with CHD. Optimal care for these patients is provided by cardiologists trained and experienced in both pediatric and adult cardiology, by surgeons with training and experience with CHD, and by anesthesiologists with interest and experience in caring for the adult with CHD. Whatever the setting, the cardiac anesthesiologists performing these cases must be thoroughly aware of the anesthetic implications for the unique pathophysiology of each patient, and must not rely on their "usual" expectations of either true pediatric CHD or acquired adult heart disease.

## Summary of anesthetic issues for congenital heart lesions most commonly encountered in adults

*Atrial septal defect:*
- Primarily left-to-right shunt, but may have paradoxical emboli.
- Many patients with hemodynamically insignificant ASDs present after embolic stroke.
- Pulmonary vascular disease usually does not develop until 40 years of age.

*Ventricular septal defect:*
- Left-to-right shunt.
- Delayed closure may leave longstanding ventricular dysfunction or irreversible pulmonary hypertension.
- Increased incidence of aortic insufficiency (AI).

*Patent ductus arteriosus:*
- Longstanding left-to-right shunt.
- May develop end-stage pulmonary hypertension.
- Ductus may be calcified or aneuysrual when repaired in adulthood.

*Coarctation of the aorta:*
- Arterial monitoring in right arm.
- Primary repair in adulthood is associated with poor outcome.
- Revision of childhood repair common, either surgically or via cardiac catheterization.

*d-Transposition of the great arteries (D-TGA):*
- Atrial arrythmias and/or sick sinus syndrome after Mustard or Senning procedure.
- Progressive right ventricle failure or tricuspid insufficiency may develop after Mustard or Senning procedure:
  Tricuspid valve repair or replacement;
  Conversion to the arterial switch procedure may be indicated, usually preceded by pulmonary artery banding.

*Congenitally corrected transposition of the great arteries:*
- Arrhythmias (heart block) is common.
- Right (systemic) ventricular failure develops with increasing age.
- Double switch procedure places the left ventricle as the systemic pump.

*Ebstein's anomaly:*
- Adults may show congestive heart failure (CHF) or cyanosis depending on right ventricular output.
- Atrial arrythmias are common, and atrioventricular (AV) block is common after tricuspid replacement.

*Tetralogy of Fallot:*
- Primary repair can be performed in adults with good outcome.
- Reoperation most commonly needed for pulmonary insufficiency or conduit failure.
- Ventricular arrhythmias are common years after repair.

*Atrioventricular canal:*
- Most frequently associated with Down syndrome.
- Residual or progressive mitral regurgitation may necessitate surgery later in life.

*Truncus arteriosus:*
- Essentially all patients require repeat operations for right ventricle to pulmonary artery conduit revision.
- Some patients will require truncal (neo-aortic) valve repair or replacement.

*Single ventricle:*

- Variable anatomy (usually atresia of AV valve or semilunar valve) with mixing of systemic and pulmonary venous blood.
- Fontan procedure performed as staged surgical repair:
  Central venous pressure is the driving force for pulmonary blood flow;
  Positive pressure ventilation will increase intrathoracic pressure and decrease pulmonary blood flow, thereby decreasing cardiac output.
- Conversion of atriopulmonary Fontan to extracardiac Fontan has been performed in adults with improvement in cardiac function.

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# 4 Management

# 14 Hemodynamic management

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Jure Marijic

## Introduction

Congenital heart disease (CHD) encompasses a diverse group of diseases with dramatic differences between patients, even with the same or similar diagnoses. Because of these dramatic differences it is fair to say that each patient is unique and requires an individually tailored approach for optimal hemodynamic management. Before deciding on the medications or the interventions that you will employ to improve the hemodynamic status of these patients, one has to understand the anatomy and physiology of the congenital heart lesion as well as the comorbid conditions that may influence the choice of inotrope and vasoactive drugs that one will use. Hemodynamic management of patients is also impacted by long-term hemodynamic perturbations that arise as a result of disease itself or compensatory changes due to uncorrected lesions and the sequelae after surgical palliation or correction (Table 14.1).

## Pathophysiology of congenital cardiac lesions

Congenital heart disease includes a wide spectrum of lesions, however all CHDs include in part or in their entirety one or more of these four lesions: (i) obstructive lesions; (ii) regurgitant lesions; (iii) shunt lesions; (iv) mixing lesions.

**Table 14.1** Hemodynamic stigmata in congenital heart disease.

| |
|---|
| Pulmonary hypertension and pulmonary vascular disease |
| Valvular regurgitation or stenosis |
| Ventricular enlargement |
| Ventricular hypertrophy |
| Impaired diastolic and systolic ventricular function |
| Outflow tract obstruction |
| Polycythemia and hyperviscosity |
| Autonomic denervation in the transplanted heart |

It is important for the anesthesiologist to understand how the presence of one or a combination of these lesions impacts the hemodynamic management of a patient with CHD.

### Obstructive lesions

Obstructive lesions, whether they are on the right or left side, impose a pressure load on the chamber proximal to the obstruction, which over a period of time leads to chamber hypertrophy and/or enlargement. Increases in oxygen demands by the hypertrophied myocardium may eventually outstrip the coronary blood supply and cause myocardial ischemia. The primary derangement seen in right-sided obstructive lesions is reduction of pulmonary blood flow and possible hypoxemia. Left-sided obstructive lesions (coarctation of aorta, hypoplastic left heart syndrome) mainly present as decreased cardiac output (*CO*) and systemic perfusion. Hemodynamic management (Fig. 14.1) in patients with obstructive lesions requires knowledge of the degree of stenosis or obstruction in the vascular tree and the ability to keep the proximal pressure higher in order to overcome the resistance and maintain antegrade flow in the circulation. It is very important to distinguish between fixed and dynamic obstruction since the management of the obstruction caused by these two mechanisms is very different. The degree of dynamic obstruction (e.g. right ventricular outflow tract obstruction or hypertrophic cardiomyopathy) is dependent upon end-diastolic volume; increased preload, decreased heart rate (*HR*), and decreased contractility decrease the obstruction and gradient, increasing forward flow as well as decreasing myocardial work and oxygen consumption. Obstructive lesions frequently coexist with shunting or mixing lesions. Under these conditions the degree of obstruction will dramatically alter the shunt fraction and in some cases may even change the direction of the shunt. Changes in systemic and pulmonary vascular resistances (*PVR*s) will also affect pulmonary-to-systemic blood flow ratio ($Qp : Qs$) in such combined lesions.

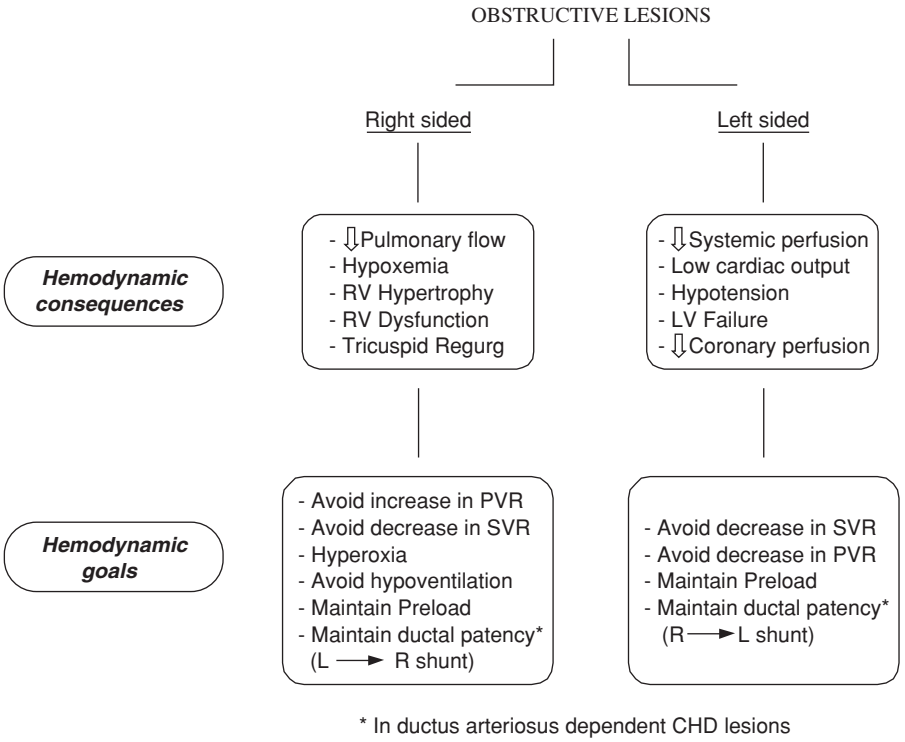


**Fig. 14.1** Hemodynamic consequences and goals for obstructive lesions. CHD, congenital heart disease; L, left; LV, left ventricle; *PVR*, pulmonary vascular resistance; R, right; RV, right ventricle; *SVR*, systemic vascular resistance.

## Regurgitant lesions

Valvular regurgitation can be seen as a primary congenital anomaly in certain congenital cardiac lesions (Ebstein's anomaly, atrioventricular [AV] canal defect, cleft mitral valve), but more commonly develops as a long-term sequelae of anatomical and physiological changes induced by pressure or volume loads that have been imposed by other associated lesions. The regurgitant fraction (portion of the total stroke volume) is dependent on preload (may change geometry of the ventricle and mitral valve), afterload (changes impedance to forward flow), and *HR* (through changes in ventricular end-diastolic volume, systolic and diastolic time). Appropriate management of the *HR*, preload, and afterload helps minimize the negative hemodynamic effect of valvular regurgitation (Fig. 14.2). Poor ventricular function results from volume loading associated with significant valvular regurgitation and alters the severity of regurgitation. This is especially true for AV valves since the ventricle is an integral part of valvular apparatus.

## Shunt lesions

Shunts can be intracardiac (atrial septal defect/ventricular septal defect) or extracardiac (patent ductus arteriosus) or surgically created (e.g. systemic-to-pulmonary artery shunt). Flow in a shunt is dependent upon the pressure gradient and relative vascular resistance in the vascular bed distal to the shunt. The degree to which each of these factors affects the amount and direction of shunting depends upon the size of the anatomical defect. In general, if the shunt size is large (non-restrictive), the pressure gradient across the defect will be small, and flow across the shunt will be affected more by the vascular resistance in the respective vascular beds and less dependent on the pressure gradient. The converse is also true when the anatomical size of the shunt is small (restrictive flow).

In the case of a left-to-right shunt, increasing the systemic vascular resistance (*SVR*) (systemic arterial pressures [*SAP*s]) or decreasing the *PVR* increases the amount of shunting leading to an excess of pulmonary blood flow (*Q*p) relative to systemic blood flow (*Q*s). This increased *Q*p *: Q*s ratio predisposes to pulmonary edema and development of pulmonary vascular disease. At the same time, systemic blood flow and oxygen supply delivery decrease. Hemodynamic management (Fig. 14.3) of patients with left-to-right shunting includes lowering of *SVR* and avoiding maneuvers that decrease *PVR* (hyperoxia, hypocarbia). In extreme cases one may need to increase the *PVR* above normal by either providing hypoxic inspired gas mixtures or by providing hypercapneic ventilation. Inotropes and vasodilators should be selected and used with these goals in mind. On the other hand, right-to-left shunts are optimally managed by lowering the *PVR* as well as avoiding decreases in *SVR*. Hyperventilation and higher concentrations of inspired oxygen have been used to lower *PVR* in patients with CHD to test the reactivity of *PVR* as well as for therapy. Other options include the use of selective pulmonary vasodilators

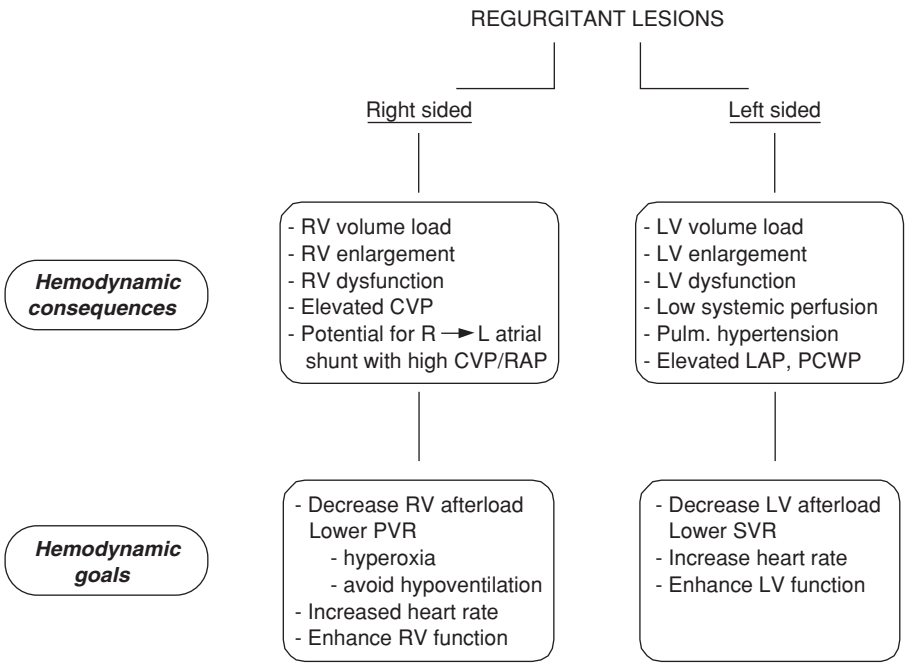


**Fig. 14.2** Hemodynamic consequences and goals for regurgitant lesions. CVP, central venous pressure; L, left; LAP, left atrial pressure; LV, left ventricle; PCWP, pulmonary capillary wedge pressure; *PVR*, pulmonary vascular resistance; R, right; RAP, right atrial pressure; RV, right ventricle; *SVR*, systemic vascular resistance.

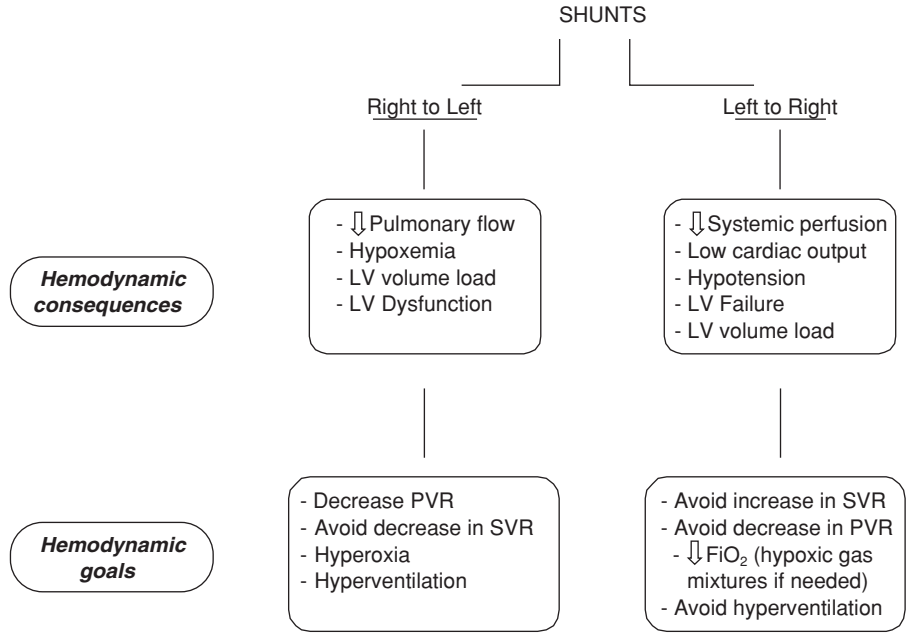


**Fig. 14.3** Hemodynamic consequences and goals for intracardiac and extracardiac shunting lesions. $Fio_2$, fraction of inspired oxygen; LV, left ventricle; *PVR*, pulmonary vascular resistance; *SVR*, systemic vascular resistance.

such as inhaled nitric oxide (iNO), prostacyclin, calcium channel blockers, and sildenafil.

## Mixing lesions

Congenital heart defects in which there is a complete mixing of oxygenated and deoxygenated blood in the cardiac chambers or the great vessels are termed mixing lesions (tricuspid atresia, univentricular hearts, truncus arteriosus, anomalies of pulmonary venous return). This complete mixing is due to the unrestricted flow of blood from right-sided structures to left and vice versa across a large communication between the two sides, leading to arterial hypoxemia of varying degrees. As in the case of large shunts, the flow of blood is significantly affected by the vascular resistance of pulmonary and systemic circulation (Fig. 14.4).

Complete mixing (as well as right-to-left intracardiac shunting) results in partially desaturated blood in the

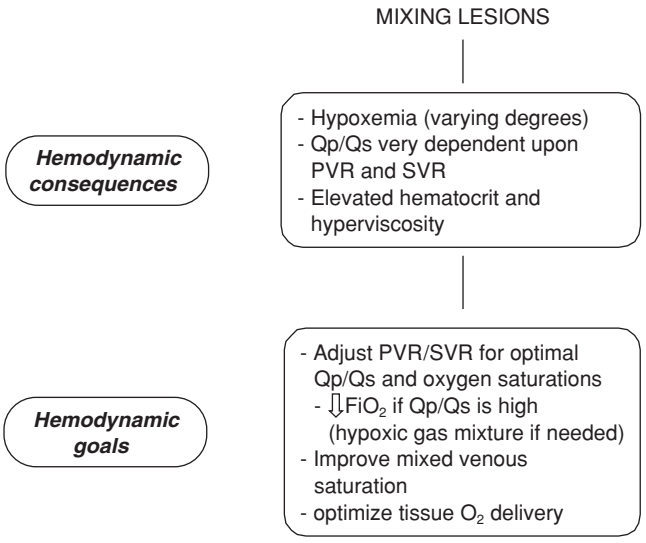


**Fig. 14.4** Hemodynamic consequences and goals for intracardiac mixing lesions. $Fio_2$, fraction of inspired oxygen; *PVR*, pulmonary vascular resistance; *Qp/Qs*, pulmonary to systemic blood flow ratio; *SVR*, systemic vascular resistance.

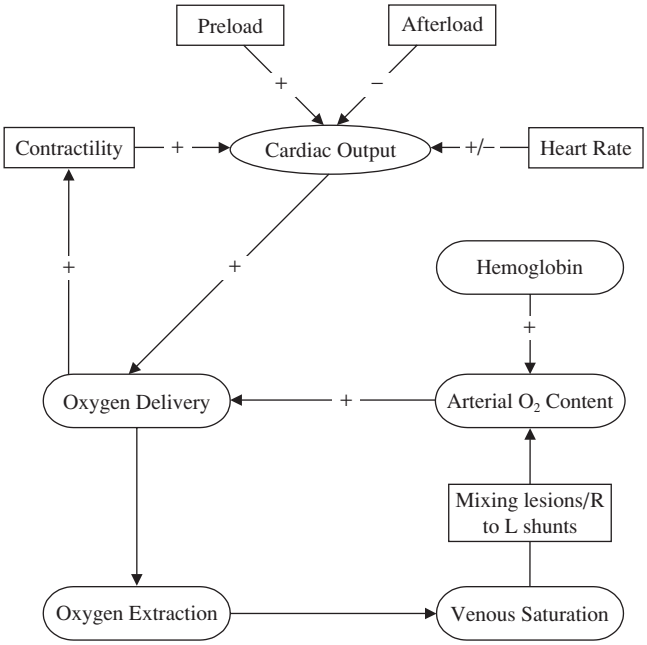


**Fig. 14.5** Determinants of cardiac output and oxygen delivery. L, left; R, right.

systemic circulation and, over a period of time, to compensatory changes in the oxygen carrying capacity of the blood (increased hemoglobin and red cell mass) and oxygen delivery to the tissues (increased 2,3-diphosphoglycerate [2,3-DPG] and fall in oxygen consumption). Potentially large increases in blood viscosity occurring as a result of elevation in serum hematocrit to 65–70% may compromise blood flow to vital organs and decrease oxygen delivery to the tissues rather than increase it.

## Determinants of cardiac output and oxygen delivery

Besides the unique factors discussed earlier that alter the hemodynamic management in patients with CHD, it is important to recognize that alterations of preload, afterload, contractility, and *HR* are the four cornerstones that affect *CO*, before and after surgical correction of congenital cardiac disease (Fig. 14.5). The oxygen carrying capacity of blood is improved by increasing the hemoglobin concentration. Each of these factors should be adjusted for the specific congenital cardiac lesion and the cardiovascular physiology that is associated with the lesion.

## Pharmacologic therapy for congenital heart disease

The goal of drug therapy in an acute setting should be to optimize *CO*; improve perfusion pressure to vital organs such as brain, heart, and kidneys; and maintain an optimal balance between systemic and pulmonary blood flows with an appropriate level of oxygenation.

The drugs that may be used in the acute hemodynamic management of patients can be categorized as belonging to one or more of these functional classes:

1. Inotropes (epinephrine, dopamine, dobutamine, milrinone, amrinone, calcium, digoxin).
2. Chronotropes (isoproterenol).
3. Vasoconstrictors (norepinephrine, phenylephrine, vasopressin).
4. Vasodilators (nitroglycerin, nitroprusside, prostaglandins, nitric oxide [NO], hydralazine, phentolamine, phenoxybenzamine).
5. Beta-adrenergic antagonists.
6. Newer cardiotonic and vasoactive agents.

These drugs will now be reviewed, and the pediatric cardiovascular anesthesiologist must keep in mind that the indications for and doses of these drugs in an individual patient are highly variable. Tables 14.2 and 14.3 summarize the effects and recommended dosages for these drugs. Factors such as age, disease state, and adrenergic receptor up or downregulation necessitate frequent titration of drugs to effect.

### Inotropes

#### Epinephrine

Epinephrine is an endogenous catecholamine that is secreted primarily by the adrenal glands and has strong α- and

**Table 14.2** Cardioactive and vasoactive drugs.

| Drug | Dose | Receptors | Inotropy | *HR* | *SVR* | *PVR* | Renal vascular resistance |
|---|---|---|---|---|---|---|---|
| Epinephrine | 0.02–0.20 μg/kg/min | | | | | | |
| | Lower dose | $\beta_1, \beta_2 > \alpha_1$ | ↑ | ↑ | ↔, ↓ | ↔, ↓ | ↓ |
| | Higher dose | $\alpha_1 > \beta_1, \beta_2$ | ↑ | ↑ | ↑ | ↑ | ↑ |
| Norepinephrine | 0.02–0.20 μg/kg/min | $\alpha_1 > \beta_1, \beta_2$ | ↑ | ↑ | ↑ | ↑ | ↓ |
| Dopamine | 2–5 μg/kg/min | $DA_1, DA_2$ | ↔ | ↔ | ↔ | ↔ | ↓ |
| | 5–10 μg/kg/min | $\beta_1, \beta_2 > \alpha_1$ | ↑ | ↑ | ↔, ↓ | ↔ | |
| | > 10 μg/kg/min | $\alpha_1 > \beta_1, \beta_2$ | ↑ | ↑ | ↑ | ↑ | ↑ |
| Dobutamine | 2–20 μg/kg/min | $\beta_1 > \beta_2, \alpha_1$ | ↑ | ↑ | ↓ | ↓ | ↔ |
| Isoproterenol | 0.01–0.2 μg/kg/min | $\beta_1, \beta_2$ | ↑ | ↑ | ↓ | ↓ | ↓ |
| Milrinone | Loading 25–50 μg/kg<br>Infusion 0.25–0.75 μg/kg/min | Phosphodiesterase III inhibitor/ ↑ cAMP | ↑ | ↑ | ↓ | ↓ | ↓ |
| Calcium chloride | 5–10 mg/kg/hr | Contractile proteins | ↑ | ↔, ↓ | ↑ | ↔, ↑ | ↔ |

cAMP, cyclic adenosine monophosphate; DA, dopamine; *HR*, heart rate; *PVR*, pulmonary vascular resistance; *SVR*, systemic vascular resistance.

**Table 14.3** Vasoactive drugs.

| Drug | Dose | Receptors | Inotropy | *HR* | *SVR* | *PVR* | Renal vascular resistance |
|---|---|---|---|---|---|---|---|
| Vasopressin | 0.0003–0.0020 U/kg/min | $V_1, V_2$ | ↔ | ↔, ↓ | ↑ | ↑ | ↑ |
| Phenylephrine | 0.02–0.30 μg/kg/min | $\alpha_1$ (agonist) | ↔ | ↓ | ↑ | ↑ | ↑ |
| Nitroglycerin | 0.2–10.0 μg/kg/min | Vascular myocyte/ guanylyl cyclase, cGMP ↑ | ↔ | ↔, ↑ | ↓ | ↓ | ↓ |
| Nitroprusside | 0.2–5.0 μg/kg/min | Vascular myocyte/ guanylyl cyclase, cGMP ↑ | ↔ | ↔, ↑ | ↓ | ↓ | ↓ |
| Phentolamine | 0.2–2.0 μg/kg/min | $\alpha_1$ (antagonist) | ↔ | ↔, ↑ | ↓ | ↓ | ↓ |
| Hydralazine | 1–5 μg/kg/min | Vascular myocyte | ↔ | ↔, ↑ | ↓ | ↓ | ↓ |
| Inhaled NO | 10–40 p.p.m. | Vascular myocyte/cGMP ↑ | ↔ | ↔ | ↔ | ↓ | ↔ |
| $PGE_1$ | 0.01–0.20 μg/kg/min | Vascular myocyte/cAMP ↑ | ↔ | ↔, ↑ | ↓ | ↓ | ↓ |

cAMP, cyclic adenosine monophosphate; cGMP, cyclic guanosine monophosphate; *HR*, heart rate; NO, nitric oxide; $PGE_1$, prostaglandin $E_1$; *PVR*, pulmonary vascular resistance; *SVR*, systemic vascular resistance; V, vasopressin.

β-adrenergic receptor activation. This action on both types of adrenergic receptors leads to the complexity of response in different organs and tissue beds. The response of exogenously administered epinephrine is to a large part dependent on the ratio of α- to β-receptors in the individual tissue beds as well as to the dose of epinephrine given (Fig. 14.6). At lower doses (< 0.05 μg/kg/minute), epinephrine causes a moderate increase in systolic blood pressure that is mainly due to the increased ventricular contraction.[1] Activation of the $\beta_2$-receptors in the vascular smooth muscles of the skeletal muscles usually leads to a drop in the *SVR* and slight decrease in the diastolic pressure. As the dose is progressively increased, more prominent peripheral vasoconstriction is seen due to the activation of the α-receptors in other vascular beds.[2] Renal blood flow is consistently decreased as vascular resistance in all segments of the renal vasculature increases.[3] Epinephrine has been used as a strong inotrope in the supporting the function of a failing myocardium.

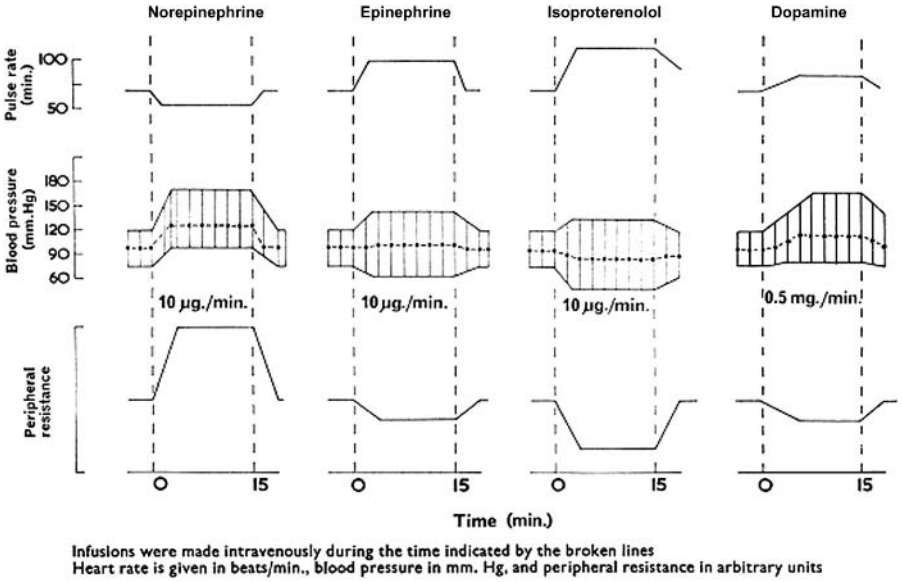


**Fig. 14.6** Effects of infusions of norepinephrine, epinephrine, isoproterenol, and dopamine in dogs. Reproduced with permission from Allwood M, Cobbold A, Ginsburg J. Peripheral vascular effects of noradrenaline, isopropylnoradrenaline and dopamine. *Br Med Bull* 1963; **19**: 132–6.

Epinephrine's action on the predominant $\beta_1$-receptors in the heart leads to an increase in contractility and an increase in the *HR*. Higher doses will lead to a decrease in the refractory period of the AV node and an increase in the automaticity of the myocardium, which may predispose to the development of atrial or ventricular arrhythmias.

During cardiopulmonary resuscitation (CPR), epinephrine is the vasopressor of choice since it has profound α-adrenergic stimulation that aids in maintaining the cerebral and coronary perfusion pressure in the face of cardiovascular collapse.[4] Survival after CPR in dog models (weight 20 kg) was markedly improved if the aortic diastolic pressure was at least 30–40 mmHg. The American Heart Association's (AHA's) recommendation of using 1 mg epinephrine in adults is based upon such dog studies. Subsequently, other studies suggested possible improved benefits of higher doses of epinephrine. This led to the recommendation by the AHA to the use of a higher epinephrine dose (5 mg) for subsequent and repeat dosing every 3–5 minutes. Benefits of the higher dose epinephrine have not been clearly demonstrated in the limited human CPR trials that have been conducted.

The AHA recommended dose of epinephrine in children for bradycardia, asystolic or pulseless arrest is 0.01 mg/kg i.v. Subsequent doses of epinephrine should be higher (0.1–0.2 mg/kg) and be given at 3–5 minute intervals.

Prolonged exposure of epinephrine and other catecholamine compounds to alkaline solutions (e.g. sodium bicarbonate) leads to the auto-oxidation and loss of their activity. Epinephrine should not be mixed with infusion bags or bottles that have alkaline solutions.

Epinephrine is used as an infusion primarily in the dose range from 0.02 to 0.2 μg/kg/minute, although doses up to 0.5 μg/kg/minute or higher are occasionally required in the short term for acute severe low *CO* in situations such as weaning from bypass, or during extracorporeal membrane oxygenation cannulation or emergency institution of bypass.

## Dopamine

Dopamine is another naturally occurring catecholamine that is an immediate precursor of norepinephrine. Most of the functions of endogenously excreted dopamine are as a central neurotransmitter, though it has been found in the peripheral circulation as well. The cardiovascular effects of exogenously administered dopamine are due to the activation of a variety of receptors that have different affinity for the drug.[5] At a lower dose (< 5 μg/kg/minute), the primary receptors that are activated are the dopaminergic-1 ($DA_1$) receptors present in the renal, mesenteric, and coronary vascular beds. Infusion of low dose dopamine can lead to an increase in renal blood flow and an increase in glomerular filtration rate (GFR).[6] Even though there are promising data in animals as well as in some uncontrolled human studies,[7] no prospective randomized controlled trial has evaluated the role of dopamine in improving acute renal failure, either alone or in combination with diuretics. It is therefore unclear if renal dose dopamine has direct beneficial effects in improving renal function. As the dose of the drug is increased, stimulation of the $\beta_1$-receptors in the myocardium leads to an increase in inotropy and chronotropy of the heart.[8] At these doses, dopamine causes an increase in *CO*, decrease in pulmonary capillary wedge pressure, and there is usually a decrease in *SVR* with only slight changes in blood pressure. The increase in *HR* is much less as compared to isoproterenol. Total peripheral resistance is usually unchanged with low or intermediate doses of dopamine, due to vasodilatory action of dopamine on regional vascular beds. At higher doses (> 10 μg/kg/minute), more $\alpha_1$-receptors are activated leading to

a more intense peripheral vasoconstriction and an increase in vascular resistance. Dopamine causes release of norepinephrine from nerve endings; this also adds to its pharmacologic effect of adrenergic stimulation.

In a study of dopamine pharmacokinetics in infants and children who were recovering from cardiac surgery or sepsis and had stable hemodynamics, the drug was reported to have a distribution half-life of 1.8 ± 1.1 minutes.[9] The volume of distribution (2952 ± 2332 mL/kg) and the clearance (454 ± 900 mL/kg/minute) were found to be highly variable, underscoring the principle of titrating this drug to effect in the individual patient. Dopamine in the dose range 5–15 μg/kg/minute is commonly used as an inotropic support to assist in the weaning of the heart from cardiopulmonary bypass.

### Dobutamine

A synthetic congener of dopamine, dobutamine's pharmacological actions are due to its activation of α- and β-adrenergic receptors. Dobutamine has not been shown to have any effect on the dopaminergic receptors or lead to the release of norepinephrine from nerve endings. The primary action of dobutamine is on the $\beta_1$-receptors with only a small action on the $\beta_2$- or $\alpha_1$-receptors. This action manifests as an increase in inotropy and chronotropy. *CO* is markedly enhanced and the left-sided filing pressures are decreased. Total peripheral resistance is unchanged or may be decreased with the use of dobutamine. This effect may be especially beneficial in treating patients with ventricular dysfunction.

There is little direct increase in renal blood flow as is seen with dopamine. Dobutamine has been shown to be effective in improving depressed cardiac index (*CI*) after cardiopulmonary bypass in children with CHD in doses ranging from 5 to 15 μg/kg/minute.[10] Comparison with newer inotropic drugs such as milrinone demonstrates similar improvements in stroke volume but a more profound decrease in left ventricular filling pressures and vascular resistance with the phosphodiesterase inhibitors.[11] Increased *HR* is more prominent with dobutamine than with milrinone. At equivalent inotropic doses dobutamine enhances the automaticity of the sinoatrial node to a much less extent than isoproterenol.[12] Higher doses of dobutamine (> 15 μg/kg/minute) can predispose to the development of atrial or ventricular arrhythmias.

The dose range of a dobutamine infusion ranges from 3 to 20 μg/kg/minute. Steady state levels were achieved in 10 minutes and the half-life was 2.37 minutes in a pharmacokinetic study in adult patients with heart failure.[13] Since almost all tissues metabolize dobutamine, dosage adjustment need not be performed even in patients with renal, hepatic, or any other organ dysfunction. Tolerance to long-term infusions (> 72 hours) may develop due to downregulation of β-receptors.[14]

### Milrinone

Milrinone is a bipyridine derivative that induces vasodilation and exerts a positive inotropic effect by blocking the phosphodiesterase III enzyme. The inhibition of phosphodiesterase leads to the accumulation of cyclic adenosine monophosphate (cAMP), independent of adrenergic receptor stimulation.[15] The increase in cAMP in cardiac myocytes improves systolic and diastolic function by altering calcium influx,[16] and by altering uptake and binding of calcium to myofilaments. Whereas in vascular smooth muscle, accumulation of cAMP predominantly affects the removal of calcium across sarcolemma and therefore vasodilation, the decrease in *SVR* allows phosphodiesterase inhibitors to increase *CO* and oxygen delivery without increasing myocardial work and oxygen demand. Because of the dual effects on the inotropic state of the heart and the vascular resistance, milrinone has been used extensively in the treatment of congestive heart failure (CHF), pulmonary hypertension, and postoperative low *CO*.

Milrinone has been shown to be an effective inotrope in adults as well as children with CHD.[17,18] Peripheral vasodilation also ensues as a result of vascular smooth muscle relaxation. Chang *et al*.[19] reported that milrinone (loading 50 μg/kg followed by an infusion of 0.5 μg/kg/minute), when administered to neonates with low *CO* after cardiac surgery, was able to lower filling pressures, systemic and *PVR*s (> 25%), and improve *CI* (cardiac index) from 2.1 to 3.1 L/minute/$m^2$. Similarly, Bailey *et al*.[20] found a mean increase in *CO* of 18% after milrinone therapy in 20 children undergoing corrective surgery for congenital cardiac defects. Milrinone also improves diastolic function. In adult patients undergoing CPB, administration of 0.5 μg/kg/minute milrinone decreased endotoxemia and other markers of inflammation, likely because of improved splanchnic perfusion. In the pediatric population, where hemodilution and activation of the inflammatory response during CPB is an even greater problem, the administration of phosphodiesterase inhibitors could potentially be of greater benefit. Hypotension and reflex tachycardia may result as a side effect of milrinone therapy. Thrombocytopenia is also seen as a side effect, though less common and less severe than with amrinone therapy.[21,22] Mehra *et al*.[21] reported a 4% incidence of thrombocytopenia in 71 patients who received long-term intravenous milrinone therapy (> 3 days). Milrinone is primarily renally excreted and higher bolus doses (50–75 μg/kg) may show prolonged hemodynamic effects in patients with impaired renal function. Serum half-life was found to be 0.8 hours in patients with CHF.[23] Milrinone has also been suggested to have a higher volume of distribution and a faster clearance in infants and children as compared to adults.[23] The dose recommended for milrinone therapy in patients with normal renal function is a bolus of 50 μg/kg followed by an infusion of 0.25–0.75 μg/kg/minute. Hypotension seen with a loading dose may

be avoided by reducing or eliminating the loading dose and simply beginning the infusion, recognizing that therapeutic plasma levels will not be achieved for several hours.

### Calcium

The calcium ion is an integral part of the excitation–contraction coupling and impulse generation in myocardial cells and is a major determinant of vascular smooth muscle tone. Administration of calcium in the form of calcium chloride or calcium gluconate helps improve the inotropic function of the heart in the presence of hypocalcemia (decreased serum ionized calcium levels).[24] Calcium functions primarily as a vasoconstrictor when the serum ionized calcium levels are normal. Routine administration of calcium salts upon termination of CPB is a subject of debate. The incidence of hypocalcemia during CPB is relatively high, but the ionized calcium levels usually are corrected to normal levels as weaning from CPB is attempted,[25] and therefore calcium administration may not be required for most patients. Moreover, increasing evidence suggests that elevated intracellular calcium levels are associated with cell death and injury during ischemia and reperfusion injury.[26] A recent study also suggests that no significant improvement in *CI* was observed in adult patients with good ventricular function upon administration of calcium chloride at the termination of CPB.[27] Murdoch *et al*.[28] reported an increase in the *SVR* index (885–1070 dyne · s · $cm^{-5}$ · $m^2$) and a decrease in *CI* (4.44–3.85 L/minute/$m^2$) after administration of 10 mg/kg of $CaCl_2$ in 12 children following cardiac surgery. Rapid administration of calcium can slow the *HR* transiently, and it should be used cautiously in patients who are taking digoxin as it may precipitate digoxin toxicity.

Calcium administration is not recommended in brady-asystoles unless severe hypocalcemia or hyperkalemia coexists or if the arrest is secondary to calcium channel antagonist drugs.[17]

A higher and more predictable amount of elemental calcium is available from the intravenous administration of calcium chloride than calcium gluconate or gluceptate.

### Digoxin

Digoxin continues to be one of the most commonly prescribed inotropic agents in children with CHD. Digoxin is mostly used for the chronic management of congestive failure and low *CO* state. Its use in acute hemodynamic settings is somewhat limited except in the management of certain arrhythmias (see Chapter 15). Digoxin increases contractility by inhibiting the $Na^+$–$K^+$ pump leading to an increase in intracellular $Na^+$. This stimulates $Ca^{2+}$ entry into the cell due to the activation of the $Na^+$–$Ca^+$ exchanger and myocardial contractility is enhanced in patients with CHF. Digoxin also causes parasympathetic activation that produces a decrease in *HR* and inhibition of AV conduction.[29]

## Chronotropes

### Isoproterenol

Isoproterenol is a potent non-selective β-adrenergic agonist with only very minimal actions on α-receptors. Due to its vasodilatory $\beta_2$ stimulatory actions as well as lack of α-receptor stimulation, isoproterenol leads to lowering of peripheral vascular resistance (see Fig. 14.6).[1,30] Its vasodilatory actions may be seen in renal, mesenteric and pulmonary vascular beds. Cardiac output is increased in patients with heart failure as a result of increased inotropy and chronotropy in the face of diminished *SVR*.[12] An intravenous infusion of isoproterenol has more chronotropic than inotropic effects as opposed to dopamine or dobutamine. Myocardial oxygen demands are greatly exacerbated by isoproterenol and this may exacerbate or induce ischemia.[31] Higher doses of isoproterenol can be arrhythmogenic and may induce ventricular tachycardia or fibrillation.

Isoproterenol has been shown to cause less hyperglycemia as compared to epinephrine, since insulin secretion is stimulated by the strong β-adrenergic stimulation. The drug has been shown to be effective in increasing the *HR* in patients with severe bradycardia or a heart block.[32] This chronotropic effect of isoproterenol remains the principal use of the drug. Isoproterenol is generally not used as a first line drug in the management of myocardial dysfunction or in the treatment of heart failure. The dose for isoproterenol infusion ranges from 0.01 to 0.2 μg/kg/minute.

## Vasoconstrictors

### Norepinephrine

Norepinephrine is an endogenous catecholamine that is primarily released by the postganglionic adrenergic nerve endings. Besides being a major source of epinephrine, the adrenal medulla also contains norepinephrine in a smaller fraction (10–20%).

The actions of norepinephrine on the heart are very similar to epinephrine, with strong stimulation of the $\beta_1$-receptors and increase in myocardial contractility.[3] There is a substantial difference in the peripheral action of the two drugs[1] and these differences account for the difference in the clinical use of these two drugs. Norepinephrine is a potent $\alpha_1$-agonist at all doses with minimal effects on the vasodilatory $\beta_2$-receptors.[1] As a result, even low doses of norepinephrine lead to an increase in the systolic and diastolic blood pressure. Systemic vascular resistance is increased as a result of the vasoconstriction of most peripheral vascular beds. Cardiac output is usually decreased or unchanged, depending upon the increase in total peripheral resistance. Heart rate may be slowed as a result of reflex increase in vagal tone, or may increase if the $\beta_1$ effects predominate in an individual patient.

Both of the endogenous catecholamines, epinephrine, and norepinephrine can lead to hyperglycemia with prolonged infusions.[33] Norepinephrine usually causes these effects at much higher doses than epinephrine.

Norepinephrine functions as a strong vasoconstrictor and is useful in the clinical situation of decreased *SVR*; however, it is used rarely in infants and children. The dose range of norepinephrine infusion varies from 0.02 to 0.20 μ/kg/minute.

### Phenylephrine

Phenylephrine is a pure peripheral $\alpha_1$-receptor agonist used as a bolus or infusion where low systemic blood pressure or *SVR* must be treated acutely. The pure α effects often result in reflex slowing of the *HR*, although this is not as pronounced in young infants. Its principal use in CHD is to acutely raise *SVR* when either ventricle is compromised by outflow obstruction, e.g. tetralogy of Fallot with low *SVR* leading to increased right-to-left intracardiac shunting and cyanosis during a "tet spell,"[34] and hypertrophic cardiomyopathy[35] or other left-sided lesions where the gradient across the obstruction is increased by low *SVR*. On CPB, small phenylephrine boluses can be used to increase perfusion pressure when other measures such as increasing bypass flow are ineffective, until *SVR* on bypass equilibrates with cooling, and viscosity changes from redistribution of red cells in the patient–bypass circuit. Infusions can be used when frequent boluses are necessary, such as in the tetralogy of Fallot patient with continuous spelling before bypass. Phenylephrine is very effective at increasing the blood pressure, but its principal adverse effect is vasoconstriction of peripheral tissue beds, including skeletal muscle, skin, renal, and mesenteric. This vasoconstriction may be intense, and theoretically may compromise end-organ blood flow and function, leading many practitioners to limit its use to extreme situations. Extravasation of phenylephrine into the skin and subcutaneous tissues may lead to ischemia, necrosis, and tissue loss.

Bolus dosing of phenylephrine is 0.5–5.0 μg/kg, and infusion dosing ranges from 0.02 to 0.30 μg/kg/minute, through a central venous catheter if possible.

### Vasopressin

Vasopressin is a neurogenic polypeptide produced by the paraventricular nucleus of the midbrain in response to low blood pressure and is secreted by the posterior lobe of the pituitary. Vasopressin produces intense vasoconstriction and an antidiuretic effect. Vasopressin exerts these effects via $V_1$-(vasoconstriction) and $V_2$-receptors (antidiuresis). In the past the most common use of vasopressin was to treat gastrointestinal bleeding. More recently vasopressin has been used as an alternative to epinephrine in acute resuscitation; however, the superiority of vasopressin over epinephrine for this indication is not clear. A theoretical advantage of vasopressin is that vasopressin does not rely on adrenergic receptors, which may be downregulated in chronically elevated catecholamine states. In conditions of metabolic acidosis signal transmission via adrenergic receptors is also ineffective. Some conditions producing low blood pressure (e.g. septic shock) were associated with low plasma vasopressin concentration, suggesting inappropriately low vasopressin secretion. In some of these patients, hypersensitivity to the administration of vasopressin has been described, possibly due to upregulation of vasopressin receptors, and is in agreement with studies showing rapid desensitization to vasopressin.[36]

Information about the use of vasopressin in the pediatric population is scarce. Rosenzweig *et al*.[37] reported their experience with use of vasopressin in moribund pediatric patients after cardiac surgery. These patients were classified as unresponsive to standard vasopressors, although in some of these patients a trial of epinephrine or dopamine was not attempted, and some of these 11 patients were clearly on extremely high doses of adrenergic stimulators. The dosage of vasopressin they used varied from 0.0003 to 0.0020 U/kg/minute. These doses of vasopressin produced an average increase in systolic blood pressure of 22 mmHg (65–87 mmHg). The authors measured plasma vasopressin levels in three patients before treatment and all of them had low levels of vasopressin. Patients who had low blood pressure and poor cardiac function before the initiation of vasopressin therapy died. Vasoconstrictor use is ill advised in the presence of a low *CO* state; therefore, we suggest one ensure good *CO* either by a clinical exam or a direct measurement before resorting to vasoconstrictors.

## Vasodilators

### Nitroglycerin

Nitroglycerin, like all other nitrates produces vasodilation by releasing NO. The release of NO from nitroglycerin, unlike that of some other NO donors is enzymatically mediated. Nitroglycerin is frequently referred to as a venodilator while sodium nitroprusside (SNP) is thought of as a preferential dilator of arteries, although these differences are difficult to demonstrate. The major indications for the use of nitroglycerin are myocardial ischemia, systemic hypertension, pulmonary hypertension, volume overload, CHF, and pulmonary edema. Venodilation associated with nitroglycerin therapy leads to a decrease in venous return. The decrease in preload leads to a lowering of the left ventricular end-diastolic volume and pressure, and therefore diminished wall stress. The net effect is usually an improvement in the ratio of myocardial oxygen demand to delivery. Nitroglycerin also dilates both diseased and normal coronary arteries.[38] Hypotension and reflex tachycardia are the potentially undesirable side effects. Nitroglycerin is used in cardiac surgical patients for the treatment of systemic or pulmonary

hypertension as well as to decrease filling pressure and improve *CI*. In a study including 20 pediatric patients with CHD, of whom 14 had preoperative pulmonary hypertension, nitroglycerin (> 2 μg/kg/minute) reduced both systemic and *PVR*.[39] Improved *CI* was seen only with higher doses. The authors suggest that the effect of the drug on the systemic and pulmonary arteries and on capacitance vessels is dose related. In lower doses (< 2 μg/kg/minute), nitroglycerin mainly produced venodilation, as evidenced by an increased requirement of volume to maintain a constant right and left atrial pressure.

Tolerance to the drug is known to occur after more than 24 hours of intravenous therapy. In patients who have been on a prolonged therapy, the drug infusion should be tapered slowly to avoid rebound hypertension. Methemoglobinemia and cyanide toxicity from the release of nitrite ions upon metabolism is an extremely rare side effect.[40]

The usual doses of intravenous nitroglycerin infusion are 0.5–5.0 μg/kg/minute.

### Sodium nitroprusside

The hypotensive properties of sodium nitroprusside (SNP) were described in the late 1800s, however the drug was not approved for clinical use until 1974. Frequently, nitroprusside is incorrectly referred to as a "direct, preferential arterial vasodilator." Nitroprusside dilates both arteries and veins by releasing NO in an interaction with tissue compounds containing sulfhydryl groups. The released NO activates soluble guanyl cyclase that increases cyclic guanosine monophosphate (cGMP). Nitroprusside is most commonly used to control blood pressure in hypertensive patients and decrease *SVR*, thereby improving forward flow in patients with poor left ventricle function or regurgitant lesions (mitral or aortic regurgitation). Because of its short half-life SNP allows precise control of blood pressure and *SVR*. In patients with diminished myocardial function, *CO* is increased from an increased stroke volume as a result of decreased aortic impedance. Despite significant reductions in *SVR*, the blood pressure drop is usually modest since an increase in *CO* compensates for the decrease in *SVR*. The drop in blood pressure is more dramatic in patients with pre-existing hypovolemia or obstructive cardiac lesions. In patients with hypertrophic cardiomyopathy SNP may increase outflow obstruction, and patients with aortic or mitral stenosis may not be able to compensate with an increase in *CO*, resulting in profound hypotension. Because of dilation of both pulmonary and systemic vasculature, SNP is of little value in patients with shunts and mixing lesions. Although frequently used in the pediatric population, the reported experience of use of SNP in neonates is limited. In one of those reports Benitz *et al*.[41] administered SNP (0.2–6.0 μg/kg/minute) to 58 neonates with various diagnoses including shock, respiratory distress syndrome and persistent pulmonary hypertension. Patients with respiratory distress syndrome had an increased $Pao_2$, decreased $Paco_2$ and peak inspiratory pressures, and 82% survived. Patients in shock showed signs of improved perfusion, increased urine output, and decreased acidosis. Response to SNP was suggested to be a good predictor of survival. Adverse effects were uncommon and there was no evidence of toxicity. The authors concluded that SNP is safe and effective in controlling these circulatory disorders in neonates.[41] One of the concerns in the administration of SNP during the neonatal period is the prevention of ductus arteriosus closure by SNP. In some congenital heart lesions survival of patients is dependent on the patency of the ductus. To our knowledge there are no human studies on the effect of SNP on ductal patency and flow; however, based on animal studies, SNP is a potent dilator of ductus arteriosus. Administration of nitroglycerin and SNP produced a greater increase in ductal blood flow (184% and 126% increase, respectively) as compared to a bolus of prostaglandin $E_1$ ($PGE_1$) (110%), in near-term lambs undergoing oxygen-stimulated ductal closure. With the potential problem of tachyphylaxis to nitroglycerin, SNP is a logical alternative to $PGE_1$ when attempting to maintain ductal patency.[42]

One of the dangers associated with the use of nitroprusside use is toxicity from the formation of cyanide. Cyanide, a byproduct of SNP metabolism, is taken up by red cells and inactivated predominantly in the liver by reacting with thiosulfate. This reaction is catalyzed by the enzyme rhodanase, and patients with liver failure are more susceptible to cyanide toxicity. If cyanide toxicity occurs, SNP should be stopped immediately and, after confirmation of diagnosis, the patient should be treated with 3% sodium nitrate followed by the administration of sodium thiosulfate. Sodium nitroprusside should be used cautiously in patients with renal failure since they may have difficulty metabolizing the thiocyanate produced during breakdown of SNP. In patients with increased intracranial pressure, SNP should be avoided since it increases cerebral blood flow, potentially increasing intracranial pressure.

The starting dose of SNP is 0.5–1.0 μg/kg/minute and the dose can be titrated up to 5 μg/kg/minute. The high doses pose greater risk for toxicity, so doses exceeding 3 μg/kg/minute should not be administered for longer than several hours and an alternative treatment should be sought.

### Prostaglandins

Prostaglandins such as $PGE_1$ and prostacyclin ($PGI_2$; epoprostenol) are the main metabolites of the arachidonic acid pathway. In the vascular tissues they are predominantly generated and subsequently released by the endothelium to bind to specific receptors on the underlying smooth muscle cells. This leads to the activation of adenylate cyclase and an increase in cAMP levels, which lowers intracellular $Ca^{2+}$ and produces vascular smooth muscle relaxation.

Prostaglandin $E_1$ is used to relax the smooth muscle and maintain the patency of the ductus arteriosus in neonates whose systemic or pulmonary circulation is dependent on ductal patency. Prostaglandin $E_1$, when administered to 27 neonates in whom pulmonary or systemic blood flow was entirely or significantly dependent upon ductal patency, led to an improvement in hypoxemia and acidemia, as well as ductus dilation.[43] It has been demonstrated to maintain ductal patency for as long as 2 months[44] and to reopen a recently closed ductus. Preoperative drug therapy with $PGE_1$ has lowered the mortality and allowed planned surgeries, rather than desperate attempts at emergency palliation, which was frequently the case in the past. Side effects of $PGE_1$ therapy occur in 20–40% of patients at higher doses (0.05–0.1 μg/kg/minute) but they are usually reversible upon lowering the dose or discontinuation of the drug. Hypotension, apnea, hyperpyrexia, and jitteriness are some of the adverse effects.

Besides management of neonatal CHD, $PGE_1$ has been used to treat pulmonary hypertension secondary to mitral valve disease,[45] after congenital cardiac surgery,[46] and after heart transplantation.[47] There has been only limited research conducted in the use of inhaled $PGE_1$.

Prostacyclin is a relatively recent addition to the drug therapy for the management of pulmonary vascular disease. Even though $PGI_2$ is probably the most selective pulmonary vasodilator of all the currently available intravenous drugs, administration of $PGI_2$ via this route will lower *SAP*. Prostacyclin is spontaneously hydrolyzed to 6-keto-prostaglandin $F_{1\alpha}$ with a half-life of 1–3 minutes. The relatively selective effect on lowering *PVR* is due to rapid inactivation in the pulmonary vasculature bed during a single circulation time. Intravenous infusions of $PGI_2$ have been shown to be useful in decreasing the *PVR* in patients with primary pulmonary hypertension, and after cardiac surgery in neonates.[48] Due to its short half-life, aerosolized $PGI_2$, like NO, can selectively dilate pulmonary vessels with minimal affects on the *SAP*. Several anecdotal reports and a few small clinical studies suggest that inhaled $PGI_2$ can reduce elevated pulmonary artery pressures (*PAP*s) and *PVR*. Schulze-Neick *et al*.[49] reported inhaled $PGI_2$ and NO to have similar advantageous effects on reducing *PVR* in patients with CHD after cardiac surgery. Another study demonstrated reduction of *PAP*s and improvement in the right ventricular function following inhaled $PGI_2$ therapy with bolus dosing (2.5, 5.0, 10.0 μg) in nine patients undergoing cardiac surgery including heart transplantation.[50] The optimal dosing of epoprostenol remains undefined and dosing of inhaled $PGI_2$ ranging from 1 to 50 ng/kg/minute have been shown to efficacious.[51–53]

### Sildenafil

Sildenafil is a phosphodiesterase-5 inhibitor that in its intravenous form appears to be a selective and highly effective pulmonary vasodilator in a piglet model of meconuim aspiration with severe pulmonary hypertension.[54] Sildenafil has been shown in case reports to ameliorate the effects of NO withdrawal in a patient after cardiac surgery with persistent pulmonary hypertension.[55] An ongoing multicenter study will address the question of its efficacy for primary treatment of postoperative pulmonary hypertension in a larger group of patients.

### Inhaled nitric oxide

A ubiquitous compound in the human body, NO is produced as a result of the conversion of the amino acid arginine to citrulline, a reaction that is facilitated by the enzyme nitric oxide synthase (NOS). Nitric oxide, being a very small and lipophilic molecule diffuses into the underlying smooth muscle cells producing an increase in intracellular cGMP levels and subsequent vasodilation.[56] Nitric oxide, when delivered via the inhaled route, readily crosses the alveolar–capillary membrane leading to pulmonary vasodilation and a decrease in *PVR*. High affinity binding and immediate inactivation of iNO activity by hemoglobin limits the action of the drug to the pulmonary circulation. Inhaled NO therapy has been shown to be useful in the treatment of pulmonary hypertension, which is frequently seen in CHD.[57,58] Pulmonary hypertension in patients with CHD is multifactorial, due to chronic hypoxemia or due to chronic elevation of pulmonary blood flow and/or pulmonary venous pressures. Pulmonary vascular resistance is also increased immediately after cardiopulmonary bypass due to endothelial dysfunction. Inhaled NO is ideally suited in selectively reducing *PVR* in this critical period. Miller *et al*.[58] reported a lowering of *PVR* (37%), while increasing *CO* by 14% using low doses of iNO in CHD patients who had high *PVR* (*PAP*/*SAP* > 0.5, mean *PAP* > 37 mmHg) shortly after their surgery. Left atrial pressure (LAP), *SVR* and *SAP* remained unaffected. Patients with low postoperative *PVR* did not show any hemodynamic effect in response to iNO. The pulmonary vascular selectivity of iNO may be especially useful in reducing the right ventricular afterload in patients undergoing heart transplant, where the donor hearts may not be accustomed to the high *PVR* usually seen in these patients.[59] Several investigators have reported the use of iNO in the preoperative period as a test of reversibility of *PVR* and in predicting post-CPB pulmonary hypertension, as well as using the preoperative evaluation to predict the use of the drug in the immediate post-CPB period.[51,60–62] In a study of 20 patients with ventricular septal defects and/or atrial septal defects, Winberg *et al*.[62] reported the lowering of *PAP* from 50 to 38 mmHg and a decrease in *PVR* by 34% after administration of 40 p.p.m. iNO in patients with elevated *PVR* at the time of preoperative cardiac catheterization. Systemic pressures remained unchanged.

Others have reported the benefit of iNO in improving oxygenation, likely by improving pulmonary blood flow and

ventilation–perfusion balance in congenital cardiac surgery patients.[56,63] Even though iNO has been shown to be effective in a variety of congenital heart lesions, it may not be helpful in reducing *PVR* in all patients. The non-responders are usually those who have longstanding pulmonary hypertension and extensive remodeling of the pulmonary vasculature. It also has not been shown to improve outcome, the cost is prohibitive at several thousand dollars per day of use, the delivery system setup is complex, as is transport with NO, and there are toxicity issues (see below). All of these issues suggest that NO should only be used as a last resort in a patient with known or suspected severe pulmonary hypertension resulting in low *CO* (in two ventricle patients), or severe desaturation in single ventricle patients after systemic arterial or venous to pulmonary artery shunts.

Nitric oxide can be administered using a face mask in a spontaneously ventilating patient, or added to the inspiratory limb of the breathing circuit in a mechanically ventilated patient. The most commonly used dose range is 20–40 p.p.m., though a decrease in *PVR* has been demonstrated with doses as low as 2–5 p.p.m. Side effects of iNO at these doses are minimal, even with prolonged therapy.

Abrupt withdrawal of NO or rapid reductions in drug dosage may lead to rebound pulmonary hypertension.[64] The binding of NO to hemoglobin gives rise to methemoglobin,[65] and methemoglobin levels should be routinely monitored especially with prolonged therapy.

Nitrogen dioxide is also formed as a byproduct of NO administration, and its levels should be maintained below 5 p.p.m. Nitrogen dioxide in high concentrations can lead to injury of the lungs.[52]

### Hydralazine

Hydralazine, a direct vasodilator, has long been used in oral form for treatment of hypertension and CHF. The combination of hydralazine and nitrates was one of the first drug combinations shown to be effective in decreasing symptoms and in improving survival in patients with CHF. These authors could find no studies of hydralazine for acute therapy of hypertension in children, and most studies were performed in the 1980s in adults following valve surgery. Hydralazine is a predominant arterial dilator with little effect on preload. The 0.1–0.5 mg/kg bolus dose of intravenous hydralazine produces a 25% reduction of *SVR* that returned to baseline after 2 hours. A bolus of 0.1 mg/kg followed by an infusion of 1.5 μg/kg/minute produced a stable decrease in the *SVR* and an increase in *CO*. In a few patients the infusion dose had to be increased to as much as 5.0 μg/kg/minute. It has been reported that hydralazine has a favorable effect on coronary flow and resistance,[53] which in combination with decreased wall stress and oxygen consumption produces favorable effects on myocardial energy state.

### Phentolamine

Phentolamine binds reversibly to and blocks the α-receptors, and several groups have demonstrated the beneficial effects of phentolamine on reducing *SVR* as a result of its strong vasodilating properties. In one study of patients undergoing cardiac surgery, administration of 0.2 mg/kg of phentolamine during cooling and rewarming periods reduced plasma lactate levels, indicating better tissue perfusion. In addition, the nasopharyngeal–rectal temperature difference was fourfold higher in the control group, while systemic oxygen consumption was higher and blood pressure was lower in the phentolamine group ($59 \pm 6$ vs. $63 \pm 7$ mmHg).[66] The superiority of one vasodilator over another has not been demonstrated in cardiac surgery, but because one of the most important reasons for the increase in *SVR* during and after CPB is an elevation in plasma catecholamines, administration of an α-adrenergic blocker seems logical.

Another potential use of phentolamine is in the treatment of extravasation of vasoconstrictors like phenylephrine, norepinephrine, or epinephrine. Local infiltration of 0.5–1.0% phentolamine is recommended for this use.

### Phenoxybenzamine

Phenoxybenzamine is an irreversible $\alpha_1$ and $\alpha_2$ -receptor blocker that is advocated by some groups for routine perioperative management in infants undergoing cardiac surgery with the use of hypothermic cardiopulmonary bypass. The advantage of phenoxybenzamine over other vasodilators is its irreversibility and unparalleled potency to dilate peripheral vasculature and shift blood from pulmonary to systemic circulation (decreased $Q$p : $Q$s ratio) leading to an increase in *CO* and oxygen delivery. Phenoxybenzamine was first advocated by the Cleveland Clinic group and then adopted and prospectively studied by Tweddell *et al*.[67] in Milwaukee for patients undergoing the Norwood operation. They administered 0.25 mg/kg phenoxybenzamine at the start of cardiopulmonary bypass. In patients that did not reach target oxygen delivery ($Svo_2 > 50\%$) and target $Q$p : $Q$s (0.8–1.2), an infusion of 0.25 mg/kg/24 hours phenoxybenzamine was administered for up to 48 hours. They concluded that phenoxybenzamine improves systemic oxygen delivery in the early postoperative period when compared to standard hemodynamic management.[67]

## Beta-adrenergic antagonists

Beta-blockers, like digoxin and angiotensin-converting enzyme (ACE) inhibitors, are more beneficial in the management of chronic heart failure where they have been shown to improve the functional status in both pediatric and adult CHD.[68,69] This effect is due to the modulation of the endogenous neurohumoral system. Several studies have demonstrated

the downregulation of β-adrenoceptors in chronic heart failure as a result of elevated sympathetic tone.[70,71] Therapy with β-blockers such as propranolol, metoprolol, and carvedilol increase the number of myocardial β-adrenoceptors and improve myocardial function in heart failure secondary to CHD.[72,73] Responsiveness to catecholmines may be preserved in these patients during the perioperative period as a result of β-blocker therapy. Besides their use in the management of chronic heart failure, these medications have several uses in the acute hemodynamic management of patients with CHD. By reducing the effects of increased sympathetic tone on the right ventricular infundibulum in tetralogy of Fallot, β-blockers are effective in the treatment of cyanotic spells.[74] Also, a decrease in *HR* allows for a longer diastolic filling time and improved preload. The use of esmolol, a short acting $\beta_1$-selective antagonist, is well suited for the hemodynamic management of tetralogy of Fallot (TOF) in the perioperative setting.[75] Esmolol in doses of 100–700 μg/kg/minute has also been successfully used to control postoperative hypertension after repair of aortic coarctation in children.[76]

## Newer cardiotonic and vasoactive agents

Currently, there exists limited scientific literature regarding the use of some new vasoactive drugs in patients with CHD, though a few of them have been well researched in other patient groups. A brief description of some of these newer agents is as follows.

### Levosimendan

Levosimendan is a positive inotrope and vasodilator. Most other positive inotropes work through stimulation of adrenergic receptors and increase intracellular calcium that may be already elevated in the failing heart. Unlike these drugs, levosimendan works by causing conformational changes in the myofilaments making them more sensitive to intracellular calcium. The vasodilation produced is mediated by the opening of potassium channels. Although the drug is not approved for routine clinical use in the USA, there are extensive clinical studies involving large number of patients with end-stage cardiac failure demonstrating that levosimendan is both safe and effective in providing symptomatic relief. Unlike other intravenous inotropic agents that usually have neutral or negative effects on survival, levosimendan improves survival. Levosimendan was also more effective in decreasing pulmonary artery wedge pressure and increasing *CO*.[77] Experience with the use of levosimendan in the perioperative period is limited. In a prospective randomized placebo-controlled trial in patients undergoing cardiac surgery, levosimendan given before separation from CPB enhanced cardiac performance, decreased *SVR*, increased myocardial oxygen consumption, and significantly decreased blood pressure, occasionally leading to hypotension.[78] The hypotension was responsive to volume administration and did not require vasoconstrictors.

### Nesiritide (B-type natriuretic peptide)

Nesiritide is a human recombinant form of B-type natriuretic peptide (BNP) that is identical to and has actions that are similar to the endogenous BNP. Human BNP stimulates increases in intracellular cGMP in the vascular endothelial cells and smooth muscles. Elevated cGMP levels with nesiritide therapy lead to venodilation and arteriodilation. Nesiritide has natriuretic, diuretic and vasodilatory properties. Currently, the primary use of nesiritide is in the treatment of acute decompensated heart failure. It produces dose dependent reductions in the pulmonary capillary wedge pressure and *SAP* in patients with heart failure. In addition, vasodilation occurs without a change in *HR* and is associated with increases in stroke volume and *CO*. In a randomized controlled trial involving 489 subjects, nesiritide when given as a bolus dose of 2 μg/kg and followed by an infusion at 0.01–0.03 μg/kg/minute, was more effective in lowering the pulmonary capillary wedge pressure as compared to nitroglycerin.[79] In another randomized controlled trial that included 103 patients with heart failure and systolic dysfunction, nesiritide was reported to decrease the pulmonary capillary wedge pressure by up to 39% as well as lower the right atrial pressure and *SVR*, along with a significant improvement in the *CI*.[80] Colucci *et al*.[81] reported that nesiritide was effective as the standard drug therapy (dobutamine, milrinone, dopamine, or nitroglycerin) in treating heart failure. The renal hemodynamic effects of nesiritide appear to be that of arteriolar vasoconstriction, which would likely augment the glomerular filtration rate and filtration fraction in the setting of compromised renal perfusion. Additionally, BNP leads to an increase in both urinary sodium excretion as well as fractional excretion of sodium (FENA).[82] A mild diuretic effect of nesiritide therapy has been reported in a few clinical trials.[82,83]

### Fenoldopam

Fenoldopam is a selective dopamine-1 receptor agonist with moderate affinity for $\alpha_2$-receptors. Despite its binding to $\alpha_2$-receptors, fenoldopam has no significant sedative effect. Fenoldopam can be given intravenously as an infusion or administered parenterally. Fenoldopam administration produces dramatic vasodilation of the peripheral vasculature including renal, mesenteric coronary, and skeletal muscle. The main indication for the use of fenoldopam is in the treatment of hypertensive emergencies and postoperative hypertension.[84,85] The theoretical advantage of use of fenoldopam is that it maintains renal perfusion while decreasing blood pressure. This is especially important in patients with decreased renal function, since in these patients a rapid drop

in blood pressure may lead to decreased renal blood flow, glomerular filtration rate, and even acute renal insufficiency. In one retrospective case series, Tobias[86] reports use of fenoldopam for controlled hypotension during posterior spinal fusion in children and adolescents (8–14 years old). The target mean arterial pressure of 50–65 mmHg was reached in an average of 7 minutes. The starting infusion rate in this report was 0.3–0.5 μg/kg/minute and target blood pressure was achieved with infusions of 0.2–2.5 μg/kg/minute (mean 1.0 ± 0.3 μg/kg/minute). The infusion of fenoldopam was associated with significant increase in *HR* (87–114 b.p.m.), most likely due to reflex response to hypotension along with a small but significant decrease in $P_{O_2}$ suggestive of increased shunting due pulmonary vasodilation. During prolonged infusion of fenoldopam there is development of tolerance with a half-life (predicted loss of 50% effectiveness of the drug) of 60 h, without a prolonged pharmacodynamic effect or rebound hypertension upon discontinuation of fenoldopam. Infusion of fenoldopam in healthy, normotensive awake individuals produced a decrease in global and regional blood flow. The decrease in cerebral blood flow was not due to decrease in cerebral blood pressure since normalization of blood pressure with concurrent infusion of phenylephrine failed to restore blood flow. Tobias *et al*. postulated that the decrease in cerebral blood flow was mediated by fenoldopam's $\alpha_2$-agonist activity. It remains unclear if the reduction of cerebral blood flow may have negative consequences in patients during intraoperative controlled hypotension or in the treatment of hypertensive emergencies where brain ischemia is a real concern.

### Dopexamine

Dopexamine is a derivative of dopamine and is an agonist at the $DA_1$-, $DA_2$- and $\beta_2$-receptors. Dopexamine hydrochloride has interesting vasodilator properties, with marked intrinsic agonist activity at $\beta_2$-adrenoreceptors and a lesser agonist activity at dopaminergic receptors ($DA_1$ and $DA_2$). Its mild inotropic activity arises primarily from baroreceptor reflex stimulation with a possible contribution from direct stimulation of myocardial $\beta_2$-adrenoreceptors. Dopexamine is responsible for an inhibition of neuronal reuptake of catecholamines, producing an indirect stimulation of cardiac $\beta_1$-receptors. This catecholamine has no effect at $\alpha_1$- and $\alpha_2$-adrenoreceptors, and only very weak and clinically insignificant $\beta_1$-adrenoreceptor agonist activity. Dopexamine improves cardiac performance by a marked vasodilation and a mild inotropic activity. The specific activity at dopaminergic receptors increases cerebral, myocardial, splanchnic, and renal blood flows. These hemodynamic effects are associated with an increase in diuresis and natriuresis. In a study of 70 post-coronary artery bypass graft (CABG) surgery patients with a *CI* less than 2.2, who were randomized to receive dopamine (up to 6 μg/kg/minute) or dopexamine (up to 2 μg/kg/minute), dopexamine was found to be effective in improving the low *CO* state and maintaining urine output greater than 0.5 mL/kg/hour.[87] The authors suggest that treatment with dopexamine was better as compared to dopamine since the hemodynamic improvements were achieved faster along with fewer side effects (arrhythmias) in the dopexamine group. In another study, the investigators reported that the beneficial hemodynamic effects (increased *CI*, lowering of *SVR*) were well maintained during the extended infusion period up to 36 hours at a mean dopexamine dose of 2.8 μg/kg/minute in 20 patients who had undergone cardiac surgery.[88] No tachyphylaxis was observed.

## Conclusion

The choice of a therapeutic drug in patients with CHD should be made after careful consideration of the alteration in hemodynamics that may occur as a result of the drugs' pharmacological effects. This requires an understanding of the anatomy and associated physiology of the various congenital heart lesions. The anesthesiologist must also consider the adequacy of each of the determinants of *CO*, including *HR*, preload, afterload, and contractility. Clinical management should be based upon the risks and benefits of the various therapies.

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# 15 Dysrhythmias: Diagnosis and management

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## Introduction

The practice of pediatric cardiac anesthesia has evolved significantly over the years, expanding beyond the operating room environment to many non-surgical locations. It is likely that anesthetic care will be provided for patients with cardiac rhythm disturbances in a variety of settings (operating rooms, intensive care units, treatment rooms, emergency facilities, cardiac catheterization/electrophysiology laboratories). Basic knowledge of dysrhythmia diagnosis and management is essential when caring for patients in any of these settings. This chapter provides a practical approach to pediatric cardiac dysrhythmias with discussions centered on diagnosis, mechanisms, and acute management strategies. A review of antiarrhythmic drug therapy in children is presented as well as the basic principles of cardiac pacing as applicable to the practice of this specialty.

## Cardiac rhythm disturbances

### Sinus bradycardia

Slow heart rates can be observed during sleep or at times of high vagal tone. When there is significant sinus bradycardia, a slow junctional escape rhythm or a slow atrial rhythm with an ectopic P wave focus may be present. Certain forms of congenital heart disease (CHD) may be more prone to slow heart rhythms. Patients with visceral heterotaxy (malpositioning of the abdominal organs) and polysplenia syndromes may be included in this category due to absence, displacement or hypoplasia of a true sinus node.[1] The sinus node is a right-sided structure and this condition is characterized by bilateral left sidedness.

In the intraoperative setting, particularly upon induction of anesthesia, with laryngoscopy, endotracheal intubation or tracheal suctioning, sinus bradycardia may occur. Sinus bradycardia may also be related to drug administration (i.e. opioids) or increased parasympathetic activity. This type of sinus bradycardia rarely poses a significant hemodynamic problem and, if so, can be easily treated with removal of the stimulus or chronotropic agents such as atropine or epinephrine (Table 15.1). In the postoperative setting, slow sinus rates may be associated with surgical interventions such as atrial septal defect repair (sinus venosus type) and cardiac transplantation. Sinus bradycardia can also be secondary to hypoxemia, hypothermia, drugs, acidosis, electrolyte abnormalities, or increased intracranial pressure. Bradycardia related to hypoxemia should be treated promptly with supplemental oxygen and appropriate airway management. The approach to other forms of secondary sinus bradycardia should focus on addressing the underlying cause. For worrisome low rates, particularly in small infants, or clinical evidence of low cardiac output, pharmacologic therapy (isoproterenol infusion) or temporary pacing should be considered.

### Sinus node dysfunction

Sinus node dysfunction, sometimes termed sick sinus syndrome, encompasses a spectrum of disorders characterized by slow or irregular heart rates with a variety of escape rhythms alternating with periods of tachycardia. The tachycardia may be atrial tachycardia, atrial flutter, or atrial fibrillation. The term tachycardia–bradycardia syndrome is frequently used to characterize this association. Surgical interventions most likely to be associated with sinus node dysfunction include extensive atrial baffling procedures, such as Mustard or Senning operations, and the Fontan procedure. Management of symptomatic patients may include pacemaker implantation, drug therapy for tachydysrhythmias, atrial antitachycardia pacing, and in some cases radiofrequency ablation (transcatheter or surgical).

### Sinus tachycardia

Sinus tachycardia is more commonly seen in the perioperative

**Table 15.1** Acute therapy of bradycardia.

*Treat primary causes:*
Hypoxemia, hypothermia, acidosis, hypotension, anemia, hypoglycemia, hypothyroidism

*Consider causative drugs:*
Opioids, β-blockers, digoxin

*Drug therapy:*

| Drug | Dosage |
|---|---|
| Atropine | 0.02–0.04 mg/kg i.v. (minimum dose 0.1 mg; maximum dose 1–2 mg) |
| Epinephrine | 10–100 μg/kg i.v. bolus (lower dose may also be effective)<br>Infusion: Start at 0.05 μg/kg/min, titrate to effect up to 2.0 μg/kg/min |
| Isoproterenol | Infusion: 0.01–2.00 μg/kg/min |

*Temporary atrial pacing:*
Transcutaneous, esophageal, transvenous, epicardial

period than sinus bradycardia. It is often the result of stress or painful stimuli, hypovolemia, anemia, fever, medications (i.e. inotropic agents), a high catecholamine state or fluid in the pericardial sac. Treatment is directed at the underlying cause. Prolonged periods of sinus tachycardia may impair diastolic filling time, limit ventricular preload, and compromise systemic output (decreased urine output, poor peripheral perfusion, metabolic acidosis). Patient groups at higher risk of hemodynamic compromise are those with significant degrees of ventricular hypertrophy or non-compliant ("stiff") ventricles and associated diastolic dysfunction and those with certain types of cardiomyopathies.

### Junctional rhythm

A junctional rhythm is characterized by QRS complexes of morphology similar to those of sinus rhythms without preceding P waves. This may be an escape rhythm in the context of sinus bradycardia, or when the faster sinus impulses fail. Junctional rhythm is thought to originate in the His bundle rather than the atrioventricular (AV) node. Atrioventricular dissociation may be present as the faster escape junctional beats and slower atrial impulses are discharged. When this rhythm completely takes over the pacemaker activity of the heart, retrograde P waves may be seen. In the intraoperative setting this is a fairly common rhythm resulting from cardiac manipulation and dissection around the right atrium. In addition to the electrocardiographic (ECG) findings described above, the invasive pressure tracings may display waveform changes. The central venous pressure contour may demonstrate prominent v waves (right atrial pressure wave at the end of systole) due to the loss of AV synchrony (Fig. 15.1). An associated decrease in cardiac output may manifest as a reduction in systemic arterial blood pressure as a result of the lack of normal atrial systolic contribution to ventricular filling.

## Conduction disorders

### Bundle branch block

In the unoperated patient, bundle branch block is an uncommon ECG finding, although incomplete right bundle branch may be seen in patients with right ventricular volume overload (atrial septal defects, anomalous pulmonary venous return, etc.). In the postoperative patient, a right bundle branch pattern is a frequent finding after surgical procedures for various congenital heart defects including tetralogy of Fallot, right ventricular outflow tract reconstructions, ventricular septal defect, and AV septal defect (AV canal or endocardial cushion defect). The bundle branch block pattern may be related to the ventriculotomy incision, damage to the moderator band, the ventricular septal defect repair, or resection of infundibular muscle. Left bundle branch block patterns are uncommon but can be seen in some patients following surgery involving the subaortic region.

## Atrioventricular block

### First-degree atrioventricular block

First-degree AV block is characterized by prolongation of the PR interval beyond the normal for age. Each P wave is followed by a conducted QRS complex. This can be a normal variant in healthy individuals but can also been seen in various disease states (e.g. rheumatic fever, structural heart

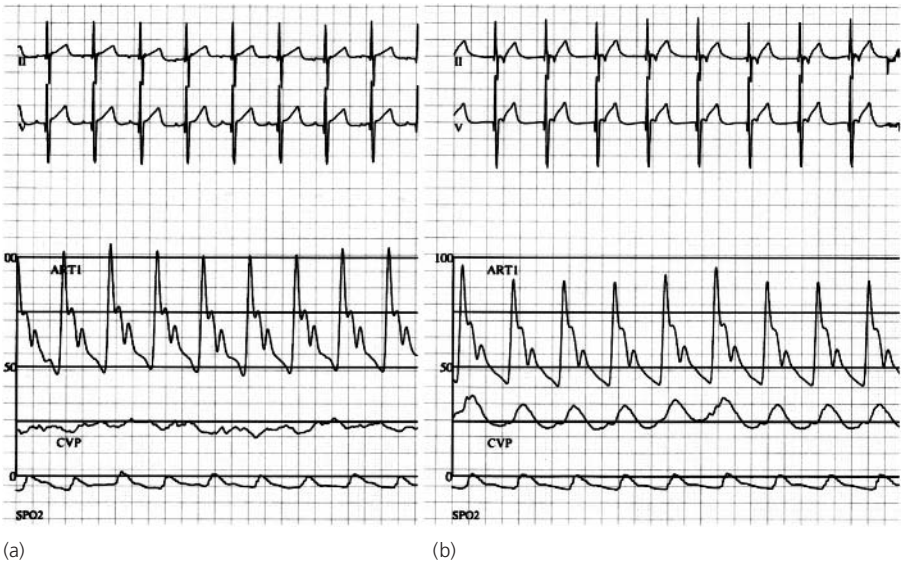


**Fig. 15.1** (a) Normal sinus rhythm. The normal atrioventricular activation sequence is shown in this intraoperative recording (P wave precedes each QRS complex). Baseline hemodynamic and oxygen saturation tracings are shown. (b) Junctional rhythm. The electrocardiograph features of junctional rhythm are demonstrated in the same patient during the pre-bypass period. Retrograde P waves are seen following the QRS complexes. Associated hemodynamic changes include a reduction in the systemic arterial blood pressure and prominent v waves on the CVP tracing related to the loss of atrioventricular synchrony. ART 1, systemic arterial blood pressure (scale 0–100 mmHg); *CVP*, central venous pressure (scale 0–60 mmHg); *Spo*$_2$, oxygen saturation.

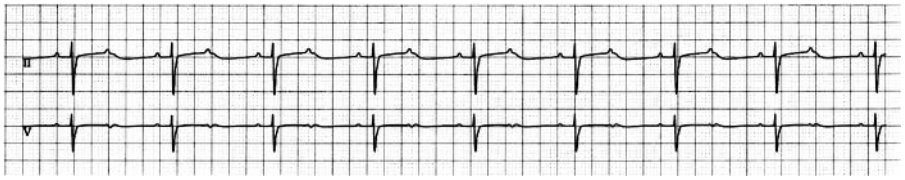


**Fig. 15.2** Mobitz type II second-degree atrioventricular (AV) block is shown with a constant PR interval and failure of every other atrial impulse to conduct to the ventricle (2 : 1 AV block).

lesions associated with stretching of the atria). In general, first-degree AV block is a benign condition and requires no specific treatment.

## Second-degree atrioventricular block

Second-degree AV block has two forms: Mobitz type I (Wenckebach) and Mobitz type II. Both forms show a periodic failure to conduct atrial impulses to the ventricle. In type I second-degree AV block, there is a progressive lengthening of the PR interval with eventual failure to conduct the next atrial impulse to the ventricle (P wave without associated QRS complex). The RR intervals concomitantly shorten. The degree of AV block is expressed as the ratio of P waves per QRS complexes (i.e. 2 : 1, 3 : 2). This condition can occur during periods of high vagal tone or in the postoperative setting. This is generally a benign phenomenon that needs no therapy. In the less frequent type II second-degree AV block, there is a relatively constant PR interval prior to an atrial impulse that suddenly fails to conduct (Fig. 15.2). This type of AV block is considered potentially more dangerous. It can be seen in patients following surgery for CHD and is thought to be secondary to damage to the His bundle or distal conduction system. Close observation of the patient's conduction is warranted as higher grade AV block may develop requiring temporary pacing.

## Third-degree (complete) atrioventricular block

Third-degree AV block is characterized by total failure of atrial impulses to conduct to the ventricle. There is complete dissociation between the atria and ventricles and the ventricular rate is usually slow and regular. The diagnostic feature on ECG is the fact that atrial impulses that should be propagated to the ventricle fail to do so (Fig. 15.3). Complete heart block may be either congenital or acquired. Congenital AV block in infants with otherwise structurally normal hearts may be due to intrauterine exposure to maternal antibodies associated with collagen vascular diseases. Anatomic substrates at high risk of complete AV block include patients with l-transposition of the great arteries with ventricular inversion (congenitally corrected transposition) and those with polysplenia/left isomerism.[1] Acquired postoperative AV block is thought to occur from damage to the compact AV node or bundle of His and may be of a transient or permanent nature. The surgical repairs most commonly associated with complete AV block are AV septal defects, ventricular septal defects, tetralogy of Fallot, resection of subaortic obstruction, and interventions in patients with l-transposition of the great arteries.[2] The incidence of surgical AV block has been reported to be as high as 2–4% of pediatric patients.[3] Eventual recovery of normal conduction occurs in over 60% of subjects and usually does so within the first 10 postoperative days

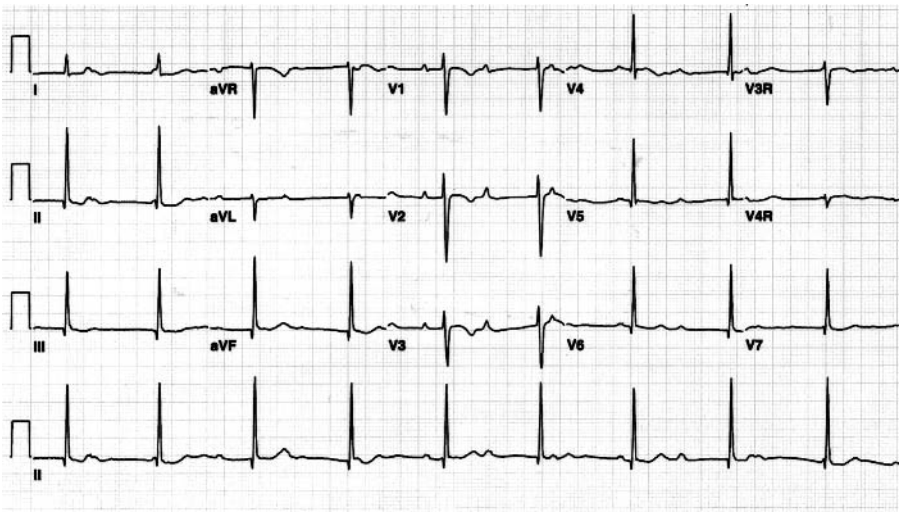


**Fig. 15.3** Complete atrioventricular block. Surface electrocardiograph shows complete dissociation between the atria and ventricles related to inability of the atrial impulses to be propagated to the ventricular myocardium. The ventricular rate is fairly regular.

with a smaller percentage showing late recovery.[3,4] Acute treatment includes temporary pacing, either AV sequential or ventricular pacing only. If the junctional escape rhythm is of adequate rate to support a stable hemodynamic state, then the temporary pacemaker may be set to a back up rate and the patient monitored. Postoperative surveillance in the patient with surgical AV block includes close observation for return of AV conduction and daily evaluation of thresholds of the temporary pacing wires. The ventricular output of the temporary pacemaker is set well above the capture threshold for increased safety. Permanent cardiac pacing is generally indicated in the patient who has not recovered from complete AV block following 10–14 days of the surgical intervention.

## Supraventricular dysrhythmias

### Premature atrial contractions

Isolated premature atrial beats, often referred to as premature atrial contractions (PACs) are relatively common in the younger age group (infants and small children). The early P waves on the ECG frequently have an axis and morphology differing from those in normal sinus rhythm and are followed by a normal QRS. On occasion, these may blocked at the AV node or conduct aberrantly (abnormal QRS). Premature atrial contractions are usually benign in nature and require no therapy. Investigation may be initiated in cases of symptomatic, frequent or complex (arising from multiple foci) PACs. If a central venous catheter or any other type of intracardiac line is present, radiographic or echocardiographic assessment of the tip position should be considered and appropriate adjustments performed to eliminate direct atrial irritability as a potential etiology.

### Supraventricular tachycardia

Supraventricular tachycardia (SVT) is the most common significant dysrhythmia in infants and children. This rhythm disturbance is characterized by a narrow or "usual" complex QRS morphology and can occur in structurally normal hearts as well as in various forms of CHD. "Usual" complex implies that the QRS morphology in tachycardia is similar to that in normal sinus rhythm. This differentiation is made because patients with CHD often have abnormalities on their baseline ECG including a wide QRS complex. On occasion, widening of the QRS in SVT may be secondary to aberrancy in the right or left bundle branches or because of the tachycardia mechanism. When the QRS complex is wide the distinction of supraventricular from ventricular tachycardia may be difficult.

There are two general types of SVT: automatic and reentrant. These can be differentiated by evaluating characteristics of the tachycardia as listed in Table 15.2. The most common mechanisms of SVT and their electrographic features are listed in Table 15.3. Evaluation of a tachydysrhythmia typically includes a surface 12-lead ECG, a continuous six-lead rhythm strip to document onset and termination, and response to medication (i.e. adenosine) or pacing maneuvers. Bedside or transport monitor strips are helpful to determine tachycardia rate, but are not sufficient for diagnosis or to differentiate among tachycardia mechanisms. In the postoperative patient, temporary atrial pacing wires can be helpful in both diagnosis and management. These wires are typically placed on the epicardial surface of the heart at the conclusion of the surgical intervention. If it is difficult to discern P waves on the surface ECG, an atrial electrogram may be obtained by the use of these wires. This may assist in clearly defining atrial activity and the relationship between

**Table 15.2** Characteristics of supraventricular tachycardia mechanisms.

| | Automatic | Reentry |
|---|---|---|
| Onset and termination | "Warm-up" at initiation | |
| | "Cool-down" at termination | Abrupt |
| Mode of initiation | Spontaneous | Premature beats |
| Ability to initiate/terminate with timed premature beats | No | Yes |
| Variation in tachycardia rate | Wide | Narrow |
| Response to catecholamines | Increased rate | None or slight rate increase |
| Response to adenosine | None | Termination |
| Response to drugs that increase refractoriness | Variable | Slowing or termination |
| Response to overdrive pacing | Transient suppression, quick resumption | Termination |
| Response to cardioversion | None | Termination |

**Table 15.3** Mechanisms of most common types of supraventricular tachycardia and electrocardiographic features.

| Diagnosis | Electrocardiographic features |
|---|---|
| *Automatic tachycardias* | |
| Ectopic atrial tachycardia | Atrial rates of 90–330 beats/min<br>Incessant rhythm<br>From atrial focus distinct from sinus node<br>Abnormal P wave morphology and/or axis<br>Distinct P waves preceding QRS complexes<br>No influence of AV block on tachycardia |
| Junctional ectopic tachycardia | Narrow QRS tachycardia<br>Incessant rhythm<br>AV dissociation frequent feature<br>Atrial rate slower than ventricular rate<br>Capture beats frequently seen (QRS complexes slightly earlier than expected from antegrade conduction of normal sinus impulses) |
| *Reentrant tachycardias* | |
| Atrial flutter | Sawtooth pattern or more discrete undulating P waves (leads II, II, AVF)<br>Various degrees of AV block may be seen |
| Atrioventricular reentrant tachycardia (accessory pathway-mediated)<br>Concealed bypass tract<br>Wolff–Parkinson–White syndrome | P waves immediately following the QRS complex, on ST segment or T wave<br>AV block results in termination of tachycardia |
| *Atrioventricular nodal reentry tachycardia* | P waves buried within QRS and not discernible<br>AV block results in termination of tachycardia |

AV, atrioventricular.

atrial and ventricular depolarization. In addition, these temporary wires may be used for rapid atrial pacing to attempt to terminate SVT due to reentrant mechanisms or to overdrive suppress an automatic focus.

Management of SVT depends on the clinical status of the patient, type of tachycardia and precise electrophysiologic mechanism (Table 15.4). If the tachydysrhythmia is associated with moderate to severe hemodynamic compromise, emergent therapy is indicated. Synchronized direct-current cardioversion should be considered for essentially all acute tachydysrhythmias associated with evidence of low cardiac output, recognizing the fact this approach may not always result in restoration of normal sinus rhythm.

## Automatic supraventricular tachycardias

Automaticity of atrial or AV junctional tissues account for this group of supraventricular tachydysrhythmias.[5] In general these rhythm disorders are more resistant to standard pharmacological therapy than reentrant types.

**Table 15.4** Acute therapy of perioperative dysrhythmias without evidence of hemodynamic compromise.

| Rhythm disturbance | Treatment considerations |
|---|---|
| Sinus bradycardia | See Table 15.1 |
| Sinus tachycardia | Correct underlying cause |
| Premature atrial contractions | Evaluate position of central venous line or intracardiac catheter |
| Ectopic atrial tachycardia | Correct fever, electrolyte abnormalities<br>Adequate sedation<br>Consider possible role or inotropes/vagolytics<br>Digoxin, usually first drug but rarely effective as single agent<br>Beta-blockers, use with caution if depressed cardiac function<br>Procainamide<br>Amiodarone, sotalol<br>Flecainide, propafenone |
| Multifocal atrial tachycardia (chaotic atrial tachycardia) | As in ectopic atrial tachycardia<br>Goals are rate control and decreased automaticity |
| Accelerated junctional rhythm | Correct fever<br>Consider possible role or inotropic agents<br>Temporary atrial pacing |
| Junctional ectopic tachycardia | Correct fever, electrolyte abnormalities<br>Consider possible role or inotropes/vagolytics<br>Surface cooling to 34–35°C<br>Temporary atrial pacing (for JET rates below 180 beats/min)<br>Hypothermia plus procainamide<br>Amiodarone |
| Atrial flutter | Adenosine to confirm diagnosis<br>Atrial overdrive pacing<br>Digoxin<br>Procainamide<br>Amiodarone, sotalol<br>Propafenone |
| Atrial fibrillation | Digoxin (except in WPW)<br>Beta-blockers<br>Procainamide, quinidine<br>Amiodarone, sotalol |
| Atrioventricular reentrant tachycardia or atrioventricular nodal reentry tachycardia | Consider vagal maneuvers<br>Adenosine<br>Atrial overdrive pacing<br>Procainamide<br>Amiodarone |
| Premature ventricular contractions | Consider and treat underlying cause<br>Lidocaine |
| Ventricular tachycardia | Lidocaine<br>Amiodarone<br>Procainamide<br>Magnesium (for torsade de pointes)<br>Beta-blockers<br>Phenytoin (for digitalis toxicity)<br>Bretylium? (no longer recommended in Pediatric Advanced Life Support Guidelines) |
| Ventricular fibrillation | Check for loose ECG electrode mimicking VF<br>Lidocaine<br>Amiodarone (to prevent recurrence) |

ECG, electrocardiogram; JET, junctional ectopic tachycardia; VF, ventricular fibrillation, WPW, Wolff–Parkinson–White syndrome.

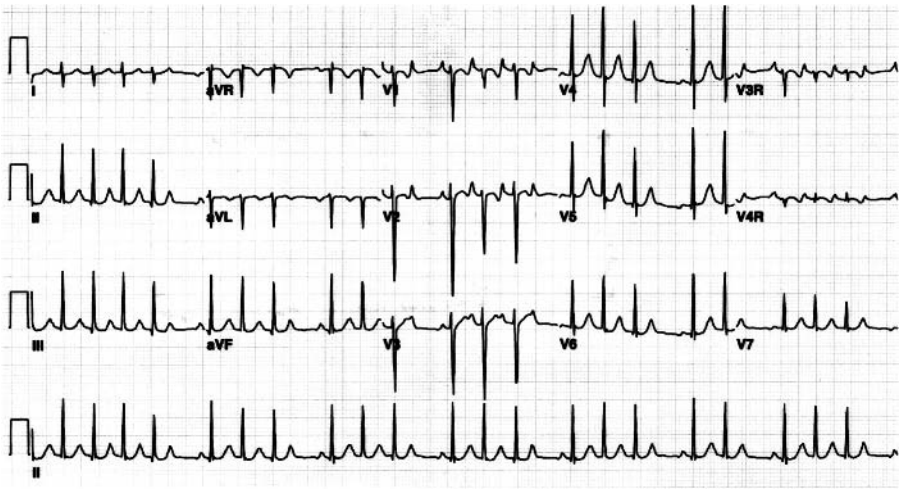


**Fig. 15.4** Twelve-lead electrocardiograph in a 6-year-old child with ectopic atrial tachycardia. The characteristic features of the tachycardia are shown including a faster heart rate than expected for age, an abnormal P-wave axis (left atrial focus in this case) and maintenance of the dysrhythmia in the presence of atrioventricular block.

### Ectopic atrial tachycardia

Ectopic atrial tachycardia (EAT) is a rhythm disturbance originating from a single focus in the atrium outside of the sinus node. The clinical characteristics of EAT follow those outlined in Table 15.2 for automatic tachycardias. Ectopic atrial tachycardia may be incessant or episodic. The diagnosis is made by evaluation of the surface ECG or rhythm strips demonstrating an abnormal P wave morphology and/or axis (Fig. 15.4). The PR interval may also differ from that in sinus rhythm. Atrial rates in EAT are faster than usual sinus rates for age and physiologic state of the patient. If the atrial rates are very rapid, some of the atrial impulses may not be conducted to the ventricle due to AV node refractoriness.

Ectopic atrial tachycardia is relatively rare and is generally found in two different clinical scenarios.[6,7] A patient with a structurally normal heart can develop EAT as a primary phenomenon. In this condition, EAT tends to be incessant and can lead to the development of a dilated cardiomyopathy because of the chronicity of the tachycardia. A patient with CHD can develop EAT in the postoperative period related to cardiac surgery. In this setting, EAT tends to be episodic and transient, usually resolving within days. In a recent report, postoperative patients who developed EAT tended to have lower preoperative oxygen saturations, increased inotropic support both pre and postoperatively, and had undergone an atrial septostomy prior to surgical intervention.[8] No specific cardiac repair was associated with the development of EAT.

The management of postoperative EAT includes:

1 Correction of fever if present.
2 Adequate sedation.
3 Correction of electrolyte abnormalities, especially potassium and calcium.
4 Decreasing or withdrawing medications associated with sympathetic stimulation (i.e. inotropic agents) or with vagolytic properties (i.e. pancuronium).
5 Institution of antiarrhythmic drugs is based on overall heart rates and the hemodynamic status of the patient. Digoxin has a minimal effect on the atrial focus, but can slow the overall heart rates by slowing AV conduction.[9] After digoxin, the choice of therapy is based on clinical judgment and myocardial function. There are no large clinical series investigating antiarrhythmic drug efficacy in postoperative EAT. Intravenous medications such as β-blockers, procainamide, and amiodarone can be effective in slowing the tachycardia rate.[10] Oral agents (class I, II, and III drugs) may also be of benefit.
6 In very rare cases in the postoperative patient, EAT may be incessant and life threatening and consideration should be given to a radiofrequency catheter ablation of the atrial focus.[11]
7 Atrial pacing and cardioversion are not likely to be effective.

### Multifocal atrial tachycardia

Multifocal atrial tachycardia (MAT) also known as chaotic atrial rhythm, is an uncommon atrial dysrhythmia characterized by multiple (at least three) P wave morphologies.[12] These different morphologies correspond to multiple foci of automatic atrial activity. Characteristic ECG features include variable P–P, R–R, and PR intervals. Multifocal atrial tachycardia may be seen in young infants without structural heart disease, in patients with cardiac defects after surgical intervention, and in children with non-cardiac medical conditions.[13,14] Treatment focuses on ventricular rate control and/or decreasing automaticity. Drugs such as digoxin, procainamide, flecainide, amiodarone, and propafenone have been found to be successful in converting MAT to sinus rhythm in children.[15] Adenosine, pacing and direct-current cardioversion are ineffective.

### Accelerated junctional rhythm

Accelerated junctional rhythm is an automatic rhythm that arises from the AV junction. Characteristics of this dysrhythmia include a narrow or "usual" QRS pattern with no preceding P wave. There is either ventriculoatrial (VA) dissociation with ventricular rates faster than atrial rates or the presence of 1 : 1 VA conduction via the AV node. Temporary atrial pacing at a rate 10–20 beats/minute faster than the junctional rate re-establishes AV synchrony and effectively suppresses the automatic junctional rhythm. Changes in the patient's physiologic state including fever, chronotropic agents, and endogenous catecholamines may act to stimulate the automatic junctional focus and increases in junctional rates may be seen. This rhythm is usually well tolerated and easily managed with temporary pacing and control of the patient's underlying physiologic state.

### Junctional ectopic tachycardia

Junctional ectopic tachycardia (JET) is differentiated from accelerated junctional rhythm by the heart rate and the hemodynamic status of the patient. Junctional ectopic tachycardia is defined as a narrow or "usual" complex tachycardia, with heart rates above 160 or 170 beats/minute, with usually no preceding P wave (Fig. 15.5).[16] There is either VA dissociation with ventricular rates faster than atrial rates or the presence of 1 : 1 VA conduction. If 1 : 1 VA conduction is noted, then a trial of adenosine or rapid atrial pacing may be beneficial to differentiate JET from other reentrant forms of SVT.

Junctional ectopic tachycardia typically occurs in the immediate postoperative period and can result in hemodynamic instability, significant morbidity and may contribute to mortality.[17–20] It occurs more commonly following surgical intervention for tetralogy of Fallot, repair of ventricular septal defects, AV septal defects, transposition of the great arteries, and total anomalous pulmonary venous connections.[20]

Numerous therapies have been advocated for JET.[18,19,21] In the acute setting strategies include:

1. Control of fever to at least normothermia. Core temperature cooling (to 34 or 35°C) in the younger patient by the use of cooling blankets, fans, or cold compresses has been shown to be of benefit in reducing the tachycardia rate.[22–24] Shivering, if significant, should be avoided by the use of muscle relaxants in view of potential detrimental increases in oxygen consumption.
2. Decreasing or withdrawing medications associated with catecholamine stimulation or vagolytic agents.
3. Correction of electrolyte abnormalities, especially potassium and calcium.
4. Temporary atrial pacing at heart rates 10–20 beats/minute above the JET rate. This establishes AV synchrony and often benefits the patient hemodynamically. However, if the JET rates are faster than 180 or 190 beats/minute, there is often little benefit with overdrive atrial pacing.
5. Initiation of antiarrhythmic medications. The two most widely used drugs for JET are procainamide and amiodarone.[21,25–27] The benefits of procainamide are that it has a faster onset of action and a shorter half-life. The concerns are that it appears to be efficacious only with the use of core cooling. It may also cause a decrease in peripheral vascular resistance and hypotension, especially during bolus infusions. Procainamide may also have negative inotropic properties. Usually, a saline bolus or other volume expander should be administered prior to or during procainamide therapy to maintain adequate hemodynamics. Amiodarone has a longer onset of action and a longer half-life as compared to procainamide. It has been shown to reduce the heart rate in JET during the initial bolus infusion.[25,26] Core cooling is often continued but is not needed for efficacy. This may avoid the challenge of having to evaluate clinical signs of adequate cardiac output (distal peripheral perfusion, skin temperature) in a hypothermic, tachycardic patient. Amiodarone does not influence

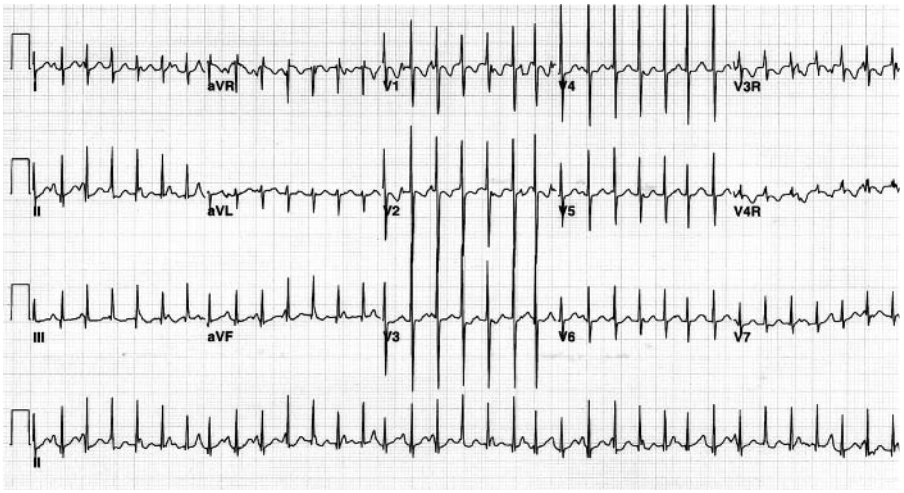


**Fig. 15.5** Junctional ectopic tachycardia. Twelve-lead electrocardiograph in postoperative patient following repair of tetralogy of Fallot. The tachycardia is characterized by a narrow QRS complex and atrioventricular dissociation.

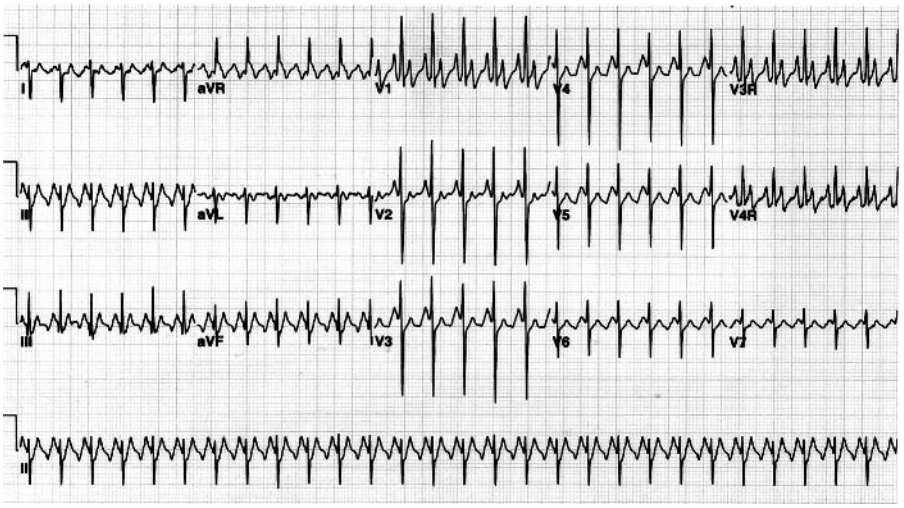


**Fig. 15.6** Atrial flutter. The typical features of the classic form of atrial flutter are shown on this surface electrocardiograph. The negative large sawtooth flutter waves in leads II, III, and aVF are seen in addition to the 2 : 1 atrioventricular block.

ventricular function and generally it causes less blood pressure changes during the initial bolus infusion. Both drugs have been shown to be effective in the treatment of JET in published retrospective studies; however, drug choice is significantly influenced by physician/center preference. Due to the fact that procainamide and amiodarone can each result in QT prolongation and proarrhythmic side effects, concomitant drug administration should be used with extreme caution and under guidance of a consultant. Anecdotally, digoxin loading may slow the JET rate, but this has not been well documented in the literature.[21] Beta-blockers and calcium channel blockers can depress myocardial contractility, a feature that limits their application in the immediate postoperative period. The use of intravenous class IC agents such as propafenone and flecainide has been reported, but these agents have not been studied extensively for JET and the intravenous form of propafenone is not yet available in the USA.[28–30]

6 Overdrive pacing and cardioversion are generally considered ineffective to terminate JET.

The natural history of perioperative JET is that it resolves within 2–5 days from the surgical intervention. Long-term antiarrhythmic therapy is usually not necessary. In extreme cases where JET cannot be controlled medically, radiofrequency catheter ablation may be indicated.[31,32]

## Reentrant supraventricular tachycardias

Reentry, also known as "circus" movement or reciprocation, implies that a single stimulus or excitation wave front returns and reactivates the same site or tissue where it came from. Reentrant forms of SVT may or may not involve accessory pathways.

### Atrial flutter

Atrial flutter is a dysrhythmia confined to the atrial myocardium. The electrophysiologic basis for this rhythm disturbance involves reentry within the atrium. The typical or classic form of atrial flutter is characterized by a negative saw-tooth P wave pattern and atrial rates of 300 beats/minute (Fig. 15.6). This form of atrial flutter may occasionally be seen in an otherwise healthy neonate but is relatively uncommon in children. The diagnosis of atrial flutter is suggested by abrupt onset of a rapid atrial rhythm that remains relatively regular over time. Atrioventricular nodal conduction accounts for the ventricular response that may be 1 : 1 or variable. Rapid clinical deterioration is likely with fast ventricular rates and prompt intervention is frequently necessary. Atypical atrial flutter or intra-atrial reentrant tachycardia (IART) usually displays slower atrial rates than the classic form of atrial flutter and varying P wave morphologies. Intra-atrial reentrant tachycardia occurs predominantly in older children and young individuals in association with structural heart disease.[33] This is one of the most common dysrhythmias in the postoperative patient and is considered the cause of significant morbidity following certain types of surgical interventions.[34] Procedures that involve extensive atrial manipulations, such as atrial redirection procedures (Senning or Mustard operations) and those associated with atrial dilation (Fontan surgery) are particularly at high risk. It has been proposed that anatomic abnormalities related to suture lines, scars or fibrosis from previous surgical interventions in atrial tissue account for the variable atrial rates in these patients.

Management approaches for atrial flutter include:

1 Pharmacologic agents such as digoxin, procainamide, and amiodarone are recommended in acute situations. Drug therapy for controlling the ventricular response in atrial flutter may include in some cases β-blockers (esmolol) or calcium channel blockers (verapamil). Important considerations regarding drug selection are patient age, underlying ventricular function, and presence of sinus node dysfunction (a concomitant problem in patients with recurrent atrial flutter). Newer class III agents (e.g. ibutilide) are

available for acute termination of atrial flutter in the adult age group, and may have applications in the postoperative adult with CHD.

2 Although adenosine will not terminate atrial flutter it may assist in confirmation of the diagnosis by enhancing AV block and uncovering flutter waves.

3 Atrial overdrive pacing (via esophagus, intracardiac pacing catheter, or epicardial wires) has been shown to be safe and effective in the acute termination of atrial flutter.[35] After determination of the atrial cycle length, rapid atrial stimulation is performed in short bursts to attempt interruption of the reentry circuit.

4 Synchronized direct current cardioversion is the treatment of choice for any patient with unstable hemodynamics associated with atrial flutter (0.5–1.0 J/kg body weight).

5 Chronic drug therapy is frequently required in patients with CHD because of the potential for recurrence and associated fast AV conduction.

6 Pacemaker therapy, atrial antitachycardia pacing, and radiofrequency ablation are additional modalities more applicable to long-term management.

### Atrial fibrillation

Atrial fibrillation is the result of many small reentrant circuits within the atrium. In the pediatric age group this tachydysrhythmia is less frequent than atrial flutter. The atrial rates are rapid and irregular ranging from 400 to 700 beats/minute. Ventricular response rates are variable but generally range between 80 and 150 beats/minute. Patients at potential risk for atrial fibrillation include those with pre-excitation syndromes, rheumatic heart disease, structural heart disease (Ebstein's anomaly, tricuspid atresia, atrial septal defects), severe AV valve regurgitation and cardiomyopathies.

Management principles in atrial fibrillation are similar to those for atrial flutter except that atrial overdrive pacing is not effective in terminating the dysrhythmia. Cardioversion is more likely to be required. Generally a higher amount of energy is necessary for cardioversion in patients with atrial fibrillation as compared to those with atrial flutter. An orientation of the cardioversion pads over the front and back of the heart in order to shock the entire atrium may be necessary. Anticoagulation and consideration of transesophageal echocardiography for evaluation of intracardiac thrombi is recommended prior to cardioversion if atrial fibrillation has been present more than a few days.[36,37]

### Atrioventricular reentrant tachycardia and atrioventricular nodal reentrant tachycardia

Atrioventricular reentrant tachycardia (AVRT) mediated by an accessory pathway between the atrium and ventricle is the most common form of SVT in infancy and childhood. Typically, the tachycardia circuit consists of conduction from the atrium, down the AV node, through the His bundle and ventricles, up the accessory pathway, and back to the atrium. This form is called "orthodromic" SVT and occurs in patients with Wolff–Parkinson–White syndrome (WPW; short PR interval, delta wave, abnormal QRS morphology), concealed accessory pathways (bypass tract utilized only as retrograde limb of reentrant circuit in SVT), and permanent junctional reciprocating tachycardia (PJRT). In contrast, in "antidromic" SVT conduction travels from the atrium, down the accessory pathway, through the ventricles, up the AV node, and back to the atrium. The QRS complex in this form of SVT is wide. Antidromic tachycardia can occur in patients with WPW and other pre-excitation variants (Mahaim tachycardia).

Atrioventricular nodal reentrant tachycardia (AVNRT), or reentry within the AV node, is more likely in the adolescent or young adult. In AVNRT there are two physiologically distinct components of the AV node designated as "slow" and "fast" AV nodal pathways. The typical form of AVNRT consists of antegrade conduction (from the atrium to the ventricle) via the slow pathway followed by retrograde conduction (back to the atrium) via the fast pathway.

Both AVRT (Fig. 15.7) and AVNRT (Fig. 15.8) have clinical characteristics of the reentrant tachycardia mechanisms listed in Table 15.2. The two can often be distinguished by close evaluation of the surface ECG in tachycardia. Patients with structurally normal hearts as well as those with CHD can have either AVRT or AVNRT. Ebstein's anomaly of the tricuspid valve is frequently associated with AVRT secondary to one or multiple accessory pathways.[38,39] The accessory pathways in this condition are usually right-sided and of either the WPW or concealed varieties. l-Transposition of the great arteries can be associated with Ebstein-like features of the left-sided AV valve and left-sided accessory pathways can be identified in a subset of these patients.

Management principles of AVRT or AVNRT include the following:

1 If the patient is hemodynamically unstable emergent direct current cardioversion (0.5–1.0 J/kg) should be carried out (Fig. 15.9). A lower energy setting is adequate for epicardial paddles. This should also be considered in the stable patient when potential rapid clinical deterioration is anticipated or after unsuccessful conventional therapy.

2 In the stable patient various modalities can be utilized to acutely terminate the tachycardia. Vagal maneuvers (ice application to face in infants, coughing, gag reflex stimulation, Trendelenburg position) enhance parasympathetic influences and may acutely terminate the tachycardia.[40] Continuous electrocardiographic monitoring is recommended as well as the availability of atropine as transient bradycardia following tachycardia termination may be seen. Adenosine has become first line therapy for SVT.[41–43] Other pharmacologic agents (digoxin, edrophonium, β-blockers, calcium channel blockers, phenylephrine) have

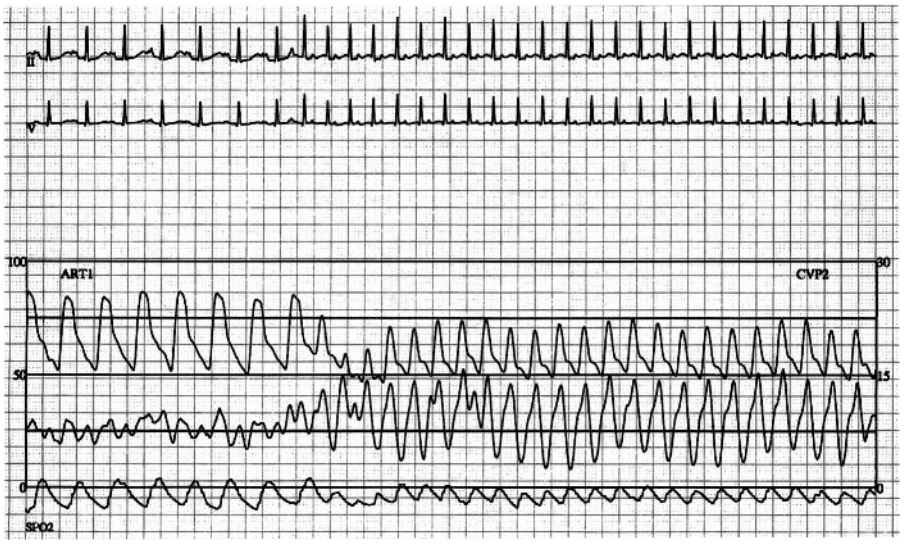


**Fig. 15.7** Atrioventricular reentrant tachycardia secondary to a concealed accessory pathway. For the first seven beats, there is normal sinus rhythm without evidence of Wolff–Parkinson–White syndrome. The next beat is an atrial premature beat which initiates the supraventricular tachycardia. The QRS complexes are narrow and there are retrograde P waves after each QRS. Note the decrease in the systemic arterial blood pressure and the increase in the central venous pressure during the tachycardia. ART 1, systemic arterial blood pressure (scale 0–100 mmHg); *CVP*, central venous pressure (scale 0–30 mmHg); *S*po$_2$, oxygen saturation.

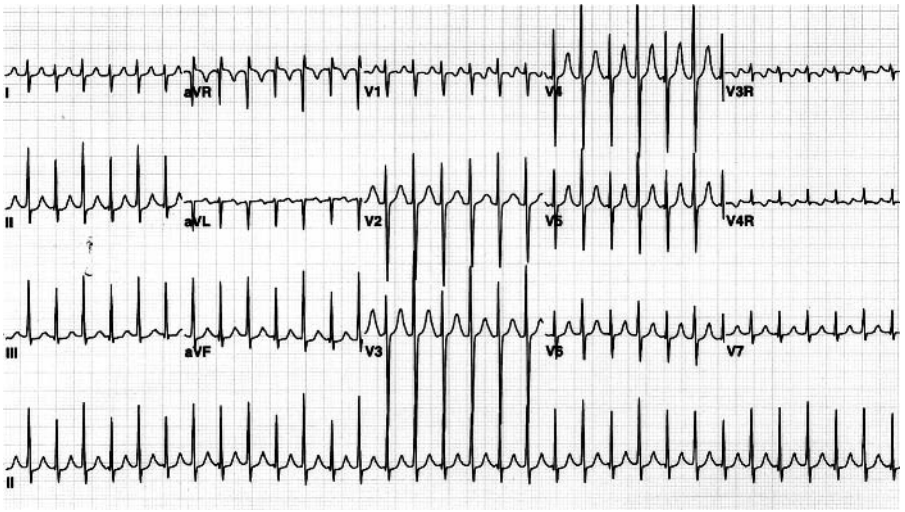


**Fig. 15.8** Atrioventricular nodal reentrant tachycardia. This electrocardiograph shows a narrow-complex tachycardia with a very regular rate. There is no evidence for retrograde P waves, secondary to the P waves occurring at the same time, and therefore being hidden by, the QRS complex.

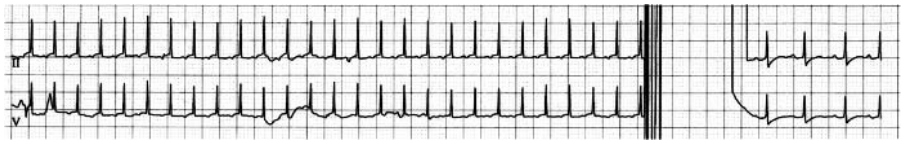


**Fig. 15.9** Direct current cardioversion. This reentrant supraventricular tachycardia is converted to normal sinus rhythm by direct current cardioversion.

been used in the acute setting with variable results; however, serious adverse effects may be seen.

3 Rapid atrial pacing may be conducted via a transesophageal electrode catheter or via temporary atrial pacing wires. One should first establish that at the pacing outputs utilized, the electrode catheter or the temporary wires do not capture the ventricle and cause ventricular contraction. Then, rapid atrial pacing is performed by pacing the atrium at 10–20% faster than the SVT rate for a period of up to 15 s, which typically terminates the tachydysrhythmia. If the tachycardia terminates but then reinitiates, antiarrhythmic drug therapy can be instituted and the maneuvers again attempted. In patients with high catecholamine states, termination of SVT can be successful but rapid recurrence may be seen. In this instance, it is helpful to sedate the patient and limit catecholamine stimulation if possible.

4 Once the tachycardia has terminated or if it terminates and then reinitiates, antiarrhythmic medication can be instituted. For perioperative patients not able to take oral medications, parenteral therapy includes digoxin, procainamide, and amiodarone. Beta-blockers and calcium channel blockers are much less desirable in view of their negative effects on myocardial contractility. Thus, their use is limited in the immediate perioperative period.

5 If the patient has incessant tachycardia and cannot be controlled with medications, radiofrequency catheter ablation may be warranted.

## Ventricular dysrhythmias

Ventricular dysrhythmias are disorders that arise distal to the bifurcation of the common His bundle. These are relatively rare in young children and more commonly seen in the adolescent or young adult with a history of operated CHD. Patients with ventricular rhythm abnormalities may have minimal to no symptomatology or be gravely ill. Evaluation of ventricular dysrhythmias should include a review of the medical history for the presence of associated cardiovascular pathology or potential cause, analysis of the ECG and, very importantly, assessment of the hemodynamic state of the patient.

### Premature ventricular contractions

Premature ventricular beats, often referred to as premature ventricular contractions (PVCs) are characterized by: (i) prematurity of the QRS complex; (ii) a QRS morphology that differs from that in sinus rhythm; (iii) prolongation of the QRS duration for age (this is a frequent finding but may not always be the case); (iv) abnormalities of the ST segment and T wave; and (v) a premature ventricular complex not preceded by premature atrial activity. Premature ventricular contractions of a single QRS morphology (uniform or monomorphic), without associated symptoms and in patients with structurally normal hearts are generally considered benign. Premature ventricular contractions that merit further investigation include those of multiple morphologies (multiform or polymorphic) on ECG, that occur with moderate frequency (runs) or in succession (couplets, triplets) and are associated with symptoms, or present in the context of an abnormal heart.

Ventricular ectopy in the perioperative period may be secondary to myocardial irritation from intracardiac catheters or direct surgical stimulation. Additional etiologies include respiratory (hypoxemia), electrolyte (hypokalemia) or metabolic (acidosis) derangements. Isolated PVCs may also be due to pharmacological agents (including recreational drugs), myocardial injury, poor hemodynamics, and prior complex surgical intervention. In some cases drug therapy (i.e. lidocaine) may be indicated to prevent degeneration of ventricular ectopy into a malignant rhythm.

### Ventricular tachycardia

Ventricular tachycardia (VT) is defined as three or more consecutive ventricular beats occurring at a rate greater than 120 beats/minute. The QRS morphology in VT is different than that in sinus rhythm but not necessarily wide for age. ECG features that favor this diagnosis include: (i) AV dissociation; (ii) intermittent fusion (QRS complex of intermediate morphology between two other distinct QRS morphologies); (iii) QRS morphology of VT similar to that of single PVCs; and (iv) tachycardia rate in children usually below 250 beats/minute. A right bundle branch block QRS morphology is most common in infants with VT, whereas in older children a left bundle branch block QRS morphology is more frequent with likely widening of the QRS.

Various qualifiers have been proposed to further characterize VT. The classification as monomorphic or polymorphic is based on the evaluation of the QRS morphology in multiple ECG leads. Ventricular tachycardia is considered to be sustained or non-sustained if it lasts more or less than 10 seconds respectively.

Acute onset of VT in pediatric patients may be due to hypoxia, acidosis, electrolyte imbalance or metabolic problems. Ventricular tachycardia may also occur in the context of depressed myocardial function, poor hemodynamics, prior surgical interventions, cardiomyopathies (hypertrophic, dilated, arrhythmogenic right ventricular dysplasia), myocardial tumors, acute injury (inflammation, trauma), and prolonged QT syndromes. Among patients with CHD and ventricular dysrhythmias, those at higher risk include older patients following tetralogy of Fallot repair. The following potential causes of ventricular ectopy in patients with structural heart disease have been proposed: inadequate myocardial protection during the surgical procedure, chronic pressure or volume loads, residual or recurrent pathology, and scar formation at the ventriculotomy site.

### Monomorphic ventricular tachycardia

Although occasionally seen in patients with presumably normal hearts, monomorphic (single dominant or constant morphology) VT is a more common phenomenon in patients with diseased hearts. In the abnormal heart the tachycardia is thought to originate from a reentry focus in scarred or damaged myocardial tissue. The electrographic findings are those of a wide regular QRS rhythm of uniform morphology (Fig. 15.10).

### Polymorphic ventricular tachycardia

#### Torsade de pointes

Torsade de pointes ("twisting of the peaks") refers to polymorphic VT. The characteristic ECG feature of this dysrhythmia is that of a varying QRS morphology manifested as positive and negative oscillations of the QRS direction that twist around an isoelectric baseline (Fig. 15.11). Polymorphic VT may occur in long QT syndromes, can be secondary to drug therapy or neurologic pathology or the result of

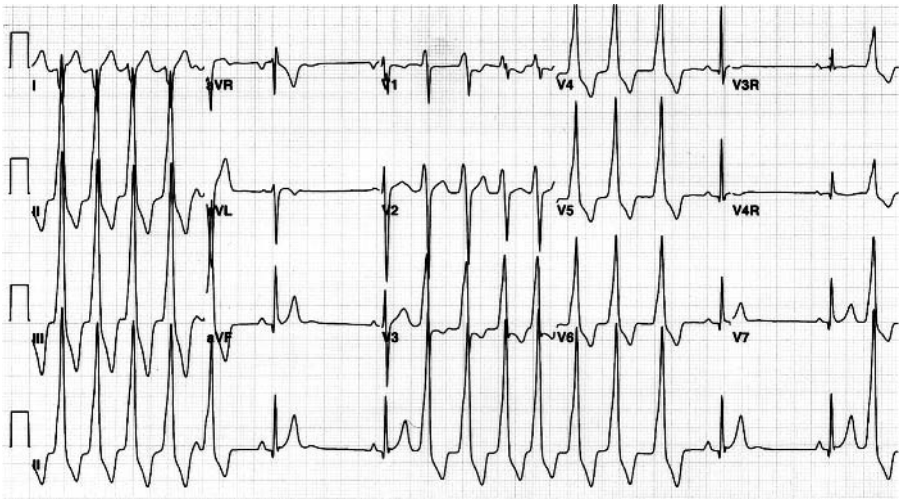


**Fig. 15.10** Ventricular tachycardia. Runs of a uniform, wide complex rhythm are seen, separated by a few beats of normal sinus rhythm.

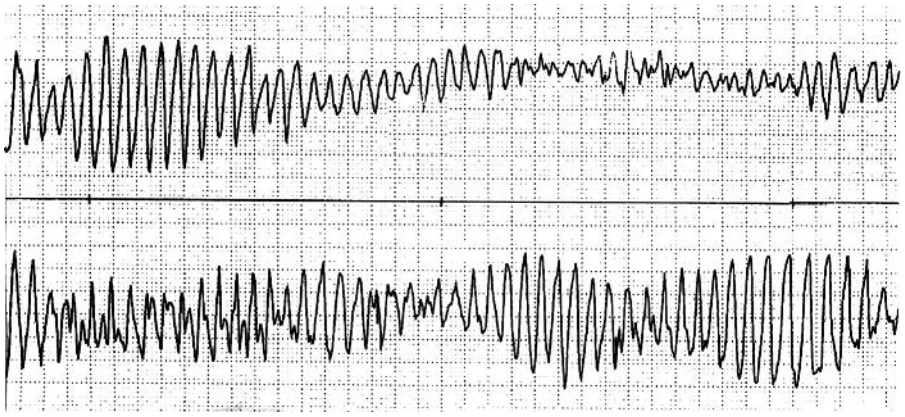

**Fig. 15.11** Torsade de pointes. The typical positive and negative oscillations of the QRS complexes in polymorphic ventricular tachycardia are shown.

myocardial ischemia. Torsade may terminate spontaneously or degenerate into ventricular fibrillation (VF).

## Long QT syndromes

The long QT syndrome can occur in the congenital (inherited) or acquired forms. This distinction is relevant to management strategies. The congenital varieties are considered to be the result of a genetic defect in the sodium or potassium channels responsible for maintaining electrical homeostasis in the heart. A diagnostic criteria has been suggested for the long QT syndrome.[44] This scoring system includes ECG findings, clinical history (deafness, syncope), and family history. A frequent, but not essential, feature is prolongation of the corrected QT interval (QTc) on the resting ECG. The QTc is derived as follows:

$$\text{Corrected QT} = \text{measured QT interval} / \sqrt{\text{of preceding } RR \text{ interval.}}$$

A QTc greater than 0.48 seconds is considered abnormal regardless of age. In addition to torsade de pointes, potential dysrhythmias in patients with long QT syndrome include VF and bradydysrhythmias. An important consideration in the care of these patients is ensuring adequate β-adrenergic blockade preoperatively and minimizing adrenergic stimulation. Conditions and drugs associated with QT interval prolongation should be avoided. Intraoperative dysrhythmias can be treated with additional doses of β-blockers. Others drugs to be considered include phenytoin and lidocaine. Bradydysrhythmias can be managed by pacing. Despite the fact that several anesthetics (intravenous medications and volatile agents) increase the QT interval, in most cases these drugs are used without untoward effects.

Acquired forms of long QT may result from electrolyte disturbances (hypokalemia, hypocalcemia, hypomagnesemia), drug therapy (antiarrhythmic agents, antipsychotic drugs, cisapride), and neurologic or endocrine abnormalities. Therapy in this setting should focus on correction of the underlying cause.

General considerations in the management of VT are as follows:

1 A wide QRS tachycardia should always be considered to be of ventricular origin although some atypical forms of supraventricular dysrhythmias may mimic VT.

2 The primary approach in the care of a patient with an acute ventricular rhythm disturbance is consideration of possible causes and prompt evaluation of hemodynamics. In general, sustained ventricular dysrhythmias are poorly tolerated and require immediate attention. Cardiopulmonary resuscitation should be instituted in the unstable patient while preparing for cardioversion.
3 Pharmacological therapy may be indicated in the stable patient or for the prevention of recurrence in VT. Lidocaine is recommended as first line drug and procainamide as second choice therapy. Additional agents that may be of benefit in refractory dysrhythmias include β-blockers and amiodarone.
4 Electrical cardioversion in torsade de pointes should be performed only if the dysrhythmia is sustained. In patients with frequent but non-sustained runs of torsade de pointes cardioversion is of no benefit and may be detrimental. Magnesium sulfate is considered to be the first line drug and lidocaine may have a role in therapy. Procainamide is contraindicated due to QT prolongation.
5 In addition to β-blockade, congenital forms of the long QT syndrome may in some cases be treated with implanted defibrillators.
6 For polymorphic VT associated with acquired QT prolongation, such as that related to the proarrhythmic effects of certain drugs, pacing and isoproterenol may be more appropriate. In this setting it is thought that the electrophysiologic mechanism that initiates the tachycardia is the result of long pauses in the cardiac cycle.

### Ventricular fibrillation

Ventricular fibrillation is an uncommon dysrhythmia in children characterized by chaotic, asynchronous ventricular depolarizations failing to generate an effective cardiac output. The ECG morphology in VF demonstrates low amplitude irregular deflections without identifiable QRS complexes. A loose ECG electrode may mimic these surface ECG features; therefore, immediate clinical assessment of cardiac output (checking for a pulse) and adequate pad contact should be performed when VF is suspected.

Considerations in the management of VF are as follows:

1 This is a lethal dysrhythmia if untreated; therefore immediate defibrillation (initial dose 2 J/kg for the transthoracic approach) is the definitive therapy. If this is unsuccessful, the energy dose should be doubled (4 J/kg) and repeated. Infant paddles are generally recommended for infants weighing less than 10 kg. Larger adult paddles are suggested for children weighing over approximately 10 kg in order to reduce impedance and maximize current flow.
2 Adequate airway control (oxygenation, ventilation) and chest compressions should be rapidly instituted while preparing for defibrillation or between shocks if several defibrillation attempts are needed. Resuscitative drugs such as epinephrine should strongly be considered without delaying defibrillation.
3 Adjunctive pharmacologic agents for VF include lidocaine and amiodarone. The intravenous preparation of sotalol may be an option in countries where available. Bretylium use in children with VF is not well documented and it is no longer considered an appropriate agent.
4 Additional therapies such as mechanical circulatory support may be an option in selected cases.

The most generally accepted management strategies for acute therapy of perioperative rhythm disturbances without associated hemodynamic compromise are summarized in Table 15.4.

## Pharmacologic therapy of cardiac dysrhythmias

Antiarrhythmic drugs exert blocking actions predominantly on sodium, potassium or calcium channels, or adrenergic receptors. These pharmacologic agents are generally classified according to their presumed mechanism of action and electrophysiologic properties (Table 15.5). The drug classification scheme described by Vaughan Williams in the 1960s and modified over the years is one frequently used and may be helpful in predicting the response to antiarrhythmic drug therapy. Appropriate selection of pharmacologic therapy by the anesthesiologist requires an understanding of dysrhythmia origin, presumed mechanism, and drug. This section discusses antiarrhythmic drug therapy focusing on the drugs most frequently used for acute management in the pediatric age group (Table 15.6).[45] It should be emphasized that perioperative consultation with a cardiologist should be considered during the care of complex rhythm disturbances or if involving patients receiving chronic antiarrhythmic drug therapy.

### Class I agents

The largest group of antiarrhythmic drugs is the sodium channel blockers. The relatively large size of this class has led to subclassification of these agents into IA, IB, and IC groups based on their cellular actions. Group IC is for oral therapy and will not be discussed in this chapter.

The class IA drugs include procainamide, quinidine, and disopyramide. The predominant electrophysiologic effects of these agents are prolongation of myocardial repolarization (QT interval) and duration of the action potential. Their mechanism of action is primarily related to inhibition of the fast sodium channels. The anticholinergic (vagolytic) properties of these drugs account for their more pronounced effects at fast heart rates.

**Table 15.5** Classification of antiarrhythmic agents.

| Class and action | Drugs |
|---|---|
| Class I: Sodium-channel blockers. Drugs may be subclassified into IA, IB, and IC categories | |
| IA agents: Moderately depress phase zero upstroke of the action potential, slow conduction, and prolong repolarization. Effectively slow conduction in atria, ventricles, and accessory connections | Procainamide<br>Quinidine<br>Disopyramide |
| IB agents: Shorten action potential duration and result in minimal alteration of conduction. These agents are usually not effective in the treatment of supraventricular tachycardia | Lidocaine<br>Mexiletine<br>Phenytoin |
| IC agents: Significantly depress phase zero upstroke, with marked slowing of conduction but impart little change in refractoriness | Flecainide<br>Propafenone |
| Class II: Beta-adrenergic receptor blockers. Antiarrhythmic effects result from conduction and decreasing automaticity, particularly in the sinoatrial and atrioventricular nodes | Esmolol<br>Atenolol<br>Metoprolol<br>Propranolol |
| Class III: Potassium-channel blockers. Primarily prolong action potential duration with resultant prolongation of refractoriness | Amiodarone<br>Sotalol<br>Bretylium<br>Ibutilide |
| Class IV: Calcium channel blockers with predominant sites of action in the sinoatrial and atrioventricular nodes | Verapamil<br>Diltiazem |
| Others | Atropine<br>Digoxin<br>Adenosine<br>Magnesium sulfate |

### Procainamide

Procainamide is a potent sodium channel blocker, and to a lesser extent, a potassium channel blocker. This agent slows atrial conduction (prolongs PR interval) and lengthens the QRS duration and QTc interval. Procainamide is useful in the management of both atrial and ventricular dysrhythmias.[21,46–48] The suppression of abnormal automaticity accounts for the role of this agent in the treatment of EAT, JET, and VT. This drug is more effective than lidocaine in acutely terminating sustained VT.

Procainamide may be administered via the oral, intravenous, or intramuscular routes. For the treatment of acute dysrhythmias, intravenous loading (doses of 10–15 mg/kg) is usually required. This is administered over a period of 30–45 minutes. The lower end of the loading dose spectrum is recommended for younger patients. Continuous ECG monitoring and frequent blood pressure assessments are recommended during the loading phase. The drug is rapidly distributed following intravenous injection. An infusion is frequently initiated at 40–50 μg/kg/minute. Monitoring of plasma levels is advisable during maintenance infusion. The infusion rate is adjusted accordingly to maintain therapeutic levels between 4 and 8 μg/mL. The drug is eliminated by the kidneys (50–60%) and via hepatic metabolism (10–30%). Hepatic acetylation accounts for the generation of *N*-acetylprocainamide (NAPA), a metabolite with antiarrhythmic (class III) properties.

Potential side effects include hypotension due to blocking of α-adrenergic receptors and decreased peripheral vascular resistance during rapid intravenous administration. Significant QTc prolongation and proarrhythmia is a known side effect. Additional non-therapeutic effects include negative inotropism and AV block. Gastrointestinal symptoms, a lupus-like syndrome, and blood dyscrasias may also occur.

## Class IB agents

Class IB drugs include lidocaine, mexiletene, phenytoin, and tocainide. These inhibit fast sodium channels and shorten the action potential duration and refractory period.

**Table 15.6** Intravenous antiarrhythmic agents.

| Agent | | Dosing |
|---|---|---|
| Procainamide | Load:<br>Infusion: | 10–15 mg/kg over 30–45 min<br>40–50 μg/kg/min |
| Lidocaine | Load:<br>Infusion: | 1 mg/kg every 5 min up to three times<br>20–50 μg/kg/min |
| Phenytoin | | 1–3 mg/kg over 10–15 min |
| Flecainide | | 1–2 mg/kg over 5–10 min (not available in the USA) |
| Propafenone | Load:<br>Infusion: | 1 mg/kg over 10 min (not available in the USA)<br>4–7 μg/kg/min |
| Esmolol | Load:<br>Infusion: | 500 μg/kg over 1–2 min<br>50 μg/kg/min starting dose, may increase gradually to 400 μg/kg/min |
| Propanolol | | 0.05–0.15 mg/kg over 5 min |
| Amiodarone | Load:<br>Infusion: | 5 mg/kg over 30–60 min<br>5–10 μg/kg/min |
| Sotalol | Load: | 0.2–1.5 mg/kg (not available in the USA) |
| Bretylium | | 5 mg/kg over 1 min, may be repeated in 15 min |
| Verapamil | | 0.05–0.30 mg/kg over 3–5 min, maximum 10 mg, not under 12 months of age |
| Diltiazem | Load:<br>Infusion: | 0.25 mg/kg up to 20 mg bolus over 2 min<br>0.1–0.3 mg/kg/h, may increase up to 15 mg/h |
| Digoxin | Load:<br>Maintenance: | 20–30 μg/kg (divide as 1/2, 1/4, 1/4 every 8 h), dose is age dependent<br>7–10 μg/kg/day divided every 12 h orally |
| Adenosine | | 100 μg/kg rapid bolus, increase by 50 μg/kg every 2 min, up to 300 μg/kg maximum |
| Magnesium sulfate | | 25–50 mg/kg (up to 2 g) over 20–30 min |

### Lidocaine

This drug is a short acting antiarrhythmic agent with primary effects on ventricular myocardium. Lidocaine shortens action potential duration and refractory period. Lidocaine is one of the antiarrhythmic drugs most frequently used in the operating room and intensive care environments. It is the drug of choice for suppression of frequent ventricular ectopy, warning dysrhythmias, and for prevention of recurrence of VT/VF.[49–52]

The recommended dosage includes an initial bolus of 1 mg/kg i.v., and if ineffective, may be repeated after several minutes. The maintenance infusion rate ranges between 20 and 50 μg/kg/minute. Lidocaine is rapidly metabolized in the liver by microsomal enzymes. Therefore drugs associated with altered microsomal enzyme activity (i.e. cimetidine) or conditions with potential reductions in hepatic blood flow (i.e. severe congestive heart failure) may result in decreased drug metabolism. Monitoring of drug levels is advisable during continuous infusion.

Lidocaine toxicity from excessive plasma concentrations may result from poor cardiac output, hepatic or renal failure. Elevated plasma levels beyond the therapeutic range may cause gastrointestinal symptoms (nausea and vomiting), central nervous system pathology (paresthesias, tremor, confusion, seizures) and in rare instances hemodynamic perturbations may be seen.

## Class II agents

The class II drugs (esmolol, atenolol, metoprolol, and propranolol) block β-adrenergic receptors to variable extents (receptor selectivity and intrinsic sympathomimetic activity) depending on the specific agent. Antiarrhythmic effects result from slowing conduction and decreasing automaticity, particularly in the sinoatrial and AV nodes. These agents universally decrease sympathetic activity through β-receptor blockade.

### Esmolol

Esmolol is a predominant $\beta_1$-selective (cardioselective) adrenergic receptor-blocking agent with a rapid onset and

very short duration of action. The primary electrophysiologic drug property is inhibition of sinoatrial and AV conduction.[53,54] The brief elimination half-life of this drug after intravenous injection (approximately 9 minutes) is a feature that has made it desirable in the perioperative and intensive care settings. Esmolol is commonly used for heart rate and blood pressure control and management of a wide number of tachydysrhythmias (supraventricular and ventricular). Following an intravenous loading dose of 500 μg/kg (over 1–2 minutes), an infusion is initiated at 50 μg/kg/minute and titrated to effect by increasing the infusion rate. Because of its short half-life, blood levels of esmolol can be rapidly altered by increasing or decreasing the infusion rate and rapidly eliminated by discontinuing the infusion.

Most adverse effects related to esmolol therapy have been mild and transient. Reported cardiovascular side effects include bradycardia, sinus pauses, AV block, hypotension, and negative inotropism. These are more likely to be seen during bolus therapy.

## Class III agents

The class III drugs (amiodarone, sotalol, bretylium, ibutilide) block potassium channels and increase action potential duration and refractoriness in atrial and ventricular muscle and in Purkinje fibers.

### Amiodarone

Amiodarone has a wide spectrum of actions with multiple and complex electrophysiologic effects which encompass all four antiarrhythmic drug classes. Class I actions include inhibition of fast sodium channels. Class II and IV effects result in depression of sinus node automaticity and function, and slowing of AV and His–Purkinge system conduction. As a class III agent, amiodarone delays repolarization and increases action potential duration resulting in prolongation of refractoriness in all cardiac tissues and accessory connections if present. In addition to blocking potassium channels, amiodarone exhibits vagolytic properties, weakly blocks calcium channels and non-competitively blocks α- and β-adrenergic receptors. The efficacy of this agent has been documented against many supraventricular (EAT, atrial flutter and fibrillation, reentrant arrhythmias involving accessory pathways, JET) and ventricular dysrhythmias (VT and VF).[25,55–58] The usefulness of this drug in the treatment of life-threatening tachydysrhythmias accounts for its increasing role in emergency cardiovascular management.

Intravenous therapy requires a loading dose because of its rapid plasma disappearance during the distribution phase. In children the suggested dose is 5 mg/kg over 1 hour. The same dose is then infused over 12 hours, and repeated if necessary. Amiodarone binds extensively to most tissues, accounting for its extremely prolonged elimination. The slow elimination rate of amiodarone leads to an unusually long half-life (25–110 days).

Amiodarone administration may result in sinus bradycardia and AV block. Hypotension is an unlikely complication of intravenous therapy. Electrocardiogram effects include PR, QRS, and QTc prolongation. There are significant drug interactions with amiodarone that merit attention. Coadministration with other antiarrhythmic agents (digoxin, procainamide, flecainide, quinidine, phenytoin) may result in increased levels of these drugs. The concomitant use of amiodarone with β-blockers or calcium channel antagonists should raise concerns of potential synergistic effects on conduction tissue. A number of adverse effects have been reported with long-term oral therapy in children. These include skin discoloration, corneal microdeposits, alterations in hepatic and thyroid function, pulmonary fibrosis, and neurologic disturbances.

### Bretylium

The clinical experience with this drug is limited in the pediatric age group.[50,59] Indications have included VT or VF unresponsive to standard therapy. In the latest guidelines of the American Heart Association for pediatric resuscitation, bretylium is no longer considered an appropriate agent because of the risk of hypotension, the lack of demonstrable effectiveness in VT, and the absence of published studies of its use in children.[60]

### Ibutilide

Ibutilide is an intravenous class III agent approved in the adult population for the acute conversion of atrial flutter and fibrillation of recent onset (< 90 days) to sinus rhythm.[61–63] Like other drugs that prolong ventricular repolarization, this agent may be associated with excessive QT prolongation and polymorphic VT requiring careful patient selection and monitoring during drug administration. The clinical experience with ibutilide in the pediatric age group is extremely limited.

## Class IV agents

The class IV drugs, also known as calcium channel blockers (verapamil, diltiazem, nifedipine) inhibit the slow inward calcium current.

### Verapamil

The actions of this drug are mediated through prolongation of conduction time and refractory period in nodal tissue. Verapamil has been shown to be efficacious in the management of SVT, certain types of VTs, and hypertrophic cardiomyopathy in children.[64–66]

Verapamil should not be used in young children (< 1 year of age) in view of the potential for severe hemodynamic compromise (refractory hypotension, myocardial depression, asystole and cardiovascular collapse) following its administration.[67,68] The detrimental effects are related to calcium channel blockade and uncoupling of excitation–contraction in myocardial cells. In older children (beyond 1 year of age) verapamil is infused in a dose of 0.1 mg/kg. The concomitant use of verapamil and β-blocking agents may result in serious cardiovascular side effects and is therefore not recommended. In the setting of WPW syndrome, verapamil may enhance the ventricular response rate of atrial fibrillation leading to hemodynamic compromise.

## Other agents

### Atropine

Atropine sulfate, an antimuscarinic, parasympatholytic drug, accelerates sinus or atrial pacemakers, and enhances AV conduction. Atropine is recommended in the treatment of symptomatic bradycardia caused by increased vagal activity or AV block, such as vagally mediated bradycardia during intubation. Atropine may be used to treat bradycardia accompanied by poor perfusion or hypotension; however, epinephrine may be a more effective therapy in this setting. Efforts to ensure adequate oxygenation and ventilation and exclude hypothermia should precede pharmacologic therapy of bradycardia.

The recommended dose is 0.02 mg/kg, with a minimum dose of 0.1 mg. The maximum single dose is 0.5 mg in a child and 1.0 mg in an adolescent or young adult. The dose may be repeated in 5 minutes, to a maximum total dose of 1.0 mg in a child and 2.0 mg in an adolescent. In the absence of intravenous access, atropine (0.02 mg/kg) may be administered tracheally or intramuscularly, although with less reliable absorption than through the intravenous route. Small doses of atropine may be associated with transient heart rate slowing. Atropine may rarely cause cardiac dysrhythmias.

### Digoxin

Digitalis glycosides have been used for many years as first-line pharmacologic agents in the management of certain dysrhythmias. The electrophysiologic properties of digoxin are the result of direct effects on cardiac tissues (through inhibition of the sarcolemmic sodium pump) and indirect effects via the autonomic (parasympathetic) nervous system. Digoxin is known to increase the refractory period and decrease the conduction velocity of the specialized cardiac conduction system, slow the sinus rate (primarily by enhancing vagal discharge), and shorten the refractory period in atrial and ventricular muscle.

Digoxin is effective in the treatment of a wide spectrum of supraventricular dysrhythmias such as SVT, atrial flutter, atrial fibrillation, and chaotic atrial tachycardia. In patients with WPW and ECG evidence of antegrade conduction via the accessory pathway in tachycardia (wide QRS complexes), digoxin is not recommended. This is related to the fact that digoxin may alter the conduction properties of the accessory pathway and lead to malignant dysrhythmias (VT and VF) during episodes of atrial flutter or fibrillation and 1 : 1 AV conduction.

Digoxin can be administered orally or parenterally. In view of the fact that the onset of the digitalis effect may be delayed (up to 5 h), this drug may be less than ideal in the treatment of acute symptomatic tachycardias. Despite this limitation, digitalis glycosides remain useful in controlling the ventricular response in atrial tachydysrhythmias, particularly during atrial flutter or fibrillation. A common loading algorithm utilizes a total digitalizing dose of 30–50 μg/kg. Half of this amount is given initially followed by two doses at 6-hour intervals of 25% of the total digitalizing dose each. For intravenous use, the total digitalizing dose is reduced to 65–75% of the total oral dose given following a similar scheme. Inappropriate dose calculations may result in drug overdose emphasizing the fact that drug calculations should be carefully performed and corroborated prior to drug administration. Maintenance doses of digoxin are 7–10 μg/kg/day. Digoxin is tightly bound to peripheral tissue proteins. Drug excretion is via the kidneys. Dose adjustments are indicated in the case of renal impairment or congestive heart failure.

The coadministration of digoxin with other antiarrhythmic agents (amiodarone, quinidine, verapamil) requires an adjustment (reduction) in the digoxin dose and monitoring of plasma levels. Toxic manifestations of digitalis therapy may be classified as cardiac and non-cardiac. Digoxin toxicity can cause virtually any type of cardiac rhythm disturbance. Non-cardiac manifestations of digitalis toxicity include gastrointestinal (nausea, vomiting, anorexia) and neurologic symptoms (headache, lethargy, weakness, confusion, seizure), and visual disturbances. Although non-specific, non-cardiac symptoms are the earliest manifestations of digitalis toxicity.

### Adenosine

Adenosine is a purine agonist, with effects mediated via the activation of the $A_1$-adenosine receptor (leading to activation of adenylate cyclase and intracellular cyclic-AMP production). The electrophysiologic effects are secondary to an increase in potassium conductance and depression of the slow inward calcium current resulting in transient sinus slowing or AV nodal block. This accounts for its therapeutic value in terminating dysrhythmias that involve the AV node. Adenosine is the drug of choice for acute treatment of SVT.[41,42,50,69–71] Reentrant supraventricular tachydysrhythmias that involve the AV node as part of the circuit are particularly sensitive to

adenosine therapy. Adenosine provides aid in the diagnosis of atrial tachycardias (no efficacy in atrial flutter, atrial fibrillation, or automatic tachycardias) and may also be useful in the differentiation of wide QRS tachycardias.[71]

To terminate the tachycardia a bolus of adenosine is rapidly injected intravenously, preferably into a central vein, at initial doses of 100–150 μg/kg/minute, followed by a normal saline flush. The dose can be doubled up to a maximum of 300 μg/kg (or adult dose of 6–12 mg). The effects of the drug are seen within a period of 10–20 seconds. It is extremely useful to obtain an ECG recording during drug administration. Sinus pauses, with or without escape rhythms, may be seen. The response to adenosine therapy may also provide insight into the mechanism of the tachycardia. Adenosine is rapidly metabolized by erythrocytes and endothelial cells accounting for its extremely short half-life (< 10 seconds).

Cardiac side effects include sinus pauses, sinus bradycardia, sinus tachycardia, and AV block. These effects are generally transient and may only require supportive care. However, some suggest availability of temporary pacing. Adenosine should be used with extreme caution in patients following cardiac transplantation in view of the reported increased duration of the electrophysiologic effect of this agent in the denervated heart and associated detrimental actions. Other unwanted effects are transient and generally well tolerated. These include flushing, shortness of breath, bronchospasm, and chest pressure. On very rare occasions hypotension may occur.

### Magnesium sulfate

Magnesium is a major intracellular cation, cofactor in multiple enzymatic reactions, and important regulator of numerous cardiovascular processes. Magnesium sulfate therapy is indicated as adjunct management for dysrhythmias in patients with documented hypomagnesemia or torsade de pointes.[72] Magnesium deficiency is frequently seen in the context of other electrolyte abnormalities (hypokalemia and hypocalcemia). Rhythm disturbances associated with hypomagnesemia resemble those with hypokalemia or digitalis toxicity. In the setting of torsade de pointes, VT intravenous infusion (over several minutes) of 25–50 mg/kg (up to 2 g) is recommended. Approximately 70% of plasma $Mg^{2+}$ is ultrafiltered by the kidney and the remainder is bound to protein. Side effects associated with magnesium administration include flushing, diaphoresis, muscle weakness, and central nervous system depression. Magnesium levels well above the therapeutic range can lead to serious morbidity such as cardiac conduction defects, respiratory depression, and circulatory collapse.

## Pacemaker therapy in children

### Pacemaker nomenclature

Pacemaker nomenclature as established by the North American Society of Pacing and Electrophysiology and the British Pacing and Electrophysiology Group is detailed in Table 15.7.[73] The generic pacemaker (NBG) code has five positions. The first position or letter of the code refers to the chamber(s) paced, the second to the chamber(s) sensed, the third to the pacemaker's response to sensing, and the fourth to programmability and rate modulation. The fifth position is restricted to antitachycardia function and is used infrequently.

### Permanent cardiac pacing

Advances in pacemaker technology, enhancements in programmability, and miniaturization of units have resulted in the increasing use of these devices in the pediatric age group.[74] The American Heart Association/American College of Cardiology published recent guidelines for permanent pacing in children and adolescents in 1998.[75] Table 15.8 lists indications for which there is general agreement that the device should be implanted (class I) and for which pacemakers are used frequently but diverging opinions exist regarding benefits (class II).

In general terms these indications can be summarized as follows:

**Table 15.7** Generic pacemaker code.

| Position I<br>Chambers paced | Position II<br>Chambers sensed | Position III<br>Response to sensing | Position IV<br>Programmability, rate modulation |
|---|---|---|---|
| O, none | O, none | O, none | O, none |
| A, atrium | A, atrium | I, inhibited | P, simple programmable |
| V, ventricle | V, ventricle | T, triggered | M, multiprogrammable |
| D, dual (A + V) | D, dual (A + V) | D, dual (I + T) | C, communicating |
| | | | R, rate modulation |

Reproduced with permission from Bernstein AD, Camm AJ, Fletcher RD *et al*. The NASPE/BPEG generic pacemaker code for antibradyarrhythmia and adaptive-rate pacing and antitachyarrhythmia devices. *Pacing Clin Electrophysiol* 1987; **10**: 794–9.

**Table 15.8** Indications for permanent pacing in children and adolescents.

*Class I*
- Advanced second- or third-degree atrioventricular (AV) block associated with symptomatic bradycardia, congestive heart failure, or low cardiac output
- Sinus node dysfunction with correlation of symptoms during age-inappropriate bradycardia. The definition of bradycardia varies with the patient's age and expected heart rate
- Postoperative advanced second- or third-degree AV block that is not expected to resolve or persists at least 7 days after cardiac surgery
- Congenital third-degree AV block with a wide QRS escape rhythm or ventricular dysfunction
- Congenital third-degree AV block in the infant with a ventricular rate < 50–55 beats/min or with congenital heart disease and a ventricular rate < 70 beats/min
- Sustained pause-dependent VT, with or without prolonged QT, in which the efficacy of pacing is thoroughly documented

*Class IIa*
- Bradycardia–tachycardia syndrome with the need for long-term antiarrhythmic treatment other than digitalis
- Congenital third-degree AV block beyond the first year of life with an average heart rate < 50 beats/min or abrupt pauses in ventricular rate that are two or three times the basic cycle length
- Long QT syndrome with 2 : 1 AV or third-degree AV block
- Asymptomatic sinus bradycardia in the child with complex congenital heart disease with resting heart rate < 35 beats/min or pauses in ventricular rate > 3 s

*Class IIb*
- Transient postoperative third-degree AV block that reverts to sinus rhythm with residual bifascicular block
- Congenital third-degree AV block in the asymptomatic neonate, child, or adolescent with an acceptable rate, narrow QRS complex, and normal ventricular function
- Asymptomatic sinus bradycardia in the adolescent with congenital heart disease with resting heart rate < 35 beats/min or pauses in ventricular rate > 3 s

Reproduced with permission from Gregoratos G, Cheitlin MD, Conill A *et al*. ACC/AHA guidelines for implantation of cardiac pacemakers and antiarrhythmia devices: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Pacemaker Implantation). *J Am Coll Cardiol* 1998; **31**: 1175–209, with permission from the American College of Cardiology Foundation.

**1** Symptomatic sinus bradycardia.
**2** Recurrent bradycardia–tachycardia syndromes.
**3** Congenital AV block.
**4** Advanced second- or third-degree AV block.

An important consideration in the setting of CHD is correlation of symptoms with recommended criteria for pacemaker placement in view of the physiologic alterations associated with structural heart disease or that may arise or persist following surgical intervention.

## Implantation techniques

Permanent pacemaker implantation is accomplished via the transvenous or epicardial approach. These procedures are typically performed under sterile conditions in the cardiac catheterization laboratory, electrophysiology suite, or operating room. Local anesthesia with supplemental intravenous sedation may be used in the older age group; however, most infants and small children require a general anesthetic.

The transvenous technique uses the subclavian, cephalic, and axillary vein for access.[76] Under fluoroscopic guidance pacing leads are advanced into the right atrium and/or ventricle and fixed to the endocardium according to the specific lead mechanism. After adequate sensing, capture thresholds and lead impedances are documented, and the leads are attached to a generator positioned in the pectoral region. The following are considered contraindications to transvenous pacing: right-to-left intracardiac shunts, prosthetic tricuspid valves, certain types of structural heart disease, anatomy not suitable for transvenous access to cardiac chambers, recurrent lead dislodgment, and small patient size (< 10 kg). Advantages of the transvenous route include longer generator longevity because of lower pacing thresholds and lower incidences of lead fractures.[77] Disadvantages are potential narrowing or thrombosis of venous pathways, lead dislocation, risk of systemic embolization in the presence of an intracardiac shunt, and possible endocarditis.

For epicardial implantation the leads are attached to the epimyocardial surface of the heart and after appropriate testing, these are tunneled to the generator pocket.[78] This approach requires a subcostal, subxiphoid, thoracotomy, or sternotomy incision. Advantages of epicardial implantation include ability for placement independent of intracardiac pathology and avoidance of considerations regarding venous thrombosis. Disadvantages include the invasiveness of the approach, higher incidence of lead failure, and early generator battery depletion.

Need for pacing, programmed settings, and device capabilities play a significant role in the longevity of pacemaker generators. These units are powered by lithium–iodide batteries with an expected service life of between 5 and 15 years.

### Hardware selection and programming of devices

A variety of hardware options are available for cardiac pacing in infants and children. The selection of the particular generator system, mode for pacing, and pacing leads is dependent upon a number of factors. In general terms considerations include patient size, indications for pacing, requirements for specific programmability options, cardiac status/underlying cardiac pathology, and anticipated need for generator longevity.

Both single- and dual-chamber units are commercially available for permanent pacing in the pediatric age group. The dual-chamber devices provide the benefit of AV synchrony and optimization of hemodynamics. The modes frequently used in single-chamber pacing are AAI or AAIR, VVI or VVIR, depending on whether atrial or ventricular leads are present. In the case of dual-chamber pacemakers, typical modes are DDD or DDDR. Under specific circumstances such as during surgical interventions, the pacing mode may be modified to asynchronous (AOO, VOO, or DOO) to prevent erratic pacemaker behavior and allow for an increased margin of safety. If active, the rate-responsiveness feature of the unit should be disabled prior to anesthetic induction.

### Pacemaker malfunction

The problems most frequently accounting for pacemaker malfunction include complications related to lead placement and function, failure to pace, failure to capture, under or oversensing, phrenic nerve stimulation, and pacemaker-mediated tachycardia.[79] Pacemaker troubleshooting may require a combination of chest radiograph, 12-lead ECG, rhythm strip, and device interrogation to determine pacing and sensing thresholds, lead impedances, battery status, and magnet rate.

Children are considered to be at higher risk for lead failure and fracture than their adult counterparts. These problems result in inappropriate pacemaker sensing or capture (underpacing or overpacing) and potential need for pacemaker revision.

With a single-chamber unit failure to pace implies no pacing artifacts or spikes on the ECG. A malfunctioning dual-chamber pacemaker may exhibit either no pacing deflections or pacing in only one chamber. The inability to pace may be intermittent or continuous. Failure to capture implies pacemaker stimuli without associated cardiac chamber response. Increasing the energy output of the pacing device may alleviate this type of malfunction. In the acute postoperative setting this problem requires immediate attention. Normally pacing thresholds increase with time emphasizing the fact that frequent testing of pacemaker function should be performed in the postoperative patient with temporary pacing wires. Steroid therapy may limit edema, inflammation and fibrosis that accounts for increases in pacing thresholds. Undersensing (inability to sense) leads to intercalation of pacing stimuli during normal atrial (P waves) or ventricular (QRS complexes) activity. Oversensing, or failure of the pacing stimulus to be delivered at the pre-programmed time, results in pacemaker pauses. Diaphragmatic contraction related to pacing stimulation can be avoided by reducing the pacemaker output to a lower value, or adjusting pulse amplitude and duration. Pacemaker mediated tachycardia is an infrequent problem in the pediatric age group. Adjustments in pacemaker settings may remedy this potential issue.

## Perioperative considerations

Device interrogation should be part of the complete preoperative evaluation in all patients with implanted pacemakers scheduled for surgical interventions (cardiac or non-cardiac). Consultation with a pediatric cardiologist/electrophysiologist to obtain details of unit type, settings, date of and indications for implantation, and underlying rhythm is highly recommended. Results of a recent 12-lead ECG should be reviewed. Reprogramming may be required prior to the planned procedure to avoid potential problems with pacemaker malfunction related to electromagnetic interference (electrocautery). Unipolar electrocautery may interfere with pacemaker function, thus bipolar electrocautery is preferred. Chronotropic agents and backup pacing modalities (transvenous, epicardial, transcutaneous) should be readily available and carefully considered in the event of pacemaker malfunction and inadequate underlying rate. Capture thresholds can be affected by pharmacological agents (i.e. amiodarone can increase thresholds) and this should be considered if pacing is required in the patient receiving antiarrhythmic drug therapy. A magnet should also be accessible to allow for asynchronous pacing if required. Most generators respond to generator magnet application by pacing at a fixed rate asynchronously (AOO, VOO, or DOO). A potential concern is that the specific magnet rate, as determined by the manufacturer for the particular device, may not be in agreement with the desired or optimal pacing rate. Thus the use of a magnet should not be considered a substitute for preoperative pacemaker interrogation/programming. At pacemaker generator end of life the pacing rate upon magnet application to the generator may differ (slower) than the pre-specified magnet rate. In addition to perioperative ECG monitoring, additional modalities that confirm pulse generation during pacing (esophageal stethoscope for assessment of heart sounds, pulse oximetry, invasive arterial blood pressure monitoring) should be strongly considered. After completion of the procedure the device should be tested and reprogrammed.

## Temporary cardiac pacing

The transvenous and epicardial routes are commonly used for temporary pacing, although the transthoracic

(transcutaneous) and transesophageal approaches are also suitable in some circumstances. Indications for temporary cardiac pacing are not clearly defined as in the case of permanent pacing. Temporary pacing is provided for during most cardiothoracic procedures by placement of wires in the atrial and/or ventricular epimyocardium near the completion of the intervention. Basic settings to be adjusted in the external temporary pulse generator (single or dual chamber device) include: (i) pacing rate; (ii) atrial and/or ventricular output amplitude (milliamperes); (iii) atrial and/or ventricular sensitivity (millivolts) or asynchronous mode; and (iv) A–V interval (milliseconds). Temporary pacing may be necessary for maintenance of adequate cardiac output in the context of bradydysrhythmias, abnormal AV conduction, AV asynchrony, and heart rates inadequate for physiologic state.[80] Temporary pacing may also be helpful in individuals at risk of high degree AV block and can be used to suppress, overdrive, or terminate tachydysrhythmias. Atrial recordings (atrial electrograms) obtained through temporary pacing wires may provide diagnostic information in certain types of rhythm disorders. Temporary pacing is discontinued with resolution of the indication for pacing or transitioned to permanent pacing. In the care of patients who depend on temporary pacing for maintenance of hemodynamics, it is extremely important to be attentive to pacemaker settings, capture thresholds, and prepare to provide alternate means of pacing in the event of lead/pacemaker failure or malfunction.

## External transcutaneous pacing

A transcutaneous external pacing unit with features superior to earlier transcutaneous systems was patented and introduced by Dr Paul Zoll in the early 1980s. This lead to renewed interest in the field and enhancements of this technology. Several of the devices currently available for commercial use combine defibrillation/cardioversion capabilities and external pacing features. In pediatric patients emergency transthoracic pacing may be considered as a temporizing measure in those with symptomatic bradycardia (secondary to abnormal sinus node function or to complete AV block).[81] It is important to understand that transcutaneous pacing allows for simultaneous atrial and ventricular activation, thus optimal hemodynamics may not be feasible. Transcutaneous pacing has not been found to be effective in the treatment of asystole in children. Pacing electrode size should be selected according to patient size (usually patients under 15 kg require smaller adhesive pads). Device settings typically include heart rate and current output (milliamperes). Most current models provide the option for fixed rate (asynchronous) and demand (synchronous) pacing. After selection of a desired heart rate and pacing modality the current is increased as tolerated until capture is achieved. If the patient is not anesthetized, sedation may be necessary to improve tolerance to transcutaneous pacing. Prolonged periods of transcutaneous pacing may result in serious burns or skin trauma in infants and young children. In addition to monitoring for pacemaker capture by ECG, ongoing clinical assessment of the adequacy of cardiac output should be undertaken.

## Esophageal overdrive pacing

A transesophageal catheter may be used for atrial sensing allowing for diagnostic information and discrimination of supraventricular tachydysrhythmias. The esophageal route also provides a minimally invasive approach for overdrive pacing a variety of supraventricular rhythm disorders (atrial flutter, SVT). For this purpose an electrode catheter is placed into the esophagus, advanced to a location that correponds roughly to the region behind the atrial mass and an atrial electrogram is obtained to refine the catheter position. Local anesthesia to the nasopharynx or oropharynx and/or sedation is generally required in order to introduce the catheter and to prevent discomfort during atrial pacing. Standard cardiorespiratory monitoring should be undertaken during the procedure, in addition to airway support as necessary. Emergency drugs and cardioversion/defibrillation equipment should be readily available.

## Implantable cardioverter–defibrillators

The primary goal of the internal cardioverter–defibrillator is the reduction of sudden death in patients at high risk. Although sudden cardiac death is an uncommon occurrence in pediatrics, certain patients groups may have a definitive risk deriving potential benefits from these devices. Individuals with arrhythmogenic right ventricular dysplasia (a specific type of cardiomyopathy), long QT syndrome, hypertrophic cardiomyopathy, and those with a history of near death events may be considered suitable candidates for pacemaker/defibrillator implantation. Additional patients are those with operated CHD and a history of malignant arrhythmias. At the present, the experience in the pediatric age group with these devices has been limited and reported mostly in retrospective fashion.[82–84] Prospective trials are required to establish guidelines for use, address safety concerns, and evaluate long-term issues specific to children. The anesthetic considerations in patients with implanted units relate primarily to potential surgical electromagnetic interference (electrocautery). Perioperative consultation with a cardiologist/electrophysiologist is therefore essential in the care of these patients. In many cases the devices may need to be adjusted or deactivated prior to surgery. Careful evaluation and device reprogramming is advisable at the conclusion of the surgical intervention.

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# 16 Airway and ventilatory management

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## Introduction

Infants and children with congenital heart disease (CHD) present unique challenges to the anesthesiologist owing to a range of congenital airway abnormalities, cardiopulmonary interactions, and adverse effects of surgery and cardiopulmonary bypass (CPB). The pediatric cardiac anesthesiologist must have expertise in the management of the pediatric airway as well as controlled ventilation. Few other clinical situations will tax the skills of an anesthesiologist as the management of a child with CHD and a difficult airway. Children with cardiovascular disease may be intolerant of the myocardial depressant effects of many anesthetics, limiting the options available in managing their airway during induction of anesthesia. Children with cyanotic CHD experience rapid oxygen desaturation during periods of apnea associated with tracheal intubation. Developing a plan that allows safe airway and ventilatory management without hemodynamic compromise requires preparation, skill, and familiarity with a range of techniques of tracheal intubation.

## Choosing the appropriate endotracheal tube

The narrowest portion of a child's larynx is at the level of the cricoid cartilage, as opposed to adult patients whose limiting airway diameter is at the level of the vocal cords (rima glottidis). Uncuffed endotracheal tubes (ETTs) are commonly used in children because a seal is created between the tracheal mucosa and the tube at the level of the cricoid cartilage.[1] The adequacy of this seal is usually assessed by performing a leak test in which a gradual increase in positive pressure is delivered through the breathing circuit while the practitioner listens over the mouth or neck for the sound of escaping gas. The circuit pressure at which a leak is auscultated is then documented. The leak test provides the best assessment of tube fit; however, significant interobserver variability has been demonstrated.[2] While the appropriate ETT size may be predicted by the patient's age (Table 16.1), a tube smaller or larger than predicted should be inserted to achieve the most appropriate tracheal fit.

**Table 16.1** Endotracheal tube sizes used in pediatric patients.

| Age | Size (mm ID) |
|---|---|
| Preterm | |
| < 1000 g | 2.5 |
| 1000–2500 g | 3.0 |
| Term neonate to 6 months | 3.5 |
| 6 months to 1 year | 4.0 |
| 1–2 years | 4.0–5.0 |
| Beyond 2 years | $\frac{Age\ (years) + 16}{4}$ |

ID, internal diameter.

A tight fitting ETT (e.g. no gas leak up to 30–35 $cmH_2O$) may cause ischemic injury to the tracheal mucosa and submucosa at the level of the cricoid cartilage. Mild ischemia and subsequent swelling may be manifest as post-extubation stridor, whereas subglottic stenosis may result from more severe injury.[3] On the other hand, placement of an ETT with a gas leak at low inflating pressures (e.g. less than 15 $cmH_2O$) results in excessive leak around the ETT and difficulty providing adequate ventilation during and after surgery. Lung compliance may be reduced, as a result of surgical traction or pulmonary edema, resulting in the need for delivery of greater inflating pressures to provide physiologic tidal volumes. With a loose fitting ETT in place, the volume of gas leak around the ETT increases as the peak inflating pressure is increased, while alveolar ventilation may remain unchanged. Gas leakage representing more than 50% of tidal volume has been demonstrated in the setting of decreasing lung compliance.[4] Associated decreases in minute ventilation may lead to dangerous elevations in $PaCO_2$.

In addition to the risk of inadequate alveolar ventilation, there are other hazards associated with placement of a loose ETT. Lung function measurements are commonly used to guide mechanical ventilation in the postoperative period. A variable leak around the ETT results in inaccurate measurements of exhaled tidal volumes, lung compliance, and airway resistance. Eliminating or minimizing the gas leak around the ETT will decrease the environmental pollution from either inhaled anesthetic agents or nitric oxide (NO).[5] Lastly, an adequate seal around the ETT may decrease the risk of pulmonary aspiration should gastric contents be regurgitated following tracheal intubation.

Most authors of pediatric anesthesia texts recommend the use of uncuffed ETTs in children under the age of 8 years.[2] However, there is limited scientific evidence to support this practice. Cuffed ETTs have been used in more than 15 000 children, none of whom developed clinically significant airway complications,[6] and the use of cuffed ETTs for short cases in the operating room reduces the need for repeated laryngoscopy, allows use of lower fresh gas flows, and limits environmental contamination with anesthetic gases.[5] There is no difference in the incidence of airway complications among pediatric intensive care patients intubated with cuffed vs. uncuffed ETTs.[7] Alterations in mucosal edema and lung compliance from the effects of CPB or altering pulmonary blood flow (*PBF*) may increase the leak around the ETT in children after heart surgery, and a cuffed ETT may be inflated to compensate for such changes.

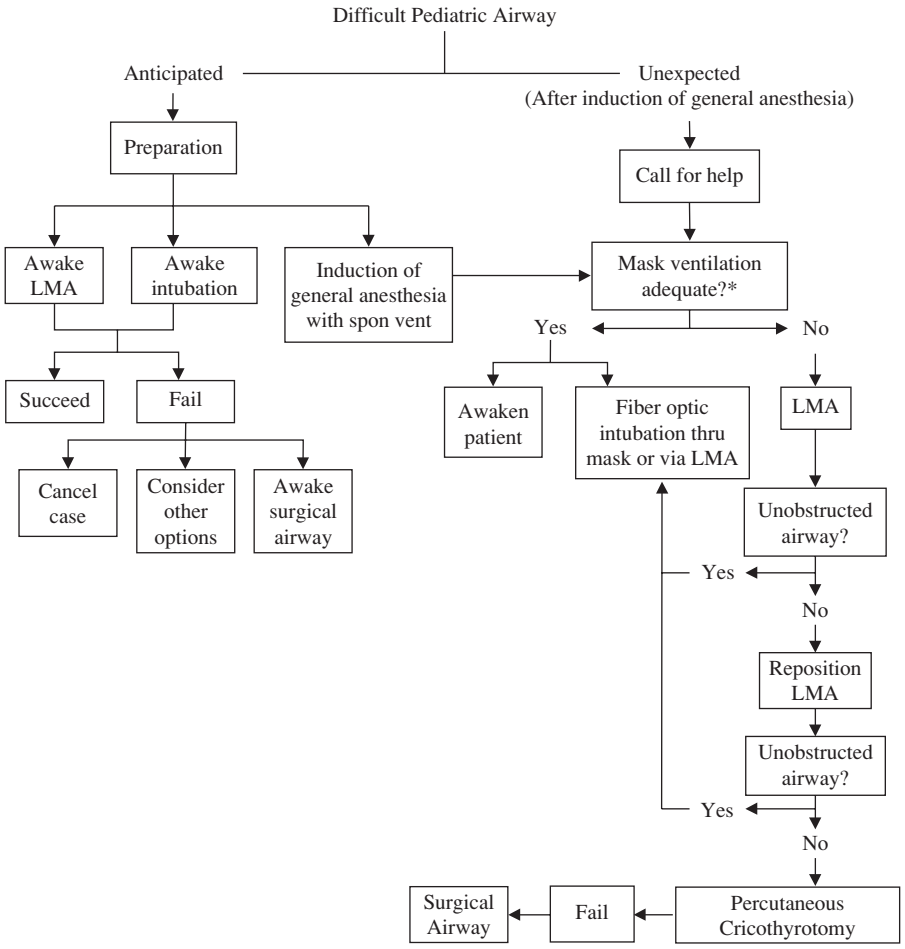
A disadvantage of using cuffed ETTs is that their outer diameter is approximately 0.5 mm larger than uncuffed ETTs with the same inner diameter. As a result, a tube with an inner diameter one size (i.e. 0.5 mm) smaller must be used when a cuffed ETT is placed. This results in greater resistance to gas flow and an increased risk of occlusion of the ETT with blood and tracheal secretions. While a reduction of the tracheal tube diameter by only 0.5 mm might not be expected to effect a clinical change, gas flow resistance increases exponentially at smaller tube diameters. While a reduction in tracheal tube size from 8.0 mm inner diameter (ID) to 7.5 mm ID increases airway resistance by 29%, a change from a size 4.0 mm ID to a 3.5 mm ID tube results in an increase of 71%, and a change from a 3.5 mm ID tube to a 3.0 mm ID tube increases resistance by 85%. The increase in resistance is even more profound if turbulent airflow occurs in smaller tracheal tubes.

### Orotracheal vs. nasotracheal intubation

While orotracheal intubation is performed more commonly than nasotracheal intubation for routine surgery in children, there may be advantages to the use of nasal tubes in children undergoing cardiac surgery. Transesophageal echocardiography (TEE), which is performed in many centers, may cause compression or dislodgement of an orotracheal tube in the oropharynx. However, Stevenson[8] found a low incidence of airway complications during pediatric TEE among children who were orally intubated. Of the 1650 patients he studied, three (0.2%) developed a right mainstem advancement of the ETT, and eight (0.5%) were inadvertently extubated. Nasal ETTs are more readily secured to the face, and movement of the ETT is less likely during manipulation of the TEE probe. At the Texas Children's Hospital over 1800 TEE studies have been performed in children who were nasally intubated with no inadvertent extubation. There is a greater risk of sinusitis and damage to nasal alae from long-term nasotracheal intubation.[9–12] The risk of bleeding from adenoidal trauma is especially problematic in the fully anticoagulated patient. This risk is minimized by the routine use of topical vasoconstriction and adequate lubrication of the ETT. Excessive pressure should not be used during advancement of the tube through the nose and nasopharynx. A soft, lubricated suction catheter can be passed through the ETT and advanced through the nasopharynx into the oral cavity. This will act as a guide permitting easier passage of the nasal ETT.[13] Because ETTs can be placed more easily and rapidly via the oral route, oral intubation is preferred for rapid sequence intubation or when intubating cyanotic infants. Once adequate ventilation and oxygenation have been provided, the stomach is suctioned, and the ETT may be exchanged for a nasal tube under direct visualization. Because it is important to properly size the ETT, we intubate most children orally, perform a leak test, and alter the size of the tube or use a cuffed ETT if necessary via the nasal route. In general, the nasal passages of children will accommodate the same size ETT as would be used for oral intubation.

## The difficult airway

The incidence of congenital airway anomalies is greater among children with CHD than in the general population.[14] Genetic syndromes associated with both airway anomalies and CHDs are frequent, and patients with syndromes such as the CHARGE (coloboma, heart anomaly, choanal atresia, retardation, and genital and ear anomalies) association and velocardiofacial syndrome must have a complete airway examination. A thorough history should be taken on all patients receiving sedation or anesthesia with attention to the recent presence of an upper respiratory infection, snoring or noisy breathing during sleep, inspiratory stridor, and previous problems associated with tracheal intubation or following extubation. In older, cooperative patients, the airway should be examined as with adult patients including mouth opening, dentition, mandibular size (hyomental distance), and neck mobility. Studies in adults have shown that examination of the airway can help predict difficulty of intubation and mask ventilation.[14] No such studies have been performed in infants and children, and it is not known whether assessing




* may need 2 person technique and/or oral airway

**Fig. 16.1** Management of the difficult pediatric airway. LMA, laryngeal mask airway. Modified with permission from A Report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. Practice guidelines for management of the difficult airway. *Anesthesiology* 1993; **78**: 597–602.

mouth opening using a tongue depressor in a non-verbal child is predictive of difficulty with intubation. Assessment of an infant's airway should include an assessment of neck mobility and the appearance of the mandibular size when viewed in profile. Children with micro or retrognathia are more likely to manifest difficult mask ventilation and/or difficult intubation.

## Intubation of the patient with a difficult airway

A modification of the American Society of Anesthesiologists algorithm for the management of the patient with a difficult airway can be applied to children (Fig. 16.1).[15] Specialized airway equipment should be prepared, checked and available in the operating room. Table 16.2 lists recommendations for equipping a difficult airway cart. In addition to equipment, additional personnel skilled in airway management should be immediately available for assistance.

When the difficult airway is recognized prior to the induction of anesthesia, control of the airway can be performed with the patient awake, following sedation, or after the induction of anesthesia with inhalation agents. Awake, non-sedated, direct laryngoscopy can be accomplished in neonates but may be difficult, traumatic, and have significant adverse hemodynamic consequences. Placement of a

**Table 16.2** Suggested contents of difficult airway management cart.

- Rigid laryngoscope blades of alternate design and size from those routinely used
- Endotracheal tubes of assorted size. Nasal and oral airways of assorted sizes
- Endotracheal tube guides and tube exchangers. Examples include (but are not limited to) semirigid stylettes with or without a hollow core for jet ventilation and light wands
- Jet ventilation equipment
- Fiberoptic intubation equipment
- Laryngeal mask airways of assorted size
- Equipment suitable for emergency surgical airway access (e.g. percutaneous cricothyrotomy size 3.5, 4.0, 6.0)
- An exhaled $CO_2$ detector.

laryngeal mask airway (LMA) after application of topical anesthesia to the airway in an awake infant has been described as an alternative to awake direct laryngoscopy.[16] Fiberoptic-guided intubation of the older, cooperative patient using topical anesthesia and intravenous sedation is a safe and effective alternative.

Inhalation induction of anesthesia using halothane or sevoflurane with maintenance of spontaneous ventilation is commonly performed in infants and children with a difficult airway. Intravenous access is established prior to mask induction. If the patient develops airway obstruction during the induction of anesthesia, immediate attempts are made to relieve the obstruction by jaw thrust, head extension, use of continuous positive airway pressure (*CPAP*), and insertion of an oropharyngeal or nasopharyngeal airway. If mask ventilation is inadequate and not improved with the above maneuvers, insertion of an LMA should be attempted. If positive pressure ventilation can be delivered via the LMA, the LMA can be used as a guide for insertion of an ETT or can be exchanged for an ETT with the use of a fiberoptic bronchoscope (FOB). If an LMA fails to provide a patent airway, preparations should be made for an emergency cricothyrotomy (see below). If mask ventilation is possible with either a face mask or LMA, neuromuscular relaxation should be used in order to optimize laryngoscopy.

If mask ventilation is possible, but tracheal intubation is not readily achieved, repeated attempts at direct laryngoscopy should be avoided. Instead, one should optimize head and neck positioning and consider use of an alternate laryngoscope blade to better visualize the larynx. Repeated attempts at direct laryngoscopy may lead to swelling and/or bleeding in the airway and the inability to perform adequate mask ventilation.[17] After a few failed attempts at direct laryngoscopy, use of an LMA should be considered. For the majority of pediatric patients, insertion of an LMA provides a patent airway and a method of delivering positive pressure ventilation, and facilitates fiberoptic intubation.

### Fiberoptic-guided tracheal intubation

The development of FOBs with small diameters has facilitated the use of fiberoptic-guided intubation in infants and young children. A pediatric intubation FOB with 2.2 mm outer diameter that will fit through a 2.5 mm (ID) ETT tube is available (Olympus LF-P, Olympus America Inc., Melville, NY 11747). A FOB with an outer diameter of 2.4 mm that passes through a 3.0 mm (ID) ETT is also manufactured (Pentax Intubation FI-7P, Pentax Precision Instrument Corporation, Orangeburg, NY). Neither of these FOBs has a suction channel. Currently, the smallest FOB that includes a suction channel is 2.8 mm in diameter (no. 11301, Karl Storz, Tuttlingen, Germany). Fiberoptic-guided tracheal intubation can be performed via the nose, mouth, or LMA, under sedation and topical anesthesia, or under general anesthesia. The nasal route may be preferred because it tends to maintain the scope in the midline, facilitating visualization of the larynx. Repeated practice in children with normal airways is recommended in order to acquire and maintain the skills essential to be proficient with the use of this equipment.

Fiberoptic guided tracheal intubation can also be performed through an LMA. Once the LMA is appropriately positioned, the FOB is passed through the opening of the LMA into the trachea. An ETT is passed into the trachea over the FOB, which is then used to confirm appropriate positioning. When a standard ETT is used, only a short length of the ETT remains outside the LMA making maintenance of ETT position and removal of the LMA difficult. A variety of techniques have been described to facilitate safe removal of the LMA while maintaining the ETT in place. First, a specially designed, long ETT can be placed over the FOB. Second, a tracheal tube exchange catheter (Cook Critical Care, Inc., Bloomington, IN) can be passed through the ETT into the trachea after which both the ETT and LMA are removed. An ETT is passed over the exchange catheter into the trachea. Third, the ETT can be made temporarily longer by wedging a half-size smaller ETT into the proximal end, or by cutting the 15 mm adapter and using it to connect two ETTs of the same size together. After placement of the combined ETTs through the LMA, the LMA and proximal ETT are removed and the 15 mm adapter is replaced. An alternative to fiberoptic intubation through the LMA is the "blind" passage of the ETT through the LMA into the trachea. An intubating LMA has been developed for this purpose and is available as small as size no. 3. In younger children, the epiglottis frequently folds inside the LMA.[17] While this may not cause airway obstruction, traumatic injury to the epiglottis may occur from blind passage of an ETT.

Several other methods for controlling the airway of patients with a difficult airway have been described. These include the use of a lighted stylet, combitube, retrograde transtracheal intubation, blind nasal intubation, use of the Bullard and other specialized laryngoscopes, and digital (tactile) techniques.[1,18,19] The reader is referred to a textbook of general pediatric anesthesiology for more detailed descriptions of these alternative techniques for intubation.

### Emergency cricothyrotomy

In the rare instance in which mask ventilation and placement of an LMA do not provide adequate oxygenation and ventilation and tracheal intubation cannot be performed, percutaneous cricothyrotomy may be life saving. Percutaneous tracheotomy kits are available (Cook Critical Care, Inc., Bloomington, IN) that are designed to facilitate pediatric tracheotomy tube placement through the cricoid membrane using the Seldinger technique.[20]

### The difficult extubation

Tracheal extubation of patients with risk factors for difficult reintubation presents a challenge to the anesthesiologist and intensive care physician. Infants and children with CHD are at high risk for adverse consequences associated with oxygen desaturation, hypercapnia, and hemodynamic instability prior to or during attempted reintubation. Respiratory distress signaling the need for reintubation may develop at a time when a physician with the greatest expertise in airway management is not immediately available. This can occur in the recovery room or intensive care unit (ICU), where equipment and other conditions may be less optimal than those encountered in the operating room. In addition, reintubation may be technically more difficult than the initial intubation due to airway edema, bleeding, secretions, and poor patient cooperation. Fiberoptic intubation or other alternative techniques may be extremely difficult or impossible under these circumstances.

Practice guidelines set forth by the American Society of Anesthesiologists Task Force for the Management of the Difficult Airway recommend that anesthesiologists have a preformulated strategy for extubating patients with a difficult airway.[21] This may include placement of a device through the indwelling ETT that serves as a stent over which the ETT can be replaced if the patient fails extubation. Accordingly, tracheal extubation of patients with a difficult airway has been performed over a FOB, a gum-elastic bougie, and a jet stylet.[22–24] The endotracheal ventilation catheter (ETVC) is a modification of the jet stylet. This device includes a Luer-lock connector in place of the removable 15-mm adaptor, allowing attachment to a high-pressure circuit for jet ventilation, capnography, or oxygen insufflation. The ETVC was used by Cooper in 202 patients over a 3-year period to maintain airway access in patients with difficult airways.[25] Oxygen insufflation and capnography were continued for up to 72 hours following tracheal extubation, during which time the catheter was well tolerated in most patients. Tracheal tube exchange and reintubation were successful in 20 of 22 attempts, with failure in two patients attributed to excessive pliability of a prototype catheter in one patient and operator inexperience in the other.

The Cook Airway Exchange Catheter (CAEC, Cook Critical Care, Bloomington, IN) has been used to maintain airway access in adult patients who were at risk for difficult reintubation.[26] Like the ETVC, this polyurethane catheter has multiple sideports proximal to its blunt tip. It is packaged with both 15-mm and Luer-locking connectors. The catheter was placed prior to tracheal extubation, after which humidified oxygen was insufflated through the lumen for a mean duration of 9.4 hours until it was deemed unlikely that tracheal reintubation would be necessary. In this study, four reintubations were performed over the CAEC on the first attempt and no complications were observed.

Because of their relatively large outer diameter, airway exchange catheters are not suitable for use in infants or small children for maintenance of airway access following tracheal extubation. The smallest available CAEC, for example, has a 3.0 mm outer diameter. In infants, this may severely limit gas flow around the catheter during spontaneous breathing. For young children, the use of a 0.018″ (0.457mm) guidewire for maintenance of airway access following tracheal extubation has been reported.[27] The guidewire used was Teflon-coated and had a floppy, curved tip designed to minimize tissue trauma during placement. This guidewire facilitates placement of the smallest CAEC over which a 3.5 mm ID ETT may be advanced, a method similar to previously described reports.[28,29]

## Airway and ventilatory management for thoracic surgery

### Ventilation/perfusion in the lateral decubitus position

Several pediatric cardiovascular surgical procedures are performed in the lateral decubitus position, including patent ductus arteriosus (PDA) ligation, insertion of a systemic to pulmonary shunt, repair of coarctation of the aorta, and unifocalization of the pulmonary arteries. Ventilation is normally distributed preferentially to dependent regions of the lung so that there is a gradient of increasing ventilation from the most non-dependent to the most dependent lung segments. Because of gravitational effects, perfusion normally follows a similar distribution, with increased blood flow to dependent lung segments. Therefore, ventilation and perfusion are normally well matched. During thoracic surgery, several factors act to adversely affect ventilation/perfusion ($V/Q$) matching. First, general anesthesia, neuromuscular blockade, and mechanical ventilation cause a decrease in functional residual capacity of both lungs. Second, compression of the dependent lung in the lateral decubitus position may cause atelectasis. Third, surgical retraction and/or single-lung ventilation (SLV) result in collapse of the operative lung. Lastly, hypoxic pulmonary vasoconstriction (HPV), which acts to divert blood flow away from the underventilated lung, thereby minimizing $V/Q$ mismatch, may be diminished by inhalational anesthetic agents and other vasodilating drugs. These factors apply equally to infants, children, and adults.

The overall effect of the lateral decubitus position on $V/Q$ mismatch, however, is unique in infants. In adults with unilateral lung disease, oxygenation is optimal when the patient is placed in the lateral decubitus position with the healthy lung dependent (down) and the diseased lung non-dependent (up).[30] Presumably, this is related to an increase in blood flow to the dependent, healthy lung and a decrease in blood flow to the non-dependent, diseased lung due to the

hydrostatic pressure (or gravitational) gradient between the two lungs. This phenomenon optimizes *V*/*Q* matching in the adult patient undergoing thoracic surgery in the lateral decubitus position.

In infants with unilateral lung disease, however, oxygenation is improved with the healthy lung "up."[31] Several factors account for this discrepancy between adults and infants. Infants have a soft, easily-compressible rib cage that cannot fully support the underlying lung. Therefore, functional residual capacity is closer to residual volume, making airway closure likely to occur in the dependent lung even during tidal breathing.[32] When the adult is placed in the lateral decubitus position, the dependent diaphragm has a mechanical advantage, since it is "loaded" from abdominal pressure. This pressure is reduced in infants, thereby reducing the functional advantage of the dependent diaphragm. The infant's small size also results in a reduced hydrostatic pressure gradient between the non-dependent and dependent lungs. Consequently, the favorable increase in perfusion to the dependent, ventilated lung is reduced in infants. This may be especially true for infants with systemic-to-pulmonary artery shunts, e.g. modified Blalock–Taussig or central surgically created shunts, PDA, or multiple aortopulmonary collateral arteries (MAPCAs), in whom systemic pressure may be maintained in the pulmonary arterial circulation.

Finally, all infants have increased oxygen consumption which predisposes them to hypoxemia. Infants normally consume 6–8 mL $O_2$/kg/minute compared with an adult's 2–3 mL/kg/minute.[33] The functional residual capacity of the lung functions as an oxygen reservoir when ventilation ceases. An infant will more rapidly consume oxygen from the diminished oxygen reservoir that is produced during surgery in the lateral decubitus position. Obviously, infants with cyanotic CHD are at increased risk of life-threatening oxygen desaturation during thoracic surgery.

## Single-lung ventilation

Prior to 1995, nearly all thoracic surgery in children was performed by thoracotomy. In the majority of cases, anesthesiologists ventilated both lungs with a conventional tracheal tube and the surgeons retracted the operative lung in order to gain exposure to the surgical field. During the past decade, the use of video-assisted thoracoscopic surgery (VATS) has dramatically increased in both adults and children. Reported advantages of thoracoscopy include smaller chest incisions, reduced postoperative pain, and more rapid postoperative recovery compared with thoracotomy.[34–36] Recent advances in surgical technique and technology, including high-resolution microchip cameras and smaller endoscopic instruments, have facilitated the application of VATS in smaller patients. Video-assisted thoracoscopic surgery is now being utilized for PDA occlusion in many centers. Open thoracotomy is generally performed for more complex procedures, including repair of coarctation of the aorta and pulmonary artery unifocalization.

Single-lung ventilation is extremely desirable during VATS as well as open thoracotomy because lung deflation improves visualization of thoracic contents and may reduce lung injury caused by the use of retractors.[37] There are several different techniques that can be used for SLV in children.

### Single lumen endotracheal tube

The simplest means of providing SLV is to intentionally intubate the ipsilateral mainstem bronchus with a conventional single lumen ETT. When the left bronchus is to be intubated, the bevel of the ETT is rotated 180° and the head turned to the right.[38] The ETT is advanced into the bronchus until breath sounds on the operative side disappear. A FOB may be passed through or alongside the ETT to confirm or guide placement. When a cuffed ETT is used, the distance from the tip of the tube to the distal cuff must be shorter than the length of the bronchus so that the cuff is entirely in the bronchus.[39] This technique is simple and requires no special equipment other than a FOB, and may be the preferred technique of SLV in emergency situations such as airway hemorrhage or contralateral tension pneumothorax.

Problems can occur when using a single lumen ETT for SLV. If a smaller, uncuffed ETT is used, it may be difficult to provide an adequate seal of the intended bronchus. This may prevent the operative lung from collapsing adequately, or fail to protect the healthy, ventilated lung from contamination by purulent material from the contralateral lung. It is not possible to suction the operative lung using this technique. Hypoxemia may occur due to obstruction of the upper lobe bronchus, especially when the short right mainstem bronchus is intubated.

Variations of this technique have been described, including intubation of both bronchi independently with small ETTs.[40–43] One mainstem bronchus is initially intubated with an ETT, after which another ETT is advanced over a FOB into the opposite bronchus.

### Balloon tipped bronchial blockers

A Fogarty embolectomy catheter or an end-hole, balloon wedge catheter may be used for bronchial blockade to provide SLV.[44–47] Placement of a Fogarty catheter is facilitated by bending the tip of its stylette toward the bronchus on the operative side. A FOB may be used to reposition the catheter and confirm appropriate placement. When an end-hole catheter is placed outside the ETT, the bronchus on the operative side is initially intubated with an ETT. A guidewire is then advanced into that bronchus through the ETT. The ETT is removed and the blocker is advanced over the guidewire into the bronchus. An ETT is then reinserted into the trachea alongside the blocker catheter. The catheter balloon

is positioned in the proximal mainstem bronchus under fiberoptic visual guidance. With an inflated blocker balloon the airway is completely sealed, providing more predictable lung collapse and better operating conditions than with an ETT in the bronchus.

A potential problem with this technique is dislodgement of the blocker balloon into the trachea. The inflated balloon will then block ventilation to both lungs and/or prevent collapse of the operated lung. The balloons of most catheters currently used for bronchial blockade have low volume, high pressure properties and overdistension can damage or even rupture the airway.[48] Guyton *et al*.,[49] however, reported that bronchial blocker cuffs produced lower "cuff to tracheal" pressures than double lumen tubes. When closed tip bronchial blockers are used, the operative lung cannot be suctioned and *CPAP* cannot be provided to the operative lung if needed.

Recently, adapters have been used that facilitate ventilation during placement of a bronchial blocker through an indwelling ETT.[50,51] Use of a new 5 Fr endobronchial blocker that is suitable for use in children with a multiport adapter and FOB has been described (Cook Critical Care, Inc., Bloomington, IN).[52] The risk of hypoxemia during blocker placement is diminished, and repositioning of the blocker may be performed with fiberoptic guidance during surgery. Even with use of a FOB with a diameter of 2.2 mm, however, the indwelling ETT must be at least 5.0 mm ID to allow passage of the catheter and FOB. The use of this technique, therefore, is generally limited to children over the age of 18 months to 2 years.

### Univent tube

The Univent tube (Fuji Systems Corporation, Tokyo, Japan) is a conventional ETT with a second lumen containing a small tube that can be advanced into a bronchus.[53–55] A balloon located at the distal end of this small tube serves as a blocker. Univent tubes require FOB for successful placement. Univent tubes are now available in sizes as small as 3.5 and 4.5 mm ID for use in children over 6 years of age.[56] Because the blocker tube is firmly attached to the main ETT, displacement of the Univent blocker balloon is less likely than when other blocker techniques are used. The blocker tube has a small lumen which allows egress of gas and can be used to insufflate oxygen or suction the operated lung, but this feature is only present in size 6.0 and larger Univent tubes.

A disadvantage of the Univent tube is the large amount of cross-sectional area occupied by the blocker channel, especially in the smaller size tubes which have a disproportionately high resistance to gas flow.[57] The Univent tube's blocker balloon has low volume, high pressure characteristics so mucosal injury can occur during normal inflation.[58,59]

### Double lumen tubes

All double lumen tubes (DLTs) are essentially two tubes of unequal length molded together. The shorter tube ends in the trachea and the longer tube in the bronchus. Marrarro[60] described a bilumen tube for infants. This tube consists of two separate uncuffed tracheal tubes of different length attached longitudinally, but it is not available in the USA. Double lumen tubes for older children and adults have cuffs located on the tracheal and bronchial lumens. The tracheal cuff, when inflated, allows positive pressure ventilation. The inflated bronchial cuff allows ventilation to be diverted to either or both lungs, and protects each lung from contamination from the contralateral side.

Conventional plastic DLTs, once only available in adult sizes (35, 37, 39, and 41 Fr), are now available in smaller sizes. The smallest cuffed DLT is 26 Fr (Rusch, Duluth, GA) which may be used in children as young as 8 years old. Double lumen tubes are also available in sizes 28 and 32 Fr (Mallinckrodt Medical, Inc., St Louis, MO) suitable for children 10 years of age and older.

Double lumen tubes are inserted in children using the same technique as in adults.[61] The tip of the tube is inserted just past the vocal cords and the stylette is withdrawn. The DLT is rotated 90° to the appropriate side and then advanced into the bronchus. In the adult population the depth of insertion is directly related to the height of the patient.[62] No equivalent measurements are yet available in children. If fiberoptic bronchoscopy is to be used to confirm tube placement, a scope with a small diameter and sufficient length must be available.[63]

A DLT offers the advantage of ease of insertion as well as the ability to suction and oxygenate the operative lung with *CPAP*. Left DLTs are preferred to right DLTs because of the shorter length of the right main bronchus.[64] Right DLTs are more difficult to position accurately because of the greater risk of right upper lobe obstruction.

Double lumen tubes are safe and easy to use. There are very few reports of airway damage from DLTs in adults, and none in children. Their high volume, low pressure cuffs should not damage the airway if they are not overinflated with air or distended with nitrous oxide while in place.

Guidelines for selecting appropriate tubes (or catheters) for SLV in children are shown in Table 16.3. There is significant variability in overall size and airway dimensions in children, particularly in teenagers. The recommendations shown in Table 16.3 are based on average values for airway dimensions. Larger DLTs may be safely used in large teenagers.

## Ventilatory management during thoracic surgery

During two-lung ventilation, tidal volumes of 10–15 mL/kg are typically used at a respiratory rate to effectively provide normocapnia. When ventilation to one lung is occluded, the delivered tidal volume should be reduced to 7–10 mL/kg and the respiratory rate increased by 20% in order to avoid excess inspiratory pressure and delivered tidal volume to the

**Table 16.3** Tube selection for single-lung ventilation in children.

| Age (yrs) | ETT (ID)* | BB† (Fr) | Univent®‡ | DLT (Fr)§ |
|---|---|---|---|---|
| 0.5–1.0 | 3.5–4.0 | 5 | | |
| 1–2 | 4.0–4.5 | 5 | | |
| 2–4 | 4.5–5.0 | 5 | | |
| 4–6 | 5.0–5.5 | 5 | | |
| 6–8 | 5.5–6.0 | 6 | 3.5 | |
| 8–10 | 6.0 cuffed | 6 | 3.5 | 26 |
| 10–12 | 6.5 cuffed | 6 | 4.5 | 26–28 |
| 12–14 | 6.5–7.0 cuffed | 6 | 4.5 | 32 |
| 14–16 | 7.0 cuffed | 7 | 6.0 | 35 |
| 16–18 | 7.0–8.0 cuffed | 7 | 7.0 | 35 |

*Sheridan® Tracheal Tubes, Kendall Healthcare, Mansfield, MA.
†Arrow International Corp., Redding, PA.
‡Fuji Systems Corporation, Tokyo, Japan.
§26 Fr—Rusch, Duluth, GA; 28–35 Fr—Mallinckrodt Medical, Inc., St. Louis, MO.
BB, bronchial blocker; DLT, double-lumen tube; ETT, endotracheal tube; Fr, French size; ID, internal diameter.

ventilated lung. Pulse oximetry and capnography are useful to reflect trends in the changes in oxygenation and ventilation, but monitoring of arterial blood gas tensions is important to accurately determine $PaO_2$ and $PaCO_2$.

Hypoxemia is commonly encountered during thoracic surgical procedures, especially in children with CHD and pre-existing hypoxemia, pulmonary hypertension, or compromised myocardial function. Hypoxemia develops from one or more of several possible mechanisms. The conducting passages of the operative lung are usually obstructed during single-lung ventilation and/or from surgical retraction and compression of the operative lung. The conducting passages of the dependent lung may also be compromised by secretions in the bronchial lumen or from surgical and hydrostatic compression. Reduction in ventilation to one lung causes regional hypoxemia, inducing HPV, which tends to minimize resultant *V*/*Q* mismatch. However, HPV may not effectively improve *V*/*Q* matching in children with CHD. In a dog model it has been shown that HPV is impaired by elevated pulmonary arterial pressure and by low mixed venous oxygen tension, both of which are commonly encountered among children with CHD.[65,66] Lastly, retraction of the operative lung may also impair cardiac filling and reduce cardiac output (*CO*), which decreases mixed venous oxygen concentration thereby worsening hypoxemia from either intracardiac or intrapulmonary shunting.

Hypoxemia should be treated immediately by increasing the $FIO_2$ to 1.0 and by confirming patency of the ETT. A suction catheter should be passed through the ETT to clear secretions and/or blood from the lumen. Irrigation with sterile saline may be performed. If the ETT remains occluded, a FOB may be used to determine the site of obstruction and to re-establish patency of the ETT. The surgeon should be informed, and compression of the lung and/or mediastinum should be minimized. Administration of intravenous fluids may improve *CO* and reduce *V*/*Q* matching by increasing perfusion pressure to the lungs. Application of *CPAP* to the non-dependent lung will reduce shunt through this lung and improve oxygenation during SLV. If hypoxemia persists despite these maneuvers, the operative lung should be reinflated with 100% oxygen. Although NO might be expected to increase *PBF* to the ventilated lung and improve oxygenation, two studies in adults failed to show benefit from NO during SLV.[67,68]

## Changes in lung function in children with congenital heart disease

Ventilation may be impaired in children with increased *PBF* due to left-to-right shunts, and both decreased lung compliance and increased airway resistance have been demonstrated in these children. Two studies in infants and young children with CHD found strong correlation between echocardiographic evidence of pulmonary artery engorgement and decreased lung compliance.[69,70] Among neonates undergoing Blalock–Taussig shunts or repair of coarctation of the aorta without CPB,[71] lung compliance decreases and airway resistance was significantly increased after surgery. Also, the return to baseline pulmonary function was prolonged after Blalock–Taussig shunt placement when compared to coarctation repair, suggesting that increases in *PBF* worsen pulmonary mechanics.[71] Some infants develop substantially increased total lung resistance following heart surgery; the severity of which can be predictive of postoperative respiratory failure.[72] Acute increases in pulmonary artery pressure (*PAP*) also produce significant changes in lung mechanics. Airway resistance increases 43% and compliance decreases 11% during periods of acute pulmonary hypertension.[73] Lung biopsy specimens from patients with the greatest increase in *PAP* had increased bronchial smooth muscle mass. Changes in lung mechanics correlate better with the magnitude of pulmonary vascular engorgement than with pulmonary artery hypertension. During cardiac catheterization, the degree of increased *PBF* is proportionate with increases in respiratory resistance among infants who are mechanically ventilated.[74] Infants with CHD and pulmonary overcirculation have reduced dynamic compliance and increased respiratory resistance that improves following surgery.[75]

Extrinsic compression of larger airways by the heart and vascular structures can also affect lung function in children with CHD. Both left and right mainstem bronchial compression have been described from enlarged pulmonary arteries. An enlarged left atrium can compress the left mainstem bronchus, and bronchial compression can occur from extrinsic compression by a right ventricle-to-pulmonary artery conduit.[76]

## Changes in lung function from cardiopulmonary bypass

Pulmonary dysfunction is common after cardiac surgery.[77] Children with increased *PBF* develop a threefold increase in lung water in the immediate postoperative period, the degree of which appears to be related to the presence of pulmonary hypertension.[78,79] In addition, both quantitative and qualitative differences in surfactant have been described in children after CPB.[80] Others have found the most common adverse pulmonary effect is the development of atelectasis, reported to be as high as 82% among children undergoing CPB.[81] Both non-cardiogenic pulmonary edema and acute bronchospasm have been reported following CPB in children and adults,[82,83] although the incidence of these complications in children is unknown. Some authors find correlation between the duration of CPB and the severity of lung injury while others find only minor changes in pulmonary mechanics related to CPB.[81,84–86] These differences may be related to improvements in CBP management over the past decade. In a study of over 100 infants undergoing heart surgery at Texas Children's Hospital, we found no correlation between the duration of CPB, the duration of aortic cross-clamp, the use of deep hypothermic circulatory arrest and pulmonary outcomes.[87]

## Cardiopulmonary interactions

Positive intrathoracic pressure typically has adverse hemodynamic effects on the right ventricle and beneficial hemodynamic effects on the left ventricle in patients with normal cardiac anatomy and function. Intrathoracic pressure is transmitted to the thin-walled, compressible superior and inferior venae cavae, reducing venous blood return to the right atrium and leading to a decrease in right ventricular filling.[88] In addition, right ventricular output will decrease if pulmonary vascular resistance (*PVR*) increases. With acute rises in *PVR*, the right ventricle may become dilated, resulting in decreased left ventricular filling as the intraventricular septum is displaced to the left.[89]

Pulmonary vascular resistance is affected by mechanical factors, chemical factors, and local humoral factors. Pulmonary vascular resistance is optimal when the resting lung volume is at functional residual capacity, and becomes elevated when lung volumes are above or below functional residual capacity. As lung volume decreases below functional residual capacity extra-alveolar (large) blood vessels are compressed. In addition, atelectasis develops when lung volume decreases, leading to HPV with associated elevation in *PVR*. When lung volumes exceed functional residual capacity, alveolar distension causes compression of smaller arterioles and capillaries, also resulting in an increase in *PVR* (Fig. 16.2).[90]

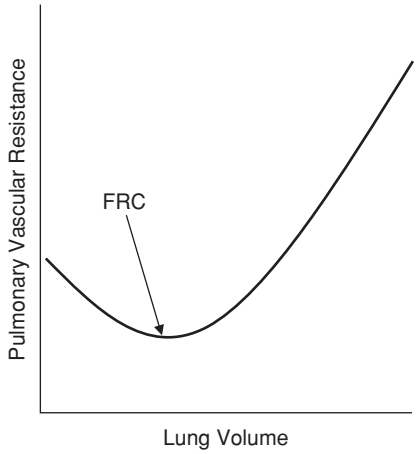



**Fig. 16.2** The relationship of lung volume to pulmonary vascular resistance. *FRC*, functional residual capacity.

Both oxygen tension and pH have significant effects on *PVR*,[91] with hypoxemia and acidemia causing an increase in *PVR*, and alkalemia reducing *PVR*. Local pH has the greatest affect on pulmonary vascular tone, and *PVR* is reduced by producing either respiratory or metabolic alkalemia. Finally, lung expansion from positive pressure ventilation causes a local release of prostaglandins, leading to pulmonary vasodilation. This may explain the decrease in *PVR* associated with the onset of hyperventilation that occurs before carbon dioxide is reduced.[91]

Changes in pleural pressure also affect left ventricular function. Ventricular output is affected by changes in afterload of the ventricle from transmitted intrathoracic pressure to the ventricular wall. The left ventricle lies within the thoracic cavity whereas most of the systemic arterial tree lies outside the thoracic cavity. Therefore, changes in pleural pressure affect the left ventricle and not the systemic vasculature. Afterload is affected by the ventricular transmural pressure, i.e. the intracavitary pressure minus the pleural pressure. During spontaneous ventilation, negative intrapleural pressure is transmitted to the ventricular wall. During systole, the ventricle must overcome systemic vascular resistance (*SVR*) and pleural pressure, therefore afterload is increased when negative pleural pressure develops as occurs during spontaneous ventilation. With positive pressure ventilation, *SVR* is unchanged, but afterload to the ventricle is reduced because positive intrapleural pressure will reduce ventricular transmural pressure (Fig. 16.3).[92–94]

## Mechanical ventilation for children with congenital heart disease

Changes in pleural pressure during inspiration have different hemodynamic effects on patients with cardiac and/or pulmonary disease. In healthy individuals, spontaneous

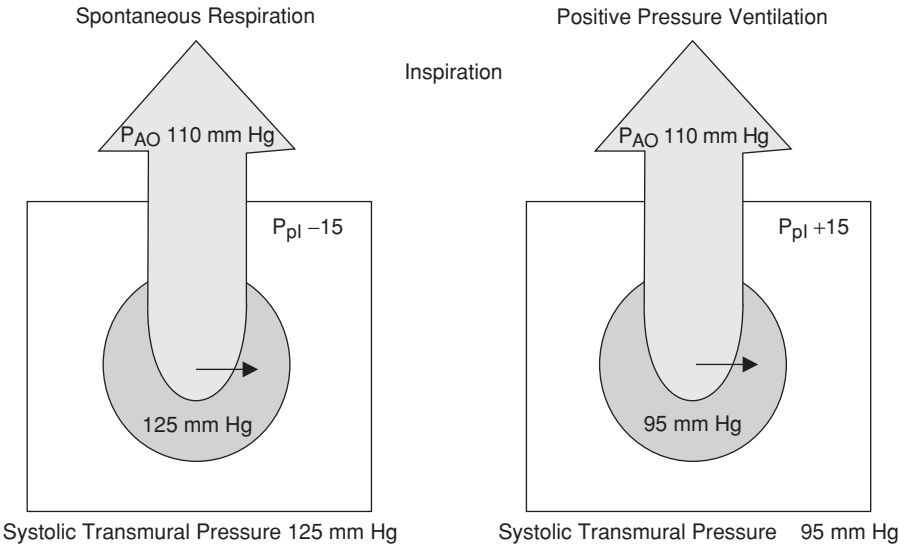



**Fig. 16.3** The effect of positive pressure ventilation on systemic ventricular transmural pressure during inspiration. $P_{AO}$, aortic pressure; Ppl, pleural pressure.

inspiration augments venous return and increases right ventricular output, while increasing left ventricular afterload and decreasing left ventricular output. The net effect on total *CO* is minor, and the conversion to positive pressure ventilation will have minimal effects on *CO*. However, in hypovolemic patients total *CO* decreases from positive pressure ventilation because the decrease in right ventricular preload becomes the predominate hemodynamic effect.

In patients with right heart failure, mechanical ventilation parameters should be selected that minimize intrathoracic pressure, maintain lung volume at functional residual capacity, avoid hypoxemia, and optimize pH in order to minimize *PVR*. Intrathoracic pressure should be minimized by avoiding excess positive end-expiratory pressure (*PEEP*) and excessively large tidal volumes. However, inadequate *PEEP* will cause lung volumes to decrease below functional residual capacity, thereby increasing *PVR* (see discussion above). Pressure–volume loops can be used to optimize pulmonary mechanics (Fig. 16.4). Hyperventilation is the traditional maneuver performed to reduce *PVR* because the associated hypocarbia produces alkalemia. However, both metabolic and respiratory alkalosis reduce *PVR*,[91,95] and local pH is the most significant factor affecting tone in pulmonary vessels. Because hyperventilation requires an increase in minute ventilation, greater intrathoracic pressure must be used which may negatively impact right ventricular preload. Creating a metabolic alkalosis through the administration of sodium bicarbonate will produce the same beneficial effect on reducing *PVR* without interfering with right ventricular filling. Inhaled NO further reduces *PVR* in patients with pulmonary hypertension and will improve right heart output.

Even though positive intrathoracic pressure reduces right ventricular filling, augmentation of *PBF* by high frequency, high volume ventilation has been described. Serra *et al*.[96] reported improved *CO* in four children with right ventricular

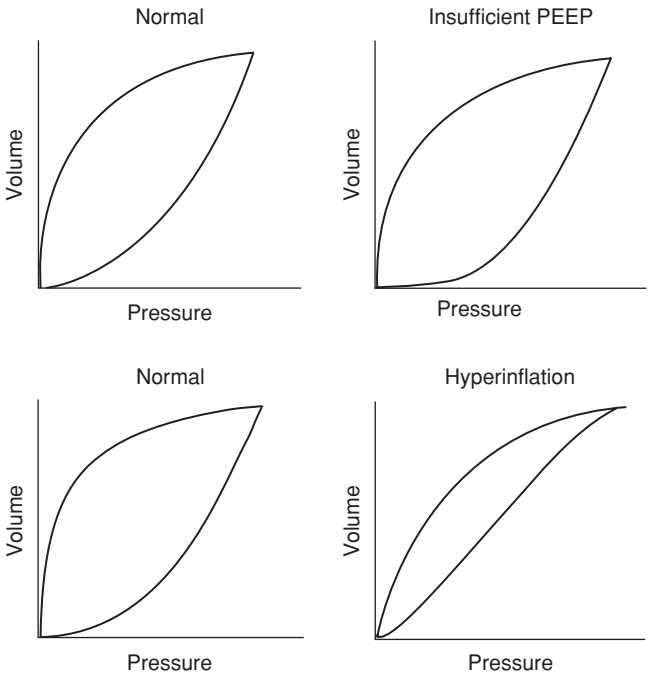



**Fig. 16.4** Effect of positive end-expiratory pressure (*PEEP*) on pressure–volume relationship in the lung.

failure with the use of high frequency (50 breaths/minute) high volume (30 mL/kg) ventilation following congenital heart surgery. These children had high central venous pressures and non-pulsatile *PBF* secondary to severe right ventricular failure. The changes in intrapulmonary blood volume from high frequency, high volume ventilation caused the lungs to function as a type of pump, increasing *PBF*, thereby augmenting left ventricular filling and improving *CO*.

Positive pressure ventilation can improve *CO* among patients with left ventricular failure.[97,98] As the left ventricle

fails left atrial pressure is increased, leading to pulmonary venous congestion and decreased lung compliance. Work of breathing is increased and greater negative pressure is generated during spontaneous ventilation, which, in turn, increases left ventricular afterload (see discussion above). Positive pressure ventilation will obviously decrease the work of breathing and thereby decrease oxygen consumption. In addition, positive intrathoracic pressure will reduce ventricular afterload enhancing *CO*.

Patients with non-pulsatile *PBF* (e.g. following the Glenn and Fontan procedures) show the most dramatic interactions between alterations in intrathoracic pressure, *PBF*, and *CO*. Because they lack pulsatile flow in their pulmonary arteries, positive intrathoracic pressure interferes with *PBF*. Likewise, elevations in *PVR* will reduce *PBF*. Reductions of *PBF* impair ventricular filling and reduce *CO*. The goals of lowering carbon dioxide in order to reduce *PVR* while diminishing intrathoracic pressure are diametrically opposed. A pattern of ventilation providing large tidal volumes, e.g. 15–20 mL/kg, with lower respiratory rates is believed to optimize carbon dioxide elimination and *PBF*. Positive end-expiratory pressure is generally avoided in order to diminish intrathoracic pressure. However, atelectasis and lung volumes below functional residual capacity will increase *PVR* and these problems can be minimized through the judicious use of *PEEP*. High-frequency jet ventilation effectively reduces carbon dioxide at a lower mean airway pressure and has been shown to improve *CO* when compared to conventional ventilation in postoperative Fontan patients.[99]

In patients with lung diseases associated with collapsed or fluid-filled alveoli (atelectasis, pulmonary edema, pneumonia, acute respiratory distress syndrome [ARDS]) gas exchange will improve when functional residual capacity is re-established through the use of *PEEP*. In this setting, the application of positive pressure and *PEEP* will have variable cardiovascular effects depending on lung compliance. Even high levels of *PEEP* have limited effect on *CO* when lung compliance is reduced, because the higher airway pressures are not transmitted to the heart and pulmonary vasculature.[100] Some congenital heart defects such as tetralogy of Fallot with absent pulmonary valve are associated with small and large airway compression from engorged pulmonary arteries. These patients develop airway collapse during exhalation and typically manifest hyperinflation of some lung segments and/or atelectasis in other areas.[101] Such children benefit from a ventilatory strategy that increases exhalatory time, i.e. a slower ventilatory rate allowing prolonged exhalation time. The optimal level of *PEEP* can be determined through the use of pressure–volume and flow–volume loops (Fig. 16.4).

## Lung management during cardiopulmonary bypass

Studies performed in animal models and adult patients have compared continued ventilation, use of intermittent sigh breaths, and maintenance of *CPAP* during CPB. Most studies show improvement in postoperative gas exchange from *CPAP*; however, this difference appears to be short lived.[102,103] No such studies have been performed in children. Because closing capacity is higher in infancy, maintaining airway patency through the application of *CPAP* would theoretically be beneficial. Lung inflation from *CPAP*, however, may interfere with adequate surgical access to the heart and complete lung collapse is usually required. An $F_{IO_2}$ of 0.21 has the theoretical benefit of diminishing absorption atelectasis during CPB, although this also has not been studied in children. Before weaning from CPB, several vital capacity breaths should be administered in order to re-establish patency of collapsed airways, reinflate atelectatic areas of the lung,[104] and to mobilize secretions into the larger airways. The tracheal tube should be suctioned prior to weaning from CPB to assure patency of the tracheal tube and large airways, but care must be taken in order to avoid tracheal mucosal injury producing hemorrhage in a fully anticoagulated patient. Inhaled $\beta_2$-agonists are commonly administered before weaning from CPB in order to decrease airway reactivity; however, the efficacy of this practice has not been proven.

## Volume-controlled vs. pressure-controlled ventilation

Volume-limited ventilation delivers a relatively constant tidal volume despite changes in the patient's total pulmonary compliance. During volume-controlled ventilation the peak inspiratory pressure varies and is dependent on the set tidal volume, *PEEP*, gas flow rate, gas flow resistance, and respiratory system compliance. The presence of high inflation pressures signals decreased pulmonary compliance or conductance (e.g. offset of neuromuscular blockade, bronchospasm) or obstruction of the breathing circuit (e.g. occluded ETT). Disadvantages of volume-limited ventilation include the potential to produce very high inflating pressures and increase the risk of barotrauma. With proper monitoring of inspiratory pressure, including the use of appropriate limits and alarms, changes in the patient's pulmonary mechanics can be observed and the risk of barotrauma minimized. Because of technical difficulties in accurately delivering very small tidal volumes (e.g. < 100 $cm^3$), volume-limited ventilators have been primarily used in patients over 10 kg body weight. More recently, however, ventilators have been introduced that may be used in a volume-limited mode for smaller patients.[105]

In the neonate and infant, ventilators that are pressure-limited and time-cycled are commonly used. These ventilators offer the advantages of avoiding excessive inflating pressures and barotrauma. However, a decrease in the compliance or conductance of the patient's respiratory system, ventilator

circuit, or tracheal tube will cause a reduction in delivered tidal volume. An increase in compliance, conversely, will result in an increased tidal volume. Pressure-limited or pressure-controlled ventilation (PCV) is frequently applied to infants and children receiving mechanical ventilatory support in whom severe pulmonary pathology dictates the need for rapid respiratory rates or high inflating pressures. Advantages of this mode of ventilation include limiting the peak-inflating pressure delivered by the ventilator, thereby limiting the transalveolar pressure and ventilator-induced lung injury.[106] The decelerating flow used to produce PCV is thought to improve the distribution of gas flow to the lungs.[107] When compared to volume-controlled ventilation there is a more rapid improvement in lung compliance and oxygenation with PCV.[108] Lastly, anesthesia ventilators may not deliver small tidal volumes accurately because of the proportionately large compression volume loss in the ventilator and circuit.[109] Therefore, setting an anesthesia ventilator in pressure control mode will deliver more consistent ventilation to infants.

### Monitoring ventilation

Ventilation is the tidal exchange of gas between lungs and the atmosphere, and is measured by the concentration of carbon dioxide in arterial blood. In the operating room, the most common non-invasive method of measuring carbon dioxide is capnography, which closely reflects changes in arterial carbon dioxide among patients without lung or heart disease. Capnography is less accurate in infants when there is a leak around the ETT and when carbon dioxide is measured at the Y-piece, due to fresh gas washout of the small volume of carbon dioxide sampled.[110,111] Another measurement of alveolar ventilation is the measurement of exhaled tidal volumes (TV). Exhaled TV is usually measured by a spirometer located at the end of the expiratory limb. This measurement tends to be an overestimate because it reflects the patient's exhaled TV and the compression volume in the breathing circuit. As a result the measured exhaled TV may be grossly inaccurate in infants. If there is a leak around the ETT, the spirometer will underestimate the exhaled gas volume. Without reliable $EtCO_2$ monitoring or exhaled TV measurements, the pediatric cardiovascular anesthesiologist must rely on chest expansion and peak inspiratory measurement (*PIP*) to make ventilator adjustments. Because adult anesthesia ventilators have large compression volumes, only profound changes in lung compliance reflect changes in *PIP*. For these reasons, blood gases should be measured frequently in order to assure adequate ventilation and to recognize changes in acid-base status. Newer monitoring systems allow for measurement of flow and pressure at the ETT, assisting the anesthesiologist in determining optimal ventilation in patients with poorly compliant lungs.

### Anesthesia ventilators

Badgwell *et al*.[109] evaluated the Ohmeda 7800 in 80 infants undergoing a variety of surgical procedures. These authors found a very large portion of the set tidal volume was lost due to gas compression in the anesthesia ventilator and circuit, requiring a set tidal volume ranging from 250–300 mL/kg for a 1 kg infant, to 25 mL/kg if the infant weighed 10 kg or more. With this type of system, changes in lung compliance have a profound affect on delivered TV in infants. For this reason, use of a neonatal or pediatric ICU ventilator may be preferable when caring for an infant with heart and/or lung disease in the operating room. Stevenson *et al*.[112] tested an anesthesia machine ventilator (Narkomed GS) with standard adult circle compared to two neonatal ICU ventilators in an infant test lung using pressure-limited ventilation. The authors found limited advantage in switching to an ICU type ventilator over the Narkomed GS. However, the Narkomed GS can deliver very high inspiratory flows, unlike the Ohmeda 7800 ventilator tested by Badgwell.

The North American Drager NAD 6000 has a piston-driven, microprocessor-controlled ventilator that compensates for variations in fresh gas flow as well as differences in compliance of the circle system. We compared the performance of the Servo 900C, an ICU ventilator, and the NAD 6000 in infants weighing less than 5 kg with CHD.[105] At identical volume control settings, the NAD 6000 delivered slightly greater minute ventilation, as evidenced by lower $EtCO_2$, $PaCO_2$, and measured tidal volumes. It generated higher *PIP* and peak inspiratory flows to do so, as well as a slightly higher mean airway pressure. Newer anesthesia ventilators have improved performance so there is little benefit in converting to an ICU-type ventilator in the operating room.

## Specialized problems

### Hypoxic gas mixture and inspired carbon dioxide

Infants and children with single ventricle physiology and excess *PBF* (e.g. those with hypoplastic left heart syndrome) may benefit from a ventilatory strategy designed to increase *PVR* and diminish *PBF*. Hypoxic gas mixtures (i.e. $FIO_2$ less than 0.21) or inhaled carbon dioxide have been used to accomplish this. Among neonatal patients with single ventricle physiology, 3% inhaled carbon dioxide improves cerebral oxygen saturation, mean arterial pressure, and oxygen delivery when compared with 17% inspired oxygen, which has no effect.[113,114]

### Surfactant

Despite the widespread use of surfactant in neonates, its therapeutic role in acute lung injury in pediatric patients

remains unclear. Therapeutic benefit in the treatment of acute lung injury has been reported in several case reports and uncontrolled studies in adults.[115,116] Aerosolized surfactant therapy has been associated with improved oxygenation and a trend toward decreased mortality in patients with sepsis-related acute lung injury in two prospective, randomized studies.[117,118]

There has been limited research regarding the changes in surfactant in pediatric patients undergoing CPB. Some studies have demonstrated an alteration in surfactant composition after CPB,[119] while others have demonstrated a decline in total pulmonary phospholipids.[120] It remains unclear whether exogenous surfactant administration will improve pulmonary outcomes. Until these issues are further resolved, surfactant therapy for non-neonatal acute respiratory failure must be considered experimental.

### Nitric oxide

Nitric oxide, an endothelium-derived smooth muscle relaxant, has been used in neonates with persistent pulmonary hypertension of newborn (PPHN)[121,122] and in infants and children with pulmonary hypertension related to CHD.[123,124] Nitric oxide has also been used in adult and pediatric patients with severe hypoxemic respiratory failure due to acute lung injury.[125–128] Inhaled NO selectively reduces *PVR* and may decrease intrapulmonary shunting. As a result, oxygenation is improved in patients with acute lung injury due to increased perfusion of relatively well-ventilated lung units.[129] Pulmonary vascular resistance and oxygenation are improved to a similar extent by doses of 11 and 60 p.p.m. in children with acute lung injury.[130] A recent study of infants with pulmonary hypertension after cardiac surgery found a decrease in *PAP*s and a 30% increase in oxygenation from the use of as little as 3–5 p.p.m. of NO, and no further benefit from increasing NO to as high as 80 p.p.m.[131] However, other studies have failed to show improvements in *PAP*s, oxygenation, or outcome.[132,133] Future studies are needed to determine the risks, benefits, optimal duration, and impact on survival of NO in children with severe respiratory disease after heart surgery.

### Liquid ventilation

Liquid ventilation, using chemically inert perfluorocarbons, has been investigated as a therapy for refractory respiratory failure.[134,135] Oxygen and carbon dioxide are highly soluble in perfluorocarbon liquids, theoretically enhancing alveolar gas exchange. Theoretical advantages of liquid ventilation include reduction in lung distending pressures, homogeneous lung expansion, maintenance of functional residual capacity, and facilitation of drug administration and alveolar lavage. The two forms of liquid ventilation are total (tidal) liquid ventilation (TLV) and perfluorocarbon-associated gas exchange (PAGE), or partial liquid ventilation. With TLV, a perfluorocarbon volume equal to functional residual capacity is instilled via a tracheal tube, and similar volumes are cycled to effect gas exchange. With PAGE, a volume of perfluorocarbon equal to functional residual capacity is instilled, after which mechanical ventilation is initiated using a conventional ventilator.

Studies using liquid ventilation in humans have been limited. Total (tidal) liquid ventilation was reported in three preterm infants with hyaline membrane disease refractory to conventional ventilation and surfactant therapy.[134] A gravity flow device was used for two brief cycles, after which an increase in lung compliance was noted. There was no circulatory compromise observed. Improved oxygenation occurred during subsequent gas ventilation, suggesting TLV-induced reduction in surface tension and/or improved lung expansion. Animal studies in neonatal swine have shown improved pulmonary function and cardiac function, and a reduction in neutrophil sequestration in the lung from liquid ventilation during hypothermic bypass.[136] Further studies are needed to define the indications, optimum modes of delivery, and possible toxicity associated with perfluorocarbon liquid ventilation.

## Summary

The pediatric cardiovascular anesthesiologist must have great knowledge and expertise in managing the airway and ventilatory issues during cardiothoracic surgery. Patients with CHD may have limited myocardial reserve as well as pre-existing cyanosis; disruptions of ventilation can lead to diminished oxygen delivery with associated organ injury or death. Many patients undergo thoracic surgery and require SLV in order to optimize surgical conditions. Lastly both pulmonary overcirculation and CPB will sometimes cause a lung injury. Therefore, the pediatric cardiovascular anesthesiologist must have expertise in managing acute lung injury.

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# 17 Regional anesthesia and postoperative pain management

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## Introduction

Treatment of pain following cardiac surgery is the subject of a growing number of publications and presentations given the current trend toward fast-track management of cardiac surgery patients. Tracheal extubation in the operating room or within a few hours of reaching the intensive care unit (ICU) has become common practice after the repair of simple cardiac defects.[1–6] This precludes the use of large doses of systemic opioids during and after surgery due to resultant respiratory depression. An alternative approach to the treatment of postoperative pain is therefore required.

Neuraxial anesthesia involves the use of intrathecal or epidural opioids with or without local anesthetic agents. The use of neuraxial anesthesia in combination with general anesthesia for children undergoing cardiac surgery has been reported to facilitate early tracheal extubation.[7,8] Reported benefits of neuraxial anesthesia in patients having cardiac surgery include attenuation of the neuroendocrine response to surgical stress, improved postoperative pulmonary function, enhanced cardiovascular stability, and improved postoperative analgesia. To the extent that neuraxial anesthesia facilitates early tracheal extubation in cardiac surgical patients, complications and costs associated with postoperative mechanical ventilation may be reduced. These benefits must, however, be weighed against the adverse effects that may accompany the use of neuraxial anesthesia. These include hypotension, postoperative respiratory depression, and epidural hematoma formation. In this chapter, the benefits and risks of neuraxial anesthesia in infants and children having open heart surgery are reviewed. In addition, specific techniques currently in use are described.

## The benefits of neuraxial anesthesia in cardiac surgery

Adverse physiologic responses which occur during and after cardiac surgery include alterations in circulatory (tachycardia, hypertension, vasoconstriction), metabolic (increased catabolism), immunologic (impaired immune response), and hemostatic (platelet activation) systems.[9,10] Together, these changes are referred to as the "stress response." The stress response associated with cardiac surgery in neonates may be profound and is associated with increased morbidity and mortality. Anand *et al*.[11] measured the stress response during and after cardiac surgery in 15 neonates anesthetized with halothane and morphine. They found elevated plasma concentrations of epinephrine, norepinephrine, cortisol, glucagon, and β-endorphin in all patients, accompanied by hyperglycemia and lactic acidemia. The four deaths in the study group occurred in neonates with the greatest stress responses.

Bromage *et al*.[12] first demonstrated in 1971 that the stress response associated with major abdominal and thoracic surgery could be attenuated with epidural blockade. Since then, several investigators have shown that the use of neuraxial anesthesia during and after cardiac surgery (i.e. intraoperative anesthesia and postoperative analgesia) may decrease the stress response as well as morbidity and mortality.[13–20] Neuraxial anesthesia (intrathecal or epidural blockade) with opioids and/or local anesthetics appears to be more effective in inhibiting the stress response associated with surgery than intravenous opioids. For example, epidural fentanyl is more effective than intravenous fentanyl in reducing the stress response after thoracotomy in adults.[21] Epidural morphine administration was shown to attenuate the adverse decrease in triiodothyronine ($T_3$) concentration in children undergoing open heart surgery compared with general anesthesia alone.[18] Epidural anesthesia with bupivacaine suppresses the increase in serum catecholamines, glucose, and adrenocorticotropic hormone (ACTH) more effectively than intravenous fentanyl in infants.[19] Epidural local anesthetics may be more efficacious than opioids in attenuating the stress response.[20] In a study of fetal lambs, total spinal anesthesia completely blocked the stress response to surgical manipulation and cardiopulmonary bypass (CPB).[22]

In contrast, intravenous anesthetic techniques do not appear to mitigate the stress response. Gruber *et al*.[23] studied the effects on the stress response of intravenous fentanyl and midazolam on 45 infants undergoing cardiac surgery. Patients were randomized to receive fentanyl 0.05–0.10 mg/kg with or without midazolam 0.10 mg/kg/hour during the surgery. Plasma epinephrine, norepinephrine, cortisol, adrenocortical hormone, glucose, and lactate were measured at five intervals during and after surgery. In all groups, plasma epinephrine, norepinephrine, cortisol, glucose, and lactate concentrations were significantly greater at the completion of surgery than prior to skin incision. The authors concluded that fentanyl dosing strategies, with or without midazolam, do not prevent a hormonal or metabolic stress response in infants undergoing cardiac surgery.

Additional benefits that may be attributed to neuraxial anesthesia include improved pulmonary function, greater circulatory stability, and reduced pain scores. Several randomized, controlled studies in adults have shown that patients receiving epidural analgesia have better pulmonary function after thoracic surgery than those treated with intravenous opioids. Thoracic epidural opioids are associated with improved pulmonary function following chest surgery compared with intravenous opioids.[24] In a study comparing thoracic epidural meperidine to intravenous meperidine for postoperative analgesia, the patients receiving epidural infusions had significantly greater forced expiratory volumes in 1 second ($FEV_1$) and forced vital capacity ($FVC$), and were more cooperative with deep breathing maneuvers than those in the intravenous meperidine group.[25] Thoracic epidural anesthesia may also improve respiratory performance postoperatively by effecting an improvement in diaphragmatic function.[26]

Early tracheal extubation is an important factor in reducing ICU length of stay and the duration of hospitalization.[4] Especially in children with single ventricle physiology (e.g. following bilateral cavopulmonary anastomosis or modified Fontan operations), spontaneous ventilation may result in improved hemodynamics by decreasing intrathoracic pressure and thereby increasing pulmonary blood flow.[27] Early tracheal extubation may also obviate or reduce complications associated with mechanical ventilation, including trauma to the lungs and airways, inadvertent dislodgement or malpositioning of the tracheal tube, and adverse hemodynamic changes associated with tracheal suctioning. The cost of mechanical ventilation can be avoided in patients who are extubated in the operating room.[4] A number of studies have shown that infants and children can be safely extubated within several hours following the completion of surgery.[1,2,28,29] The majority of reports of early extubation following open heart surgery in infants and children include a period of 6–8 hours of mechanical ventilation in the ICU after surgery. A limited number of reports describe tracheal extubation in the operating room at the completion of surgery.

## Early extubation without neuraxial anesthesia

In an early report of tracheal extubation in the operating room following congenital heart surgery, Schuller *et al*.[30] reviewed the records of 209 children who had undergone repair of congenital heart defects. Fifty-two percent of infants between the ages of 3 and 12 months and 88% of patients over the age of 12 months were extubated in the operating room. Four patients were reintubated in the operating room or ICU. Inhaled agents were supplemented with low doses of fentanyl to provide anesthesia. Similarly, Burrows *et al*.[3] reviewed the management of 36 children undergoing repair of secundum atrial septal defects under isoflurane and fentanyl anesthesia. The tracheas of 19 children (53%) were extubated in the operating room. Compared to those children receiving postoperative mechanical ventilation, these patients had shorter CPB times (24 vs. 32 minutes) and received lower doses of fentanyl (5.9 vs. 35.1 μg/kg).

Laussen *et al*.[5] reported tracheal extubation in the operating room after atrial septal defect repair as part of a clinical practice guideline in children. Of 66 children reviewed subsequent to the implementation of the practice guideline, 25 patients (38%) were extubated in the operating room while the remainder received postoperative mechanical ventilation. The children in the early extubation group received less fentanyl (6.0 vs. 27.5 μg/kg), were more likely to have a respiratory acidosis on admission to the ICU, and had an increased frequency of vomiting in the ICU. Eight children in the early extubation group received caudal morphine 50–75 μg/kg vs. two children in the postoperative mechanical ventilation group. There was no difference in ICU stay or in clinical outcomes. The patients extubated in the operating room had significantly lower hospital charges due to the absence of postoperative mechanical ventilation.

Cray *et al*.[6] reported the use of propofol with "low dose" opioid anesthesia to facilitate early tracheal extubation following cardiac surgery in children between the ages of 6 months and 18 years. Isoflurane and fentanyl (up to a maximum dose of 20 μg/kg) were given prior to and during CPB. In patients for whom early tracheal extubation was considered, a propofol infusion was started at 50 μg/kg/minute as well as a morphine infusion at a dose of 10–40 μg/kg/minute. The median time to tracheal extubation was 5 hours. The goal of extubation within 6 hours was achieved in 56 children (62%). Causes for prolonged intubation included bleeding and phrenic nerve palsy. One child was reintubated shortly following extubation due to excessive respiratory depression.

## Neuraxial anesthesia and early extubation

Neuraxial anesthesia techniques have been used to facilitate

early tracheal extubation following cardiac surgery, improve postoperative analgesia, and reduce the incidence of side effects caused by intravenous opioids. Jones *et al*.[31] reported the use of intrathecal morphine for postoperative analgesia in 56 children undergoing cardiac surgery. Following induction of anesthesia, patients received intrathecal morphine 0.02 or 0.03 mg/kg. Tracheal extubation was performed in all patients after admission to the ICU shortly following the completion of surgery. The duration of analgesia in both groups was similar, with two-thirds of patients requiring no supplemental analgesia for more than 18 hours.

In a retrospective review of pain control in 91 children undergoing cardiac surgery, Shayevitz *et al*.[32] compared lumbar epidural morphine infusions to intravenous opioid analgesia. In the epidural analgesia group, lumbar epidural catheters were placed following induction of anesthesia. Preservative-free morphine sulfate was administered in an initial dose of 0.05 mg/kg followed by a continuous infusion of 0.003–0.004 mg/kg/hour during and after surgery. Children in the intravenous analgesia group received an initial dose of fentanyl 0.05 mg/kg i.v. followed by a continuous infusion of 0.018 mg/kg/hour i.v. during surgery. The fentanyl infusion was reduced to 0.006 mg/kg/hour i.v. postoperatively. Patients in the epidural analgesia group had significantly lower pain scores and received significantly less supplemental analgesia postoperatively than patients in the intravenous analgesia group.

In a prospective, randomized, controlled study, Rosen and Rosen[33] evaluated the efficacy of caudal epidural morphine compared with intravenous morphine in 32 children following open cardiac surgery. Patients in the study group received a caudal injection of preservative-free morphine sulfate 0.075 mg/kg in the operating room following surgery prior to awakening and tracheal extubation. Children in the control group received intravenous morphine alone for postoperative analgesia. Supplemental doses of intravenous morphine were given to children in both groups as needed, prior to which pain scores were recorded. Children having received caudal morphine required significantly less intravenous morphine and had significantly lower pain scores postoperatively than patients in the control group. The mean duration of complete analgesia in children receiving caudal morphine was 6 hours (range 2–12 hours), but decreased analgesic requirements were noted for the entire 24-hour study period.

In another prospective, randomized, controlled study, Hammer *et al*.[34] compared postoperative analgesia in children receiving a remifentanil-based anesthetic with or without spinal anesthesia for open heart surgery. Patients in both groups were extubated in the operating room immediately following the completion of surgery. Intravenous fentanyl was administered according to age appropriate pain scores postoperatively. Patients in the spinal anesthesia group received significantly less fentanyl during the initial 8- and 24-hour periods following surgery than those in the control group ($P < 0.01$, $P = 0.02$, respectively). There was a trend toward lower pain scores in patients receiving spinal anesthesia compared with those in the control group.

In addition to the benefits of improved lung function and pain control, patients receiving neuraxial anesthesia have fewer opioid-related side effects than patients treated with intravenous opioids. Patients receiving epidural anesthesia have more rapid return of bowel function following surgery compared with those receiving intravenous analgesics. In a recent review of 16 studies comparing epidural and systemic analgesia with regard to postoperative recovery of gastrointestinal function, all eight studies with epidural catheter placement above T12 showed more rapid recovery of bowel function when epidural analgesia was used.[35] The use of postoperative thoracic epidural analgesia with bupivacaine and morphine was associated with earlier return of gastrointestinal function and decreased hospital costs due to shortened hospital stay compared with intravenous morphine patient-controlled analgesia (PCA).[36] A study comparing epidural vs. intravenous fentanyl analgesia following thoracotomy also reported a lower incidence of nausea, shorter duration of ileus, and earlier hospital discharge in the epidural analgesia group.[21]

## Adverse effects of neuraxial anesthesia for cardiac surgery

Although neuraxial anesthesia offers many benefits, adverse effects may occur. The most serious complications that may be associated with neuraxial anesthesia for cardiac surgery are hypotension, respiratory depression, and epidural hematoma formation.

Systemic arterial hypotension is an undesired effect of intrathecal and epidural local anesthetic blockade. In adults with coronary artery stenosis and myocardial ischemia, local anesthetic-induced blockade of cardiac sympathetic nerve activation alleviates angina and improves coronary blood flow and ventricular function.[20,37–39] However, local anesthetic blockade to upper thoracic dermatomes produces hypotension accompanied by a decrease in coronary artery perfusion.[13,40] In infants and young children, local anesthetic blockade to T3–T5 does not produce significant changes in blood pressure nor heart rate.[41] This may be attributable to decreased sympathetic innervation of the lower extremities and/or immaturity of the sympathetic nervous system in young children. In two recent studies of high spinal blockade in children undergoing open heart surgery, hemodynamic stability was demonstrated in all patients.[7,42]

Respiratory depression may be seen in children following the administration of epidural opioids in doses exceeding 0.05 mg/kg.[43] However, in a study of children undergoing cardiac surgery and receiving epidural morphine in an initial

dose of 0.05 mg/kg followed by a continuous infusion, respiratory depression did not occur.[32] Several other studies in children have shown excellent analgesia and no evidence of respiratory depression when the dose of epidural morphine does not exceed 0.05 mg/kg.[44–46]

Similarly, doses of intrathecal morphine exceeding 0.02 or 0.03 mg/kg may result in significant respiratory depression following cardiac surgery in children.[31] Intrathecal morphine 0.01 mg/kg has also been associated with respiratory depression postoperatively when combined with midazolam and intravenous fentanyl 0.02 mg/kg in adult patients undergoing cardiac surgery.[47] However, in a review of children given intrathecal morphine in a dose of 0.02 mg/kg in whom no intravenous opioids were administered during surgery, no patient had postoperative respiratory depression.[48] In addition, no child required supplemental opioid analgesia for at least 15 hours following surgery. In a recent study comparing intrathecal morphine in doses of 0.005, 0.007, and 0.010 mg/kg in children having open heart surgery, the trachea of each patient was extubated at the conclusion of surgery and no patient had signs of respiratory depression.[49] Hammer *et al*.[50] reported results of a study of postoperative respiratory depression in children anesthetized with remifentanil with or without spinal anesthesia for open heart surgery. The authors found only mild elevation in arterial carbon dioxide tension in children in both groups following surgery. No patient required intervention for respiratory depression.

Epidural hematoma formation following epidural or spinal anesthesia is a rare but potentially catastrophic complication of neuraxial blockade. In an analysis of 20 series, including more than 850 000 cases of epidural blockade and 650 000 cases of spinal anesthesia in adult patients, only three case reports of epidural hematoma were documented.[51] Based on these data, the author estimated the risk of epidural hematoma to be 1 : 150 000 following epidural anesthesia and 1 : 220 000 following spinal anesthesia. Unfortunately, it is unknown what the incidence of clotting disorders, use of anticoagulants, or traumatic procedures was in these reports.

In a thorough review of the literature from 1906 through 1994, Vandermeulen *et al*.[52] found 61 published cases of epidural or subdural hematoma following epidural or spinal anesthesia in adult patients. Of these 61 cases, 42 occurred in patients with impaired coagulation prior to epidural or spinal needle placement, including 25 patients receiving heparin. In 15 patients, the procedure was reported to be difficult and/or traumatic. A clotting disorder or difficult/traumatic needle placement was present in 53 of the 61 cases (87%).

In a series of over 4000 epidural or spinal anesthetics performed prior to anticoagulation with heparin for vascular surgery, no cases of epidural hematoma were reported.[53] The authors highlighted important precautions that were undertaken in these patients, including delaying surgery for 24 hours in the event of traumatic needle placement, and allowing at least 1 hour between needle placement and heparin administration. Other recommended precautions include use of the smallest dose of heparin necessary to achieve therapeutic objectives and removal of epidural catheters only when normal coagulation function has been restored.[54] Although traumatic needle placement may increase the risk of hemorrhage, there are no data to guide the practitioner as to whether or not surgery should be cancelled. Patients must be monitored postoperatively for signs of unexpected motor blockade suggestive of epidural hematoma formation. When epidural analgesia is used following surgery, the minimum effective concentration of local anesthestic should be administered to allow early detection of an epidural hematoma.[55] Epidural hematoma formation has not been reported in a patient following spinal anesthesia performed prior to CPB.

Pediatric data regarding neuraxial hematoma are sparse, but a symptomatic intraspinal hematoma has been reported in a neonate undergoing non-cardiac surgery from a caudal epidural catheter threaded to the lumbar level.[56] In the largest series reported to date, 961 pediatric patients undergoing cardiothoracic surgery who received catheter epidural techniques were studied.[57] Caudal, lumbar, and thoracic sites were studied, and heparinized and non-heparinized cases, as well as coarctation of aorta repairs were included. There was a 7.9% incidence of observing blood through the needle or catheter during placement, and 88% of these incidents were with caudal catheters. Surgery apparently was not delayed in these cases, but a median of 90 minutes elapsed between catheter placement and heparinization for caudal catheters, and 183 minutes for thoracic epidurals. No neurologic deficits attributable to the epidurals were noted in any patient, including 60 patients undergoing coarctation repair, three of whom bled during catheter placement. Despite the lack of reports of neurologic injury with neuraxial techniques and their benefits to facilitate early extubation and pain control, neuraxial anesthesia for cardiac surgery in children remains a very controversial topic, and awaits large-scale controlled studies.[58]

## Neuraxial anesthesia techniques

A variety of neuraxial blockade techniques have been reported in children undergoing cardiac surgery. These include intrathecal (spinal) and epidural techniques utilizing opioids and/or local anesthetics. Epidural approaches include single dose ("single shot") caudals as well as thoracic, lumbar, and caudal catheter techniques.

### Intrathecal (spinal) techniques

The use of spinal opioid analgesia as an adjunct to general anesthesia was first described by Mathews and Abrams[59] in 1980. In this report, 40 adults received intrathecal morphine

in a dose of 1.5–4.0 mg prior to surgery. All patients remained comfortable for more than 24 hours. Subsequently, many studies have demonstrated the efficacy of spinal opioids, primarily morphine, in producing analgesia following cardiac surgery in adult patients. These reports have been summarized elsewhere.[54] Although intrathecal morphine alone has not been shown to attenuate the stress response associated with cardiac surgery per se, it may attenuate the stress response in the immediate postoperative period.[60]

In order to augment the effects of intrathecal opioids in reducing the stress response and circulatory instability in patients undergoing cardiac surgery, local anesthetics have been used in combination with intrathecal opioids. In adults, however, intrathecal injection of local anesthetics in doses needed to attain high spinal blockade results in hypotension.[61] Young children, on the other hand, do not develop hypotension following high spinal blockade. Finkel *et al*.[42] studied the hemodynamic effects of spinal anesthesia in children undergoing cardiac surgery. In this study, 30 children between the ages of 7 months and 13 years received intrathecal morphine mixed with tetracaine following induction of general anesthesia and tracheal intubation. The dose of tetracaine was adjusted for age, according to the estimated volume of cerebrospinal fluid. Patients aged 6–12 months received intrathecal tetracaine 2.0 mg/kg, those between the ages of 1 and 3 years received 1.0 mg/kg, and those over the age of 4 years received 0.5 mg/kg. Tetracaine was mixed with 10% dextrose to yield a 0.5% hyperbaric solution, and all patients received preservative-free morphine in a dose of 0.005–0.010 mg/kg. Patients were placed in a 30° head-down (Trendelenberg ) position for a minimum of 10 minutes following administration of the intrathecal solution. Although there was mild slowing of the heart rate in children over age 4 years, there was no clinically significant bradycardia nor hypotension observed. Hammer *et al*.[7] have also reported hemodynamic stability following intrathecal tetracaine/morphine in children undergoing cardiac surgery.

The use of spinal anesthesia in combination with general anesthesia has been reported in children for whom tracheal extubation is planned prior to leaving the operating room following open heart surgery.[7] Surgical procedures included repair of atrial and/or ventricular septal defects, anomalous pulmonary venous return, aortic or pulmonary valvuloplasty, right ventrical-to-pulmonary artery conduit placement or exchange, bidirectional cavopulmonary shunt, and the modified Fontan procedure. Spinal anesthetic blocks were performed immediately after tracheal intubation (i.e. prior to placement of arterial and central venous catheters) in order to maximize the time interval between spinal anesthetic block and heparinization for CPB. Patients were placed with the head of the table 30° down for a minimum of 15 minutes following spinal anesthetic block. No intravenous opioids were administered intraoperatively. The authors' dosing regimen for spinal anesthetic blocks is shown in Table 17.1.

**Table 17.1** Dosing regimens for spinal anesthesia.

| Age (years) | Tetracaine (mg/kg) | Morphine (mg/kg) |
|---|---|---|
| < 1 | 2.0 | 0.007 |
| 1–3 | 1.0 | 0.007 |
| 4–8 | 0.5 | 0.007 |
| > 8 | 0.0 | 0.010 |

## Epidural techniques

The use of postoperative epidural analgesia in patients undergoing open heart surgery was first described by Hoar *et al*.[62] in 1976. Subsequently, El-Baz and Goldin[17] reported the use of epidural blockade initiated prior to surgical incision. In 1989, Rosen and Rosen[33] first reported the efficacy of epidural morphine analgesia in children undergoing cardiac surgery. Since then, many studies have reported favorable results with epidural anesthesia and analgesia for cardiac surgery.[54]

In general, epidural anesthesia is used in patients undergoing open heart surgery for whom tracheal extubation is planned in the operating room following the completion of surgery or shortly thereafter. The epidural technique most commonly used in children is the administration of a single dose of morphine injected into the caudal epidural space. Morphine is favored for caudal epidural administration due to its low lipid solubility and tendency to spread cephalad to thoracic dermatomes.[63,64] Following induction of general anesthesia and tracheal intubation, preservative-free morphine sulfate is injected in a dose of 0.05–0.10 mg/kg into the caudal epidural space via an epidural needle or intravenous catheter. Intravenous opioids, if administered intraoperatively, are given in restricted doses (e.g. fentanyl 0.01–0.02 mg/kg).

Alternatively, a caudal epidural catheter may be inserted to facilitate continuous administration of morphine during and after surgery. Following an initial dose of epidural morphine 0.04 mg/kg, a continuous infusion is begun in a dose of 0.0075 mg/kg/hour. The infusion is continued throughout the intraoperative period and maintained postoperatively for 48–72 hours. If the patient appears overly somnolent the infusion is decreased in increments of 0.0025 mg/kg/hour (pers. comm., D. Rosen to G.B. Hammer, January 2000).

In order to attenuate the stress response associated with cardiac surgery and CPB as well as optimize postoperative analgesia, a combination of epidural opioids and local anesthetic agents may be used. Although local anesthetic agents may spread to thoracic dermatomes when administered via the caudal epidural space, potentially toxic doses of local anesthetics may be required to achieve thoracic analgesia.[65,66] Thoracic epidural blockade may be achieved with greater safety and efficacy by placing the epidural catheter tip in proximity to the spinal segment associated with surgical

**Table 17.2** Local anesthetic dosing regimens for thoracic epidural anesthesia.

| Epidural local anesthetics | Intraoperative dosing | Postoperative infusion |
|---|---|---|
| Bupivacaine | 0.25%: 0.5 mL/kg initial, then 0.3 mL/kg every 90 seconds | 0.1%: 0.15–0.30 mL/kg/h, max. dose 0.4 mg/kg/h |
| Ropivacaine | 0.2%: 0.5 mL/kg initial, then 0.3 mL/kg every 90 seconds | 0.1%: 0.15–0.30 mL/kg/h, max. dose 0.4 mg/kg/h |

**Table 17.3** Thoracic epidural opioids.

| Agent | Intraoperative bolus | Postoperative infusion |
|---|---|---|
| Fentanyl (thoracic) | 1–2 μg/kg | 1–5 μg/mL: 0.25–1.00 μg/kg/h |
| Hydromorphone (caudal/lumbar) | 7–8 μg/kg | 10–30 μg/mL: 2–3 μg/kg/h |
| Morphine (caudal/lumbar) | 50–75 μg/kg | 50 μg/mL: 4–6 μg/kg/h |

Reduce doses of all agents 50% for infants under 3 months of age; use local anesthetic doses at lower end of range for thoracic epidural catheters.

incision. Segmental anesthesia may then be achieved with lower doses of local anesthetic than those needed when the catheter tip is distant from the surgical site. In infants, a catheter can be advanced from the caudal to the thoracic epidural space.[67] For example, with the infant in the lateral decubitus position, a 20-gauge epidural catheter may be inserted via an epidural needle or an 18-gauge intravenous catheter placed through the sacrococcygeal membrane. The epidural catheter is then advanced 16–18 cm to the mid-thoracic epidural space. Minor resistance to passage of the catheter may be overcome by simple flexion or extension of the spine. If continued resistance is encountered, no attempt should be made to advance the catheter further, as the catheter may become coiled within or exit the epidural space. A newly described method to guide placement of caudal epidural catheters at thoracic dermatomes is to use the electrocardiogram (ECG).[68] All catheters in this report were within two vertebrae of the target. Radiographic confirmation of tip location may be undertaken following placement or postoperatively. In older children, a thoracic epidural catheter may be inserted directly between T4 and T8 to provide intraoperative anesthesia and postoperative analgesia. As with spinal anesthetic block, epidural catheter placement should be performed immediately following tracheal intubation in order to maximize the time elapsed prior to heparin administration for CPB. Hammer *et al*.[7] reported the use of an initial dose of hydromorphone 0.007–0.008 mg/kg and 0.25% bupivacaine 0.5 mL/kg. Subsequent doses of 0.25% bupivacaine 0.3 mL/kg are administered intraoperatively at approximately 90 minute intervals. No intravenous opioids are given during surgery. Postoperatively, a continuous infusion of 0.10% bupivacaine and hydromorphone 0.003 mg/mL is administered at a rate of 0.3 mL/kg/hour. Intraoperative and post-operative thoracic epidural local anesthetic regimens are listed in Table 17.2. An advantage of epidural catheter compared with "single shot" techniques is that adjustments can be made in dosing postoperatively according to the patient's level of comfort. For example, a "bolus" of epidural anesthetic agents may be given and the infusion rate increased if the patient is experiencing pain. Alternatively, the infusion may be decreased if the patient becomes somnolent. Table 17.3 lists suggested regimens for thoracic epidural opioids.

Ropivacaine is a newer long-acting local anesthetic agent that has the advantage of reduced cardiotoxicity and neurotoxicity compared to bupivacaine.[69,70] It also has less propensity to cause motor blockade in children.[71] Its pharmacokinetics for long-term (2–4 days) infusion via lumbar or low thoracic epidural catheter has been studied, and plasma levels are well within the safe range in children 4 months to 7 years in age undergoing major abdominal surgery.[72] Analgesia was excellent and side effects few with 0.2% ropivacaine infused at 0.4 mg/kg/hour. Of note is that starting doses for neonates and young infants under 3 months of age should be reduced by 50% because of reduced clearance of all agents due to renal and hepatic immaturity in this age group.

## Treatment of side effects

Side effects related to neuraxial opioids include nausea and vomiting, pruritus, somnolence, respiratory depression, and urinary retention. Nausea and vomiting as well as pruritus appear to be relatively uncommon in infants and are primarily seen in children over the age of 3 years. These side effects are more common with morphine compared with hydromorphone and fentanyl.[73] Due to greater rostral spread, respiratory depression is also more common when morphine is used compared with hydromorphone.[63,73] Urinary retention is seen most commonly during the initial 24 hours of therapy, during which time the majority of patients have urinary

**Table 17.4** Treatment for side effects of neuraxial opioid administration.

| Side effect | Treatment | Comments |
|---|---|---|
| Nausea/vomiting | Metoclopromide 0.1–0.2 mg/kg/dose i.v. Q 6 h<br>Maximum dose: 10 mg | Extrapyramidal reactions may occur but are uncommon |
| | Droperidol<br>0.025–0.05 mg/kg i.v. Q 6 h p.r.n.<br>Maximum dose: 1.25 mg | Very sedating—avoid if somnolent |
| | Diphenhydramine<br>0.5–1.0 mg/kg i.v. Q 6 h p.r.n.<br>Maximum dose: 50 mg | Very sedating—avoid if somnolent |
| | Ondansetron<br>0.1–0.2 mg/kg i.v. Q 6 h p.r.n.<br>Maximum dose: 4 mg | May substitute other 5-$HT_3$ antagonist, e.g. granisetron or dolasetron |
| | Nalbuphine<br>0.1 mg/kg i.v. Q 6 h p.r.n. | |
| | Naloxone 0.001–0.005 mg/kg/h infusion | Excessive doses may compromise analgesia |
| | Propofol<br>0.001–0.010 mg/kg/h infusion | |
| Pruritus | Diphenhydramine 0.5–1.0 mg/kg i.v. Q 6 h p.r.n.<br>Maximum dose: 50 mg | Very sedating—avoid if somnolent |
| | Nalbuphine 0.1 mg/kg i.v. Q 6 h p.r.n. | |
| | Naloxone 0.001–0.005 mg/kg/h infusion | Excessive doses may compromise analgesia |
| Somnolence | Decrease epidural opioid infusion<br>Consider low dose naloxone infusion (above) | |
| Respiratory depression | *Severe*: Administer 100% oxygen via facemask<br>Initiate positive pressure ventilation p.r.n.<br>Naloxone 0.001–0.010 mg/kg i.v.<br>Stop epidural infusion<br>*Subsequently/Mild–moderate depression*:<br>Increase $F_{IO_2}$<br>Reduce epidural opioid infusion<br>Naloxone 0.001–0.005 mg/kg/h infusion | |
| Urinary retention | Replace urinary catheter p.r.n. | |

catheters in place. Suggested treatment for side effects related to spinal and epidural opioids is shown in Table 17.4. Most of these patients will initially be cared for in a monitored unit, but many will be discharged to a ward setting within 24–48 h, and need appropriate monitoring for respiratory depression and motor blockade while receiving epidural infusions.

## Adjuncts and alternatives to neuraxial analgesia

In order to decrease the incidence and magnitude of side effects associated with spinal and epidural opioids, a variety of drugs may be used to provide supplemental analgesia. Recently, the use of epidural and intrathecal clonidine to provide postoperative analgesia has been described. Clonidine has been shown to prolong and potentiate the effects of local anesthetics by as much as 50–114%.[74–76] The administration of clonidine in an initial dose of 1–2 μg/kg followed by a continuous infusion of 0.08–0.12 μg/kg/hour with bupivacaine or ropivicaine appears safe and effective for use in children. Motsch *et al*.[77] compared caudal clonidine 5 μg/kg with 0.175% bupivacaine to 0.175% bupivacaine alone. The authors reported a prolongation of caudal blockade with the

**Table 17.5** Intravenous patient-controlled analgesia regimens.

| Agent | Bolus dose (μg/kg) | Continuous rate (μg/kg/h) | 4-h limit (μg/kg) |
|---|---|---|---|
| Morphine | 15–25 | 4–15 | 300 |
| Hydromorphone | 3–5 | 1–3 | 60 |
| Fentanyl | 0.25 | 0.15 | 4 |

Patient should be developmentally normal 6–7 years of age or older; meperidine is contraindicated for patient-controlled analgesia.

addition of clonidine, but some sedation, hypotension and bradycardia were seen at this dose.

For patients who are not receiving a regional anesthetic technique to provide postoperative analgesia, systemic opioids are used to treat postoperative pain. Although intermittent intramuscular and subcutaneous injections have been used widely in the past, these routes of administration are painful and are associated with unpredictable and erratic uptake and distribution. Intermittent intravenous injections with opioids of short or moderate duration are also associated with periods of excessive sedation and inadequate analgesia. Continuous analgesia may be achieved when opioids are administered by continuous intravenous infusion with or without PCA dosing.

Morphine is commonly used for postoperative analgesia. In neonates less than 1 month of age, clearance is reduced and elimination half-life is prolonged and is about three times that in adults.[78] For continuous infusions of morphine, a loading dose of 0.025–0.075 mg/kg followed by infusion rates of 0.005–0.015 mg/kg/hour result in therapeutic plasma concentrations in neonates.[79] Older infants and children require a loading dose of 0.05–0.10 mg/kg/hour followed by an initial infusion rate of 0.01–0.03 mg/kg/hour. In children receiving PCA, dosing in the range of 0.01–0.03 mg/kg with a lock-out interval of 6–10 minutes with or without a continuous infusion has been recommended.[80] In children at risk for morphine-induced histamine release, fentanyl (0.0005–0.001 mg/kg/hour ± 0.0005–0.001 mg/kg PCA dose) or hydromorphone (0.003–0.005 mg/kg/hour ± 0.003–0.005 mg/kg PCA dose) may be used.[81] Patient-controlled analgesia dosing regimens are listed in Table 17.5.

The use of methadone, which has a half-life of approximately 19 hours in children over the age of 1 year, may provide more continuous analgesia than shorter-acting agents.[81,82] For moderate-to-severe pain, intermittent intravenous doses of methadone between 0.05 and 0.08 mg/kg as needed may be given.[83]

The side effects that may occur with intravenous opioid administration are similar to those described with epidural opioids, and may be treated similarly (see Table 17.4). With epidural or intravenous techniques, improved analgesia and a decrease in opioid dosing (and side effects) may be achieved with concomitant administration of non-opioid analgesic agents. Ketamine has been administered in a subhypnotic dose by continuous infusion to achieve sedation and analgesia in adults during mechanical ventilation after major surgery.[84] In a study by Hartvig *et al*.[85], 10 children were given continuous infusions of ketamine supplemented with intermittent doses of midazolam to provide analgesia and sedation after cardiac surgery. Ketamine infusions were administered in doses of 1 and 2 mg/kg/hour. Both ketamine infusion regimens provided acceptable analgesia and sedation during and after weaning from mechanical ventilation. Psychomimetic effects were not seen and may have been suppressed by the supplemental use of midazolam. Ketamine infusions can also be used to decrease morphine requirements and may be useful in patients developing signs of spinal cord sensitization.[86]

Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used as an adjunct to other forms of analgesia after thoracic surgery, but their use after cardiac surgery is controversial.[87] Non-steroidal anti-inflammatory drug use in cardiac surgical patients has been limited by the risks of gastritis, renal impairment, and inhibiton of platelet aggregation. Non-steroidal anti-inflammatory drugs exert their antinociceptive action by blocking the peripheral synthesis of prostaglandins through inhibition of the cyclo-oxygenase enzymes (COX-1 and COX-2). A central mechanism has also been proposed. Inhibition of COX-2 causes gastritis, platelet dysfunction, and renal impairment.[88] Studies evaluating the use of NSAIDs after cardiac surgery have concluded that a morphine-sparing effect is present. In 120 patients scheduled for elective CABG surgery, diclofenac, ketoprofen, and indomethocin were compared to placebo. Diclofenac appeared to have the best analgesic effect as evidenced by reducing the need for morphine and other analgesic agents postoperatively.[89] The short-term use of NSAIDs in the postoperative period does not appear to be associated with increased bleeding from the surgical site nor with an increased incidence of gastrointestinal bleeding.[90] New COX-2 inhibitors, including celecoxib and rofecoxib, specifically inhibit synthesis of prostaglandins that produce pain, inflammation, and fever.

Acetaminophen suppositories are a frequently overlooked but effective adjunct to other analgesic methods in infants and children following major surgery. An initial dose of 30–45 mg/kg (maximum dose 1000 mg), followed by 20 mg/kg every 6 hours, for 48–72 hours, has a narcotic sparing effect, with negligible danger of toxicity.[91,92]

## Conclusion

The use of epidural and spinal anesthesia in infants and children may attenuate the stress response and thereby decrease morbidity and mortality associated with cardiac surgery. In

addition, the use of these neuraxial anesthesia techniques during and after cardiac surgery may result in improved pulmonary function, greater circulatory stability, and better postoperative pain control compared with general anesthesia and postoperative intravenous opioid analgesia. To the extent that neuraxial anesthesia may facilitate tracheal extubation in the operating room immediately following surgery, complications and the expense associated with mechanical ventilation in the postoperative period may be avoided. In those patients who undergo tracheal extubation in the ICU, cost savings may be achieved due to reductions in time of mechanical ventilation and ICU length of stay, as well as earlier resumption of a regular diet.

The risks of epidural and spinal anesthesia in these patients include undesired side effects (nausea and vomiting, pruritus), hypotension, respiratory depression, and epidural hematoma formation. The incidence of side effects does not appear to exceed that associated with intravenous opioid analgesia. Hypotension, associated with local anesthetic spinal and epidural blockade in adult patients, is uncommon in infants and young children. Postoperative respiratory depression is greatly reduced by avoiding intraoperative opioids and using prudent doses of spinal and epidural opioids.

The risk of epidural hematoma formation is small but finite. This risk can be minimized by employing reasonable safeguards. Appropriate precautions include selecting patients with normal coagulation function prior to needle placement, abandoning the neuraxial anesthesia technique if needle placement is difficult, and delaying surgery in the event of return of blood via the needle or epidural catheter. The time interval between needle placement and heparin administration should be maximized, allowing for an interval of at least 60 minutes. Epidural catheters should be removed only after normal coagulation function has been restored following surgery.

Future studies may provide additional information regarding the dose–response relationships of neuraxial anesthetic agents in patients undergoing cardiac surgery. Modulation of the stress response in neonates, e.g. utilizing spinal anesthesia, warrants investigation. In addition, strategies to decrease the incidence of opioid-related side effects (e.g. prophylactic antiemetic therapy) may be developed.

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# 5 Anesthesia for specific lesions

# 18 Anesthesia for left-to-right shunt lesions

Sabrina T. Bent

## Introduction

Left-to-right shunt lesions are the most common congenital heart defects, accounting for approximately 50% of all lesions, and are defined by a communication between the systemic and pulmonary circulations that allows shunting of better saturated (systemic) blood to the less saturated (pulmonary) circuit; whether the anatomic structures are located on the left or right side anatomically. For instance, a child with a ventricular septal defect (VSD) and ventricular inversion will shunt blood from the systemic (right-sided) ventricle to the lower pressure (left-sided) ventricle. Left-to-right shunt lesions can be categorized on a physiologic basis according to the size of the defect and the resistance to blood flow. For example, shunting between high-pressure systems like the great arteries or ventricles is dependent upon the size of the defect and the ratio of pulmonary vascular resistance (*PVR*) to systemic vascular resistance (*SVR*). However, the amount of left-to-right shunting through a lower pressure atrial septal defect (ASD) is dependent upon the size of the defect and the relative compliance of the right and left ventricles. Because shunting occurs primarily with atrial contraction (i.e. during diastole and opening of the atrioventricular valves), the resistance is related to the diastolic compliance of the ventricles.

All left-to-right shunts produce a volume burden on the cardiovascular system. Shunting at the level of the great arteries results in increased pulmonary artery blood flow, increasing pulmonary venous return to the left atrium leading to increased left ventricular end-diastolic volume, and left ventricular stroke work by the Frank–Starling mechanism. Shunting at the level of the great arteries produces a decrease in diastolic blood pressure from runoff of blood into the low-pressure pulmonary circuit after closure of the aortic valve. Low diastolic pressures decrease coronary perfusion, potentially creating ischemia from the imbalance of decreased myocardial oxygen delivery and increased oxygen demand. Due to this volume burden, the left ventricle eventually will dilate and hypertrophy producing increased left ventricular end-diastolic pressure followed by increased left atrial pressure. The final result is pulmonary edema from pulmonary venous congestion and left heart failure. As *PVR* increases, there is an increased pressure burden on the right ventricle and eventual right heart failure. Shunting at the atrial or ventricular level, if large in size, results in an increased right ventricular volume load in addition to the hemodynamic effects present with shunting at the great artery level. Prolonged exposure of the pulmonary vasculature to increased flow and pressure results in a fixed increase *PVR*. When *PVR* exceeds the *SVR*, shunt reversal occurs resulting in cyanosis and erythrocytosis known as Eisenmenger's syndrome.

Hemoglobin concentration is another contributing factor to the amount of left-to-right shunting. As the hemoglobin concentration increases blood viscosity will increase producing greater pulmonary and *SVR*; however the net effect is a reduction in left-to-right shunting. The physiologic decline in hemoglobin concentration in the first 3 months of life is thought to have a substantial role in the normal fall of *PVR* after birth. Figure 18.1 presents a schematic representation of the pathophysiology of the left-to-right shunting lesions.

The normal compensatory mechanisms that maintain systemic cardiac output (*CO*) and myocardial performance in the patient with a left-to-right shunt include the Frank–Starling mechanism, the sympathetic nervous system, and hypertrophy of the myocardium. Sweating and tachycardia are manifestations of these compensatory mechanisms in infants with left-to-right shunt lesions. Infants are typically tachypneic from decreased lung compliance associated with increased pulmonary blood flow. They do not feed well because of tachypnea and growth failure develops from both decreased caloric intake and increased caloric utilization. As noted above, significant left-to-right shunts induce biventricular failure. However, unlike adults, infants rarely manifest peripheral edema or jugular venous distension; the most consistent sign of right-sided failure is hepatomegaly.

Anesthetic management for left-to-right shunt lesions

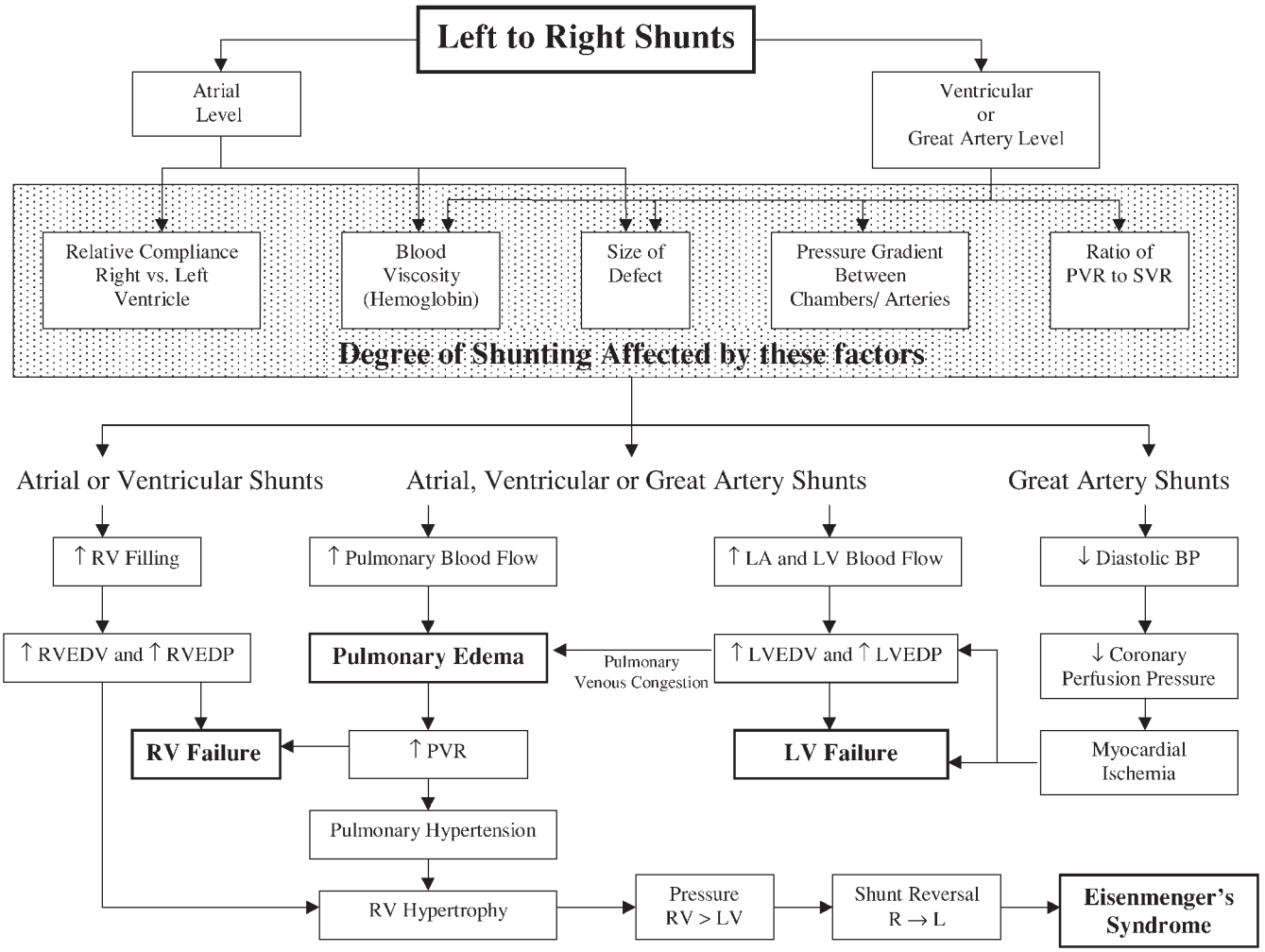


**Fig. 18.1** Pathophysiology of left-to-right shunting lesions. The flow diagram depicts factors that affect left-to-right shunting at the atrial, ventricular and great artery level and the pathophysiology produced by these shunts. A large shunt will result in left ventricle failure, right ventricle failure and pulmonary edema. Increased pulmonary blood flow and pulmonary artery pressures leads to pulmonary hypertension and eventually Eisenmenger's syndrome. These final common outcomes are highlighted in bold lettering. See text for detailed discussion. *BP*, blood pressure; L, left; LA, left atrium; LV, left ventricle; *LVEDP*, left ventricular end-diastolic pressure; *LVEDV*, left ventricular end-diastolic volume; *PVR*, pulmonary vascular resistance; R, right; RV, right ventricle; *RVEDP*, right ventricular end-diastolic pressure; *RVEDV*, right ventricular end-diastolic volume; *SVR*, systemic vascular resistance.

should be individualized to the patient, but certain generalities do exist. Premedication with intravenous or oral drugs such as midazolam (0.05–0.10 mg/kg i.v. or 0.75–1.0 mg/kg p.o.) can be safely administered decreasing anxiety and providing more controlled induction of anesthesia.[1] Standard American Society of Anesthesiologists (ASA) monitors, along with the use of invasive arterial, central venous pressure, and urine output, are recommend for all cases involving cardiopulmonary bypass (CPB). Transesophageal echocardiography (TEE), cerebral oximetry, and cerebral blood flow monitoring are useful adjunctive monitors (see Chapters 8 & 9 for more detailed discussion). Patients with severe, poorly controlled congestive heart failure (CHF) may be intolerant to the myocardial depressant effects of inhalational anesthetics, and for this group of patients intravenous anesthesia with fentanyl and midazolam is preferred.[2–4] In most situations, however, inhalation induction with sevoflurane is a viable option when intravenous access is not initially available. Sevoflurane has been shown to better preserve myocardial function in patients with congenital heart disease (CHD) as compared with halothane.[2]

Additional anesthetic issues include avoidance of air bubbles in intravenous lines to prevent paradoxical emboli. The anesthesiologist must be cognizant of the pulmonary vasodilatory effect of oxygen and hypocarbia and manipulate ventilation in order to balance the pulmonary and *SVR*s. Such measures generally include minimizing the $F_{IO_2}$ and avoiding hyperventilation ($P_{ACO_2}$ between 40 and 50 mmHg).

## Patent ductus arteriosus

The ductus arteriosus is an essential component in normal fetal circulation; it becomes functionally closed within 10–15 hours after birth, and permanently closes by thrombosis, intimal proliferation, and fibrosis in the first 2–3 weeks after birth. Functional closure is initiated by several mechanisms including aeration of the lungs, removal of prostaglandins produced in the placenta, increased arterial $P_{O_2}$, and release of vasoactive substances (bradykinin, thromboxanes, and endogenous catecholamines).[5–7]

Isolated persistent patent ductus arteriosus (PDA) occurs in approximately 1 : 2500 to 1 : 5000 live births, the incidence is higher for premature births and this defect is two to three times more common in females than in males.[5,8] PDA is also found as part of other complex congenital heart defects and is usually the source for pulmonary or systemic blood flow in patients with a functional single ventricle before palliative repair.

### Anatomy

Embrylogically, the ductus arteriosus arises from the distal portion of one of the sixth paired aortic arches.[5] The PDA is a vascular communication between the descending aorta and pulmonary artery. The PDA most commonly arises from the aorta, just distal to the left subclavian artery and attaches to the left pulmonary artery (Fig. 18.2).

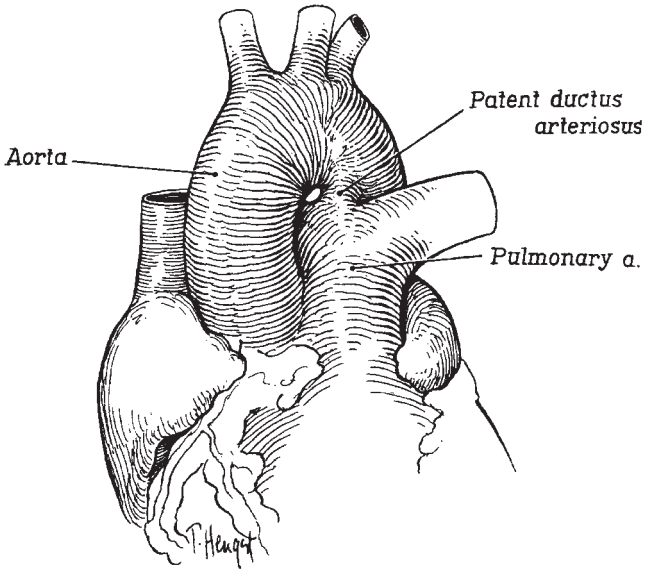


**Fig. 18.2** Patent ductus arteriosus. Reproduced with permission from Cooley DA, Norman JC. Closure of patent ductus arteriosus. In: Cooley DA, Norman JC. *Techniques in Cardiac Surgery*. Houston, TX: Texas Medical Press, 1975: 10–17.

### Pathophysiology and natural history

The degree of left-to-right shunting depends on several factors, the actual dimensions of the shunt as well as the relative ratio of *PVR* and *SVR*. The shunt dimensions of importance include the diameter and length of the PDA; shorter connections with larger diameters produce less resistance, i.e. allow greater flow. In patients with large PDAs, the diastolic runoff into the pulmonary artery results in lowered aortic diastolic pressure, which may increase the risk of myocardial ischemia, especially in the presence of anemia or lowered *SVR*.

The consequences of a PDA left untreated depend on many factors. A small PDA may be hemodynamically insignificant and unrecognized. The larger the PDA or left-to-right shunt, the more likely the progression to CHF, pulmonary hypertension, and in extreme cases, reversal of the shunt. In premature infants, PDA is associated with increased morbidity from associated respiratory distress syndrome, necrotizing entercolitis, and intracranial hemorrhage.

### Surgical approaches

In newborns, surgical treatment is usually reserved for patients who fail medical treatment with indomethacin. The usual surgical options include posterolateral thoracotomy with ligation or division of the PDA or video-assisted thoracoscopic surgery (VATS). Surgical approaches have mortality approaching 0% and minimum morbidity; however, mortality rates in premature neonates is slightly higher.[6] Complications of surgical treatment include, bleeding, chylothorax, vocal cord paralysis (injury to recurrent laryngeal nerve), pneumothorax, atelectasis, recurrence of patency, and inadvertent ligation of the pulmonary artery or descending aorta.[6]

Video-assisted thoracoscopic surgery has increasing popularity due to decreased pain, decreased hospital cost (secondary to decreased hospital stay), and avoidance of post-thoracotomy syndrome (rib fusion, chest wall deformities, scoliosis, and compromise of pulmonary function). Disadvantages of VATS include intraoperative desaturations and hypercarbia, as well as higher morbidity during the surgical learning curve.[9–11]

### Transcatheter closure techniques

Many catheter methods have been developed to non-surgically close a PDA and include the Gianturco coils, the Gianturco–Grifka coil bag and the Amplatzer duct occluder (not Food and Drug Administration [FDA] approved).[8,12,13] These methods are considered safe, efficacious, and cost effective when compared to surgical closure. Risks of transcatheter approaches include arrhythmias, embolization of the device, and incomplete closure.[12–14] In addition, there are size limitations in small infants.

### Anesthetic considerations

The anesthetic management for PDA ligation depends upon factors such as patient's clinical condition, prematurity, coexisting disease, body weight, and surgical technique. Standard ASA monitors are used, along with pulse oximetry of both upper and lower extremities which will assist in detecting inadvertent ligation of the descending aorta. In addition, placing a non-invasive blood pressure cuff on both upper and lower extremites will assist in determining if the PDA ligation produced some degree of coarctation of the aorta. Large volume venous access (which may be a 22 or 24 gauge i.v. in a premature infant) and forced air-warming devices are also recommended. Among patients with coexisting disease, intra-arterial pressure monitoring provides a method of assessing arterial blood gases, electrolytes, hematocrit, and acid-base status.

Neonatal patients commonly develop hemodynamic instability from exposure to inhaled anesthetics and benefit from an intravenous anesthetic technique using opioids such as fentanyl and possibly a benzodiazepine along with muscle relaxation. Fentanyl-based anesthesia reduces the neonatal stress response and improves postoperative outcome.[15]

Neonatal PDA ligation is often performed in the newborn intensive care unit to avoid the additional risks of transport, need for ventilator changes, and hypothermic exposure. High spinal anesthesia, caudal and thoracic epidural techniques have all been described as safe and producing faster recovery.[16]

Lung isolation improves surgical exposure, especially for VATS surgical techniques, but may require ventilation with 100% inspired oxygen to maintain acceptable oxygenation. Prior to lung isolation, efforts should be used to limit the degree of left-to-right shunting by maintaining or improving pulmonary vascular tone: minimize the $F_{IO_2}$ and maintain $P_{aCO_2}$ between 40 and 50.

## Aortopulmonary window

Aortopulmonary window (APW), also know as aortopulmonary septal defect, is a rare congenital heart defect with an incidence of approximately 0.1–0.6% of all congenital heart defects.[17,18] Fifty to eighty percent of patients with APW have associated defects including: PDA (72%), right pulmonary artery from aorta (32%), anomalous origin of a coronary artery from the pulmonary artery (23%), VSD (20%), agenesis of the ductus arteriosus (20%), and other lesions.[17,19] Aortopulmonary window is thought to have separate embryologic etiologies accounting for the three morphologic subtypes described by Kutsche and Van Mierop.[20] Non-fusion of the embryonic aortopulmonary and truncal septi is responsible for the first type, malalignment of the aortopulmonary and truncal septi results in the second type, and absence of the embryonic aortopulmonary septum leads to the third type.[17,20]

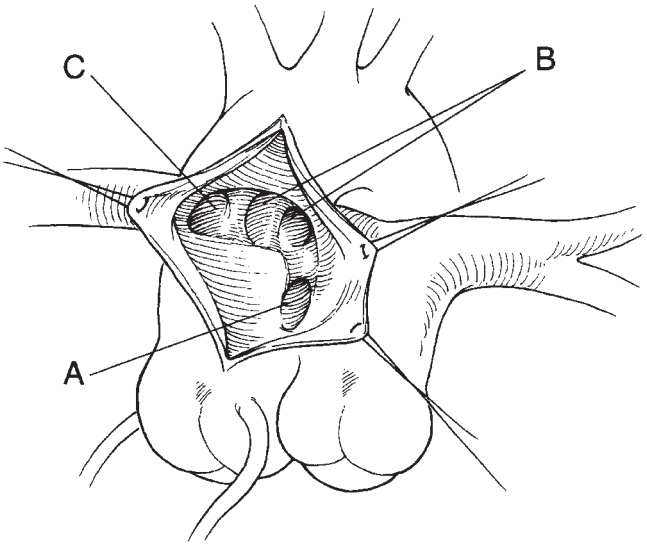


**Fig. 18.3** Composite of the types of aortopulmonary window. A, Communication between the ascending aorta and main pulmonary artery. B, Communication between the aorta and both the main and right branch pulmonary artery. C, Right pulmonary artery originating separately from the aorta. Reproduced with permission from Chang AC, Wells W. Aorticopulomonary window. In: Chang AC, Hanley FL, Wernovsky G, Wessel D, eds. *Pediatric Cardiac Intensive Care*. Philadelphia, PA: Lippincott, Williams & Wilkins, 1998: 201–2.

### Anatomy

The basic anatomical defect in APW consists of a communication between the aorta and the pulmonary artery. Type I is a proximal defect midway between the semilunar valves and the bifurcation of the pulmonary arteries, type II is a distal defect with ill-defined or absent posterior border and anomalous origin of the right pulmonary artery from the aorta, and type III is a large defect combining the first two types (Fig. 18.3).[17]

### Pathophysiology and natural history

The pressure gradient between the aorta and pulmonary artery will produce significant left-to-right flow depending upon the size of the defect and the relative resistances between the pulmonary vs. systemic vascular. Coexisting associated cardiac anomalies may alter the pathophysiology. Irreversible pulmonary hypertension can develop as early as 1 year of age,[21] and if uncorrected, results in a 40% mortality in the first year of life.[19] A report of 20 patients from India, aged 2–38 years, found 29% of patients over the age of 15 years developed Eisenmenger's syndrome.

### Surgical approaches

A variety of surgical techniques have been described to separate the aorta and pulmonary artery and repair the remaining defect; however, in general they include ligation and/or division with suture closure and patch closure.[18,19] The repair is usually performed via median sternotomy with the use of CPB and deep hypothermic circulatory arrest. Surgical repair of the aortic defect can be accomplished using a pulmonary artery flap with subsequent repair of the pulmonary artery with pericardial patch.[22,23] Care must be taken to explore and repair associated anomalies of the pulmonary and coronary arteries, and to repair coexisting cardiac abnormalities. Actuarial survival after repair of APW is approximately 90% at 1, 5, and 10 years.[19] Transcatheter closure of APW has been reported utilizing the Rashkind double umbrella as well as the Amplatzer occlusion device.[24,25]

### Anesthetic considerations

The anesthetic management of APW is similar to that of truncus arteriosus. Younger patients may have considerable diastolic runoff from low *PVR*. Prior to CPB, efforts should focus on maintaining pulmonary vascular tone by lowering of the $F_{IO_2}$ and allowing the oxygen saturation to fall to levels between 80% and 85%, and by maintaining elevated $P_{aCO_2}$ thereby allowing respiratory acidosis to develop. Surgical snaring of the pulmonary artery prior to bypass is helpful. In patients undergoing later repair, after *PVR* is elevated, the anesthetic management goal is to avoid increases in *PVR*.

These patients are at risk to develop perioperative pulmonary hypertension, especially those with elevated *PVR* prior to surgical repair. The administration of inhaled nitric oxide (NO) as well as other maneuvers described above may be necessary to lower *PVR*. Those patients exhibiting signs of pulmonary hypertension should initially be maintained under deep sedation with or without neuromuscular blockade during the immediate postoperative periods (see Chapter 27).

## Atrial septal defects

The right and left atria are normally divided from fusion of two septa, the septum primum and the septum secundum. The septum primum develops during the fourth week and the septum secundum develops during the fifth week of gestation.[5] The septum secundum forms an incomplete partition and leaves an opening called the foramen ovale. The septum primum becomes the valve of the foramen ovale.[5] Five different types of atrial septal defects exist: (i) secundum; (ii) primum; (iii) sinus venosus; (iv) patent foramen ovale (PFO); and (v) coronary sinus (Fig. 18.4). Isolated ASDs are more common in females than males by a factor of 2 : 1. Atrial septal defects make up approximately 5–10% of all congenital heart defects with the secundum ASD comprising nearly 80% of ASD.[6] A probe patent foramen ovale (PFO) is found in approximately 30% of normal adult hearts. Atrial septal defect may be isolated or associated with other congenital heart defects, where it may be a life saving communication allowing mixing of blood between the pulmonary and systemic circulations, such as total anomalous pulmonary venous return (TAPVR), tricuspid atresia, and transposition of the great arteries.

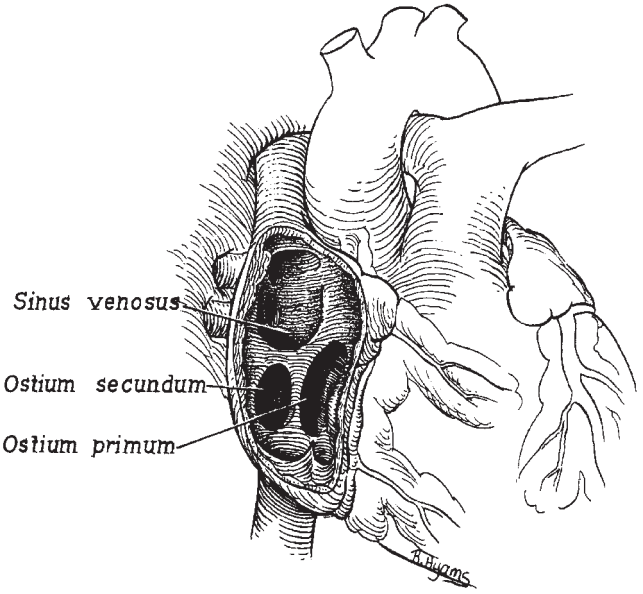


**Fig. 18.4** Composite of major types of atrial septal defect. See text for explanation. Reproduced with permission from Cooley DA, Norman JC. Closure of atrial septal defect. In: Cooley DA, Norman JC. *Techniques in Cardiac Surgery*. Houston, TX: Texas Medical Press, 1975: 70–9.

### Anatomy

#### Secundum atrial septal defect

The secundum ASD is contained within the area bordered by the limbus of the fossa ovalis.[26] It results from an abnormal reabsorption of the septum primum or defective formation or shortening of the septum secundum. Combinations of these abnormalities may contribute to large defects.

#### Primum atrial septal defect

The primum ASD results from abnormalities in formation of the septum primum. It is frequently associated with atrioventricular canal (AVC) defects, especially the partial atrioventricular canal (PAVC) that includes a cleft in the anterior leaflet of the left atrioventricular valve. These AVC defects are due to defects in fusion of the endocardial cushions.

### Sinus venosus atrial septal defect

Sinus venosus defects result from abnormal development of the septum secundum or the sinus venosus, the primitive venous collecting chamber. The most common type is located near the superior vena cava (SVC) orifice and is associated with partial anomalous pulmonary venous return (PAPVR) involving the right upper and middle pulmonary veins. Defects near the orifice of the inferior vena cava also exist and may involve PAPVR of the right lower pulmonary vein.[6]

### Patent foramen ovale

Patent foramen ovale results from failure of fusion of the septum primum to the limbus of the septum secundum. Patent foramen ovale is normal during fetal life as blood passes from right to left bypassing the lungs in fetal circulation. Following birth, as the *PVR* drops and *SVR* increases, the foramen ovale closes, but may not fuse.

### Coronary sinus ASD

Coronary sinus ASD, also called an unroofed coronary sinus, results from an absence in the wall between the coronary sinus and the left atrium. This allows blood from the left atrium to drain into the right atrium via the coronary sinus. Persistent left SVC is also associated with this defect.[26]

## Pathophysiology and natural history

The amount of left-to-right shunting at the atrial level is dependent upon two factors, the size of the defect and the relative compliance of the right and left ventricles. Shunting occurs primarily during diastole, when the atria contract and atrioventricular valves open, and produces a volume burden on the cardiovascular system that is proportionate to the amount of shunting (see the discussion in the Introduction). Isolated ASDs are usually asymptomatic in infants and during childhood despite the increased volume load on the right ventricle. Congestive heart failure usually occurs after the second or third decade of life due to chronic right ventricular volume overload.[6] Pulmonary hypertension can occur in up to 13% of unoperated patients younger than 10 years of age; however, progression to Eisenmenger's syndrome is unusual.[6] The increase in right atrial size may predispose to atrial arrhythmias, and patients with a $Qp : Qs$ of 2 : 1 or less have an 11% incidence, whereas those with a $Qp : Qs$ of 3 : 1 or greater have a 38% incidence of atrial arrhythmias.[27] An ASD is sometimes discovered during a neurologic work-up for transient ischemic attacks or strokes from paradoxical emboli.[26]

## Surgical approaches

Surgical repair of an ASD is usually recommended between the ages of 3 and 5 years.[28] Spontaneous closure of small secundum type ASD can occur in up to 87% of infants in the first year of life,[6] and controversy exists regarding the closure of small ASDs that are asymptomatic. Conventional surgical treatment involves median sternotomy with the use of CPB to perform a primary repair or patch closure, with surgical mortality approaching 0%.[6] Sinus venosus defects are usually repaired using a patch to close the ASD and baffle the anomalous pulmonary veins to the left atrium. Many centers now favor minimally invasive surgery via a partial sternotomy,[29–31] because of the advantage of improved cosmetic result with similar morbidity and mortality to complete sternotomy. Postoperative dysrhythmias are reported in 23% of patients, and as many as 2% of patients may need a pacemaker following surgery.[6]

## Transcatheter closure techniques

Transcatheter ASD closure in the cardiac catheterization laboratory has dramatically reduced the number of operative repairs. The CardioSEAL septal occluder (Nitinol Medical Technologies, Inc., Boston, MA) and the Amplatzer septal occluder (AGA Medical Corp, Golden Valley, MN) are the most common devices used.[13] These procedures are usually performed under general anesthesia with the use of TEE to guide placement. However, new intracardiac echocardiography using intravascular two-dimensional imaging may eliminate the need for TEE and reduce the need for general anesthesia.[32] Transcatheter closure is safe, associated with decreased hospital stay, lack of a surgical scar, avoidance of CPB, and limits the need for general anesthesia. Limitations to transcatheter closure of ASD are based on patient size (large introducer sheaths), type of ASD (usually only PFO or secundum), and requires the presence of an adequate tissue rim for the device to attach.

## Anesthetic considerations

Patients with ASD are generally asymptomatic, and do not have pulmonary hypertension. Therefore, the induction of anesthesia can be easily tailored to either inhalation or intravenous technique. Whenever possible, patients should have an intraoperative TEE performed prior to incision, because transthoracic echocardiographic studies are sometimes unable to visualize all four pulmonary veins, thereby excluding the possibility of PAPVR. During surgery, TEE can be helpful to assess de-airing of the left heart and adequacy of the repair. The majority of patients have good myocardial function and do not require inotropic support perioperatively. Maintenance of anesthesia may consist of inhaled agents, intravenous agents, regional anesthesia, or a combination. Regional techniques are favored by some to assist in early extubation.[33,34] Tracheal extubation in the operating room has been shown to decrease patient charges, without

compromising patient care when compared to extubation in the intensive care unit.[35] Whatever technique is chosen, the primary goal for the uncomplicated ASD patient should include preparation for an early extubation either in the operating room or within the first 4 hours postoperatively.

## Ventricular septal defects

Ventricular septal defect is the most common congenital heart defect, comprising approximately 20% of all congenital heart defects, with an incidence between 2.6 and 5.7 in 1000 live births.[36–38] Ventricular septal defect is associated with a variety of inherited conditions, including trisomy 13, 18, and 21 as well as the VACTERL (vertebral, vascular, anal, cardiac, tracheoesophageal, renal, and limb anomalies) association and CHARGE (coloboma, heart anomaly, choanal atresia, retardation, and genital and ear anomalies) syndrome.[39] Ventricular septal defects are found as isolated defects and as part of other complex congenital heart defects. Embrylogically, the primitive left ventricle is formed from the ventricular portion of the bulbis cordis and the primitive right ventricle is formed from the proximal portion at approximately 23–25 days gestation. A communication between the right and left ventricles defines a VSD and five different types of VSD exist: (i) perimembranous; (ii) subpulmonary; (iii) muscular; (iv) malalignment; and (v) canal (Fig. 18.5).

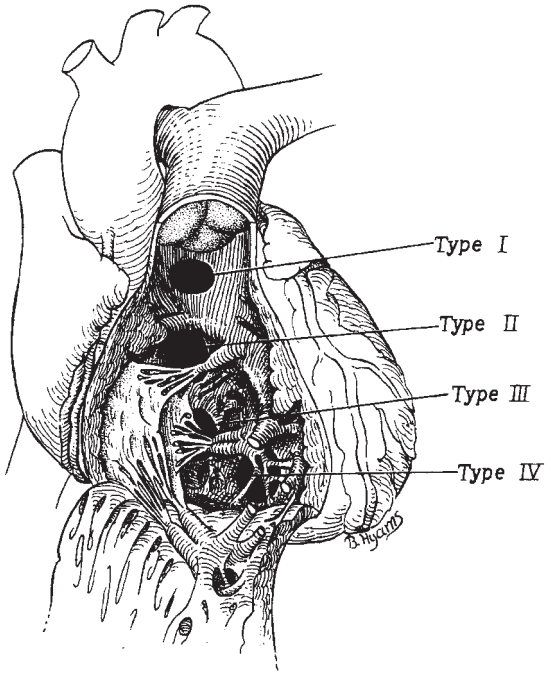


**Fig. 18.5** Composite of major types of ventricular septal defect. Type I, subpulmonary; type II, perimembranous; type III, canal or inlet-type; type IV, muscular. See text for further explanation. Reproduced with permission from Cooley DA, Norman JC. Closure of ventricular septal defect. In: Cooley DA, Norman JC. *Techniques in Cardiac Surgery*. Houston, TX: Texas Medical Press, 1975: 80–7.

### Anatomy

#### Perimembranous ventricular septal defect

The perimembranous VSD is a communication adjacent to a portion of the membranous septum and the fibrous trigone of the heart, where the aortic, mitral, and tricuspid valves are in fibrous continuity with the tricuspid, aortic, and mitral valves.[6] These infracristal defects are the most common VSD subtype, occurring in approximately 80%.

#### Subpulmonary ventricular septal defect

The subpulmonary VSD is located within the outlet septum, above the crista supraventricularis and border of the semilunar valves; and comprises approximately 5% of all VSDs. As a result of the location of this defect, a Venturi effect may be produced by the jet of blood flowing through the VSD causing the right or non-coronary aortic cusp of the aortic valve to prolapse toward the defect producing aortic insufficiency.[6] This type of lesion is more common in the Asian population.[40]

#### Muscular ventricular septal defect

Muscular VSDs are located within the muscular portion of the interventricular septum. These defects can be multiple and represent approximately 2–7% of VSDs.

#### Malalignment ventricular septal defect

Malalignment VSDs occur from malalignment of the infundibular septum and the trabecular muscular septum. These defects usually occur as a component of a more complex cardiac defect, most commonly tetralogy of Fallot.[6]

#### Canal type ventricular septal defect

Canal type VSDs are located in the posterior region of the septum beneath the septal leaflet of the tricuspid valve.[32] These inlet defects accounts for approximately 10% of VSDs.

### Pathophysiology and natural history

Isolated VSDs produce left-to-right shunting at the ventricular level, predominantly during systole. The term restrictive VSD refers to a limitation in the amount of flow across the defect based on size; and in this case a pressure gradient exists between the left and right ventricles. An unrestrictive VSD has flow limited only from the relative pulmonary to

*SVR*; and therefore, no pressure gradient exists between the left and right ventricles. Fifteen percent of patients with large VSDs develop pulmonary hypertension which will progress to the development of pulmonary vascular obstructive disease by the age of 20 years.[41]

Symptoms range from asymptomatic to signs and symptoms of CHF. The rate and degree of progression of symptomatology depends on the patient age, size of the defect, and the degree of left-to-right shunting. Infants who have unrestrictive VSDs develop symptoms of CHF in the first 3 months of life because of the physiologic decline in *PVR*. Spontaneous closure of small perimembranous and muscular VSDs occurs in as many as 50% of patients,[41–43] and such patients are typically asymptomatic.

## Surgical approaches

Surgical repair of VSD usually involves patch closure or occasionally primary closure using CPB via median sternotomy. Perimembranous and canal type VSDs are most commonly repaired via a right atriotomy, which may require detachment of the septal leaflet of the tricuspid valve for exposure. Subpulmonary VSDs are most commonly repaired via the transpulmonary approach. Midmuscular VSDs are most commonly repaired via right atriotomy, and anterior or apical muscular VSD may be approached using right ventriculotomy. However the use of right ventriculotomy carries the risks of conduction disturbances and ventricular dysfunction later in life. At many institutions, symptomatic patients with lesions that are not approachable via right atriotomy are usually treated with pulmonary artery banding until the patient is larger allowing transatrial repair. Pulmonary artery banding is also utilized for multiple muscular VSDs and in patients that are high-risk candidates for CPB. Partial median sternotomies as well as small right anterolateral thoracotomies are advocated by some because of improved cosmetic results.[44,45] Video-assisted cardioscopy (VAC) is used in some centers to improve visualization of small intracardiac structures in limited spaces during open heart surgery for congenital heart repairs.[31,46–48] Video-assisted cardioscopy has been successfully utilized for a variety of intracardiac repairs including ASD, VSD, tetralogy of Fallot, double outlet right ventricle (DORV) and AVC.

Timing for surgical repair varies depending on age, signs, and symptoms. Patients less than 6 months of age are repaired if they manifest uncontrollable CHF and failure to thrive. Patients between 6 and 24 months of age undergo repair to treat CHF symptoms or pulmonary hypertension. Patients older than 24 months undergo repair for $Q$p : $Q$s greater than 2 : 1. Among patients with subpulmonary VSD, the presence of aortic insufficiency is an indication for surgical repair to prevent further progression of the valvular insufficiency,[49,50] A defect size greater than 5 mm is repaired to avoid progression to aortic cusp prolapse and aortic insufficiency, and defects less than 5 mm can be managed conservatively.[40]

Mortality for uncomplicated VSD in older patients is less than 1–2%.[51] Mortality for VSD repair in infants during the first year of life is less than 5%.[52]

## Transcatheter closure techniques

Transcatheter closure of muscular VSDs has been performed successfully.[53–56] The use of the CardioSEAL septal occluder (Nitinol Medical Technologies, Inc., Boston, MA) is approved for use in the USA, and the Amplatzer septal occluder (AGA Medical Corp., Golden Valley, MN) is undergoing clinical trials in the USA. Indications for use of the devices include all types of muscular VSDs, including apical and multiple. Transcatheter techniques may serve as an adjunct to surgery or an alternative to surgery in selected patients. Intraoperative use of VSD closure devices during CPB for defects with difficult surgical closure has been described,[57] and postoperative residual VSDs or "Swiss cheese" type muscular VSD may be preferentially treated by this technique. The major limitation in the application of this technique is related to the size of the sheaths necessary for device delivery, precluding use in infancy. Complications of device closure include need for blood transfusion, tricuspid valve regurgitation, and device embolization.[53,55]

## Anesthetic considerations

Anesthetic management for the patient with VSD is similar to that of ASD. Pulmonary hypertension may develop early, especially in patients with trisomy 21, and preoperative chest radiograph revealing decreased pulmonary vascular markings is indicative of pulmonary hypertension.[58–61] Such patients may respond to the use of inhaled NO prior to termination of CPB and/or in the postoperative period. Right heart failure with decreased *CO* may result if pulmonary hypertension is not controlled, and is improved from the use of dopamine, milrinone, dobutamine, or isoproterenol.

Conduction disturbances, particularly atrial-ventricular heart block may be transient or permanent and is reported to occur in up to 10% of patients post-VSD repair;[6] however, the experience at Texas Children's Hospital is that less than 1% of patients require permanent pacing after VSD closure. If heart block develops, treatment with atrioventricular synchronous pacing using temporary pacing wires is indicated. Junctional ectopic tachycardia is sometimes observed in patients less than 1 year of age after repair for lesions that involve VSD repair, most commonly after tetralogy of Fallot repair. Treatment includes cooling to 35°C, increased anesthetic depth, paralysis, procainamide, esmolol, or amiodarone.[6]

Intraoperative use of TEE will help recognize residual VSDs, intracardiac air, and assess ventricular volume and function. Small muscular VSDs will become apparent after

closure of larger VSDs. Frequently these smaller defects, especially if near the apex, may not be amenable to surgical repair or worth the risk of returning to CPB.

Patients with uncomplicated VSDs are good candidates for extubation in the operating room or early after arrival in the intensive care unit.

## Common atrioventricular canal

Common atrioventricular canal (CAVC) results from failure of the endocardial cushions to fuse during the fifth week of fetal development.[5] Four to five percent of CHD involves defects of the atrioventricular septum, and CAVC defects occur in 0.19 in 1000 live births.[7,62] Common atrioventricular canal is associated with multiple syndromes and occurs in approximately 20% of persons with trisomy 21; it accounts for 15% of congenital heart defects in persons with Noonan's syndrome, and nearly 50% in persons with Ellis–van Creveld syndrome.[63]

### Anatomy

Anatomically, CAVC consist of three basic defects: (i) ostium primum defect resulting in an interatrial communication; (ii) abnormal atrioventricular valves; and (iii) inlet VSD resulting in an interventricular communication.[36] Three types of CAVC exist: (i) partial; (ii) transitional; and (iii) complete.

#### Partial atrioventricular canal

The PAVC defect consists of an interatrial communication or ostium primum defect and a cleft in the anterior leaflet of the mitral valve, usually resulting in some degree of insufficiency. The tricuspid valve is often abnormal as well, and no interventricular communication exists.

#### Transitional atrioventricular canal

The transitional atrioventricular canal (TAVC) defect consists of an ostium primum defect, abnormal atrioventricular valve, which may be partially separated into two valves, and usually a small or moderate interventricular communication that may be partially closed by bridging tissue of the atrioventricular valve to the crest of the ventricular septum.[6,26] Like the PAVC defect, the left atrioventricular valve is usually associated with a cleft and has some degree of insufficiency.

#### Complete atrioventricular canal

The complete AVC defect usually consists of a large nonrestrictive ostium primum and interventricular septal defect as well as a large common single atrioventricular valve. The left atrioventricular portion of the valve usually contains a cleft that is insufficient. Three classifications of the CAVC defects exist based on the chordal attachments of the anterior bridging leaflet of the common atrioventricular valve, and are commonly referred to as Rastelli type A, B, and C.[64]

In Rastelli type A, the anterior leaflet is attached to the crest of the ventricular septum by thin chordae tendinae. The interventricular communication is present above the crest of the ventricular septum and between the anterior and posterior bridging leaflets, and the VSD does not extend to the aortic cusps. The left ventricular outflow tract is narrowed and elongated with this defect.[26] The Rastelli type B is characterized by the anterior leaflet attachment via chordae tendinae to a papillary muscle in the right ventricle near the septum. The interventricular communication is below the common valve and extends to the aortic valve cusps. This defect is also associated with a narrowed and elongated left ventricular outflow tract.[26] The Rastelli type C is defined by an anterior leaflet that lacks any ventricular septal attachments and "floats" above the septum. The interventricular communication lies below the atrioventricular valve and extends to the aortic cusps. As in the other Rastelli subtypes, the left ventricular outflow tract is narrowed and elongated. The Rastelli type C defect is the most common type, and may be associated with other major cardiac or extracardiac anomalies such as tetralogy of Fallot or trisomy 21.[26]

Other variants of AVC also exist, including right or left ventricular dominant types in which one ventricle is hypoplastic. The physiology produced by such lesions are similar to other single ventricle lesions, and the reader is referred to Chapter 22. Multiple other associated lesions may also occur including PDA, tetralogy of Fallot, coarctation of the aorta, subaortic stenosis, left SVC, asplenia, and polysplenia.[6]

### Pathophysiology and natural history

A left-to-right shunt may occur at the atrial, ventricular, and atrioventricular valvar level, depending on the type of AVC present. This shunting, in addition to atrioventricular valve regurgitation, results in volume overload of both the atria and ventricles. Volume overload soon develops into CHF and may result in pulmonary hypertension as the ratio of pulmonary to systemic blood flow increases. As with other left-to-right shunts, pulmonary hypertension may develop by 1 year of age and eventually lead to Eisenmenger's syndrome.[65] The severity of CHF and symptoms will depend on the degree of left-to-right shunting and the severity of atrioventricular valvar regurgitation with PAVC being the least symptomatic followed by transitional, and then complete being the most symptomatic of the three. Patients with PAVC, if left untreated, may do well through childhood, but have increased likelihood of developing CHF in adulthood especially as atrial dysrhythmias develop.[26] The presence of moderate to severe atrioventricular valvar regurgitation

leads to earlier development of CHF and higher morbidity and mortality if untreated.[26] Those patients with PAVC presenting with CHF in the first year of life should be suspected of having additional lesions, most commonly left-sided obstructive lesions.[66] Patients with CAVC develop CHF, failure-to-thrive, and frequent respiratory infections in the first year of life, and those with trisomy 21 develop pulmonary hypertension earlier and with increased severity as compared to other children. Twelve percent of children with CAVC develop irreversible pulmonary hypertension within the first year of life, and a chest radiograph demonstrating black lung fields, indicating decreased pulmonary blood flow, is an ominous sign.[58]

## Surgical approaches

Surgical repair of the PAVC is usually performed at age 2–5 years unless there are signs of CHF or other lesions which necessitate earlier repair. Patients with transitional atrioventricular canal (TAVC) may be relatively asymptomatic and may tolerate surgical repair at an older age.

Primary complete surgical repair for patients with CAVC is performed between 3 and 6 months of age because it is safe, controls CHF, prevents the development of fixed pulmonary hypertension, and reduces annular dilation (a cause of atrioventricular valvar regurgitation).[3,66,67]

Surgical techniques vary, but generally consist of a right atriotomy with patch closure of the ASD, closure of clefts in the anterior leaflet of the left atrioventricular valve, and the VSD closed with a patch or, occasionally in the case of the TAVC, pledgetted sutures.[6,26,67] A one or two patch technique can be used (Fig. 18.6). Pulmonary artery banding is reserved for cases of severe respiratory illness, sepsis, or anatomy not suitable for biventricular repair. Presence of other associated cardiac anomalies such as tetralogy of Fallot, DORV, left-sided obstructive lesions, and unbalanced canals (hypoplastic ventricle), further complicate the repair and result in higher mortality, especially in the patients with a hypoplastic ventricle.[68,69]

Mortality for repair of the PAVC is less than 5%, and the mortality for complete repair of CAVC is between 3.0% and 10.5%.[6,70–72] The pulmonary artery banding is associated with mortality near 5%.[6,26] The presence of preoperative pulmonary hypertension and increasing size of the VSD is associated with higher morbidity and mortality among patients undergoing complete repair of CAVC.[26,70]

## Anesthetic considerations

Anesthetic management of the AVC defects depends primarily on the degree of left-to-right shunting, and the presence and severity of pulmonary vascular hypertension. As with other septal defects, balancing the ratio of *PVR* to *SVR*, thereby limiting the amount of pulmonary overcirculation, is paramount to successful management, and is usually accomplished by manipulations in $F_{IO_2}$ and ventilation (see above). Transesophageal echocardiography is very helpful in detecting residual intracardiac shunts, assessing atrioventricular valvar function, and determining ventricular function and volume following repair.

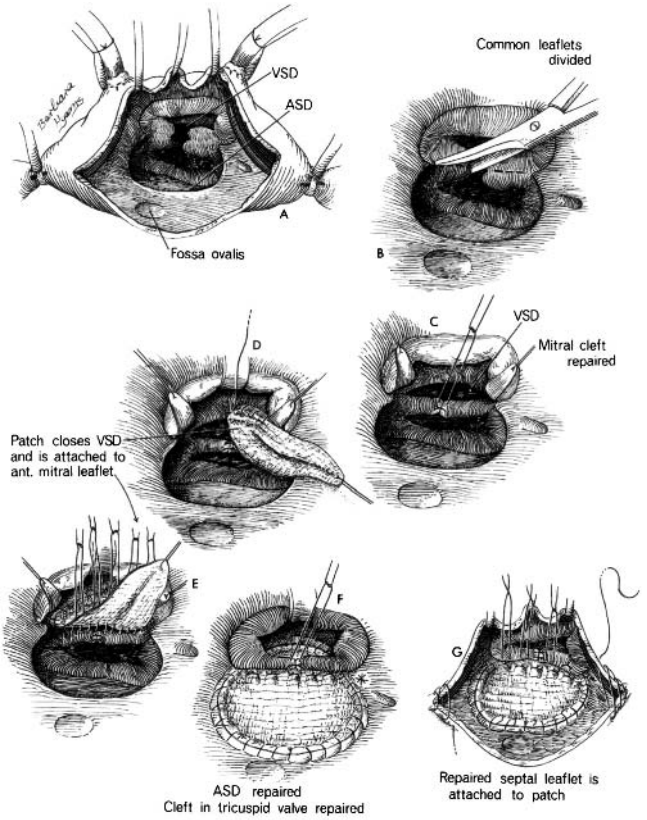


**Fig. 18.6** Single patch technique for repair of complete atrioventricular canal defect. ASD, atrial septal defect; VSD, ventricular septal defect. Reproduced with permission from Cooley DA, Norman JC. Repair of atrioventricularis communis. In: Cooley DA, Norman JC. *Techniques in Cardiac Surgery*. Houston, TX: Texas Medical Press, 1975: 88–93.

Surgical placement of left atrial and pulmonary arterial pressure lines may be used to guide management of inotropes, use of NO, and volume replacement. Persistent pulmonary hypertension and acute increases in pulmonary hypertension contribute to acute right heart failure and increased mortality.[6,70] Pulmonary hypertension commonly develops in these patients and is treated with hyperventilation, 100% oxygen, opioid anesthetics like fentanyl, systemic alkalinization and NO. Increasing the pH is more effective than lowering of the $P_{CO_2}$ in controlling pulmonary pressures and may be accomplished by the administration of sodium bicarbonate. Pulmonary hypertension that is refractory to NO may respond to magnesium sulfate, at initial doses of 20 mg/kg/hour, or magnesium chloride.[70]

Most patients require inotropic support upon weaning from CPB, and those with residual atrioventricular valvar regurgitation and/or VSD benefit from use of milrinone or

other afterload reduction. Hypotensive patients who have elevated left atrial pressures should be evaluated for the presence of severe residual left atrioventricular valvar regurgitation or stenosis, a residual VSD, left ventricular outflow tract obstruction, or left ventricular dysfunction.[6] Intraoperative TEE is essential for initial diagnosis of these conditions, and reinitiation of CPB and repair may be necessary.

Common atrioventricular canal repair is associated with conduction abnormalities, especially atrioventricular and sinoatrial nodal dysfunction resulting in complete heart block. In this situation, atrioventricular sequential pacing is necessary to minimize atrioventricular valvar regurgitation and to improve *CO*.[6]

## Double outlet right ventricle

Double outlet right ventricle describes a spectrum of congenital heart defects, anatomically defined by having both great arteries arise from the morphologic right ventricle.[73] Double outlet right ventricle comprises approximately 1.0–1.5% of all patients with CHD with an incidence estimated at 1 in 10 000 live births.[73] Trisomy 13 and trisomy 18 are associated with DORV.[73] Double outlet right ventricle results from bulboventricular malformations with failure of proper alignment of the conotruncus with the ventricular septum.[73] Characterization of the anatomy of DORV is crucial in understanding the physiologic consequences as well in determining the surgical approach for palliation or correction. Complete characterization of the anatomy will include: (i) the relationship of the VSD to the great arteries; (ii) the relationship of the great arteries with respect to one another; (iii) the morphology of the ventricles and their outflow tracts; and (iv) the presence of other associated anomalies.[73] Double outlet right ventricle may also occur with an intact ventricular septum, but is extremely rare.[74] Four different anatomic types of DORV are defined based on the relationship of the VSD to the great arteries: (i) subaortic VSD with or without pulmonary stenosis; (ii) subpulmonary VSD with or without subaortic stenosis and/or arch obstruction; (iii) doubly committed VSD; and (iv) non-committed VSD.[73]

### Anatomy

#### Double outlet right ventricle with subaortic ventricular septal defect

Subaortic VSD represents approximately 51–56% of DORV,[74,75] and involves normally related great vessels where the aorta is posterior and rightward or when the aorta is anterior and left-ward. When this defect is associated with pulmonary stenosis, the resulting physiology is similar to tetralogy of Fallot.

#### Double outlet right ventricle with subpulmonary ventricular septal defect

Subpulmonary VSD represents approximately 30% of DORV;[75,76] the aorta is to the right and/or anterior to the pulmonary artery. This type is associated with left-sided obstructive lesions such as subaortic obstruction or coarctation of the aorta, but may also occur without aortic obstruction.[73] The Taussig–Bing malformation is included in this classification and is defined as having a juxtapulmonary pulmonary, supracristal VSD, with absence of the superior aspect of the ventriculoinfundibular fold, bilateral conus or infundibulum and malposed great arteries, commonly side-by-side.[73,77]

#### Double outlet right ventricle with doubly committed ventricular septal defect

Doubly committed VSD represents approximately 3% of DORV.[75,76] The doubly committed VSD results from the hypoplasia of the infundibular septum and variable degrees of override of the VSD by both great arteries.[73]

#### Double outlet right ventricle with non-committed ventricular septal defect

Non-committed VSD represents approximately 12–17% of DORV,[74,75] and the VSD is an apical muscular or membranous-inlet type. The VSD is remote from the great arteries and is most frequently associated with AVC defects.[73]

### Pathophysiology and natural history

The pathophysiology of DORV is dependent on the specific anatomy of the lesion and degree of pulmonary vs. aortic blood flow as well as the degree of mixing of pulmonary and systemic venous blood. Three basic physiologic subtypes are tetralogy of Fallot, large VSD, and transposition of the great arteries.

Double outlet right ventricle associated with pulmonary stenosis resembles the physiology of tetralogy of Fallot with varying degrees of cyanosis depending on the severity of pulmonic stenosis. The patients have right-to-left shunting across the VSD and may have hypercyanotic spells, polycythemia, and failure to thrive.[73] Although there is a fixed component of obstruction, pulmonary blood flow may vary due to alterations in *PVR*. Pulmonary stenosis is present in approximately 50% of patients with DORV.[73]

Subaortic VSD without pulmonary stenosis and non-committed VSDs produce physiology similar to that of a large VSD. Because the VSD is typically large, the degree of left-to-right shunting will depend upon the relative ratio of *PVR* to *SVR*.

Subpulmonary VSD without pulmonary stenosis usually produces physiology similar to transposition of the great

arteries. Streaming of pulmonary venous blood to the pulmonary artery and systemic venous blood toward the aorta, results in a relative parallel circulation with variable degrees of mixing of oxygenated and deoxygenated blood. The patients can present early with both cyanosis and CHF followed by development of pulmonary vascular occlusive disease if left untreated.

Double outlet right ventricle may be associated with multiple other anomalies such as multiple VSD, atrioventricular septal defects, PDA, aortic arch obstruction, interrupted aortic arch, subaortic stenosis, hypoplastic ventricle, as well as mitral valvar abnormalities that may further affect the physiology.[75–79]

### Surgical approaches

The surgical approach to DORV varies depending on the type of DORV and the associated anomalies, and the preoperative delineation of anatomy is crucial to determine the operative strategy. However, echocardiography, angiography, and magnetic resonance imaging may still result in incomplete information due to the complexity and anatomic variations of this lesion.[78,80] Often times only intraoperative inspection of the heart by the surgeon leads to the definitive operative plan. Four surgical treatment options generally exist: (i) palliative procedures such as Blalock–Taussig shunts, coarctation repairs, and pulmonary artery banding; (ii) intraventricular repair with a baffle from the left ventricle to the aorta; (iii) intraventricular baffle from the left ventricle to the pulmonary artery followed by arterial switch; and (iv) bidirectional cavopulmonary shunt staged to the Fontan procedure (univentricular heart repair);[75–79] with the primary goal of achieving a biventricular repair when possible.

The overall early mortality for the repair of DORV is approximately 9%.[75,76,79] Ten-year survival is 81–86%.[75,76] Significant risk factors for early mortality include congenital mitral valve anomalies, side-by-side great arteries, multiple VSDs and age at operation less than 1 month.[75–77] Staged operations to Fontan or univentricular repair has the lowest early mortality of all repairs even though this group of patients usually have more complex forms of DORV.[75]

### Anesthetic considerations

Anesthetic management varies greatly depending on the specific type of DORV and associated anomalies. Management of palliative procedures, such as modified Blalock–Taussig shunts, is reviewed in Chapter 20. Patients with pulmonary stenosis who present with physiology similar to tetralogy of Fallot should be managed to minimize the right-to-left shunting (see Chapter 20). Patients with subpulmonary VSD without pulmonary stenosis who have physiology similar to transposition of the great arteries should be managed as such (see Chapter 21). Patients with subaortic VSD without pulmonary stenosis, as well as the noncommitted VSD types present with physiology similar to that of a large VSD as described earlier in this chapter. Patients with complex DORV and other associated anomalies that proceed through the single ventricle staged palliation to the Fontan procedure are reviewed in Chapter 22. Common to all patients with DORV, intracardiac shunting must be balanced with manipulation of *PVR* and *SVR* to optimize systemic *CO* and oxygen delivery.

Arrhythmias are common especially with repairs involving baffling and enlargement of the VSD. Ventricular tachyarrhythmias and complete heart block can occur in as many as 9% of patients postoperatively and may require permanent pacing.[73,75,76] Frequently, repair of DORV is complex and requires periods of circulatory arrest. Patients may have residual VSDs, valvar insufficiency, outflow tract obstruction, or ventricular dysfunction. Postoperative TEE and left atrial pressure monitoring is helpful in determining the diagnosis and guiding management.

## Truncus arteriosus

Truncus arteriosus is an uncommon congenital heart defect representing less than 3% of all congenital heart defects,[6,81–83] and is defined by the presence of a single great artery arising from the base of the heart that supplies the coronary, pulmonary, and systemic circulations, and a VSD. Embryologically, this defect results from failure of the truncus arteriosus to divide into the aorta and pulmonary artery. Deletion of chromosome 22q11 is present in approximately 11–35% of patients with truncus arteriosus, and this chromosomal abnormality is associated with DiGeorge and velocardiofacial syndrome. Patients with these syndromes have other associated non-cardiac anomalies such as aplasia or hypoplasia of the thymus and/or parathyroid glands (T-cell deficiency), hypocalcemia, palatal abnormalities, speech and learning disabilities, neuropsychological disorders, and craniofacial dysmorphia.[84–86] As many as 77% of patients with 22q11 deletion are immunocompromised.[86]

### Anatomy

Truncus arteriosus has been classified by two main systems, the first and most widely used classification system was initially described by Collett and Edwards[87] in 1949 and the second by Van Praagh and Van Praagh[88] in 1965 (Fig. 18.7). The Collett and Edwards classification is based upon the embryologic arrested development of the pulmonary arteries from the sixth aortic arches and is categorized into four different subtypes.

#### Type I truncus arteriosus

Type I truncus arteriosus accounts for 70% and is defined by

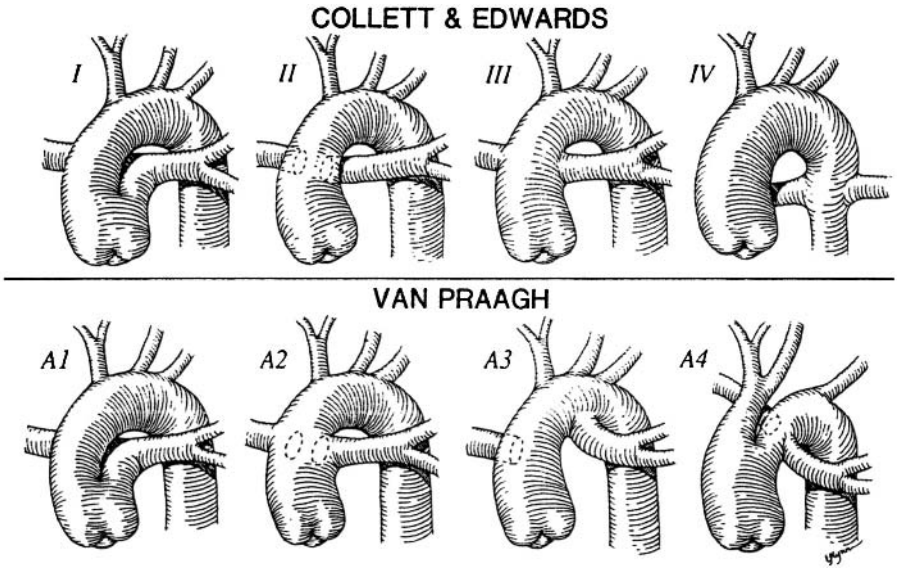


**Fig. 18.7** Major classification systems for truncus arteriosus. Type I is the same as A1. Types II and III are grouped together as a single type A2. Type IV is a variant of tetralogy of Fallot with pulmonary atresia and major aortopulmonary collaterals. Type A3 is unilateral pulmonary artery atresia with collateral supply to the affected lung. Type A4 is associated with interrupted aortic arch. See text for full explanation. Reproduced with permission from Hernanz-Schulman M, Fellows KE. Persistent truncus arteriosus. Pathologic, diagnostic and therapeutic considerations. *Semin Roetgenol* 1985; **20**: 121–9.

the origin of the main pulmonary artery from the truncus dividing into left and right pulmonary arteries.

### Type II truncus arteriosus

Type II truncus arteriosus accounts for 30% and is defined by separate origination of the left and right pulmonary arteries from the posterior surface of the truncus, with the branch pulmonary arteries arising very close to one another.

### Type III truncus arteriosus

Type III truncus arteriosus also has separate origination of the left and right pulmonary arteries, but in this case, the arteries arise from the lateral aspects of the truncus and are widely separated. This type accounts for approximately 1% of cases.

### Type IV truncus arteriosus

Type IV is not a form of truncus arteriosus, but is of historical note in the classification system. It is now defined as a variant of tetralogy of Fallot with pulmonary atresia. There is complete absence of the pulmonary arteries in this defect, with bronchial and collateral arteries of the descending aorta providing the blood supply to the lungs.

Truncus arteriosus is most commonly associated with a VSD, but intact septums can occur. The truncal valve may be abnormal with both abnormal numbers of leaflets, varying between two and six leaflets, as well as dysplastic.[6,88] Truncal valve insufficiency is estimated to occur in 25–50% of patients.[88] Anomalies of the coronary arteries may also exist. Additionally, truncus arteriosus is associated with other cardiac anomalies such as aortic arch obstruction, ASD (62%), right aortic arch (21–36%), aortic arch interruption (11–19%), PDA (18%), aberrant subclavian artery (4–10%), absence of one pulmonary artery (10%), and persistent left SVC (4–9%).[6,81,83]

## Pathophysiology and natural history

Truncus arteriosus by definition has a common arterial trunk that provides blood flow to the coronary, pulmonary, and systemic arteries. As *PVR* falls in the early neonatal period, pulmonary blood flow progressively increases and results in CHF. A variable degree of mixing of the systemic and pulmonary venous blood occurs at the ventricular level through the VSD. The large runoff provided by the pulmonary arteries results in low diastolic pressures, which may be worsened by the presence of truncal valve insufficiency. Low diastolic pressures in the face of increased myocardial work and increased ventricular pressures place the patient at risk of developing myocardial ischemia. Early CHF and increased pulmonary blood flow leads to rapid development of pulmonary vascular occlusive disease in infancy if left untreated.

Patients without surgical treatment have a 74–100% mortality in the first year of life.[80–82] Surgical repair in patients greater than 2 years of age is contraindicated when *PVR* is greater than 8 Wood units or if Eisenmenger's syndrome is present.[6,81]

## Surgical approaches

Definitive surgical repair is usually recommended in the neonatal period, although some centers individualize patients, performing surgery between 2 and 3 months of age.[81–83,89] Early repair is indicated due to the rapid development of pulmonary hypertension and high mortality rate in patients

in the first year of life if left untreated. Palliative surgery involving pulmonary artery banding has largely been abandoned except for those very few patients who are not suitable candidates for definitive repair.[83] Definitive surgical repair involves removal of the pulmonary arteries from the truncal root and closing the resulting defect either primarily or with a patch. The VSD is usually closed via a transatrial or transventricular approach with a patch. A right ventricle to pulmonary artery connection is provided by a valved homograft. Direct anastomosis of the pulmonary artery with the right ventricle has been described, but may distort the pulmonary arterial architecture. A small ASD is sometimes created if high right ventricular pressures are anticipated in order to improve *CO* at the expense of cyanosis.[6,81,82,89,90] This ASD creation can be closed at a later date by a transcatheter technique in the cardiac catheterization laboratory. Moderate to severe truncal valve regurgitation is repaired by valvuloplasty, "double-homograft" technique with coronary reimplantation, or mechanical valve implantation.[81,91,92] Valve repair has been successful even in neonates and avoids or delays serial truncal valve replacements.[91] Early mortality after repair of truncus arteriosus is 5–18%,[81,82,89,90] and mortality rates are higher among infants less than 3 kg, or from the presence of other associated cardiac anomalies.[82,89,92]

### Anesthetic considerations

Anesthetic management is dependent upon the patient's anatomy and age at presentation. Depending on the severity of CHF, the patient may require preoperative inotropic support, and the induction of anesthesia should be accomplished with drugs that maintain *SVR* and preserve myocardial function. Therefore intravenous induction of anesthesia utilizing fentanyl and midazolam or etomidate with either vecuronium or pancuronium is ideal. Inhalational induction with careful titration of sevoflurane should be performed with extreme caution. Doses of fentanyl exceeding 50 μg/kg are most commonly employed. Efforts to balance *PVR* and *SVR* to make the ratio of *Q*p : *Q*s approach unity are essential. Care must be taken to avoid hyperventilation and excessive oxygenation which may result in lowering of *PVR*, further contributing to pulmonary overcirculation and lower diastolic blood pressure. Patients with truncal valvar insufficiency combined with excessive pulmonary blood runoff will be particularly susceptible to myocardial ischemia due to coronary hypoperfusion, and it may be necessary for the surgeon to temporarily place a vessel snare around the pulmonary artery to limit pulmonary blood flow and increase diastolic blood pressure in the pre-bypass period. Those patients presenting late in infancy who have developed significant pulmonary hypertension from long-standing pulmonary overcirculation may require increased $F_{IO_2}$ to maintain oxygen saturations between 80% and 90%. Unless a chromosomal evaluation is known, patients with truncus arteriosus should be given irradiated blood products due to the high incidence of DiGeorge syndrome and associated T-cell deficiencies. Upon weaning from CPB most patients require inotropic support, afterload reduction, ventricular volume assessment, and efforts to minimize pulmonary arterial pressures in order to improve right heart function.

Pulmonary hypertension is commonly present after CPB, and these patients have signs of right heart failure with high central venous pressures, desaturation, tachycardia, hypotension, acidosis, and oliguria.[6] Management includes hyperventilation, 100% oxygen, correction of acidosis, and NO as needed. These patients are usually kept sedated and paralyzed for at least 24 hours postoperatively to minimize early pulmonary hypertensive crises. Signs similar to right ventricular dysfunction may also occur from residual VSDs or truncal valve stenosis or regurgitation. Ventricular septal defect closure or right ventricular incision may produce complete right bundle branch block, complete heart block (3–5%), junctional ectopic tachycardia, atrial tachycardias, and atrioventricular block in the postoperative period.[37] After bypass many patients benefit from calcium infusions because of the hypocalcemia associated with DiGeorge syndrome and the citrate binding of ionized calcium from blood products administered.

## Partial and total anomalous pulmonary venous return

Partial and total anomalous pulmonary venous return (PAPVR and TAPVR) may be more appropriately defined as anomalous pulmonary venous connection. Since a patient may have normal pulmonary venous anatomy with the presence of an ASD which allows abnormal return to the right atrium. Partial anomalous pulmonary venous return is defined as at least one pulmonary vein connected to the right atrium either directly or indirectly through a venous tributary.[93] In TAPVR, all of the pulmonary veins connect anomalously to the right atrium.[93] Both PAPVR and TAPVR are rare cardiac lesions with an incidence of approximately 0.6% and less than 5.0% of CHD respectively.[93–95]

At 27–30 days of gestation, the pulmonary veins are derived from the splanchnic plexus which communicates with the cardinal and umbilicovitelline system of veins. Anomalous drainage to the left common cardinal system results in pulmonary venous connections to the coronary sinus or left innominate vein. Drainage to the right common cardinal system results in pulmonary venous connections to the SVC and/or the azygous vein. Drainage to the umbilicovitelline system results in pulmonary venous connection to the portal vein, ductus venous, or inferior vena cava.[93] Early atresia of the common pulmonary vein while primitive pulmonary–systemic venous connections are still present results in TAPVR. If only the right or left portion of the

common pulmonary vein becomes atretic, persistence of the primitive pulmonary venous–systemic venous connection on that side leads to PAPVR.[93]

Both PAPVR and TAPVR can be associated with other cardiac lesions. Partial anomalous pulmonary venous return is most commonly associated with sinus venosus type ASDs. Congenital mitral stenosis, DORV, VSD, tetralogy of Fallot, coarctation of the aorta, and PDA have all been described with PAPVR.[93] Nearly 33% of patients with TAPVR have other associated anomalies, including single ventricle, CAVC, hypoplastic left heart, PDA, and transposition of the great arteries. Abnormalities of the atrial and visceral situs with the heterotaxy syndrome, asplenia, and polysplenia, are also common among patients with TAPVR.[93] Scimitar syndrome consists of either partial or complete anomalous drainage of the right pulmonary veins to the inferior vena cava, and sequestration of the right lower lobe producing a classic "scimitar" appearance on chest radiograph.[6]

## Anatomy

Multiple types of PAPVR exist. The most common is connection of the right pulmonary veins to the right SVC or right atrium, which represents approximately 74% of patients.[93] The next most common type is the right pulmonary veins to the inferior vena cava. The least common type is the connection of the left pulmonary veins to the left innominate vein or to the coronary sinus. Four different types of TAPVR exist based on the location of the anomalous connection (Fig. 18.8).

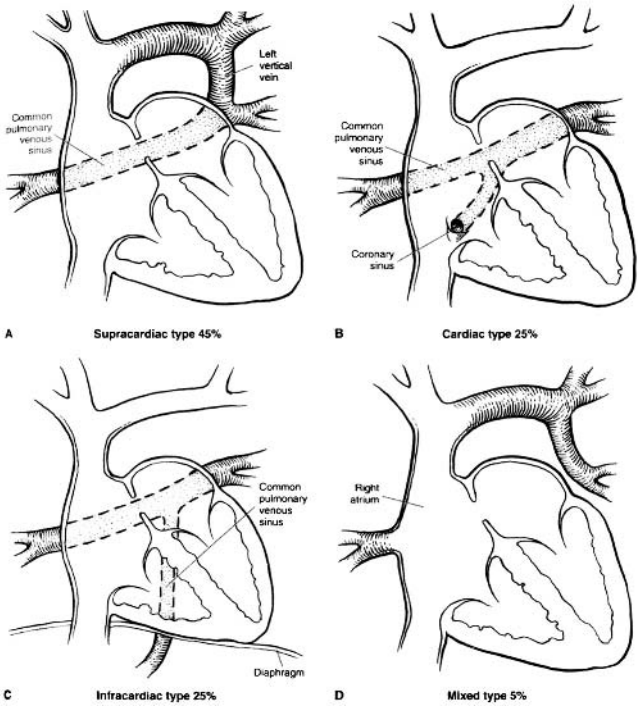


**Fig. 18.8** Four major subtypes of total anomalous pulmonary venous return. See text for further explanation. Reproduced with permission from Hanley FL. Total anomalous pulmonary venous connection. In: Kouchoukos NT, Blackstone EH, Doty DB, Hanley FL, Karp RB, eds. *Kirklin/Barratt-Boyes Cardiac Surgery*, 3rd edn. Philadelphia, PA: Churchill Livingstone, 2003: 753–79.

### Supracardiac total anomalous pulmonary venous return

Supracardiac connection comprises approximately 45–55% of cases of TAPVR.[93] In supracardiac TAPVR the two pulmonary veins from each lung converge posterior to the left atrium. A vertical vein then arises from the left side of the confluence and usually passes anterior to the left pulmonary artery and the left mainstem bronchus to drain into the left innominate vein which then drains to the right SVC.[93] Pulmonary venous obstruction is unusual, but may occur as a result of either intrinsic narrowing or extrinsic compression of the vertical vein. Although anomalous connection can occur to the right SVC via a right-sided vertical vein, this is much less common.[93]

### Cardiac total anomalous pulmonary venous return

The cardiac type of TAPVR accounts for approximately 25–30% of cases. The pulmonary veins in the cardiac type develop a confluence at the coronary sinus or posterior to the right atrium. Obstruction to the pulmonary veins is uncommon, but may occur in up to 22% of TAPVR to the coronary sinus.[96]

### Infracardiac total anomalous pulmonary venous return

Infracardiac TAPVR comprises approximately 13–30% of cases, and is commonly referred to as infradiaphragmatic TAPVR.[93] This type of connection usually forms a confluence of pulmonary veins from both lungs posterior to the left atrium. A descending vein then courses anterior to the esophagus through the diaphragm at the esophageal hiatus.[97] In 70–80% of patients, the descending vein joins the portal venous system at the splenic or the confluence of the splenic and superior mesenteric veins.[97] Nearly all of patients with infracardiac type of TAPVR have obstructed pulmonary veins, with the level of obstruction, either intrinsic or extrinsic, occurring at any location along the path.

### Mixed total anomalous pulmonary venous return

Mixed type of TAPVR makes up approximately 2–9% of cases. This type of TAPVR consists of anomalous connections at two or more levels. The most common connection involves the left pulmonary veins draining into the left innominate vein and the right pulmonary veins draining to the right atrium or the coronary sinus.[93] Obstruction to these pulmonary venous connections can occur.

## Pathophysiology and natural history

Partial anomalous pulmonary venous return results in a variable amount of left-to-right shunting that depends upon several factors: the number of anomalously draining veins as a percentage of the total pulmonary venous return, the pulmonary lobes or segments from which the anomalous veins originate from, and the relative resistances of the normally and anomalously drained pulmonary vascular beds and the compliance of the receiving chambers. The left-to-right shunt leads to increased pulmonary blood flow and enlargement of the right atrium and ventricle as well as dilation of the pulmonary artery.[93]

Most patients with an isolated single vein PAPVR and intact atrial septum are asymptomatic if left untreated and have normal life expectancy. Those patients with greater than 50% of the pulmonary veins draining anomalously or those with an associated ASD usually remain relatively asymptomatic until the third to fourth decades of life when progressive symptoms of dyspnea, recurrent bronchitis, hemoptysis, chest pain, and palpitations with supraventricular arrhythmias occur. These patients may also present with right heart failure or with pulmonary hypertension and cor pulmonale.[93]

The pathophysiology of TAPVR depends largely upon whether or not obstructed or unobstructed pulmonary venous return is present. In the presence of obstructed pulmonary veins, pulmonary venous hypertension exists with associated pulmonary edema. It is commonly confused with lung disease because of bilateral infiltrates secondary to pulmonary edema with a small heart size on chest radiograph. Pulmonary arteriolar vasoconstriction occurs as a compensatory mechanism to minimize the pulmonary edema. As *PVR* increases, the right ventricular systolic and end-diastolic pressures increase resulting in increased right atrial pressure and right-to-left shunting at the atrial level. Progressive systemic hypoxemia ensues with metabolic acidosis and multisystem organ failure. Left untreated, death occurs in the first few months of life.[6,93]

In unobstructed TAPVR, the left-to-right shunt of pulmonary venous blood results in right atrial and ventricular enlargement with pulmonary overcirculation and subsequent right heart failure. The presence or absence of a restrictive interatrial communication is another major determinant in the pathophysiology of TAPVR, and 70–80% of infants have a PFO which restricts filling of the left atrium and ventricle. The tremendous pulmonary overcirculation and right-sided dilation and mimimal left-sided filling results in decreased size of the left atrium and ventricle. The abnormal displacement of the interventricular septum along with the chronic underfilling of the left ventricle leads to decreased systemic *CO*. Symptomatic CHF usually develops in the second month of life and may be partially or totally relieved by transvenous balloon atrial septostomy.[93,98] Twenty percent of patients have an unrestrictive interatrial communication consisting of a secundum type ASD. These patients have a large left-to-right shunt with increased pulmonary blood flow, but may not develop signs of right heart failure or pulmonary hypertension until the third or fourth decade of life if left untreated.[93,98]

## Surgical approaches

Timing of surgical repair of PAPVR is dependent in part upon symptomatology. Patients with a single anomalous pulmonary vein with an intact atrial septum may never require surgical treatment. Surgical therapy is generally reserved for those patients with: (i) hemodynamically significant left-to-right shunting with $Qp : Qs$ greater than 2 : 1; (ii) patients with recurrent pulmonary infections, especially those associated with Scimitar syndrome; (iii) patients having surgical repair of other major cardiac lesions; and (iv) patients with anomalous connections which affects surrounding structures by compression or obstruction.[93] Surgical repair for PAPVR varies depending on the specific anatomy present. The repair can consist of a direct anastomosis of the anomalous veins to the left atrium or an indirect communication is developed utilizing a patch to baffle the anomalous veins to the left atrium.

Obstructed TAPVR should be corrected emergently at time of diagnosis.[99] Patients with unobstructed TAPVR with restrictive interatrial communications may be palliated with blade and/or balloon atrial septostomies and medically managed for elective surgical repair in the first year of life. Those patients with non-restrictive interatrial communications may be repaired electively, usually in the first year of life.

Techniques for surgical repair of TAPVR depend upon the specific anatomy involved, and in some cases, a period of deep hypothermic circulatory arrest may be necessary. Surgical repair generally includes incision and enlargement of the anomalous pulmonary venous confluence and direct anastomosis with the left atrium. Occasionally, a patch is needed to baffle the veins to the left atrium.

Operative mortality for repair of asymptomatic PAPVR should approach zero, and in older symptomatic patients is less than 6%.[93,100] However, operative mortality for patients with TAPVR ranges from 8% to 13%, and TAPVR with heterotaxy approaches 100%.[93,95]

## Anesthetic considerations

The anesthesiologist's first encounter of the patient with PAPVR may be in the cardiac catheterization laboratory when scheduled for a transcatheter closure of an ASD, and the presence of an anomalous pulmonary vein is discovered, thereby preventing the utilization of the device. However, the first encounter with the patient with TAPVR may be in radiology, because an increasing number of newborns with

suspected TAPVR undergo magnetic resonance imaging, which may be superior to echocardiography and angiography in the evaluation of TAPVR.[101,102]

Intraoperative considerations for patients with PAPVR are similar to management of ASD, with increased pulmonary blood flow. Minimizing pulmonary blood flow by control of ventilation and consideration for early extubation following repair should be the primary goals.

The pre-bypass management of the patient with obstructed TAPVR generally includes maximizing $P_{O_2}$, correcting metabolic acidosis, and maintaining hemodynamic stability with use of inotropic medications as necessary. Transesophageal echocardiography is usually contraindicated due to risk of further compression and obstruction to pulmonary veins even in the presence of non-obstructed TAPVR. Perioperative monitoring of central venous, left atrial, and pulmonary arterial pressures is helpful for management.

After bypass, NO should be used empirically in the case of obstructed TAPVR and should be readily available for immediate use in unobstructed TAPVR. Perioperative pulmonary hypertension occurs in as many as 50% of patients, and is a major risk factor for early mortality.[103,104] Pulmonary hypertensive crises may be avoided by employing hyperventilation, use of 100% oxygen, systemic alkalinization, sedation, and paralysis along with NO. Magnesium sulfate and prostaglandin $E_1$ have been used in some patients to treat severe pulmonary hypertension.[105] Paradoxical pulmonary hypertension and systemic hypotension has been reported from the postoperative use of NO in patients with preoperative atrial obstruction and poorly compliant left ventricles with ventricular dysfunction. This paradoxical pulmonary hypertension is thought to be due to acute increases in pulmonary blood flow and resultant preload to the non-compliant left side.[106]

Pulmonary function may be compromised after bypass as a result of two pulmonary insults: (i) preoperative pulmonary edema secondary to pulmonary venous obstruction; and (ii) the inflammatory response from CPB. Pulmonary compliance is decreased and a large arterial-to-alveolar gradient develops. Pulmonary gas distribution may be optimized with the use of pressure control ventilation and altering positive end-expiratory pressure (*PEEP*) to improve lung compliance.

Following repair, left atrial filling pressures may be elevated due to the small size and non-compliant left ventricle. Accepting low blood pressures while weaning from CPB will help avoid overdistending the "unprepared" left side. Careful fluid management along with optimization of heart rate and rhythm and inotropic support will improve *CO*. Perioperative dysrhythmias, especially supraventricular tachycardias, occur in as many as 20% of patients.[106]

Optimize heart rate and rhythm with inotropic support and/or temporary pacing as needed. If tolerated, an inovasodilator like milrinone will decrease left ventricular work and improve *CO*. It is important to recognize that the Frank–Starling curve is very flat in the small non-compliant left ventricle and administration of only a few milliliters of fluid to an infant may cause the left ventricle to become overdistended and to fail.

## Key points for anesthetic management of lesions

### Patent ductus arteriosus

1. Avoid air bubbles in intravenous lines due to risk of paradoxical emboli.
2. Critically ill neonates may require a high dose narcotic technique to minimize the stress response to surgery.
3. Lung isolation is usually required for video-assisted surgery to allow adequate surgical exposure.

### Aortopulmonary window

1. Patients with pulmonary overcirculation should be managed to maintain pulmonary vascular tone.
2. Surgical snaring of the pulmonary artery can assist in increasing diastolic blood pressure and coronary perfusion.
3. Perioperative pulmonary hypertension frequently requires hyperventilation, 100% oxygen, systemic alkalinization, deep sedation, and paralysis.

### Atrial septal defects

1. Avoid air bubbles in intravenous lines due to risk of paradoxical emboli.
2. Tailor anesthetic techniques to allow early extubation.

### Ventricular septal defects

1. Maintain pulmonary vascular tone in those patients with pulmonary overcirculation prior to repair.
2. Diagnose and treat possible dysrhythmias, especially heart block.
3. Patients with uncomplicated VSDs should be considered for early extubation.

### Common atrioventricular canal

1. Maintaining pulmonary vascular tone is usually necessary.
2. Perioperative pulmonary hypertension frequently requires hyperventilation, 100% oxygen, systemic alkalinization, deep sedation, and paralysis.
3. Transesophageal echocardiography is helpful for post-repair assessments.
4. Inotropic support is frequently required with dopamine and/or milrinone.
5. Diagnose and treat dysrhythmias.

### Double outlet right ventricle

**1** Patients with physiology associated with pulmonary overcirculation should be managed by maintaining or increasing *PVR*.
**2** Patients with physiology associated with inadequate pulmonary blood flow should be managed to improve pulmonary blood flow.
**3** Perioperative pulmonary hypertension frequently requires hyperventilation, 100% oxygen, systemic alkalinization, deep sedation, and paralysis.
**4** Diagnose and treat dysrhythmias.
**5** Inotropic support is frequently required.

### Truncus arteriosus

**1** Patients with pulmonary overcirculation should be managed to maintain or increase *PVR*.
**2** Surgical snaring of the pulmonary artery can assist in increasing diastolic blood pressure and coronary perfusion.
**3** Perioperative pulmonary hypertension frequently requires hyperventilation, 100% oxygen, systemic alkalinization, deep sedation, and paralysis.
**4** High incidence of DiGeorge syndrome may require perioperative calcium infusions and use of irradiated blood products.
**5** Inotropic support is frequently required perioperatively.

### Partial and total anomalous pulmonary venous return

**1** Maximizing oxygenation by mechanical ventilation, $F_{IO_2}$ = 1.0, hyperventilation, and other maneuvers to decrease *PVR*, as well as inotropic support for cyanotic patients.
**2** Perioperative pulmonary hypertension frequently requires hyperventilation, 100% oxygen, systemic alkalinization, deep sedation, and paralysis.
**3** Avoid use of TEE, which may worsen obstructed pulmonary veins and obstruct non-obstructive veins.
**4** Avoid overfilling the left heart.
**5** Inotropic support is frequently required perioperatively.
**6** Diagnose and treat dysrhythmias.

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# 19 Anesthesia for left-sided obstructive lesions

Anil de Silva
Greg Stratmann

## Introduction

Obstruction of the left ventricular outflow tract (LVOT) occurs at varying anatomic locations. The various disease states associated with the condition have different implications with regard to hemodynamic derangement, outcome, and anesthetic management. Categories of left heart and aortic obstructive disease include aortic valve stenosis, subvalvar stenosis, hypertrophic cardiomyopathy, coarctation of aorta, interrupted aortic arch, and Shone's anomaly.

## Aortic valve stenosis

### Anatomy

Most left ventricular obstruction has a valvular basis. The anatomic basis for the stenosis is frequently a structural anomaly in which the aortic valve is missing one or more of its commissures. Up to 6% of children with congenital heart disease suffer from some form of valvar aortic stenosis.[1] There is often a coarctation or hypoplastic aorta associated with the valvular defect since fetal aortic blood flow *in utero* is reduced.

### Pathophysiology and diagnosis

The degree of stenosis affects the age of presentation. Ten percent of patients with aortic stenosis present before 1 year of age: these patients have severe aortic stenosis with transvalvar gradients that are usually greater than 55 mmHg. Symptoms include tachypnea, poor feeding, and failure to thrive. In the most severe instance, the child may present with metabolic acidosis, and cardiogenic shock. In the past, when treatment was impossible, children with critical aortic stenosis had a 23% probability of mortality. More recently, however, the mortality for children who survive the first year was only about 1.2% for the first 20 years.[2]

Critical aortic stenosis is part of a continuum of left heart dysplasia. In addition to an isolated aortic valve abnormality, critically ill neonates will frequently have biopsy evidence of endomyocardial fibroelastosis. One hundred percent of hospital deaths after aortic valvotomy had endomyocardial fibroelastosis.[3,4] It is possible that severe left heart ischemia during intrauterine development causes a reduction in subendocardial oxygen delivery which initiates subendocardial fibrotic changes in the fetal myocardium.[5] Myocardial distensibility is decreased which reduces left ventricular end-diastolic volume and depresses the ejection fraction.[6]

Moderate aortic stenosis will provide a markedly noticeable jugular venous "a" wave. The "a" wave is caused by encroachment of the hypertrophied left ventricle into the space normally occupied by the filled right ventricle. A chest radiograph may show cardiomegaly, possibly even pulmonary edema.[7]

Echocardiography can provide an excellent assessment of aortic stenosis in the pediatric age group. This diagnostic modality may show the stenosed valve with a possibly reduced number of commissures and any decline in leaflet mobility. Doppler flows through the stenotic valves can be calculated with a satisfactory equivalence to pressure gradients obtained by cardiac catheterization.[8]

### Surgical and interventional approaches

Infants with critical aortic stenosis can present in cardiogenic shock. The closure of the ductus disrupts blood flow to the lower body; the administration of prostaglandin will be required to maintain ductal patency, thus possibly bypassing the obstructive valvular lesion and providing blood flow into the distal aorta. Endotracheal intubation and inotropic support may be necessary.

The child with critical aortic stenosis will require a balloon angioplasty of the stenotic valve, a surgical valvuloplasty resulting in a two-ventricle repair, or possibly a Norwood procedure (one-ventricle repair) if the left ventricle is hypoplastic. The Norwood procedure for the hypoplastic left heart

is discussed in Chapter 22. Percutaneous balloon valvuloplasty has been shown to be an acceptable alternative to surgery in selected neonates with aortic stenosis. One study showed 80% of newborn patients with severe aortic stenosis had successful balloon dilations of their stenotic valves. Of those patients, 30% developed mild to severe aortic insufficiency. None of the patients with a small left ventricle survived, and 20% who received balloon dilation also required surgery within 1–14 days.[9] A recent multicenter study from Japan reviewed the results of 77 patients (mean age of 8 years) with critical aortic stenosis who had undergone balloon valvuloplasty. The pressure gradient decreased immediately from an average of 68 to 34 mmHg. Fourteen percent of the patients had major complications including aortic regurgitation, aortic aneurysm, and femoral artery thrombosis. Of 55 patients who were seen at an average of 34 months later, 56% required no further intervention.[10]

The surgical valvotomy was originally conceived of as a merely palliative procedure; however, a recent study encompassing long-term results with aortic valvotomy is more hopeful. Patients with congenital valvular aortic stenosis (n = 116) with a mean aortic gradient of 78 mmHg were studied over 37 years. The early mortality was 2.5%, while the 37-year survival was 72.5%. Restenosis was associated with a 2.3%/year reoperation rate.[11,12]

Infants with critical aortic stenosis may not survive after a classic valvotomy despite a seemingly adequate left ventricular size. Surgical decisions made on the basis of left ventricular size alone appear to be inadequate. A study by Rhodes *et al*.[13] showed that it was possible to determine the survival probability of a neonate with critical aortic stenosis after a two-ventricle repair if the prediction was based on mitral valve area (*MVA*), long-axis dimension of the left ventricle relative to the long axis of the heart (*LAR*), diameter of the aortic root (*ROOT*), and the patient body surface area (*BSA*). The Rhodes' formula:

$$\text{Score} = 14.0(BSA) + 0.943(ROOT) + 4.78(LAR) + 0.15\,(MVA) - 12.03$$

shows an approximately 90% probability that a neonate would survive a two-ventricle repair if the Rhodes' score was greater than –0.35. Risk is increased when the left ventricular long axis to heart long axis ratio is 0.8 or less; the indexed aortic root diameter is 3.5 $cm/m^2$ or less; or the indexed mitral valve area is 5.75 $cm^2/m^2$ or less. Other authors suggest that additional criteria also be included such as a mitral annulus less than 9 mm[14] and a heart apex formed by the right ventricle.[15]

Older patients and those with less critical anatomy may undergo aortic valve repair or replacement. Replacement of the aortic valve in growing children often involves placement of an aortic root homograft, or the Ross procedure (pulmonary autograft), in which the patient's own pulmonary valve and root becomes the neo-aorta. These operations require reimplantation of coronary arteries (Fig. 19.1). Mechanical or prosthetic valves are normally reserved for older teenaged patients who have undergone the majority of their somatic growth, and who are candidates for chronic anticoagulation.

## Anesthetic considerations

The anesthetic management for aortic stenosis requires that the myocardial oxygen supply is adequate for the increased oxygen demand of thickened myocardium. Hypotension can be precipitated by tachycardia, hypovolemia, or dysrhythmias. Tachycardia may prevent the establishment of adequate ventricular filling during diastole. Dysrhythmias

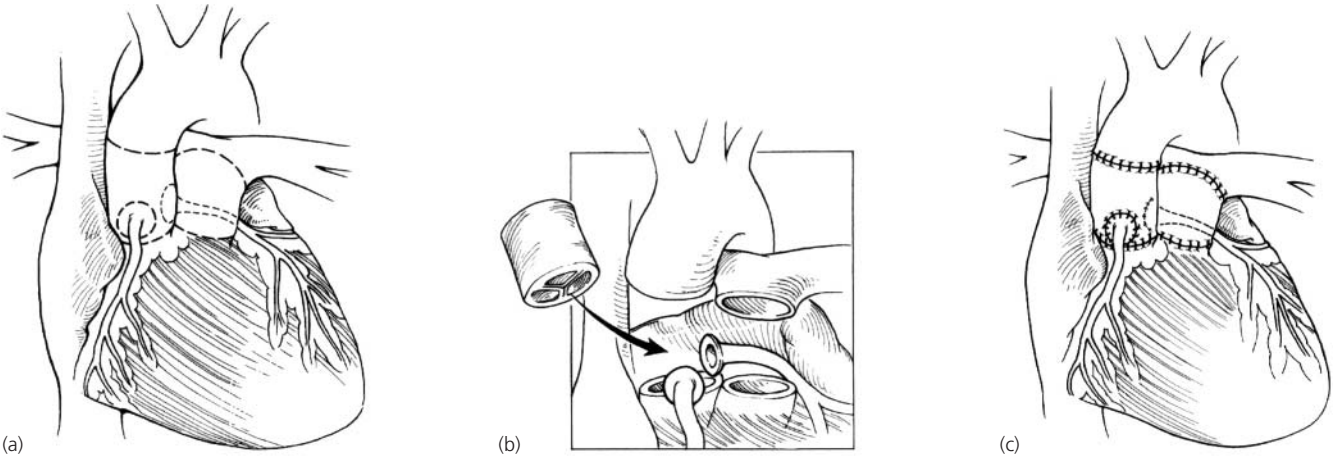


**Fig. 19.1** The Ross procedure (pulmonary autograft). (a) Incisions on the aorta, pulmonary artery, and the coronary buttons. (b) Pulmonary autograft and reimplantation of the coronary arteries. (c) Completed operation with a right ventricle to pulmonary artery conduit to replace the native pulmonary valve. Reproduced with permission from Chang AC, Burke RP. Left ventricular outflow tract obstruction. In: Chang AC, Hanley FL, Wernovsky G, Wessel DL, eds. *Pediatric Cardiac Intensive Care*. Philadelphia, PA: Lippincott, Williams & Wilkins, 1998: 233–56.

should be treated aggressively, as atrial function is critical to the maintenance of an adequate cardiac output. The use of lidocaine, overdrive pacing, and cold saline applied directly to the cardiac surface may be beneficial. Should there be a precipitous decline in blood pressure secondary to an atrial rhythm disturbance, cardioversion is required as inadequate diastolic pressure results in myocardial ischemia.

## Subvalvar aortic stenosis

### Anatomy

There are two distinct types of subvalvular aortic stenosis (subAS). The first type consists of either a thin membrane surrounding the LVOT and positioned just 2 or 3 mm under the aortic valve, or a thicker more fibrous collar with a muscular base that rings the LVOT. The second and more severe type is a fibromuscular narrow tunnel that courses the length of the LVOT. There may be a higher male preponderance to the disease state of about 2.5 to 1.[16] Subvalvular aortic stenosis can be both a congenital and progressive heart defect.

A variety of congenital heart defects may exist in association with subAS. Thirty-nine percent of patients with a membranous collar and 75% of patients with a fibromuscular tunnel had associated congenital heart lesions.[17] Structural anomalies that are most prevalent are bicuspid valves, aortic stenosis, ventricular septal defect, and coarctation (Table 19.1).

### Pathophysiology and diagnosis

Subvalvular aortic stenosis frequently appears after the first year of life and is progressive. There is a significant positive correlation between the LVOT gradient and patient age; patients with ages less than 25 years had mean LVOT gradients of 21 mmHg, which progressively increased with age.[18]

Progressive aortic regurgitation may occur in association with subAS.[19] Up to 50% of patients with subAS (even those with minor gradients) eventually develop aortic regurgitation. The aortic regurgitation appears due to injury caused by the rhythmic impact of turbulent blood on the leaflet tissue. A thick fibrous membrane may eventually coat the leaflets, causing scarring and contractures which results in regurgitation.[20]

On auscultation one may hear an ejection murmur at the left sternal border radiating toward the carotid arteries. Electrocardiograph may show evidence of left ventricular hypertrophy. The chest radiograph may show signs of cardiac enlargement. Echocardiography should show the area of narrowing within the left ventricular cavity.

**Table 19.1** Concurrent congenital anomalies in patients with subvalvular aortic stenosis.

| Lesions | Percentage of patients |
|---|---|
| Bicuspid valves | 40 |
| Aortic stenosis | 28 |
| Ventricular septal defect | 24 |
| Coarctation of aorta | 12 |
| Patent ductus arteriosus | 12 |
| Atrial septal defect | 4 |

Adapted from Tentolouris K, Kontozoglou T, Trikas A *et al*. Fixed subaortic stenosis revisited. *Cardiology* 1999; **92**: 4–10, with permission from S. Karger AG, Basel.

### Surgical approaches

The surgical procedure consists of the excision of the fibromuscular collar or membrane (Fig. 19.2) but the timing of the intervention is controversial. The progressive development of higher gradients and the possibility of the development of aortic regurgitation is the rationale behind early surgical intervention. Such a recommendation has been made even in the absence of a subaortic gradient or aortic regurgitation. Recurrence of an LVOT gradient after surgery has been a significant problem with rates as high as 55%. In addition the number of patients with aortic regurgitation actually increases from 23% to 54% postoperatively, although the degree of postoperative aortic regurgitation is mild.[21] Therefore early surgery is not necessarily beneficial.

Of 83 patients with subAS, 91% had a fibromuscular collar, and 9% the tunnel variation. The patients were separated into an early and late surgery group. The overall peak LVOT gradient was reduced from an average of 45 mmHg preoperatively to 4 mmHg postoperatively in both groups. No deaths or major complications were noted.[22] The late surgery group had a much higher recurrence rate at 5 and 10 years (28% and 57%) compared to the early surgery group (6% and 0%), justifying the rationale for early surgical intervention.

### Anesthetic considerations

The anesthetic management of the patient with subAS is very similar to that for aortic stenosis. Care must be taken to maintain myocardial and other end-organ perfusion. A decrease in myocardial oxygen demand and maintenance of afterload and preload are essential.

## Supravalvar aortic stenosis

Supravalvar aortic stenosis is often seen with Williams' syndrome, and may be complicated by involvement of the coronary artery ostia in the stenotic segment. This may lead to coronary ischemia, especially with low systemic vascular resistance when the ostia are distal to the stenotic segment.

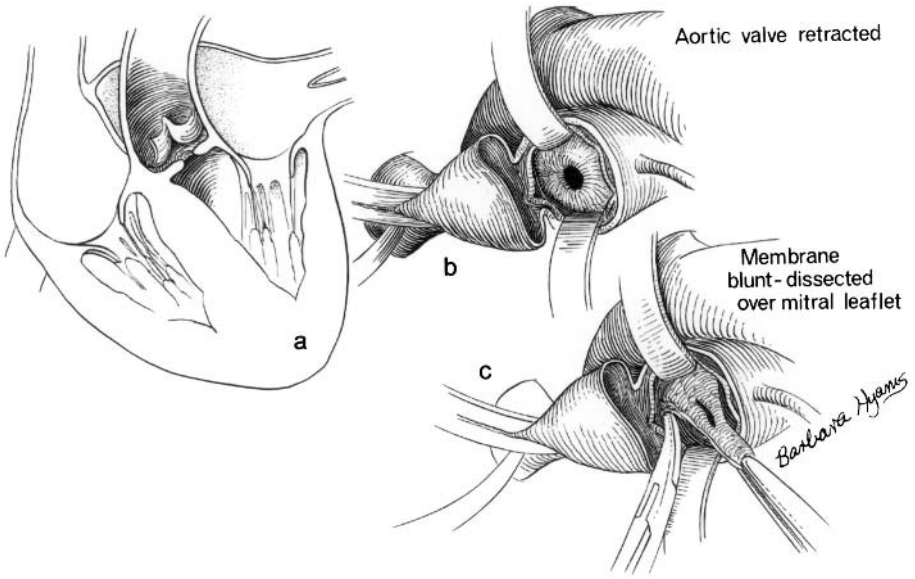


**Fig. 19.2** Surgical repair of subaortic stenosis. Reproduced with permission from Cooley DA, Norman JA. Aortic valve procedures. In: Cooley DA, Norman JA, eds. *Techniques in Cardiac Surgery*. Houston, TX: Texas Medical Press, 1975: 129–37.

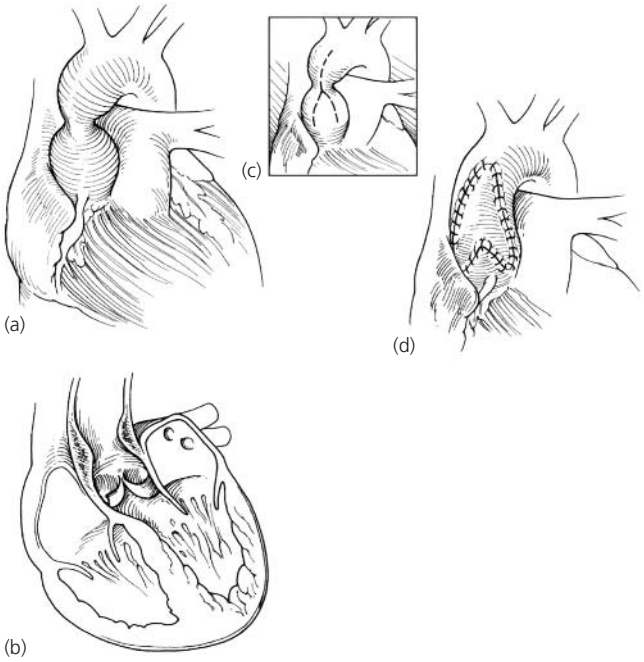


**Fig. 19.3** Repair of supravalvar aortic stenosis. (a) External appearance. (b) Coronal plane view of the defect. (c) Inverted Y incision in the ascending aorta. (d) Placement of an autologous pericardial patch. Reproduced with permission from Chang AC, Burke RP. Left ventricular outflow tract obstruction. In: Chang AC, Hanley FL, Wernovsky G, Wessel DL, eds. *Pediatric Cardiac Intensive Care*. Philadelphia, PA: Lippincott, Williams & Wilkins, 1998: 233–56.

Some of these patients are at risk for sudden death and cardiac arrest with general anesthesia.[23] Surgical repair is by incision of the ascending aorta and placement of a patch usually made of autologous pericardium cured with glutaraldehyde (Fig. 19.3).

## Hypertrophic cardiomyopathy

### Anatomy

Hypertrophic cardiomyopathy (HOCM) is an autosomal dominant disease which occurs in about 1 of 500 live births (about 0.2% of the population).[24] The annual mortality in tertiary care centers is higher than 4%. In the unselected population the mortality rate may be less than 1%.[25] Hypertrophic cardiomyopathy is caused by mutations in the genes that code for the myocardial sarcomere, and is in fact one of the most widespread genetic diseases of the myocardium.[26]

In more than 80% of the cases the location of the hypertrophied myocardium is at the ventricular septal level. However, the disease process can occur at other locations such as the apex (9%) or mid-ventricle (4%). The hemodynamic severity of the HOCM is dependent on its location.[27]

### Pathophysiology and diagnosis

Most patients with HOCM and neonates, in general, exhibit no symptoms at all.[25] The clinical course of the disease is inconsistent and is dependent on whether the HOCM is an obstructive or non-obstructive form. If obstructive, more than 25% of infants will develop symptoms of congestive heart failure manifested by feeding intolerance or failure to thrive.[28]

The hypertrophied left ventricle can become fibrotic and there is a subsequent decrease in left ventricular diastolic relaxation. The hypertrophy may eventually result in a fixed obstruction causing continuing hemodynamic difficulties, or there may be a dynamic component that is only present during times of increased ventricular contractility. A large

muscular intraventricular septal prominence can cause mitral regurgitation secondary to systolic anterior motion (SAM) of the mitral valve leaflets.

A histological examination of the myocardial architecture of the patient with HOCM shows myocardial fiber disarray that occupies large portions of the left ventricular muscle mass. Although fiber disarray is present even in normal hearts, the extent to which this happens in the heart with HOCM is significantly increased.[29] The intramural coronary arteries supplying the ventricular muscle mass are thick-walled, narrowed and tortuous.[30–32]

Echocardiography is extremely helpful in determining the extent, location, and severity of the disease. Quantitative echocardiographic findings in patients with HOCM include increased left ventricular wall thickness, decreased left ventricular end-diastolic cavity size, and increased left ventricular fractional shortening. An important diagnostic characteristic is the increased hypertrophy of the interventricular septum compared to the left ventricular posterior free wall.[28] Systolic anterior motion of the mitral valve can occur. Suggested mechanisms for the occurrence of SAM include a structural deformation of the papillary muscles; crumpling of the chordae tendinae during the brisk emptying of the left ventricle; and a Bernoulli effect from high velocity flow in the left ventricle outflow tract.[33]

The in-hospital annual mortality is about 2% or 3%. Sudden death may occur up to 35 years of age.[34] Exercise appears to be an etiologic factor. If the ventricular obstruction is uncorrected, systolic and diastolic ventricular function becomes increasingly impaired. However, as the disease process continues the ventricle may dilate, at which point systolic function fails as well. At this point, mitral regurgitation increases and congestive heart failure occurs.

### Surgical approaches

Although surgical excision of the obstructing muscle is a traditional treatment, the risk of sudden death may not be alleviated despite an adequate surgical outcome. Patients with an outflow gradient greater than 50 mmHg and who are unresponsive to medical therapy are considered to be surgical candidates. Intraoperative risk of adverse cardiac events may be as high as 40%. A study of patients with HOCM undergoing non-cardiac surgery showed a high frequency of complications such as congestive heart failure, hypotension, and stable dysrhythmias.[35]

### Anesthetic management

The primary hemodynamic goals of the anesthetic should be the reduction of the LVOT gradient, with induction that decreases myocardial contractility and maintains afterload. The use of halothane in such cases has been well tolerated as has intravenous opioids such as fentanyl.[36] The anesthetic management of the patient with HOCM should include an arterial line and central venous pressure line, and if the LVOT gradient is very high, the placement of the arterial line prior to induction should be considered. However, one must judge whether a child's anxiety and pain over the procedure might precipitate an adverse event. The placement of a central venous line for this disease state is not a trivial occurrence. Care must be taken to avoid irritation of the atrial wall and the occurrence of an atrial dysrhythmia. Rapid treatment of dysrhythmias is important as hemodynamics may deteriorate swiftly.

## Coarctation of the aorta

### Anatomy

Coarctation of the aorta most commonly is characterized by a narrowing of the aortic lumen opposite the opening to the ductus arteriosus and just distally to the opening of the left subclavian artery. Up to 8% of all congenital cardiac patients may have an associated aortic coarctation.[1] It is more prevalent in males than females by a 3 : 1 margin.[37] The etiological basis for the coarctation arises from a folding of the medial tissue of the aortic wall such that it encroaches upon the aortic lumen. Blood flow to the distal aorta is dependent on a ductus arteriosus. If the coarcted segment remains uncorrected for sufficient time, collateral blood flow will develop thus allowing for adequate perfusion distal to the aortic obstruction.

### Pathophysiology and diagnosis

The symptomatic neonate generally presents in the first few weeks of life with tachypnea and failure to thrive. The closure of the ductus arteriosus, which served to ameliorate the hemodynamic impact of the coarctation upon the neonate, causes a vastly increased left ventricular afterload.[1] The aortic obstruction precipitates congestive heart failure and cardiogenic shock.

Moderate narrowing of the aorta results in a less emergent presentation. However, without correction of the underlying structural abnormality, the untreated patient will develop systemic hypertension proximal to the coarctation, eventually causing left ventricular failure. Over 90% of untreated patients with coarctation of the aorta die by the age of 50 years.[38] The mean age for death following repair is 38 years of age.[39] Problems such as late onset hypertension, accelerated coronary artery disease, stroke, and aneurysm formation are among the more prevalent.[40,41] Therefore, these patients need to be followed for possible complications.[42]

The diagnostic feature of coarctation of the aorta is systolic and mean blood pressure differences between the upper extremities and lower extremities. A gradient greater than 10 mmHg is considered significant.

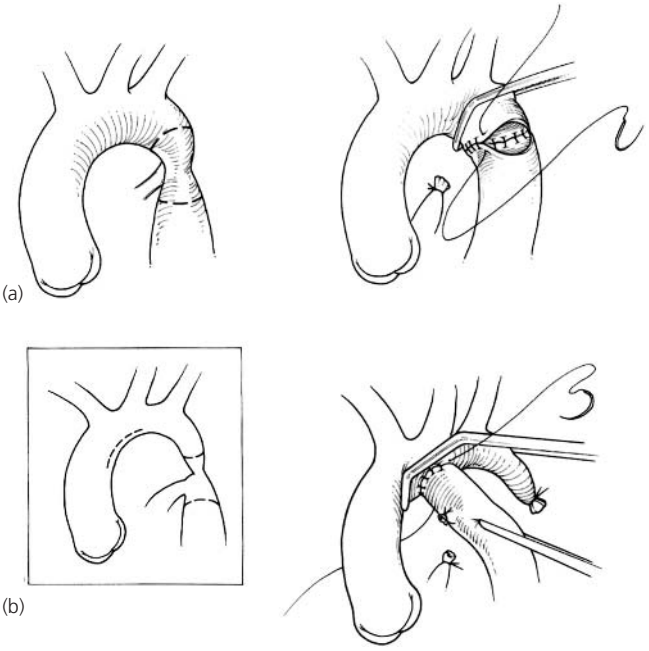


**Fig. 19.4** Two surgical approaches for repair of coarctation of the aorta. (a) Resection of coarctation with end-to-end anastomosis. (b) End-to-side or aortic arch advancement technique. Reproduced with permission from Chang AC, Burke RP. Left ventricular outflow tract obstruction. Reproduced with permission from Chang AC, Burke RP. Left ventricular outflow tract obstruction. In: Chang AC, Hanley FL, Wernovsky G, Wessel DL, eds. *Pediatric Cardiac Intensive Care*. Philadelphia, PA: Lippincott, Williams & Wilkins, 1998: 233–56.

## Surgical approaches

There is continued uncertainty as to the optimal long-term management strategy for the infant with coarctation of the aorta. At the present time, neonates are thought to have a better outcome with a surgical repair, while older patients may benefit more from balloon dilation.[43] The options for surgical repair include a subclavian flap aortoplasty, a resection of the narrowed portion of the aorta with an end-to-end anastomosis, an end-to-side reconstruction, or tube graft interpositioning (Fig. 19.4). A study of cases from 1982 to 1994 suggested that mortality was somewhat higher in infants who had undergone a subclavian flap repair (8%), compared to those who had undergone an end-to-end anastomosis (5%), although all the deaths had an associated ventricular septal defect.[44] Additional early complications include paraplegia although this is rare (0.4%).[45,46] Recurrent coarctation is defined as the existence of a pressure gradient greater than 10 mmHg across the operative site.[47] Earlier studies showed a high incidence of recoarctation if the operation was performed in the first 3 years of life; the recurrence rate was less than 3% if performed afterward.[48] More recently, recurrence rates of approximately 10% have dropped in infants under 3 months of age with either the end-to-end anastomotic or the subclavian flap techniques.[44]

## Anesthetic considerations

The medical management of infants with coarctation consists of inotropic support and diuretics. Should the infant be less than 1 month of age intravenous prostaglandin is utilized to open the closed ductus arteriosus. Intubation may be necessary to decrease the work of breathing and reduce left ventricular demand. Metabolic acidosis should be corrected to improve left ventricular function.

The anesthetic management of the patient with coarctation of the aorta should include a right-sided arterial catheter in a preductal artery, in addition to the usual anesthetic monitors. The placement of the intra-arterial catheter ensures that blood pressure will be monitored during the phase of the operation when the left subclavian artery and/or aorta may be clamped or compressed.

There have been reports that infants with a core temperature greater than 38°C are at increased risk for spinal cord ischemia. Most centers choose to allow the child to cool to about 35°C in order to protect against this complication.[49] Induction of anesthesia can be accomplished either by intravenous or inhalational anesthesia; however, care must be taken to avoid hypertension as these patients can have an exaggerated response to inotropic drugs.[50] The application of the cross-clamp can cause upper body hypertension. The blood flow to the lower body and spinal cord is reliant on collateral flow that can vary depending on the systolic pressure generated by the myocardium. It is possible that the failing ventricle may be unable to mount an appropriate blood pressure, in which case dopamine or other inotropic agent may need to be administered.[51]

The early postoperative period is often complicated by the onset of hypertension. Greater than one-half of patients who undergo repair of a coarctation experience significant increases in blood pressure for up to 2 weeks.[52] It has been postulated that the increase in blood pressure may be secondary to stimulation of the sympathetic system distal to the anastomotic site, with the subsequent increases in plasma renin activity. Untreated hypertension can result in mesenteric arteritis.[53] Vasodilators, calcium channel blockers and β-blocker therapy are used to treat this condition.

# Interrupted or hypoplastic aortic arch

## Anatomy

An interrupted aortic arch (IAA) exists in about 1% of patients with congenital malformations of the heart. The interruption may be divided into three anatomical variants: type A, which is characterized by a location just distal to the

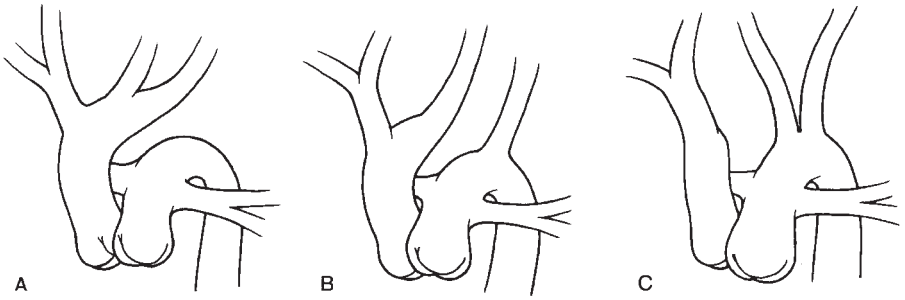


**Fig. 19.5** Interrupted aortic arch. Type A, interruption between the left subclavian artery and the ductus arteriosus. Type B, interruption between the left carotid and left subclavian arteries. Type C, interruption at the proximal aortic arch between the innominate and left carotid arteries. Reproduced with permission from Chang AC, Burke RP. Left ventricular outflow tract obstruction. In: Chang AC, Hanley FL, Wernovsky G, Wessel DL, eds. *Pediatric Cardiac Intensive Care*. Philadelphia, PA: Lippincott, Williams & Wilkins, 1998: 233–56.

left subclavian artery (25% incidence); type B, located in the space between the left subclavian artery and left common carotid artery (70% incidence); and type C between the left common carotid artery and innominate arteries (5% incidence) (Fig. 19.5).[54,55]

All types of IAA have an associated high incidence of additional congenital cardiac anomalies. A ventricular septal defect is most prevalent and is present in 94% of type B interruptions, and 57% of type A interruptions.[56] Other cardiac defects include bicuspid aortic valve, truncus arteriosus, transposition, and double inlet left ventricle.[57]

## Pathophysiology and diagnosis

The neonate often appears normal initially but over the course of a few days or weeks can become precipitously ill with duct closure. Early signs include congestive heart failure and metabolic acidosis as blood flow below the obstruction becomes compromised.

Twenty-seven percent of patients with IAA may have coexisting DiGeorge syndrome.[58] Common features of the infant with DiGeorge include hypocalcemia, an absent thymus, and anomalies of the ears, face, and palate. Of 161 patients with DiGeorge, 43% had IAA.[59]

The diagnosis of IAA is best established with transthoracic echocardiography, aortography, or MRI. In addition to delineating the extent of the lesion, additional cardiac anomalies may be seen.

## Surgical approaches

Surgical strategies for treatment have varied. The direct primary one-stage repair restores anatomic continuity and any associated cardiac defects in one operation. A left thoracotomy approach results in poor exposure of the proximal aorta and can result in difficulty in palliating coexisting proximal lesions. An approach through a midline sternotomy for a total repair of the arch and any coexisting intracardiac anomalies is now favored. A 6% overall mortality rate has been cited for neonates with IAA, regardless of other cardiac defects, utilizing this approach.[60]

A recent study of preterm and low-birth-weight infants with IAA and associated ventricular septal defect who had undergone a primary repair showed an in-hospital mortality rate of 14%.[61] The overall perioperative mortality rate for procedures done since 1990 was 12%, compared to an overall mortality rate of 42% prior to 1985.[58,62] It is possible that newer intraoperative techniques such as deep hypothermia and circulatory arrest reduced the perioperative mortality.[63,64]

## Anesthetic considerations

The use of prostaglandins, inotropic support, and diuretics is standard. The use of dopamine may be used to enhance renal perfusion and possibly avoid renal failure. However, the prognosis for survival without surgical intervention is poor. Up to 76% of patients die within the first few weeks of life, and 90% die within the first year.[65] Those who survive past the first year have developed a collateral circulation that allows for adequate lower body perfusion despite the aortic interruption.[66]

Generally intravenous access will have been established in children with IAA scheduled for surgery. Induction of general anesthesia can be accomplished using agents that are hemodynamically stabilizing with an opioid, benzodiazepine, in combination with a non-histamine releasing muscle relaxant.

The anesthetic management for the infant with IAA requires careful consideration of the optimal placement of the arterial catheter. The right subclavian artery may originate in an anomalous fashion from the descending aorta, especially when there is a type B IAA with associated subaortic stenosis.[67] In one study, 15 of 49 patients (31%) with type B IAA had a coexisting anomalous right subclavian artery.[68] The best monitoring site is probably the umbilical or femoral artery. This helps assure the monitoring of blood pressure even when the left subclavian artery outflow is involved in the repair. Two large intravenous catheters should be placed

as significant blood loss can be expected especially following discontinuation from cardiopulmonary bypass (CPB). Central venous access is helpful for the infusion of inotropic agents and monitoring of intracardiac pressures. However, some centers utilize intracardiac lines placed during CPB. A pediatric transesophageal probe can effectively guide the inotropic and fluid management. The use of deep hypothermia and circulatory arrest results in significant bleeding after CPB. Packed red cells, fresh frozen plasma, platelets, and cryoprecipitate should be given. In the case of an infant with DiGeorge syndrome, the use of irradiated blood will avoid graft-vs.-host reactions.[59] Since the infant myocardium is extremely sensitive to high potassium solutions, washed red cells may be preferable. In addition to blood products, aprotinin may also be used relatively routinely for complex procedures.[69] A regimen of 30 000 U/kg infused prior to institution of CPB followed by an additional 30 000 U/kg on CPB is used.

Separation from CPB usually requires inotropic support. Once the hemodynamics are stabilized and the bleeding is controlled, sternal closure is attempted. Inotropic support, fluid management, as well as ventilatory parameters may need adjustment at this time. Should sternal closure result in unacceptable instability due to a reduction in cardiac output or pulmonary function, a Goretex® patch may be placed over the open chest for subsequent closure in 2 or 3 days.

## Shone's anomaly

### Anatomy

Shone's anomaly consists of a parachute mitral valve, supravalvar mitral ring, subaortic stenosis, and a coarctation of the aorta. This complex was first described by Shone *et al*.[70] in 1963. The parachute mitral valve is a term used to describe a mitral valve where two mitral valve leaflets are supported by only one papillary muscle. Because the mitral leaflets are pulled together in proximity, the mitral valve can become stenotic. The supravalvar ring is a ridge of connective tissue circumferentially on the atrial side of the mitral leaflets. The tissue protrudes into the mitral inflow tract causing an obstruction. The subaortic stenosis may be formed either by a hypertrophied left ventricular septal wall, or a membranous thickening in the outflow tract. The coarctation is located in the descending aorta in proximity to the left subclavian artery.

In 30 consecutive patients with Shone's anomaly: 73% had a supravalvar mitral ring, 87% a parachute mitral valve, 87% had subaortic stenosis, and 97% had coarctation of the aorta. Additional lesions also present in these patients were a bicuspid aortic valve (61%) and ventricular septal defect (67%).[71]

Cor triatriatum must also be considered in the setting of left-sided obstructive disease. The anomaly is characterized by the pulmonary venous return entering an accessory left-sided chamber that connects with the left atrium through a slender passageway. The left atrial appendage and fossa ovalis are always distal to the obstructing membrane. In contrast, a supravalvar stenosing ring (which is often associated with Shone's complex) has a left atrial appendage in connection to the upper portion of left atrium and proximal to the stenosing formation.[72]

### Pathophysiology and diagnosis

Patient symptoms depend on the anatomic location of the most critical stenosis within the heart. Patients with a parachute mitral valve or supravalvar mitral ring may show signs of increased pulmonary congestion. Those patients with a high degree of subaortic stenosis will exhibit left ventricular hypertrophy.

Echocardiography and angiography are the primary diagnostic modalities for detecting and defining the extent of the Shone's anomaly.[73,74] It is extremely important to be aware of all levels of obstruction since the intraoperative repair of one obstruction may often reveal other less critical stenoses that now impede the blood flow. Unforeseen structural anomalies cause an increased perioperative risk to the patient.

### Surgical approaches

The surgical repair generally consists of resection of the supravalvar ring, fenesteration of the tensor apparatus, the repair or replacement of the mitral valve, and a resection of any encroaching muscular tissue in the LVOT. In the case of a hypoplastic aortic annulus an aortoventriculoplasty (Konno's procedure) is sometimes performed.[75] Surgical outcome in large part depends on the age at presentation and the hemodynamic impact of the stenoses.[1,71]

### Anesthetic considerations

The medical management of these patients depends on the location of the critical stenosis. Neonates with coarctation of the aorta will require prostaglandins to maintain the patency of the ductus arteriosus. Children with a dynamic LVOT obstruction may require β-blockers to improve intracavitary laminar blood flow. The development of congestive heart failure requires diuretics and inotropic support. Pulmonary venous congestion with postoperative pulmonary hypertension may require phospodiesterase inhibitors (such as milrinone)[76] and possibly nitric oxide.[77]

The anesthetic management of the patient with Shone's anomaly requires a thorough knowledge of the levels of stenosis and the location of the dominant lesion. A patient with dominant fixed mitral stenosis needs sufficient preload to maintain forward flow, and an inotrope to maintain blood pressure. Careful preoperative assessment is critically important.

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# 20 Anesthesia for right-sided obstructive lesions

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## Introduction

Right-sided obstructive congenital heart lesions encompass a wide variety of presentations of congenital heart disease. Some minimally affected teenagers or adults may present only with vague complaints of exercise intolerance or fatigue. At the other extreme, right-sided obstructive congenital heart disease (CHD) may be immediately apparent in the neonate who manifests severe cyanosis or congestive heart failure (CHF). All lesions of this category have the potential for right-to-left shunting of blood flow. The severity of the disease depends upon the degree of structural malformation of the heart and great vessels.

Congenital malformations that impede blood flow through the right heart may occur at a single or combination of critical anatomical areas. These include the right atrioventricular (AV) valve, the outflow tract of the right ventricle (RV), the pulmonary valve (PV), and the main pulmonary artery (MPA) and/or branch pulmonary arteries (BPAs). Commonly, congenital malformations affect several of these critical areas simultaneously, such as in the tetralogy of Fallot (TOF). Malformations may occur directly as a result of aberrant movement of tissues during development, or indirectly as a result of impaired flow hemodynamics due to malaligned structural anatomy. Often the resultant congenital heart deformity is a combination of both processes.

Patients with obstructive right-sided congenital heart anomalies may present in the neonatal period with either cyanosis or CHF. Right-sided lesions, which have potential for right-to-left shunting, may produce cyanosis, such as with right-to-left shunt through an atrial septal defect (ASD) or patent foramen ovale (PFO) in severe Ebstein's anomaly or through a ventricular septal defect (VSD) in TOF. The shunt direction may vary, becoming right-to-left as right-sided pressures exceed those in the comparable left-sided chamber, providing a "pop-off" mechanism for right-sided obstructive hypertension. Neonates with restrictive right-to-left communications or without anatomical potential for shunt develop congestive right heart failure. Infants with obstructive right-sided lesions such as critical pulmonary stenosis (PS) or pulmonary atresia (PA) may be ductal-dependent, achieving pulmonary flow either in part or entirely from a patent ductus arteriosus (PDA). Unless patency is maintained by exogenous prostaglandin, increasing cyanosis may occur when the ductus arteriosus begins to close shortly after birth.

The physiology of right-sided obstructive defects and the changes that occur with surgical intervention in the context of perioperative anesthetic care and planning for such patients are described in this chapter for Ebstein's anomaly, TOF, PS/PA with intact ventricular septum (IVS), and PA/VSD with multiple aortopulmonary collateral arteries (MAPCAs). Other right-sided obstructions such as those that result in a single functional ventricle (e.g. tricuspid atresia) are covered elsewhere in this volume.

## Ebstein's anomaly

### Anatomy

Ebstein's anomaly is by far the most common congenital malformation of the tricuspid valve (TV). The earliest description of TV malformation was by Ebstein in 1866.[1] Ebstein's anomaly is present in only about 0.3–0.7% of patients with CHD and occurs in approximately 1 in 20 000 live births.[2] Other tricuspid anomalies such as TV stenosis, TV insufficiency (TI), and various malformations of leaflets, chordae tendoneae, and papillary muscles are much less common.[3]

Ebstein's anomaly consists of: (i) a downward displacement of septal and posterior leaflet attachments at the junction of the inlet and trabecular portions of the RV; (ii) an "atrialized" portion of the RV between the tricuspid annulus and the attachment of the posterior and septal leaflets; and (iii) a malformed RV chamber (Fig. 20.1). The dysplastic characteristics of the anomaly are quite variable in functional severity, leading to a wide range of functional presentations from infancy to adulthood.

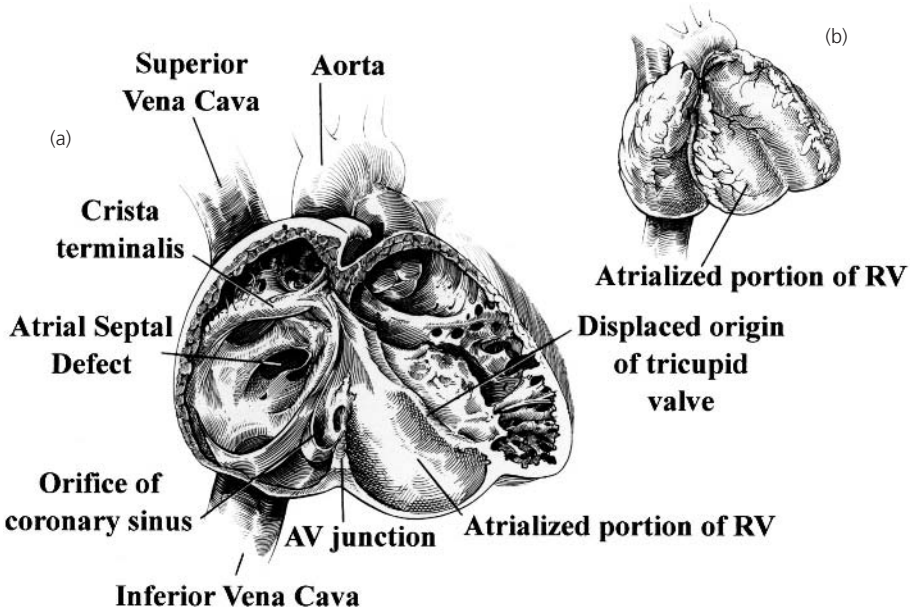


**Fig. 20.1** Ebstein's anomaly: Anatomic features. (a) Displacement of the posterior and septal leaflets into the right ventricle results in a large atrialized chamber and tricuspid valve incompetence. (b) External appearance. AV, atrioventricular; RV, right ventricle. Modified with permission from Casteñeda AR, Jonas RA, Mayer ME, Jr, Hanley FL. *Cardiac Surgery of the Neonate and Infant*. Philadelphia, PA: Saunders, 1994: 274.

The position, size, and shape of the posterior and septal leaflets are quite variable.[4] The posterior and septal leaflets may insert at varying distances below the AV annulus or may be closely adherent to the ventricular wall rather than displaced in one-third of patients. Shortened chordae often attach to papillary muscles that may be deformed. Over one-third of the hearts have an ASD, while most of the remaining two-thirds contain a PFO.[4] The anterior leaflet is attached at the AV annulus superior to the other leaflets, but it is always abnormal. It is often large and redundant, shaped like a sail, with abnormal attachments to the border of the inlet and trabecular portions of the RV. The anterior leaflet and/or the chordae can act as a barrier to blood flow from the atrium/atrialized RV to the trabecular RV. The aperture between the atrialized and trabecular portions of the RV may be restricted to slits or perforations in the anterior leaflet. As a result of the distally displaced valves the trabecular portion of the RV is often very small, lacking an inlet chamber. The walls of the RV may be normal, or thin with impaired contractile function.[2–4]

The RV wall above the line of insertion of the distally displaced leaflets functions as part of the right atrium (RA), but is anatomically ventricular. This inlet portion of the RV is often thin and dilated. Although it is exposed to atrial pressures, this atrialized RV manifests electrical conduction of an abnormal ventricular pattern. In some cases, the wall of the inlet portion is so thin that it moves paradoxically during ventricular systole, dilating with RA contraction. The RA is dilated, sometimes massively.

Left ventricular geometry may be compromised by the abnormal position of the interventricular septum, resulting in a small left ventricle (LV) chamber. In addition, mitral valve prolapse may occur because the chordae tendoneae of the normally situated mitral valve leaflets are altered in shape and size by the LV distortion.[5]

## Pathophysiology and natural history

The clinical presentation of Ebstein's anomaly varies greatly depending upon the extent of the downward displacement of the TV leaflets. Severe hemodynamic compromise may present in the neonate, and when it does death may occur from massive right heart failure, hypoxemia and arrhythmias. The neonate with Ebstein's anomaly shows rapid improvement of hemodynamics in the postnatal period due to gradual reduction of pulmonary vascular resistance (*PVR*). Ebstein's cases with lesser anatomical aberration may have no signs during the neonatal period and only mild to moderate signs and symptoms later in childhood. Unless the foramen ovale is not patent, there is little exercise intolerance. Paroxysmal supraventricular tachycardia may occur in up to 20–25% of children, but other electrophysiologic abnormalities are also common (Table 20.1).

Without surgical intervention, death from Ebstein's anomaly is usually secondary to CHF in the second or third decades of life. The more severe the cyanosis in the child or young adult, the poorer the prognosis. The onset of CHF often is a harbinger of death within a few years.

## Surgical approach

The natural history of the disease varies with its severity and accordingly, the management of Ebstein's anomaly is based on its severity. The size of the trabecular portion of the RV usually determines whether the patient is eligible for a two ventricular, one and a half ventricular, or single ventricular repair/palliation.

The first TV replacement was performed in 1963 as valvuloplasty techniques were rapidly evolving. Large numbers of patients have survived with a valvuloplasty technique

**Table 20.1** Major electrophysiologic abnormalities in Ebstein's anomaly.

- Intra-atrial conduction disturbance—"RA P wave abnormalities," PR interval prolongation
- AV nodal conduction disturbance—PR interval prolongation
- Infranodal conduction disturbances
  (a) Intra- or infra-His disturbances
  (b) Right bundle branch block
  (c) Bizarre "second" QRS attached to preceding "normal" complex
- Type B Wolff–Parkinson–White
- Supraventricular tachycardia
- Atrial fibrillation or flutter
- Electromechanical dissociation in atrialized RV
- Irritability of atrialized RV
- Q waves in leads $V_{1-4}$

RA, right atrium; RV, right ventricle.
Reproduced with permission from Perloff JK. Ebstein's anomaly of the tricuspid valve. In: Perloff JK, ed. *The Clinical Recognition of Congenital Heart Disease*, 4th edn. Philadelphia, PA: Saunders, 1994: 247–72.

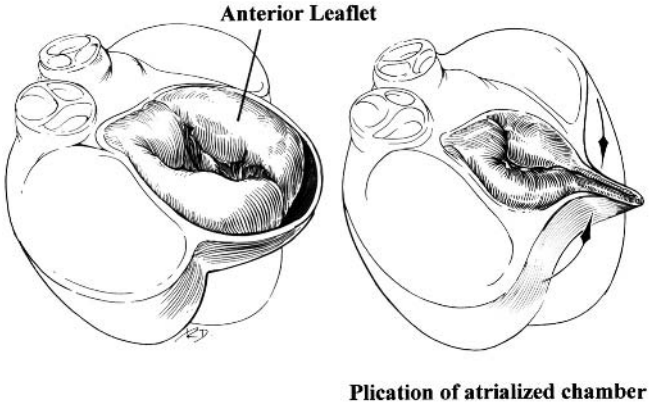


**Fig. 20.2** Carpentier repair of Ebstein's malformation. (a) Anterior and posterior leaflets of tricuspid valve are detached at annulus. (b) Atrialized chamber is obliterated in a circumferential direction. The anterior and posterior leaflets are reattached to the new, smaller annulus. Modified with permission from Casteñeda AR, Jonas RA, Mayer ME, Jr, Hanley FL. *Cardiac Surgery of the Neonate and Infant*. Philadelphia, PA: Saunders, 1994: 279.

described by Danielson[6] which includes a reduction atrioplasty and ablation of accessory conduction pathways. Of 189 patients aged 11 months to 64 years, 75% had successful atrial plication and annuloplasty, with the remainder having atrial plication and placement of a bioprosthetic valve. Operative mortality was 4.9%. Carpentier *et al*.[7] (Fig. 20.2) and Quaegebeur *et al*.[8] (Fig. 20.3) have described variations on the Danielson repair. Quaegebeur reported nine of 10 patients had good TV function on intraoperative echocardiography, and that seven of the nine continued to have reduced TV regurgitation by echocardiography on follow-up (2–23 months, mean 11.7 months).[8]

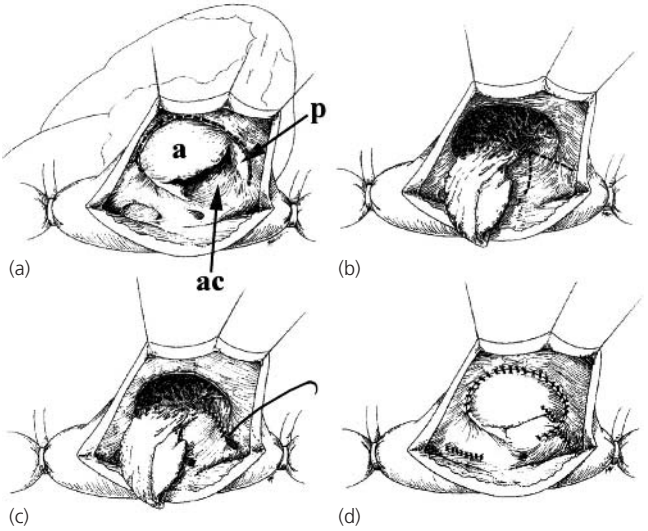


**Fig. 20.3** Operative technique as described by Quaegebeur *et al*.[8] (a) Surgeon's view after opening the right atrium. a, anterior leaflet of the tricuspid valve; ac, atrialized ventricular chamber; p, posterior leaflet. (b) Detachment of the anterior and posterior tricuspid valve leaflets and their chordal attachments to the ventricular wall. The dashed lines denote the suture insertion points. (c) Longitudinal plication of the atrialized portion of the right ventricle. (d) Clockwise spread of the anterior and posterior leaflets on the newly created tricuspid valve annulus, and direct closure of the atrial septal defects without right atrium reduction. Modified with permission from Quaegebeur JM, Sreeram N, Fraser AG *et al*. Surgery for Ebstein's anomaly: The clinical and echocardiographic evaluation of a new technique. *J Am Coll Cardiol* 1991; **17**: 722–8.

Dysrhythmias are often problematic after surgical repair of Ebstein's anomaly, and temporary pacing wires placed on the RA and RV during surgery may be useful in some patients for monitoring of rhythm postoperatively or pacing. For teenaged and adult patients with preoperative arrhythmias, intermediate follow-up post-repair indicates substantial reduction of arrhythmia in survivors who did not require placement of pacemakers.[9] Outcomes analysis[10] has shown a hospital mortality of 10% (largely due to acute postoperative RV failure), but a long-term actuarial survival of 75% at 10 years for children and adults (no infants). High-risk patients (severely impaired RV function, difficult tricuspid valve repair, and/or permanent atrial fibrillation) seemed to benefit from a cavopulmonary anastomosis.

Surgical intervention is infrequently necessary in the infant and child unless tricuspid incompetence results in progressive right heart failure. Moderate congestive failure due to TI can be managed with digoxin in combination with diuretic therapy. Dysrhythmias are medically controlled. Teenagers and young adults do well with TV replacement as progressive valvular deterioration may preclude valvuloplasty. Children who survive infancy have a greater likelihood of undergoing successful valvuloplasty or prosthetic TV replacement. For the child with an RV capable of adequate right

cardiac output (*CO*), resection of redundant atrialized RV tissue and realignment of TV leaflets or placement of a prosthetic TV have all provided reasonable surgical outcomes.

Although severe TV dysplasia in the neonate is often not reparable with surgical valvuloplasty, a recent report suggests that aggressive two ventricular repair can be successful in some cases. Favorable 5 year follow-up was found for three neonatal repairs that included reconstruction of a monocuspid TV, ventriculorrhaphy, reduction atrioplasty, subtotal closure of the ASD, and repair of other associated defects.[11] In the early 1990s, the Starnes procedure was proposed for prostaglandin $E_1$ ($PGE_1$) dependent neonates with Ebstein's anomaly and physiologic PA, converting the cardiac physiology effectively to that of the single ventricular system. A pericardial patch was placed over the TV in such a fashion as to include the coronary sinus on the ventricular side, the foramen ovale was enlarged and the RA free wall plicated. A central 4 mm Gortex® aortopulmonary shunt was placed. Ultimately, infants were able to undergo definitive surgical palliation with a Fontan procedure.[12]

Patients with a severely hypoplastic or poorly functioning RV may ultimately require a single ventricle repair with cavopulmonary anastomosis or Fontan circulation. However there are instances when a hypoplastic or small RV is still capable of ejecting partial *CO* to the pulmonary arteries. These patients may benefit from a one and a half ventricular repair, allowing the diminutive RV to pump part of the systemic venous return to the lungs. The venous drainage of the upper body returns by passive flow via a cavopulmonary anastomosis to the pulmonary circulation. In brief, the one and a half ventricle repair includes valvuloplasty, possible repair of the ASD, and creation of a cavopulmonary anastomosis. A small ASD may be left if there is an anticipated need for a "pop-off" for systemic venous return to the "half" pulmonary ventricle. The pulmonary arteries must be of adequate size and *PVR* must be low for successful implementation.

Advantages exist in utilizing a semifunctional pulmonary ventricle. Preservation of some pulsatile flow to the pulmonary artery may, possibly, reduce the risk of development of MAPCAs. Also, a hypoplastic pulmonary ventricle may be able to respond to increased demand by increasing *CO* beyond what might result with a Fontan circulation.[13] Van Arsdell *et al*.[14] have proposed that the one and a half ventricular repair may be of benefit to the patients with Ebstein's anomaly who have a partial RV outflow tract (RVOT) obstruction due to billowing of the anterior leaflet.

Reported mortality with the one and a half ventricular repair for all lesions (including Ebstein's anomaly) is variable between 0% and 12%.[15] Long-term outcomes have not been compared to the Fontan procedure, but the one and a half ventricle repair seems not to have the short-term and intermediate-term complications of cyanosis, chronic atrial arrhythmias, and protein-losing enteropathies associated with the Fontan physiology.[15] However, an increase in perioperative effusions and chylothorax has been found. Other complications have included chronically increased superior vena cava (SVC) pressure, early-morning periorbital edema, and one instance of a SVC aneurysm. Another instance is reported of development of pulmonary arteriovenous fistulas with a one and a half ventricle repair in combination with the classic Glenn procedure.[15]

Decision-making for the type of surgical repair or palliation relies on two critical assessments: the morphology of the TV and the size of the pumping chamber of the pulmonary ventricle. Valvuloplasty is preferred in infants and young children due to the need to upsize valves as the child grows. The teenager who has reached near adult size may do better with a prosthetic valve as the native valve may have incurred much damage due to abnormal dynamics over time. Patients with less than adequate pumping chambers will generally present for definitive surgical management in infancy or early childhood.

## Perioperative anesthetic management

### Preoperative

Pre-anesthetic evaluation of the child or infant with TV abnormalities includes an assessment of severity of the disease. Specifically, the patient is assessed for symptoms of fatigue, dyspnea, and increasing frequency and severity of cyanotic episodes. An assessment of exercise tolerance may often be delineated in reference to the child's healthy peers. In the infant, questions are focused on the usual baby activities; poor feeding ability, failure to thrive, and/or signs of dyspnea, irritability, cyanosis, or diaphoresis are indicative of a poorly functioning heart. A history of syncope, chest pain, and palpitations suggests arrhythmia in the older child.

With Ebstein's anomaly, physical examination may be notable for triple or quadruple heart sounds, often with a soft, high-pitched systolic murmur. A soft, scratchy mid-diastolic murmur heard best at the left sternal border and apex may be present. The second heart sound is widely split with little respiratory variation due to delayed emptying of the RV. With failure, the child may be diaphoretic, tachypneic, and irritable with rales present on chest auscultation and hepatomegaly on abdominal palpation. The chest roentgenogram may reveal moderate to severe cardiomegaly with a large RA and diminished pulmonary vascular markings. The heart often has a globular shape. Electrocardiogram (ECG) usually suggests RA hypertrophy, an increased PR interval, and complete or incomplete right bundle branch block. Interestingly, the pre-excitation patterns of Wolff–Parkinson–White syndrome are seen in 10–15% of individuals. Two-dimensional echocardiography is usually diagnostic, revealing a large tricuspid orifice complete with apical displacement of the septal leaflet of the TV. Cardiac catheterization is seldom indicated and may be complicated by induction of tachyarrhythmias.

Anxiolysis may be accomplished with midazolam, either given orally (0.5–0.75 mg/kg up to 15–20 mg) or intravenously (0.1–0.15 mg/kg up to 2–4 mg). Infants who manifest stranger fear (approximately 9 months of age and older) may also benefit from such sedation.

### Intraoperative

Inhalation induction of anesthesia may be accomplished with nitrous oxide and sevoflurane for those infants and children with mild to moderate disease. Lowered *CO* or a small right-to-left shunt at the atrial level may slow induction by the inhalation route. Alternatively, intravenous induction with ketamine (1–4 mg/kg) or thiopental (4 mg/kg) will be consistent with reasonable induction hemodynamics. For patients with moderate to severe TV pathology, intravenous induction with glycopyrrolate and ketamine (1–4 mg/kg) can be accomplished smoothly in most instances without excessive myocardial depression or reduced afterload. Etomidate may also be used as an alternative (see Chapter 4) Since these patients are dependent upon adequate preload, increases in vascular compliance due to anesthetic vasodilation need to be met with intravenous volume replacement such as with 5% albumin. Choices of muscle relaxant depend upon the expected duration of the procedure and the need for rapid sequence or modified rapid sequence induction techniques. Pancuronium, a long-acting muscle relaxant, is sufficient for most cases and provides vagolysis via ganglionic blockade for a sustained increase in baseline heart rate. The maintenance technique is largely narcotic based (fentanyl 30–50 μg/kg) with low dose isoflurane (e.g. 0.4%) for myocardial preconditioning prior to institution of cardiopulmonary bypass (CPB). For repeat sternotomy, antifibrinolytic drugs such as plasmin binding inhibitors (e.g. ε-aminocaproic acid) or the plasmin active site inhibitor, aprotinin, may reduce blood loss during the pre- and post-CPB period.

Five-lead ECG with an ability to display multiple lead tracings is useful in monitoring changes in rhythm both during the pre- and post-repair periods. Other than standard monitoring, near-infrared spectroscopy is useful for monitoring brain tissue oxygenation during periods of cannulation and CPB. Transcranial Doppler-flow velocity may provide alternative information about cerebral blood flow during cannulation and CPB as well (see Chapter 8).

Patients with severely dilated right hearts are at high risk for potentially lethal ventricular arrhythmias post-repair. Prior to separation from CPB, intravenous infusion of an antiarrhythmic agent such as lidocaine or amiodarone may prophylactically protect against ventricular arrhythmias. Inotropic support that encourages forward flow in the right heart (e.g. milrinone 0.3–0.5 μg/kg/minute or dobutamine 5 μg/kg/minute) may improve hemodynamics for hearts with pre-existing myocardial dysfunction in the post-CPB period. Generous RV filling pressures may be needed to maintain adequate preload with a poorly functioning ventricle.

### Postoperative

At the end of surgery, patients are transported to the cardiovascular intensive care unit (ICU) with continuous monitoring for rhythm and arterial blood pressure. Pain can be well controlled with narcotic infusions such as morphine sulfate (20–80 μg/kg/hour, depending on the need for sedation beyond analgesia). Patients with minimal pre-existing myocardial dysfunction may be weaned from mechanical ventilation and extubated within hours of arrival in the cardiovascular ICU. For other patients, it is prudent to allow the patient to emerge more slowly from narcotic sedation and inotropic support in order to assess the remodeled tricuspid competency and allow more time for recovery of myocardial function. Midazolam (0.1–0.2 mg/kg/hour) may be added simultaneously with narcotic analgesic infusion to provide long-term sedation for patients who need longer myocardial recovery times (beyond 1–2 days) (see Chapter 27).

As mentioned previously, dysrhythmias are common in the immediate postoperative period after repair of Ebstein's anomaly, and may persist as a late complication of repair. Supraventricular tachycardia, junctional rhythm, or intermittent AV block may complicate recovery. Risk for ventricular arrhythmias and sudden death persists through the first postoperative month. Those patients who demonstrate perioperative ventricular tachycardia or ventricular fibrillation are likely at greatest risk.[16] Patients with intermittant AV block or junctional rhythm may benefit from temporary pacing to enhance *CO* in the immediate postoperative period. As myocardial edema subsides, return of functional conduction pathways may allow return of normal sinus rhythm. As mentioned above, intravenous amiodarone or lidocaine may be helpful in the early postoperative period, and switching to oral amiodarone for several months may be warranted for high risk individuals.

In the early postoperative period, echocardiography often shows poor coaptation of the TV leaflets. This finding is likely due to post-bypass dysfunction of the papillary muscle bundles (possibly of ischemic etiology) as the leaflet coaptation often improves with subsequent echocardiographic examinations.

## Tetralogy of Fallot

### Anatomy

Tetralogy of Fallot represents 10% of all congenital heart defects and is the most common form of cyanotic heart disease. A Danish scholar, Nicholas Steno, first described the defect in 1673, 200 years before Fallot. One hundred years

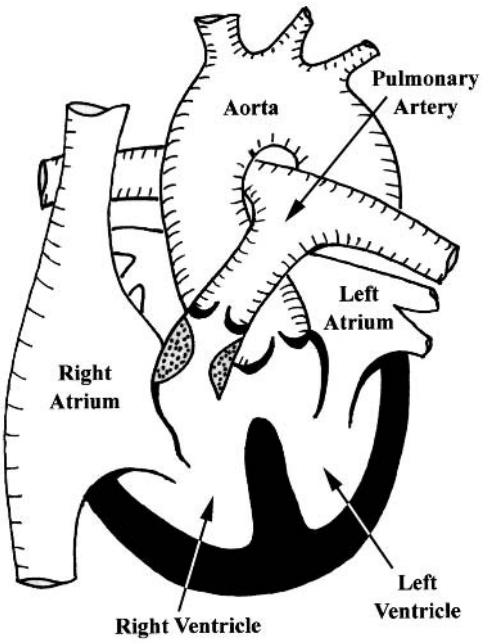


**Fig. 20.4** Schematic diagram of tetralogy of Fallot illustrating the infundibular stenosis (stippled area), ventricular septal defect, overriding aorta, and right ventricle hypertrophy.

later, numerous other reports were published from post-mortem cardiac examinations. The French physician, Arthur Fallot, was the first to make an accurate bedside diagnosis with later validation at post mortem. He later published a review of the French literature on the *maladie bleue* in 1888, his name then becoming popularly associated with the malformation.[17] Tetralogy of Fallot comprises four anatomical abnormalities: (i) a large unrestrictive VSD; (ii) RVOT obstruction; (iii) overriding of the aorta above the RVOT; and (iv) RV hypertrophy (Fig. 20.4). In reality, there is a spectrum of abnormalities ranging from TOF with PA, where there is total obstruction to RV outflow, through TOF with PS (the "classic" tetralogy), to TOF with absent PV. Embryologically, TOF is believed to result from incomplete rotation and faulty partition of the conotruncus during septation.

The VSD is perimembranous, large (usually the same size as the aortic valve), and unrestrictive. It is also important to note that the cardiac conduction tissue lies in close proximity to the margins of the VSD and may be damaged during repair producing temporary or permanent heart block. Because of clockwise rotation, the aorta overrides the VSD and thus has a biventricular origin. Additionally, the aortic arch lies to the right in 25% of TOF patients and may be associated with mirror image branching of the head vessels. There may be an aberrant origin of the ipsilateral subclavian artery from the descending aorta in some patients, and rarely, there may be an isolated origin of the left subclavian artery from the pulmonary artery. These abnormalities have important implications when selecting the surgical approach for the placement of palliative shunts.

Coronary abnormalities occur in 5–12% of patients with TOF. Failure to detect these preoperatively can have serious consequences for a successful outcome because they may be damaged during surgery. The most common abnormality consists of a left anterior descending artery that originates from the right coronary artery, and crosses the RVOT inferiorly. This arrangement makes it very susceptible to damage if the transannular incision is carried too far inferiorly across the RVOT. Indeed, an alternative surgical approach may be needed in relieving the subpulmonary obstruction, or a RV to MPA conduit may be required. Other coronary anomalies include a right coronary artery originating from the left coronary artery, and left coronary artery originating from the MPA. Precise definition of the coronary anatomy may be possible with echocardiography alone.[18] If there is uncertainty, then aortic root or selective coronary angiography may be used.

Other coexisting cardiac lesions include left SVC (LSVC), AV septal defect, PDA, ASD, and interrupted inferior vena cava. All of these require modifications to the surgical repair. It is particularly important to be aware of the presence of a LSVC because this usually drains into the coronary sinus in the RA. During surgery a venous drainage cannula is placed in the LSVC and this vessel is usually tied off at the end of the procedure. Therefore, a central venous line placed via the left internal jugular route will be rendered useless postoperatively.

Two important variants of TOF are PA with VSD and the absent PV syndrome. Pulmonary atresia with VSD is characterized by hypoplasia of the central and peripheral pulmonary arteries. The MPA may be absent or the branch PAs may be non-confluent or stenotic. Pulmonary blood supply is usually via MAPCAs. The surgical correction of this lesion is very different from that of classical TOF as described later in this chapter.[19,20] The absent PV syndrome is characterized by combined PS and incompetence which *in utero* leads to increased pulsatile pulmonary blood flow (*PBF*) producing massive enlargement of the main and branch PAs. This produces the central characteristic feature of airway compression and tracheobronchomalacia. These babies typically present in the neonatal period with severe respiratory distress, cyanosis, and air trapping. Tracheal intubation with high levels of positive end-expiratory pressure (*PEEP*) may be useful in stenting the airways. Prone positioning may also be useful in relieving some of the obstruction. Infants with significant lung disease require urgent surgical intervention. However, symptoms commonly persist due to the underlying intrinsic airway abnormalities and such patients may need long-term ventilator support.

In the common form of TOF, the obstruction to the RVOT usually has dynamic and fixed components. The dynamic component consists of hypertrophied infundibulum and muscle bundle fibers in the RVOT. The hypertrophy occurs in response to the pressure load on the RV. Fixed obstruction

may be valvular, consisting of a thickened, hypoplastic, and often bicuspid PV. In 15–25% of patients the PV is atretic producing complete obstruction to the RVOT. These patients require an alternative of *PBF* such as a PDA, bronchial arteries or MAPCAs.

Beyond the PV, impedance to RV outflow occurs due to abnormalities in the pulmonary arterial tree. There is usually some degree of central pulmonary artery hypoplasia in all patients. There may also be localized narrowing of the MPA or BPAs. Atresia or discontinuity of the MPA or BPAs may occur, which will further complicate surgical correction, as restoration of continuity or augmentation of the pulmonary arteries will be required.

There is a weak association of familial inheritance of TOF. Indeed TOF is associated with major extracardiac malformations and may occur as part of a syndrome. Some examples are the VACTERL (vertebral, vascular, anal, cardiac, tracheoesophageal, renal, and limb anomalies) association, DiGeorge syndrome, velocardiofacial syndrome, and CHARGE (coloboma, heart anomaly, choanal atresia, retardation, and genital and ear anomalies) association. Recent genetic studies have shown that TOF is associated with chromosome 22q11 deletion (catch 22 syndrome). This chromosomal abnormality is also responsible for DiGeorge syndrome, velocardiofacial syndrome, and conotruncal anomaly face syndrome. In one study of TOF patients, the prevalence of 22q11 deletion was 13%. This deletion is considered to be the most common genetic cause of TOF-associated syndromes.[21]

## Pathophysiology and natural history

The clinical manifestation of TOF ranges from extreme cyanosis at one end of the spectrum, because of profound right-to-left shunting through the VSD, to normal saturation for patients who have minimal RVOT obstruction and who exhibit a net left-to-right shunt. The latter group is sometimes known as "pink tets" because of the absence of cyanosis. They may even show signs of CHF from pulmonary overcirculation. The presentation of symptoms with TOF is determined primarily by the degree of RVOT obstruction because the large non-restrictive VSD effectively equalizes the pressures in both ventricles. If the VSD is restrictive RV pressure may be suprasystemic. The RV undergoes hypertrophy in response to the high afterload and the wall thickness may become similar to the LV. Right ventricle hypertrophy is undesirable for several reasons. It can lead to diastolic dysfunction; surgical correction of the VSD and RVOT obstruction becomes more difficult through a thickened ventricle; and it becomes more difficult to protect the hypertrophied RV during aortic cross-clamping, which may contribute to postoperative RV dysfunction. In order to limit RV hypertrophy, surgical correction is undertaken in early infancy.

With a non-restrictive VSD and equalization of RV and LV pressure, the main determinants of the degree of shunting are the relative resistances of the systemic and pulmonary circuits. Both of these change depending on various factors and, therefore, the degree of cyanosis will vary. Right ventricle outflow tract obstruction usually has a dynamic and fixed component; producing different propensities for cyanosis. An acute form of this RVOT obstruction occurs during a hypercyanotic or "tet spell" producing severe cyanosis and hypoxemia, which can lead to syncope or a stroke. The obstruction is thought to result from infundibular spasm leading to an acute decrease in *PBF* and shunting of desaturated blood into the systemic circulation. These spells can occur spontaneously, but are usually in response to crying, defecation, agitation, injury or fright which increases sympathetic tone leading to increased contractility producing infundibular spasm. As well as acute increases in RVOT obstruction, "tet spells" may be precipitated by an acute fall in systemic vascular resistance (*SVR*). This may happen during induction of anesthesia (especially if the patient is hypovolemic), and it is very important that the anesthesiologist is well prepared in advance to treat a spell. The goal of treatment is to use maneuvers (described later in this chapter) which reverse the direction of right-to-left shunting. Other factors which can worsen cyanosis are anemia, acidosis, infection, stress and posture. "Tet spells" in the awake patient are usually accompanied by hyperventilation secondary to the metabolic acidosis and the hypoxemia. Children classically adopt a squatting posture during a spell to alleviate discomfort. Squatting increases intra-abdominal pressure leading to increased venous return and RV preload, which helps to "enlarge" the RVOT. This position also increases *SVR*, which favors left-to-right shunting.

### Clinical features

The presenting features of TOF are variable depending on the degree of RVOT obstruction. Prenatal diagnosis is possible with ultrasonography. In the neonate, cyanosis and the presence of a murmur will lead to further diagnostic evaluation. In newborns with critical PS and ductal-dependent *PBF*, the clinical presentation may be delayed until ductal closure. Very rarely, the baby will be in CHF from pulmonary overcirculation if there is only mild RVOT obstruction—the so-called "pink tet." Sudden severe desaturation will occur during a hypercyanotic spell characterized by infundibular spasm and severe reduction in *PBF*.

Physical findings are not specific for TOF. The degree of cyanosis will vary, and pulse oximetry will demonstrate low hemoglobin saturation. Clubbing is a relatively late finding. Cardiac auscultation reveals a crescendo–decrescendo systolic murmur best heard at the upper left sternal border. The intensity of the murmur will be diminished during a hypercyanotic spell. Chest radiograph shows a characteristic "boot

shaped" heart, which is a reflection of RV hypertrophy and a concave upper left heart border from a small or absent MPA. The lung fields are oligemic from diminished blood flow. The ECG usually shows RV hypertrophy and right axis deviation.

### Morbidity and mortality

Survival beyond the fourth decade is very rare in untreated patients. Without surgery, 25–35% of children with TOF die in the first year of life, 40–50% by year 3, 70–76% by year 10, 90% by year 21, and 95% by year 40. The outcome is even worse for the subset of patients with PA. Without surgery, most of these children do not survive beyond infancy. Even those children who are completely palliated show delayed growth and development compared with their normal counterparts. This is usually due to the associated non-cardiac conditions. The clinical course of patients with TOF is determined primarily by the degree of PS. Mortality in untreated patients is usually a result of hypoxemia or its hematologic consequences, or the result of problems such as endocarditis or brain abscess. With complete repair in early infancy or childhood, over 85% of patients are expected to survive to adulthood.

## Surgical approach

In the present era, most of the diagnostic information needed for surgical decision-making can be obtained from echocardiography, with cardiac catheterization only necessary in selected cases. As well as delineating the anatomy of the heart chambers, PV, MPA, BPAs, and aortic arch, Doppler studies can demonstrate the severity of RVOT obstruction and the location, type, and number of VSDs. In addition, it aids in localizing alternative sources of *PBF*. Coronary anatomy can also be described in many cases. However, echocardiography cannot reliably image pulmonary artery anatomy beyond the proximal branches. If echocardiography is insufficient in providing all the information needed for determining the surgical plan, then cardiac catheterization and angiography are performed. If only a palliative procedure is planned, echocardiography may be adequate. However, for planned complete surgical correction, and for patients who have had a palliative procedure (where there may be distortion of the vascular anatomy), cardiac catheterization may be indicated. Cardiac catheterization is not a benign procedure in the tetralogy patient, especially for those at high risk for hypercyanotic spells which may be precipitated by manipulation of the catheter across the RVOT. Such patients should be managed by experienced personnel with appropriate emergency drugs and equipment immediately available for the management of "tet spells" in the catheterization laboratory.

Interventional catheterization procedures are having an increasing role in the management of CHD. In some centers, balloon dilation of the RVOT is considered as a palliative alternative to a systemic to pulmonary artery shunt.[22] Correct technique avoids the disadvantages of surgical intervention, including distortion of pulmonary vascular anatomy, which can occur with shunting procedures. Balloon dilation and stent placement also has an important role in those patients who have undergone complete surgical correction, but are left with residual pulmonary artery or conduit stenosis.

All patients diagnosed with TOF require some form of surgical intervention. However, there is ongoing debate regarding the timing of repair, and whether this should be done as a staged technique (palliative shunt followed by complete repair) or primary total repair.[23,24] There is a trend now towards early total correction, whether the patient is asymptomatic or not, with some institutions performing surgery in the neonatal period with good results.[25–27] Others prefer to adopt a slightly more conservative approach, opting for repair at 3–6 months of age or even later.[28,29] Other factors to consider are the institution's capability of providing perioperative critical care of neonates and small infants undergoing complicated cardiac surgery, or specific anatomical features that are contraindications to primary repair. Examples of unfavorable anatomy include the presence of coronary abnormalities such as the left anterior descending arising from the right coronary and crossing the RVOT, the presence of multiple VSDs, and inadequate pulmonary artery anatomy. In these cases it is reasonable to place a palliative shunt and allow the baby to grow, facilitating the eventual complete repair. The two-stage approach does have certain disadvantages.[30] It subjects the baby to an additional surgical procedure with attendant risks and complications. These include injury to the recurrent laryngeal and phrenic nerves, inadequate or excessive *PBF* requiring subsequent shunt revision, potentially fatal shunt obstruction, and potential distortion of the pulmonary artery at the anastomotic site. If the shunt is placed centrally through a median sternotomy, subsequent surgery may be more hazardous due to increased risk of damage to the heart or major vascular structures during dissection. As far as timing of surgery, there are certain disadvantages to operating in the neonatal period. In addition to the risks of performing complicated surgery on tiny neonates and the effects of CPB (and possibly circulatory arrest) on immature organ systems, the surgical procedure is technically more challenging. Although most centers perform the repair using a transatrial–transpulmonary approach, smaller patients more commonly require a ventriculotomy to facilitate repair. Ventriculotomy may result in late RV dysfunction and dysrhythmias. Nevertheless, some centers strongly favor this approach.[25] Proponents of early repair point out the desirability of operating before significant RV hypertrophy has occurred. Right ventricle hypertrophy may require extensive myectomy, making VSD closure more difficult. Severe RV hypertrophy may also impair myocardial protection during the period of aortic cross-clamping. Early repair may also lead to more normal growth and development of

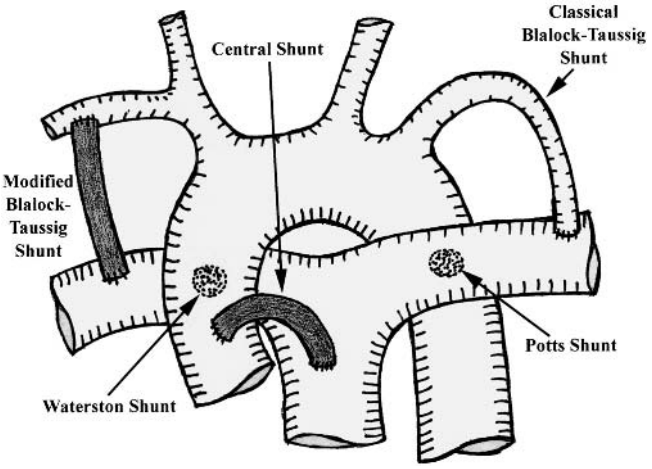


**Fig. 20.5** Diagram showing the various types of shunts used to increase pulmonary blood flow. The modified Blalock–Taussig shunt and central shunts are the only shunts used in the modern era.

the pulmonary vasculature and avoids the long-term effects of cyanosis and hypoxemia. It is not possible to perform a complete repair on all patients with TOF and the debate over the optimal surgical approach will continue.

### Surgical palliation

The proposal by Blalock and Taussig to anastomose the subclavian artery to the pulmonary artery in an end-to-side fashion to alleviate cyanosis resulted in the first successful palliation of TOF in 1944. This "classic" Blalock–Taussig (BT) shunt is very rarely used today. Potts and Waterston later described direct aorta to pulmonary artery shunts. Although these shunts provided good palliation, their size was difficult to control and commonly resulted in too much *PBF*. They were also extremely difficult to take down during corrective surgery and thus were largely abandoned. A "modified" BT shunt (MBTS) is created by interposition of a graft of synthetic material, usually polytetrafluoroethane, between the subclavian artery or brachiocephalic artery and the ipsilateral pulmonary artery. This is the most common palliative procedure carried out in the current era (Fig. 20.5). The advantages of the MBTS are many: (i) it preserves blood flow to the arm; (ii) it can be used on either side, although most are done on the right side because the pulmonary anastomosis can be placed more centrally allowing easier control of the shunt during subsequent repair; and (iii) it avoids excessive *PBF* when appropriately sized. A central shunt, between the ascending aorta and the MPA, using graft material is used as an alternative to the MBTS when the vascular anatomy precludes placement of the latter.

### Complete surgical repair

Lillehei carried out the first successful repair of TOF in 1954. There are three major goals of the TOF repair: (i) maximal relief of RVOT obstruction; (ii) separation of the systemic and pulmonary circulation by closure of the VSD; and (iii) preservation of RV function in the short and long term. It is particularly important to delineate the coronary anatomy, determine the levels of obstruction of the RVOT, and the size and continuity of the pulmonary arteries. The details of the operative procedures are well described elsewhere.[31,32] After cardioplegic arrest the repair is done using a transatrial–transpulmonary approach. Right ventriculotomy is avoided if possible to preserve RV function.[33] The PV is examined through a longitudinal incision in the MPA, and if necessary, a commissurotomy is performed. The RVOT is exposed through the RA and TV and resection of the infundibular septum is carried out. Hegar dilators are passed through the TV into the MPA to calibrate the RVOT. If the size of the RVOT is judged to be inadequate, the MPA incision is extended downwards across the annulus and onto the RV free wall. The VSD is then closed through the RA. Any ASD is also closed although some surgeons prefer to leave an atrial communication to act as a "pop off" valve in case of severe RV dysfunction postoperatively. This will produce some hypoxemia via right-to-left shunting. The adequacy of repair is assessed using several methods. The RV : LV pressure ratio can be measured, less than 0.75 being considered acceptable. It is important to emphasize, however, that pressure measurements in the early post-CPB period do not reflect measurements made at follow-up and may lead to unnecessary revisions of the repair.[34] Transesophageal echocardiography (TEE) is useful in demonstrating gradients across the RVOT, showing residual VSDs, and assessing ventricular function.[35,36] Blood gas measurements from the vena cava and the MPA are also useful in detecting residual shunts.

In patients who have a coronary artery which crosses the RVOT, a transatrial–transpulmonary repair is still feasible if the transannular incision is limited.[37] Many of these patients, however, require a valved RV–PA conduit to avoid damage to the coronary artery.

## Perioperative anesthetic management

### Management for surgical palliation

Many of these patients are critically ill due to severely reduced *PBF*. They may be mechanically ventilated and receiving an infusion of $PGE_1$ to maintain ductal patency. If intravenous access is available then anesthesia can be induced with a combination of ketamine and fentanyl and maintained with low concentrations of a volatile agent. It is important to maintain adequate *SVR* in order to limit right-to-left shunting through the VSD; in this regard, sevoflurane is a good choice as this agent has the least effect on *SVR*.[38] The myocardial depressant effect of volatile agents is also useful in limiting infundibular spasm. Low *SVR* is treated with phenylephrine or

norepinephrine; and preload is augmented with fluid boluses. It is important to avoid most inotropes, as these will worsen infundibular spasm by increasing heart rate and contractility. If there is no intravenous access, induction can be carried out rapidly and smoothly with sevoflurane. An alternative is to use intramuscular ketamine in unstable patients. Central venous access is obtained for the infusion of fluids and vasoactive agents. A radial arterial line is placed on the side opposite to that of the MBTS in order to get a true assessment of the blood pressure because after the shunt is opened there may be significant "steal" from the ipsilateral subclavian artery. A femoral arterial line can also be placed as long as care is taken to observe for evidence of distal lower extremity ischemia.

Most MBTS are performed via a thoracotomy. The median sternotomy approach is used when the surgeon feels that the patient will not tolerate lung retraction or side-clamping of the PA, when there is a possibility that CPB may be required, and for central shunt placement. Low dose heparin (100 U/kg) is administered prior to shunt placement. Lung retraction can severely impair oxygenation and ventilation, and intermittent reinflation may be required. Similar decompensation can occur during partial clamping or obstruction of the PA during the construction of the anastomosis. Such decompensation is managed with fluids, vasopressors, and ventilation adjustments. However, attempting to normalize $P_{CO_2}$ during single lung perfusion may overdistend the dependent lung, increasing *PVR* and impairing venous return. For central shunts, partial clamping of the ascending aorta is required, but it may be poorly tolerated in the presence of LV dysfunction. Inotropic support with dopamine is usually helpful. Once the shunt is open, oxygen saturation usually improves immediately. However, blood pressure may drop significantly, requiring volume infusion and vasopressors. If the diastolic pressure becomes very low, coronary flow will be reduced and ischemic changes may be seen on the ECG. Ventilation and inspired oxygen are adjusted to mimic spontaneous, non-anesthetized values for an accurate assessment of the shunt flow. An oxygen saturation of near 80% is optimal as this represents balanced pulmonary and systemic blood flow. A high saturation suggests pulmonary overcirculation and the shunt size may have to be reduced. Conversely, a low saturation suggests inadequate *PBF*, and a larger diameter shunt may be needed. In cases of persistent hypoxemia after apparently uneventful shunt placement, it is important to rule out the possibility of endobronchial intubation because failure to do so may lead to unnecessary shunt revision or even sternotomy. After chest closure, the patient is transferred to the cardiac ICU where mechanical ventilation is typically necessary for at least 12–24 hours. Increased *PBF* can cause unilateral pulmonary edema or pulmonary hemorrhage. Diastolic hypotension may cause myocardial ischemia, requiring close monitoring of intotropic medications and volume. Other complications include injury to the phrenic and recurrent laryngeal nerves, Horner's syndrome, chylothorax, and shunt thrombosis. Patency of the shunt can be clinically confirmed by briefly disconnecting the patient from the ventilator and auscultating over the end of the endotracheal tube. The murmur is transmitted via the tracheal tube due to the proximity of the shunt to the bronchus. A low dose heparin infusion is started (8–10 U/kg/hour) to maintain shunt patency when the risk of post-surgical hemorrhage has diminished. After enteral intake has begun, the patient is prescribed aspirin until the time of corrective surgery. Platelet transfusions are generally avoided for patients undergoing shunt placement due to the risk of shunt thrombosis.

### Management for complete repair

Procedures for complete repair necessitate additional considerations of the effects of CPB. The anesthetic induction does not differ from that described above. Generally, we utilize a total dose of fentanyl to 20–50 μg/kg and administer inhalational agents to supplement anesthesia. A recent study showed that a ketamine infusion provided more hemodynamic stability by preserving *SVR* in the pre-CPB period when compared with isoflurane.[39] The lower dose of fentanyl usually allows for extubation within 4–8 hours after surgery. Transesophageal echocardiography is used for almost all patients. However, it is important to monitor the effects of probe insertion on ventilation. The TEE probe may compress the trachea or mainstem bronchi, compromising ventilation, requiring removal. If TEE is not possible or unavailable, epicardial echocardiography can be performed post-CPB to assess repair. In addition to routine monitors, brain oxygen saturation trends can be followed with near infrared spectroscopy. Other monitoring alternatives include electroencephalography and transcranial Doppler. Neurologic monitoring is discussed elsewhere in this volume.

Patients who do not have a palliative shunt may develop a "tet spell" during the pre-CPB period and without prompt and aggressive treatment severe hypoxemia may progress to cardiovascular collapse. Particularly vulnerable periods are during anesthetic induction before surgical stimulation, when reduced sympathetic tone causes a fall in the *SVR* leading to increased right-to-left shunting. Manipulation of the great vessels by the surgeon may also result in sudden right-to-left shunting. The primary goal of management of a spell is to correct the hypoxemia by relieving the infundibular spasm and reversing the shunt. Some or all of the following maneuvers can be employed:

1. Administer oxygen. This does not relieve the spasm but helps reduce hypoxic pulmonary vasoconstriction.
2. Phenylephrine, 5–10 μg/kg and titrated to effect to increase *SVR*.
3. Volume infusion to support the blood pressure and increase right heart filling thereby reducing RVOT obstruction during systole.

4 Compress the abdomen to directly compress the aorta and place the child in a knee–chest position to increase the *SVR*.
5 Titrate esmolol, 50 μg/kg to effect. The negative inotropic effect and reduction in heart rate will help to reduce the infundibular spasm. Propranolol (0.1 mg/kg given slowly) also works but is slower in onset.
6 Increase the depth of anesthesia with a volatile agent to decrease contractility thereby reducing the infundibular spasm. Although halothane is traditionally used for this purpose, a recent echocardiographic study showed that sevoflurane has less effect on the *SVR* index than halothane or isoflurane at 1.5 minimum alveolar concentration[38] and therefore may be superior. Isoflurane is a poor choice because it is a potent vasodilator and also causes tachycardia, which increases contractility. Although morphine is frequently recommended for the treatment of "tet spells" in the awake patient, it produces excess vasodilation under anesthesia and is, therefore, not recommended.
7 If all these measures fail and the patient continues to deteriorate, the chest may have to be opened quickly, and the aorta may need to be compressed to reverse shunting.

During the rewarming phase of CPB, preparations are made for weaning from CPB. In general, three problems may be anticipated:

1 Right ventricle dysfunction, especially if the transannular incision was extended down the RV free wall. The mainstays of treatment are fluid loading to higher filling pressures, inotropic support, and reduction of RV afterload. Dopamine at 5 μg/kg/minute is started when rewarming commences. Nitroglycerin is also added at 2 μg/kg/minute to decrease RV afterload. Other acceptable alternatives for inotropic support are dobutamine or milrinone. These also have beneficial effects on the pulmonary vasculature. Ventilation is adjusted to reduce *PVR* prior to weaning.
2 Arrhythmias and heart block. These are common after VSD repairs because of the close proximity of the conduction system. Epicardial pacing may be needed to accomplish weaning from CPB. In most instances heart block is a transient phenomenon due to the edema around the VSD patch. If it does not resolve after 7–10 days, permanent pacing may be required. Junctional ectopic tachycardia is seen occasionally, although the onset is usually 12–24 hours later. This is characterized by AV dissociation and rapid junctional rates as high as 200–230 beats/minute. Treatment consists of cooling the patient to 34–35°C, and drug therapy with amiodarone or procainamide. Atrial overdrive pacing can also be used to re-establish AV synchrony.
3 Post-CPB bleeding. Coagulopathy results from hemodilution of coagulation factors and the effects of CPB on platelet number and function, and may require transfusion of multiple component blood products. The use of antifibrinolytics such as ε-aminocaproic acid, or protease inhibitors such as aprotinin, may reduce post-CPB bleeding and minimize the use of blood products.

Once the chest is closed the patient is transferred to the ICU. Analgesia is provided with a continuous infusion of morphine at 20–40 μg/kg/hour, supplemented with intermittent boluses of midazolam for sedation. Hemodynamically stable patients with minimal bleeding are good candidates for early extubation, usually within 4 hours. After the patient is extubated, analgesia can be reliably provided with a combination of acetaminophen and a non-steroidal anti-inflammatory agent such as ibuprofen, with morphine as needed.

## Pulmonary stenosis with intact ventricular septum

### Anatomy

Pulmonary stenosis/intact ventricular septum is relatively common, accounting for 8–10% of congenital heart defects. Pulmonary stenosis may be valvular, subvalvular, or supravalvular. In valvular PS, the PV is dome-shaped with a centrally placed orifice. The RV is usually normal in dimension with the exception of infundibular hypertrophy that occurs as a result of outflow obstruction. Valvular PS is frequently associated with Noonan's syndrome. Although isolated subvalvular PS is rare, obstruction may occur within the RV cavity due to abnormal hypertrophied muscle bands, which run between the ventricular septum and the anterior wall, effectively dividing the RV cavity into a proximal high-pressure chamber and a distal low-pressure chamber ("double chambered RV"). Supravalvular PS involving the MPA may be seen with congenital rubella and Williams' syndrome. The etiology of the defect is unknown, but there is likely a genetic factor as the incidence of the defect in siblings of the affected patient is 2–4%.

### Pathophysiology and natural history

In its most severe manifestation, PS/IVS presents in the neonatal period with cyanosis and right heart failure. However, most children develop signs and symptoms more slowly, with the onset based on the severity of the PS and the relative sizes of a PFO or ASD. Many patients are initially identified by the presence of a harsh systolic ejection murmur and perhaps a thrill over the PV auscultation area. There is often post-stenotic dilation of the MPA and BPAs which may be visible on chest roentgenogram. Radiographic cardiomegaly is a late sign, coincident with signs of failure. Electrocardiogram often shows right axis deviation, prominent P waves, and evidence of RV hypertrophy. Echocardiography with Doppler evaluation of the valve gradient can be

used to measure the severity of the lesion and serial measurement used for follow-up studies. Cardiac catheterization, in addition to its value in obtaining further measurements, can also be used to perform balloon valvuloplasty.

### Surgical approach

Symptomatic patients and those with severe gradients and impending RV failure are treated primarily with balloon valvuloplasty, which has replaced surgery as the first line treatment. In fact, repeat balloon valvuloplasty is employed for cases of recurrent stenosis. The incidence of pulmonary insufficiency after balloon valvuloplasty is 80%, but is usually mild in clinical severity. Surgical repair may be attempted with or without CPB via a median sternotomy approach. With the CPB technique, a transverse incision is made in the MPA. Fused valve leaflets are incised. The annulus may be enlarged with Hegar dilators. Subvalvar obstruction in the infundibular region may be excised. Rarely, a transannular patch may be needed. A right atriotomy is used to close a PFO or ASD, and may also be used to perform an infundibular resection through the TV. Surgical pulmonary valvotomy may also be performed off CPB via a transventricular approach through a purse string suture in the anterior RV. Hegar dilators are inserted in increasing diameters across the valve. The CPB pump is kept primed and on standby for this approach. With either surgical technique, residual valve gradients may be measured utilizing needle pressure transducers.[40]

### Perioperative anesthetic management

Optimizing inotropic therapy, instituting adequate diuresis, and correcting metabolic acidosis and electrolyte abnormalities medically optimizes the patient with CHF prior to surgery. Neonates with critical PS should be stabilized with $PGE_1$ and taken for cardiac catheterization without delay. Most patients will be eligible for elective repair.

After CPB, attention is given to optimizing RV filling pressures and keeping pulmonary arterial pressures low to induce forward right-sided *CO*. Pulmonary vasodilators begun in the early postoperative course or in the late CPB period may increase pulmonary flow and reduce RV afterload. Although most patients tolerate pulmonary insufficiency that results from either open or closed pulmonary valvotomy, inotropic support is often needed to assist the transient RV dysfunction that often presents after anterior right ventriculotomy with the closed approach. Inotropic support is utilized cautiously in patients that may have a dynamic subvalvar obstructive component due to infundibular hypertrophy, but may be needed to achieve adequate RV function for a few days after repair. Residual infundibular hypertrophy often resolves with time after the valvuar obstruction is relieved.

## Pulmonary atresia with intact ventricular septum

### Anatomy

Unlike PS/IVS, PA/IVS does not have a familial association. The defect comprises approximately 1.0–1.5% of congenital heart defects. Although the etiology of the defect is unknown, the inciting event appears to be severe intrauterine RVOT obstruction, leading to maldevelopment of the TV, RV, and coronary arteries. The degree of abnormality varies with the gestational age at which the RVOT obstruction occurred. Patients with a diminutive RV, small TV, and extensive RV to coronary artery communications would be presumed to have incurred PA at an earlier stage of gestation. Multiple morphologic abnormalities occur with this lesion, all of them proximal to the PV (in contrast to PA with VSD in which the major associated defects occur distal to the valve). There is almost always a PFO or secundum ASD, restrictive in 5–10%. The TV is usually smaller than normal, but may range from extremely stenotic to the dilated annulus of Ebstein's anomaly (5–10%). The RA is dilated proportionately to the degree of tricuspid regurgitation. The RV is hypertrophic with reduced size of the cavity. In about 50% of cases, there are endothelial-lined blind channels within the RV myocardium known as sinusoids. These sinusoids are in direct communication with the RV cavity and may form coronary artery to RV fistulae. The prevalence of these sinusoids is inversely proportional to the diameter of the TV, RV cavity size, and magnitude of TI, but directly proportional to RV systolic pressure. In the least affected individuals, RV blood may be sent as part of a dual supply of blood to small areas of myocardium in tandem with normal aortocoronary flow. But approximately 20% of patients with PA/IVS have a RV-dependent coronary circulation with absence of anterograde aortocoronary flow. In these patients the coronary bed is perfused with desaturated systemic venous blood directly from the RV and, therefore, the myocardium may be chronically ischemic. Sometimes the PV is seemingly intact, but with fused commissures. Most often, there is a fibrous tissue at the ventriculoarterial junction. The pulmonary arteries usually have normal branching and may be hypoplastic in about 6% of cases. There is almost always a PDA. The LA is enlarged and hypertrophic, sometimes exhibiting fibroelastosis. Subaortic stenosis has occurred due to bulging of the ventricular septum into the LV from RV hypertension.[41]

### Pathophysiology and natural history

Untreated, PA/IVS results in death in 50% of neonates, and in 85% of infants by 6 months of age. Fetuses with small, hypertrophied ventricles often survive to birth; those with

dilated RVs and severe TI may die of fetal hydrops. In the presence of moderate to severe TI, RV pressure will remain low and sinusoids and coronary fistulae will not evolve. Alternatively, if TI is mild or nil, the RV will hypertrophy and remain small, developing systolic hypertension. The increased flow across the foramen ovale *in utero* causes a volume overload of the left heart, resulting in neonatal LV hypertrophy and dilation, and potential aortic root dilation.

The affected newborn is dependent upon the PDA and is resuscitated with $PGE_1$. Generally, the left heart functions normally and *CO* is maintained with the presence of an adequate PDA. If there is LV hypertrophy from septal hypertrophy/LV outflow tract obstruction, there may be coronary fistulae and resulting myocardial ischemia. Single ventricle physiology is manifested. Tricuspid valve insufficiency is common, partly because of the RVOT obstruction and, in approximately one-third of cases, due to structural abnormalities of the TV. Over 90% of patients will present with cyanosis and a ductal flow murmur within the first 3 days of life. Electrocardiogram reveals lack of RV forces and often a large P wave, indicative of RA enlargement. Chest roentgenogram can show decreased to normal pulmonary vascular markings depending upon the amount of ductal flow. The cardiac silhouette is normal unless RA and RV enlargement occur due to severe TI. Echocardiography can define the RVOT, RV dimensions, the TV, and the PDA. Right ventricle pressure can be derived from Doppler measurement of the TI. Ventricular function can be assessed, but dependency of coronary blood flow cannot be determined solely with echocardiography. Cardiac catheterization is essential in all cases to define major stenoses and fistulae in the coronary anatomy.

## Surgical approach

In the early 1960s, palliative shunts and closed pulmonary valvotomies were done. But survival was dismal given that an estimated 2.5% of patients lived to 3 years of age. Right ventricle outflow procedures were combined with systemic to pulmonary shunts in the 1970s. Since that time, repair techniques have varied among surgeons, partly based on the spectrum of anatomic dysmorphology and partly on the individual surgical outcome experiences. Current corrective procedures include: (i) neonatal RVOT patch augmentation with continued infusion of $PGE_1$ (average of 6 days); (ii) neonatal RVOT patch augmentation with concurrent systemic to pulmonary artery shunt; and (iii) pulmonary valvotomy (open or closed) and a systemic to pulmonary artery shunt. Success rates in achieving ultimate biventricular repair have varied from 40% to 60%. However, all congenital heart surgeons generally avoid RV decompression if there is a complete dependency of myocardial blood supply on the RV. In these cases, initial palliation consists only of placing a systemic to pulmonary artery shunt. Patients with partial RV dependency for myocardial blood supply are managed variably by different surgeons, but regional LV wall motion abnormalities can worsen after RV decompression.[41]

The major determinants of the most appropriate surgical approach for a particular patient are: (i) the degree of RV and TV hypoplasia; (ii) presence of RV-dependent coronary circulation; and (iii) the degree of tricuspid regurgitation. The surgical options include: (i) complete biventricular repair with later closure of the interatrial communication; (ii) biventricular repair with allowable mixing of blood at the atrial level (ASD/PFO left open, or surgically adjustable ASD[41]), but using the RV to pump blood to the lungs; (iii) one and a half ventricular repair using cavopulmonary anastomosis to reduce RV load; (iv) ultimate modified Fontan procedure; and (v) cardiac transplantation (last resort).[42,43]

Reddy and Hanley[40] outline the goals of initial surgical therapy as: (i) minimize mortality; (ii) promote growth of the RV such that chances are improved for a later two ventricular repair; and (iii) minimize the need for non-definitive later surgeries. They point out that: survival after systemic to pulmonary artery shunt is at least as successful as any other initial surgical procedure; the RV will not grow if it is not decompressed and RVOT relief will be needed if two ventricular repair is thought to be possible later; and the ultimate functional potential of the RV is often unclear in the neonate with PA/IVS. The initial procedure often determines the final repair/palliation outcome (Fig. 20.6).[41]

## Perioperative anesthetic management

Given the variety of surgical options available for this particular lesion, general considerations are outlined. For any patient with a small hypertrophic, hypertensive RV, RV filling pressures must be maintained such that the RV cavity does not collapse, causing it to be an ineffective pump. This is especially important after RV outflow obstruction is relieved with the biventricular repair. Inotropic RV support is often essential as RV dysfunction is present after CPB in the presence of increased afterload of an unadjusted pulmonary vascular circulation. Minimizing ventilation pressures and vasodilating the pulmonary vasculature with drugs such as milrinone or dobutamine may reduce RV afterload. With severe pulmonary hypertension after RVOT relief, nitric oxide is useful post-repair to aid in pulmonary vasodilation for the immediate post-repair period until the pulmonary vascular bed adjusts to the increased flow. Also, pulmonary edema causes oxygenation difficulties and bronchospasm after pulmonary flow increases acutely. The one and a half ventricular repair requires a balance of adequate preload to a partially unloaded RV and maintenance of low *PVR* for upper body passive venous return to the pulmonary vasculature. Along with the ventilation and pharmacological

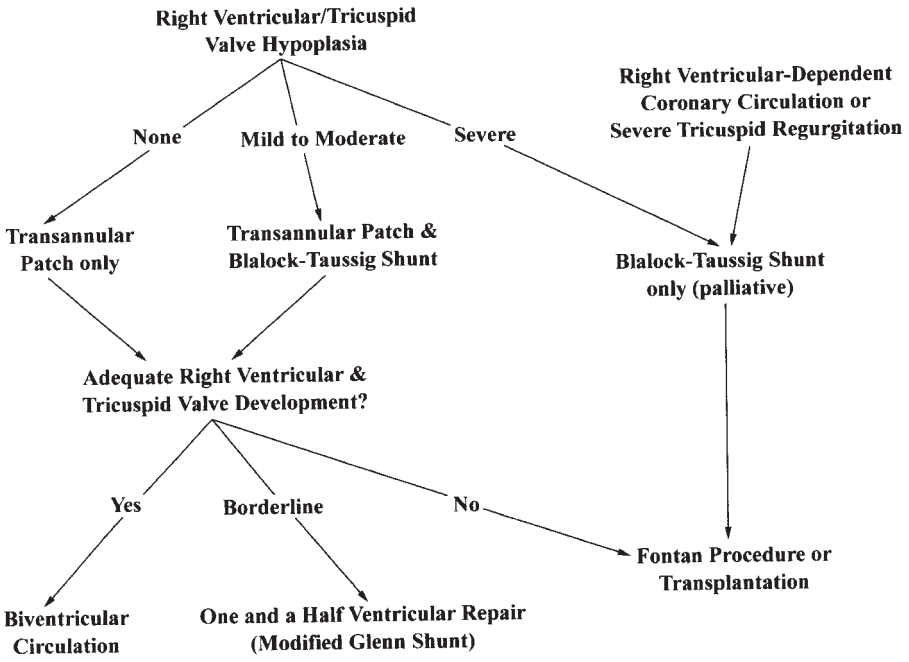


**Fig. 20.6** Consensus approach to pulmonary atresia with intact ventricular septum as described by the Congenital Heart Surgeons' Society (CHSS). Modified from Hanley FL, Sade RM, Blackstone EH *et al*. and the Congenital Heart Surgeons' Society. Outcomes in neonatal pulmonary atresia with intact ventricular septum. A multiinstitutional study. *J Thorac Cardiovasc Surg* 1993; **105**: 406–27.

maneuvers listed above for the biventricular repair, these patients are positioned with 30° head-up to assist upper body venous return to the pulmonary vascular bed. When RV function becomes adequate to support work of breathing, spontaneous respiration in an extubated patient generating negative intrathoracic pressure will boost pulmonary flow. With palliative aortopulmonary shunt placement, consideration is given to continued balance of pulmonary and systemic parallel circulations (described elsewhere in this volume). Low *CO* in the postoperative period may occur secondary to unrecognized RV-dependent coronary circulation or from a phenomenon known as a "circular shunt." The latter occurs in patients who have had a transannular patch and a systemic to pulmonary artery shunt. Because the transannular patch produces free pulmonary regurgitation, blood ejected from the LV flows through the systemic to pulmonary artery shunt and enters the RV in a retrograde fashion. If there is significant TI, blood flows back into the RA and then into the LA through the interatrial communication. This effectively "steals" blood from the systemic circuit and may lead to hypoperfusion of the distal organs and metabolic acidosis. Conservative measures such as raising the *PVR* and reducing the *SVR* may be helpful, but quite often surgical intervention to revise the shunt and treat the tricuspid regurgitation is required.

Sedation with benzodiazepines and pain control with narcotic infusions such as morphine are balanced with the patient's condition and anticipation of duration of mechanical ventilation and time needed for pulmonary vascular adjustment/RV recovery.

## Pulmonary atresia/ventriculoseptal defect/multiple aortopulmonary collateral arteries

### Anatomy

In its simplest form, with normal pulmonary vasculature, this lesion can be considered an extreme variation of TOF. However, in most cases, there is great morphologic variability regarding pulmonary artery architecture and sources of *PBF*, posing major challenges for corrective surgery. With PA, there is no continuity between the RV and the pulmonary trunk. The VSD is usually large and malaligned. The pulmonary arteries may be normal in size or have varying degrees of hypoplasia. The left and right pulmonary arteries may be confluent or non-confluent. An additional major source of *PBF* is derived from multiple collateral arteries arising from the aorta or its major branches. A given lung segment may be supplied solely from the true pulmonary arteries, solely from the aortopulmonary collaterals, or from both.

### Pathophysiology and natural history

The great heterogeneity in *PBF* determines the natural history of this lesion. Excessive *PBF* through the collateral arteries will produce pulmonary congestion and a clinical picture of CHF with LV volume overload. Moderate stenoses of the collateral arteries may result in a balanced *PBF* and minimal symptoms. Severe stenoses of the collateral arteries will lead

to inadequate *PBF*, cyanosis, and hypoxemia. Survival is poorest in those who have either excessive or inadequate *PBF*. Patients with a balanced blood flow can survive to adulthood with minimal symptoms, but eventually LV failure and aortic insufficiency ensue from chronic left-to-right shunting and volume overload.

Although the diagnosis of PA/VSD/MAPCAs can be made with echocardiography, virtually all patients require cardiac catheterization to delineate the true pulmonary artery architecture and collateral artery anatomy in order to plan the surgical approach.

## Surgical approach

The ultimate goal of surgery is to achieve a biventricular repair by completely separating the systemic and pulmonary circulations by closing the VSD and restoring continuity between the RV and the pulmonary circuit. The success of this repair is dependent on having an adequate pulmonary vascular bed, which will accommodate the entire RV output. An inadequate pulmonary vascular bed will eventually cause RV failure due to chronic increased afterload. The most important factor for a successful outcome is the post-repair RV pressure, which should be as low as possible. The pulmonary vascular bed is reconstructed by a procedure known as "unifocalization" in which as many of the aortopulmonary collateral arteries as possible are detached from the aorta and anastomosed to the central pulmonary arterial tree, in order to provide unobstructed blood flow from the RV to the pulmonary microcirculation. This centralization of multiple sources of *PBF* was traditionally done in two or three stages via bilateral thoracotomies, followed by a definitive repair through a median sternotomy.[44] However, some centers are obtaining good results with a single-stage unifocalization and repair, and this approach does have some advantages.[20,45] It avoids subjecting the patient to multiple surgeries, which if performed via thoracotomies, can make subsequent procedures extremely hazardous (especially lung transplants) due to increased adhesions and the potential for massive bleeding. Additionally, serious neurological injury can occur during CPB-assisted unifocalization because increased runoff into the pulmonary circuit can result in cerebral hypoperfusion despite adequate pump flows. Obviously, a single-stage approach will not be applicable in all patients, and this group will need a systemic-to-pulmonary artery shunt or a conduit from the RV to the pulmonary artery to allow growth before definitive repair. Reddy *et al*.[20] in their series of 85 patients, were able to complete one-stage unifocalization and intracardiac repair in 56 patients. In 23 patients single-stage unifocalization was done but the VSD was left open, and six patients required staged unifocalization through sequential thoracotomies. In the subgroup of patients with excessive *PBF*, the collateral arteries may have to be narrowed at their origin to limit overcirculation (conceptually similar to pulmonary artery banding).

## Perioperative anesthetic management

The anesthetic management will vary according to whether a staged approach to unifocalization via a thoracotomy or one-stage unifocalization with intracardiac repair is being contemplated. The general principles for induction, maintenance, and monitoring are similar to those described above for TOF repair. There are several major anesthetic challenges for unifocalization via a thoracotomy.[46] These include difficulties with oxygenation and ventilation from one-lung anesthesia, hemodynamic instability, and metabolic acidosis. In the older child, lung separation with either a double-lumen tube or a bronchial blocker will greatly facilitate surgical exposure and minimize lung contusion from surgical retraction. Extensive intrapulmonary and major airway bleeding from multiple vascular anastomoses will also compromise ventilation. In addition, major blood loss should be anticipated, and large-bore intravenous access is essential. Warming of fluids before transfusion will reduce the chance of hypothermia. Finally, thoracotomies are extremely painful, and a thoracic epidural catheter will provide excellent postoperative analgesia. The benefits of epidural anesthesia are balanced against the potential risk of neurological damage from catheter placement in an anesthetized child.

One-stage unifocalization (with or without definitive repair) is carried out via a median sternotomy or bilateral trans-sternal thoracotomy ("clamshell" incision). As many MAPCAs as possible are ligated, mobilized, and unifocalized without CPB. As each MAPCA is ligated, the arterial saturation will decrease because a proportion of the *PBF* is being cut off. At the point at which the patient nears compromise from arterial desaturation, CPB (with moderate hypothermia and a beating heart) is initiated. The rest of the unifocalization is then completed. As mentioned above, it is vital to control as many of the MAPCAs as possible prior to initiating CPB to prevent cerebral injury due to increased runoff into the pulmonary circulation. A valved conduit is then placed between the RV and the central pulmonary artery to restore continuity. Next, the surgeon determines whether the VSD should be closed at the time of one-stage unifocalization. This is a critical step because if the VSD is closed, and the "new" pulmonary vascular bed is inadequate to receive all of the *CO*, RV failure will rapidly ensue. One approach[19,47] is to do an intraoperative pulmonary flow study to estimate the resistance of the new vascular bed. The lungs are perfused with the equivalent of one *CO*, and if the mean pulmonary artery pressure is less than 30 mmHg, the VSD is closed.

Three major problems can be anticipated post-CPB:

1 RV dysfunction, which is usually secondary to increased afterload due to an inadequate pulmonary vascular bed.

The mainstays of treatment are inotropic support with dopamine, dobutamine, or milrinone; increased preload; and ventilatory maneuvers to lower *PVR*. Nitric oxide may also be helpful as a pulmonary vasodilator.

2 Intrapulmonary bleeding due to multiple vascular suture lines, systemic anticoagulation, and the effects of CPB.

3 Lung reperfusion injury due to increased blood flow to many previously underperfused lung segments. This injury manifests as pulmonary edema, bronchospasm and difficulties with ventilation and oxygenation. Frequent endotracheal suctioning, fiberoptic bronchoscopy, and *PEEP* will be helpful in managing this problem. In general, these patients are not good candidates for early extubation.

These patients benefit from sedation with benzodiazepines and aggressive pain control to keep pulmonary and systemic blood pressures from becoming excessive as multiple arterial anastomoses and suture lines may predispose to post-surgical bleeding.

## Summary

Right-sided obstructive congenital heart lesions manifest a variable presentation. Depending upon the severity of the structural anomaly(-ies), such lesions may present a spectrum of illness in the congenital heart patient, ranging from the ductal-dependent, cyanotic neonate in CHF to the minimally affected young adult who manifests mild to moderate exercise intolerance. All are characterized by the nearly universal presence of a septal defect that has the potential for right-to-left flow. An understanding of the physiology of the defect and effects of the proposed surgical intervention are essential for the meticulous and well-planned perioperative anesthetic management of such patients.

## Key points

### Ebstein's anomaly

**1** Patients with extreme cardiomegaly or perioperative ventricular arrhythmias should receive prophylactic antiarrhythmic treatment, such as amiodarone.

**2** Patients with poorly functioning RVs may be dependent upon high filling pressures to maintain adequate *CO*.

### Tetralogy of Fallot

**1** Hypercyanotic spells are treated with oxygen, phenylephrine, intravenous fluid and esmolol.

**2** During BT shunt placement difficulties may be encountered with oxygenation and ventilation, and hypotension after the shunt is open.

**3** Postoperative ventilation is recommended for 12–24 hours after BT shunt because of the risk of pulmonary edema.

**4** Following complete repair, RV dysfunction, heart block, arrhythmias, and bleeding should be anticipated.

### Pulmonary stenosis or atresia with intact ventricular septum, and pulmonary atresia with ventricular septal defects and major aortopulmonary collaterals

**1** Inotropes are used cautiously with patients with PS/IVS in which there is a component of dynamic infundibular stenosis, so as to not worsen outflow obstruction.

**2** Small hypertrophic RVs require meticulous attention to preload to maintain function.

**3** An RV-dependent coronary circulation requires maintenance of RV intracavitary pressure to prevent myocardial ischemia.

**4** After repair of PA/IVS and PA/VSD, severe RV dysfunction is often present due to the high afterload of an insufficient pulmonary vasculature: inotropes, ventilation adjustments, and vasodilators are helpful.

**5** Enhanced post-repair lung perfusion may result in pulmonary edema, intrapulmonary bleeding, bronchospasm, and difficulties with oxygenation and ventilation.

**6** Antifibrinolytic agents may be useful for minimizing bleeding after unifocalization of MAPCAs.

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# 21 Anesthesia for transposition of the great vessels

Kathryn Rouine-Rapp

## Introduction

Transposition of the great arteries (TGA) is found in about 5% of patients with congenital heart disease and is thought to be an alteration in conotruncal development of the heart.[1,2] Nomenclature for this defect is inconsistent, thus this chapter will use nomenclature established recently by members of the Society of Thoracic Surgeons and the European Association for Cardiothoracic Surgery.[3] Three general categories of TGA are described: TGA with intact ventricular septum (IVS), TGA with ventricular septal defect (VSD), and TGA with VSD and left ventricular outflow tract obstruction (LVOTO). In this chapter, TGA will refer to a physiologically uncorrected defect. Another defect, congenitally corrected transposition of the great arteries (ccTGA), will be discussed separately using the nomenclature established by the aforementioned groups.

## Anatomy

In TGA, the distinguishing feature is an abnormal connection between the ventricles and great vessels known as discordant ventriculoarterial connections, or VA discordance. The atria most commonly are normal in orientation and connections between the atria and ventricles also are normal (atrioventricular [AV] concordance). In the presence of VA discordance the aorta arises from the morphologic right ventricle (RV) and the pulmonary artery (PA) arises from the morphologic left ventricle (LV).

In the normal heart, the position of the aorta is posterior and to the right of the pulmonary trunk. There is a subpulmonary muscular infundibulum and the annulus of the aortic valve is in fibrous continuity with the mitral valve annulus.[4] In TGA, the aorta most often is anterior and to the right of the pulmonary trunk. There is a subaortic muscular infundibulum in most patients and the pulmonary valve is in fibrous continuity with the mitral valve (Fig. 21.1).[5,6] Typical anatomic characteristics in TGA include normal intracardiac attachments of the tricuspid and mitral valves and a PA diameter that equals or often exceeds that of the aorta.

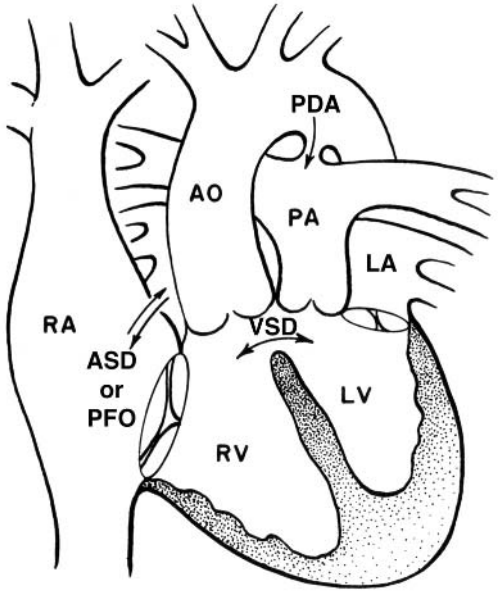


**Fig. 21.1** Basic anatomy and sites of mixing between the systemic and transposition of the great arteries. Arrows indicate mixing at the atrial level through an atrial septal defect or patent foramen ovale, through a patent ductus arteriosus, or through a ventricular septal defect. AO, aorta; ASD, atrial septal defect; LA, left atrium; LV, left ventricle; PA, pulmonary artery; PDA, patent ductus arteriosus; PFO, patent foramen ovale; RA, right atrium; RV, right ventricle; VSD, ventricular septal defect. Reproduced with permission from Garson A, Bricker JT. Transposition of the great arteries. In: Garson A, Bricker JT, Fisher DJ, Neish SR, eds. *The Science and Practice of Pediatric Cardiology*, 2nd edn. Baltimore, MD: Williams & Wilkins, 1998: 1470–503.

Other terms are used to define TGA and include d-TGA and complete transposition. The term d-TGA commonly is used to define the aorta as anterior and to the right of the pulmonary trunk. This term is misleading because four additional aortic positions have been described and the

letter "d" refers to cardiac loop formation that occurs during development of the heart.[2,6]

### Transposition of the great arteries with intact ventricular septum

Up to 85% of patients with TGA are in the category of TGA with IVS. Additional findings include a persistent patent foramen ovale (PFO) and in 50% of patients, a persistent patent ductus arteriosus (PDA).[3,7–9] A right aortic arch is present in up to 4% of patients in this category and a comparable number who undergo surgical correction have tricuspid valve abnormalities.[3]

### Transposition of the great arteries with ventricular septal defect

Another category of TGA is TGA with VSD. An estimated 10–25% of patients undergoing surgical correction have a VSD.[8,10] It is the most common defect associated with TGA, and although most are perimembranous, the size, location and hemodynamic significance of the VSD can vary as they do in the otherwise normal heart.[5,11] In addition, abnormalities of the aorta can occur in association with TGA and VSD. Up to 20% of patients in this category have a right aortic arch, and of the 5% of patients with TGA who have interrupted aortic arch and coarctation of the aorta, most have TGA and VSD.[3]

Physiologically similar to TGA, the so-called Taussig–Bing malformation occurs when malalignment of the infundibular septum increases until the VSD becomes subpulmonic and both great vessels, typically side-by-side in location, arise predominantly from the RV. Physiologic similarity exists in Taussig–Bing malformation because blood "streams" from the LV to the PA and RV to the aorta. Since both great vessels arise from the RV, Taussig–Bing malformation is considered part of the cardiac malformation known as double-outlet RV. Aortic arch obstruction is relatively common in patients with Taussig–Bing malformation.[12]

### Transposition of the great arteries with ventricular septal defect and left ventricular outflow tract obstruction

A third category of TGA is TGA with VSD and LVOTO. Anatomic LVOTO is rare in TGA with IVS but a functional form of LVOTO may occur when the RV systemic pressure load shifts the IVS into the LV. Up to 30% of patients with TGA and VSD have anatomic LVOTO. In some classification systems LVOTO, particularly when limited to the pulmonary valve, is known as pulmonary stenosis. Left ventricular outflow tract obstruction can be diffuse or discrete and can occur at several levels along the outflow tract of the left ventricle. Causes include annular hypoplasia, pulmonary valve stenosis, and subvalvar obstruction from abnormal attachments of the mitral valve apparatus, redundant tricuspid valve tissue that migrates into the LVOT through a VSD, and a membranous ring or fibromuscular tunnel that causes a fixed stenosis.[3]

### Coronary artery anatomy

Coronary artery anatomy is variable in patients with TGA. In the normal heart the coronary arteries almost always arise from the aortic sinuses of Valsalva that face or are adjacent to the pulmonary trunk. The usual aortic sinuses of Valsalva are defined as right, left, and non-coronary. In addition, one commissure from the aortic and one from the pulmonary valve are in direct alignment, whereas direct commissural alignment is absent in about 13% of pathologic specimens from patients with TGA.[6] Similarly, in patients with TGA, the coronary arteries most often arise from the aortic sinuses of Valsalva that face the pulmonary trunk, but the epicardial course of the coronary arteries frequently is abnormal.[5] Many classification systems exist to define coronary artery anatomy in patients with TGA but the Leiden classification system appears most commonly in surgical literature and will be used here.[3,13] In this classification system, the sinuses of Valsalva from which the coronary arteries originate are renamed sinus 1 and sinus 2. The usual coronary artery patterns found in patients with TGA are shown in Fig. 21.2. Most often, the left and right coronary arteries arise from sinus 1 and sinus 2, respectively, and are described as 1 LCx and 2R. About 5% of patients have a coronary artery that is intramural and provides a challenge for arterial switch reconstruction although alteration in operative technique can lead to satisfactory results.[14]

Abnormal (i.e. non-1 LCx and 2 R) coronary patterns are more commonly seen in TGA with VSD and have been used as predictors of postoperative morbidity and mortality in some published series.[8,15,16]

## Physiology and natural history

In the normal infant several physiologic changes occur following birth and lung expansion that are relevant to review prior to a discussion of abnormal physiology. Changes relevant to this discussion are summarized in Table 21.1. For a more detailed discussion the reader is referred to Chapter 3.

In normal infants, following birth, pulmonary and systemic blood circulates in series. Thus deoxygenated blood from the systemic circulation enters the right atrium (RA), the RV, and then enters the pulmonary circulation via the PA. After crossing the pulmonary capillary bed, oxygenated blood from the pulmonary circulation enters the left atrium (LA) via the pulmonary veins, flows into the LV then exits via the aorta and ultimately returns as deoxygenated blood to the RA. In the

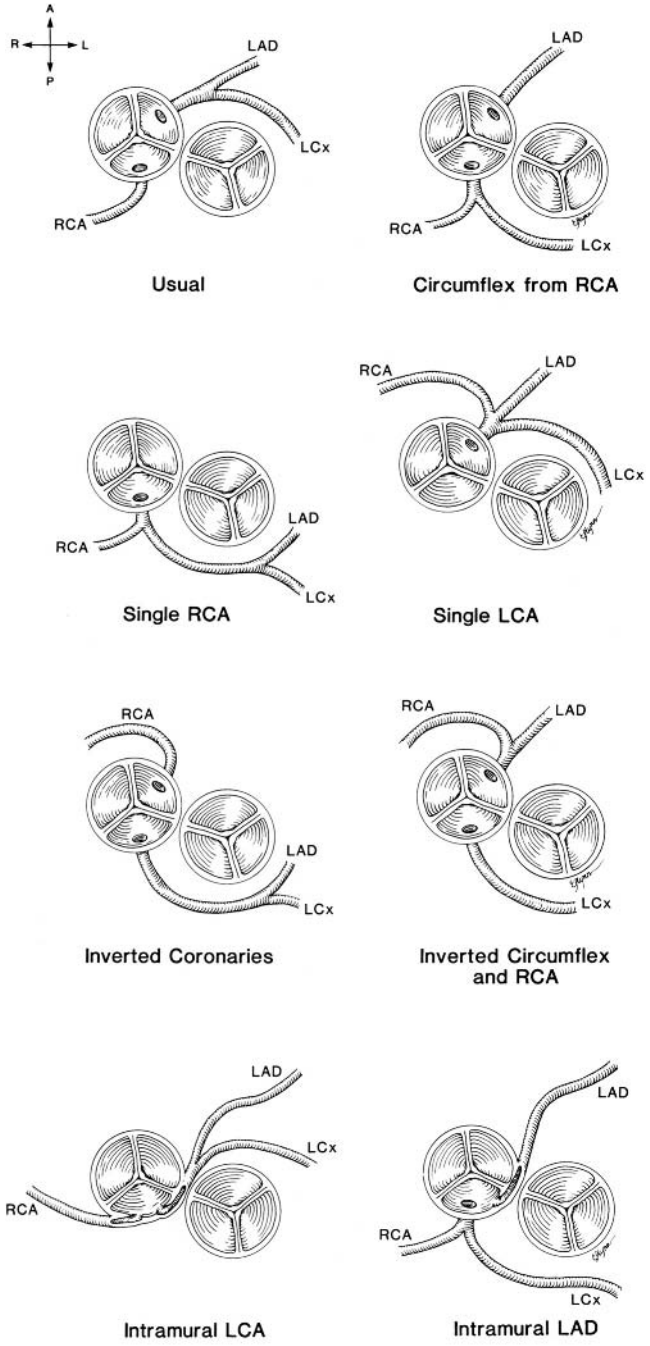


**Fig. 21.2** Coronary patterns found in patients with transposition of the great arteries. LAD, left anterior descending; LCA, left coronary artery; LCx, left circumflex; RCA, right coronary artery. Reproduced from DiDonato RM, Casteneda AR. Anatomic correction of transposition of the great arteries at the arterial level. In: Sabiston DC, Spencer FC, eds. *Surgery of the Chest*, 6th edn. Philadelphia, PA: Saunders, 1995: 1592–604, with permission from Elsevier.

infant with TGA, the pulmonary and systemic blood circulates in parallel rather than in series. Deoxygenated blood from the systemic circulation enters the RA then RV and returns to the systemic circulation via the aorta. Oxygenated blood from the pulmonary circulation enters the LA, the LV and returns to the pulmonary circulation via the PA. Thus mixing between the systemic and pulmonary circulations is essential for survival in infants with TGA. Although mixing may occur at several levels including the atrial level (atrial septal defect [ASD]), ventricular level (VSD), or arterial level (PDA) (see Fig. 21.1), the amount of mixing of systemic and pulmonary venous blood at the atrial level is an important determinant of hemoglobin oxygen saturation and the severity of the clinical picture.[17] The most common clinical finding in an infant with TGA is cyanosis (arterial partial pressure of oxygen 25–40 mmHg). The degree of cyanosis varies among infants with TGA, but neonates with TGA and IVS or a restrictive PFO or ASD usually have more pronounced cyanosis at birth. In these neonates, supplemental oxygen may increase pulmonary blood flow (*PBF*) and thus increase arterial oxygen saturation, but cyanosis persists in most. Infants with TGA and IVS but with a large PDA and better mixing are less likely to develop cyanosis, but they are more likely to develop congestive heart failure (CHF).

Blood flow through a PDA may improve arterial oxygen saturation but infants, especially smaller infants without adequate interatrial mixing, can develop pulmonary venous congestion and are at risk for preoperative death or sudden death at birth following premature closure of a PFO.[18,19] Others can develop acidosis and cardiovascular collapse and require resuscitation with mechanical ventilation and prostaglandin $E_1$ ($PGE_1$) to maintain patency of the ductus arteriosus, and a procedure to provide interatrial mixing. One such procedure is known as a balloon atrial septostomy (BAS) and can be performed in the cardiac catheterization laboratory or at the bedside using echocardiographic guidance. Developed by Rashkind and Miller in 1966, this procedure uses a balloon septostomy catheter introduced via percutaneous venous access into the RA, through the PFO, and into the LA where it is inflated then pulled downward to tear the inferior fossa ovalis and enlarge the ASD.[20] In infants less than 1 month of age, the atrial septum tends to be thin so it can be torn by the inflated balloon, providing improvement of interatrial mixing and hemoglobin oxygen saturation, relief of pulmonary venous congestion, and subsequent decompression of the LV. Poor results after BAS suggest pulmonary hypertension.[21] Even with good results following BAS, survival without surgical intervention is bleak.[22]

Infants with TGA and VSD often have mixing of blood at the atrial and ventricular levels. Interatrial mixing tends to be from the LA to RA and interventricular mixing tends to be from the RV to LV, but bidirectional shunting is possible at both levels. Thus, these infants are less likely to develop cyanosis and more likely to develop CHF. Although many infants are symptomatic during the neonatal period, clinical symptoms of CHF may develop around 4–6 weeks of life when pulmonary vascular resistance reaches its postnatal nadir. Infants with TGA and IVS or VSD with aortic obstruc-

**Table 21.1** Summary of physiologic changes in the normal neonate following birth and lung expansion.

| | |
|---|---|
| Pulmonary vascular resistance | Decreases |
| Pulmonary artery pressure | Decreases |
| Pulmonary blood flow | Increases |
| Pulmonary venous return | Increases |
| Left atrial pressure | Increases with increase in pulmonary venous return |
| Right atrial pressure | Decreases with loss of blood flow from placenta |
| Patent foramen ovale | Functional closure at birth following decrease in right atrial pressure and increase in left atrial pressure<br>Anatomic fusion in 80% of infants at about 1 year<br>Can reopen if right atrial pressure increases |
| Patent ductus arteriosus | Functional closure within 12–15 h of birth |
| Left ventricular volume load | Increases |
| Left ventricular pressure load | Increases due to loss of low resistance placenta and closure of patent ductus arteriosus |

tion are prone to develop early pulmonary vascular disease due to excess *PBF*.[23]

Nearly all infants with TGA and LVOTO have a VSD. The *PBF*, enhanced by flow across the VSD, is limited by the LVOTO, so that the balance between the pulmonary and systemic blood flow is determined by the degree of LVOTO. The reduction of *PBF* caused by the obstruction exacerbates the cyanosis found in infants with TGA; however, cyanosis can occur later in infancy when LVOTO is not severe and may be evident only when the infant is crying or feeding.[17]

## Options for surgical correction

Prior to the 1950s, up to 90% of infants with a diagnosis of TGA died within the first year of life.[24] Early surgical therapy was palliative and began when Blalock and Hanlon created a defect in the atrial septum to provide interatrial mixing of blood.[25] Physiologic correction of TGA was achieved in 1959 by Senning who redirected systemic venous blood to the LV, then PA and pulmonary venous blood to the RV and then aorta using autologous atrial flaps. This procedure was called the Senning operation or baffle, and later was modified by Mustard who created a large interatrial baffle of pericardium to redirect systemic and pulmonary venous return. The Senning and Mustard procedures were the predominant surgical approaches until the 1980s. After good early results, many patients developed late complications largely due to retention of the discordant VA connection. These complications included atrial tachyarrhythmias, baffle leaks and obstructions, failure of the systemic RV, and systemic (tricuspid) AV valve regurgitation.[26–28] In 1975, Jatene performed the first arterial switch operation (ASO), a procedure that provided anatomic and physiologic correction of TGA through translocation of the great vessels and coronary arteries (Fig. 21.3). Initially only infants with TGA and VSD underwent successful ASO.[29,30] Older infants with TGA and IVS were at risk preoperatively for regression of LV myocardial mass, and at risk postoperatively for the LV to fail as the systemic ventricle when presented with a sudden increase in pressure load.[15] Thus the initial stage of ASO for infants with TGA and IVS became placement of a pulmonary artery band (PAB) to increase LV pressure load then mass, so-called LV "retraining."[31] Subsequently the ASO was performed on neonates within the first week of life before regression of LV myocardial mass, with good early and late results.[32,33] The upper age limit before significant regression of the LV myocardium ensures failure after ASO is unknown and may be as late as 2 months of age.[34] Currently, when patients are diagnosed later in infancy with TGA and IVS, the initial surgical procedure likely will be PAB placement for LV "retraining." These patients often require concurrent placement of an arterial to PA shunt to provide adequate *PBF*.[35] In addition, older children or adults who have systemic RV dysfunction or systemic (tricuspid) AV valve regurgitation following a Senning or Mustard operation may undergo PAB placement as the initial step in a staged conversion to ASO.[36]

Infants with TGA and VSD with LVOTO require a different surgical approach predicted by the nature of the LVOTO, but many can undergo successful ASO.[37] Other procedures may be required in patients with more complex TGA and VSD with LVOTO and a detailed discussion of such surgical techniques can be found in a textbook of cardiothoracic surgery.[38] Overall, ASO remains the surgical option of choice for TGA with IVS, VSD, and in the minority of suitable candidates, VSD with LVOTO.

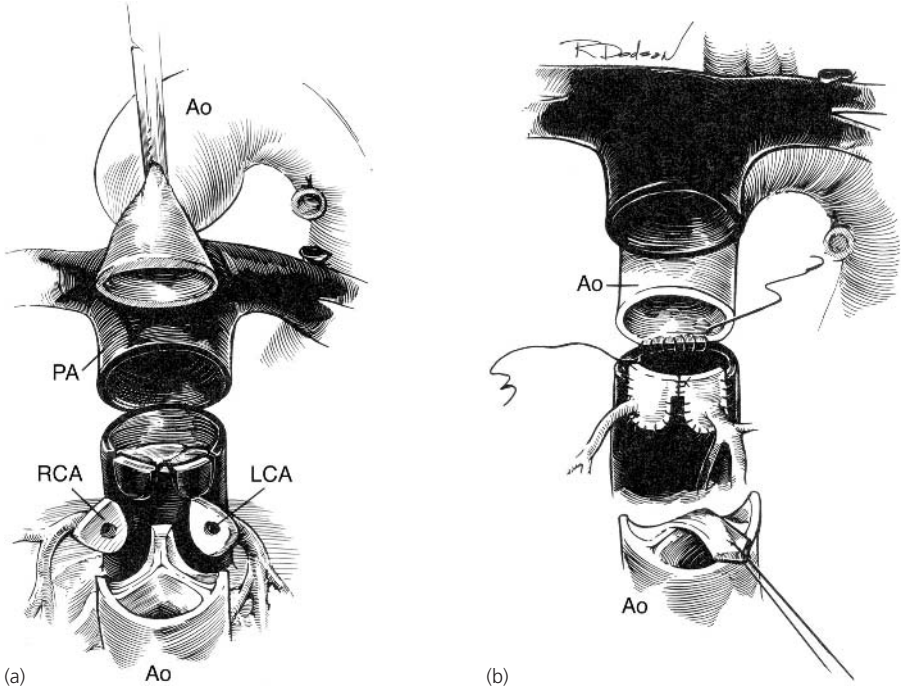


**Fig. 21.3** Arterial switch operation. (a) The aorta and pulmonary artery are transected and translocated. (b) The coronary arteries have been excised with surrounding tissue "buttons" and reimplanted in the neoaorta site. Ao, aorta; LCA, left coronary artery; PA, pulmonary artery; RCA, right coronary artery. Reproduced with permission from Castaneda AR, Jonas RA, Mayer JE *et al*. Transposition of the great arteries. In: *Cardiac Surgery of the Neonate and Infant*. Philadelphia, PA: Saunders, 1994: 420–1.

## Anesthetic considerations

Two-dimensional echocardiography provides bedside noninvasive imaging to diagnose and define features of TGA, thus cardiac catheterization is reserved for selected infants who have associated intracardiac or extracardiac abnormalities.[38] Review of the echocardiogram by the anesthesiologist should include evaluation of patterns of shunting, presence of associated defects, coronary artery anatomy, AV valve abnormalities, and evaluation of biventricular function.[39]

Preoperative evaluation of an infant scheduled to undergo surgical correction of TGA includes careful assessment of hemodynamic status, level of inotropic support, cardiac arrhythmias, peripheral, central or umbilical intravenous access, intra-arterial access, laboratory values, chest radiograph, electrocardiogram, ventilatory status and airway issues, and status of non-cardiac organ systems.[40] The anesthesiologist should be aware of risk factors for preoperative or postoperative mortality in infants with TGA. Risk factors for preoperative mortality include restrictive PFO or ASD, persistent pulmonary hypertension, low birth weight, prematurity, and time of diagnosis.[18,41] Infants with a prenatal diagnosis of TGA by fetal echocardiography, feasible as early as 18 weeks gestational age, are less likely than infants with a postnatal diagnosis to develop hemodynamic compromise, an important predictor of preoperative and postoperative mortality.[9,41] Evaluation of the infant with TGA and IVS frequently includes assessment of adequacy of interatrial mixing following BAS. In addition, infants receiving $PGE_1$ intravenous therapy to maintain patency of the ductus arteriosus, especially in doses exceeding 0.05 mg/kg/minute, should be assessed for side effects including apnea, hypotension, fever, central nervous system excitation, and decreased intravascular volume. Patency of the ductus arteriosus and associated reduction of systemic blood flow and hypotension can lead to a decrease in blood flow to the bowel and contribute to the development of necrotizing enterocolitis in some of these infants.[42] Assessment of the infant with TGA and VSD includes evaluation for signs of pulmonary overcirculation and CHF including increased heart rate, cardiomegaly, decreased skin temperature, diaphoresis, low body weight, tachypnea, intercostal and substernal retraction, and prolonged capillary refill.

Intraoperatively, routine monitors are placed prior to induction of anesthesia. Options for induction of anesthesia in the unusual infant presenting for ASO without intravenous access include inhalation or intramuscular delivery of induction agent. More often, these infants will undergo an intravenous induction using a narcotic agent. The safety and efficacy of a narcotic-based anesthetic for cardiac surgery in infants has been established for years.[43] However, narcotics alone have had inconsistent effects on stress hormone release and outcome in neonates who undergo cardiac surgery.[44,45] Thus, a balanced narcotic-based anesthetic that includes an anesthetic vapor may control hemodynamic and stress responses better in these infants.[46,47] For a more detailed discussion of anesthetic agents and their cardiovascular effects see Chapter 3. Occasionally, a patient with TGA/IVS with adequate mixing at the atrial and PDA level preoperatively

has profound arterial desaturation with the induction of general anesthesia and positive pressure ventilation. The cause for this is an acute decrease in mixing, which is multifactorial. The positive pressure ventilation and paralysis, along with the inhibition of endogenous catecholamine secretion caused by high dose narcotic anesthesia may combine to decrease preload and contractility of both ventricles, leading to lower flow of oxygenated blood across the atrial septum. An inadequate BAS may be masked by mixing at the level of the PDA, which is closing because $PGE_1$ has been discontinued. Pulmonary hypertension caused by inadequate ventilation, or inappropriate modes of ventilation, may contribute. Treatment consists of assuring adequate oxygenation and ventilation, increasing anesthetic depth without decreasing contractility if pulmonary hypertension is suspected, increasing cardiac output (*CO*) with volume infusion and rapid institution of cardiopulmonary bypass (CPB) if these measures do not rapidly correct the profound hypoxemia that may occur.

A catheter placed in an umbilical artery preoperatively provides reliable intraoperative monitoring of arterial blood pressure. Other options for invasive monitoring of arterial blood pressure include placement of a catheter via percutaneous puncture of the radial or femoral artery or cutdown to provide direct visualization of the radial artery. Ventilation should be adjusted to maintain normocarbia. A catheter placed in the umbilical vein preoperatively provides reliable monitoring of central venous pressure when positioned in the inferior vena cava or RA. Central line placement may be difficult in infants less than 4 kg and more successful when ultrasound guidance is used to locate the vessel.[48,49] In some centers, surgeons place intracardiac lines before weaning from CPB that can be used to monitor intracardiac pressures and to infuse inotropes.

Following placement of the lines, gastric contents are suctioned and a transesophageal echocardiography (TEE) probe is placed. Pediatric biplane probes have been placed in infants as small as 2.9 kg; however, the anesthesiologist should watch for hemodynamic compromise or a change in peak airway pressures during probe placement and manipulation, and remove the probe if problems occur.[50] In the infant with TGA, TEE can be used following bypass to detect residual defects, assess regional and global ventricular function, valvular function, evaluate neo-aortic valve regurgitation, and detect a gradient at the supravalvar anastomotic sites of the great arteries.[51] Regional wall motion abnormalities may be detected after bypass, but the functional implications remain unknown.[52]

Antifibrinolytic agents are used in many centers where neonates undergo ASO and include aminocaprioc acid, tranexamic acid, and aprotinin. These agents and coagulation related issues are discussed in detail in Chapter 10. The conduct of CPB is unique to each institution but may include a flow rate of 150 mL/kg/minute and avoidance of low flow or circulatory arrest, infant temperature of 30–32°C, use of blood cardioplegia, and a procedure known as modified ultrafiltration immediately following termination of CPB. See Chapter 5 for a complete discussion of CPB and modified ultrafiltration. Following separation from CPB, TEE and left atrial pressure (*LAP*) monitoring can help assess global and regional LV function, and may indicate inadequate myocardial perfusion or compromised LV performance. Arrhythmias may develop although sinus rhythm persists in most of these neonates.[53] Most of these patients will require inotropic support, often in the form of dopamine at 3–10 μg/kg/minute. Many centers add nitroglycerine infusion at 1–2 μg/kg/minute to maximally dilate coronary arteries and reduce preload, and calcium chloride infusion to normalize ionized $Ca^{2+}$, which is so important to myocardial contractility in the newborn. There are several considerations unique to the ASO which deserve mention. Although uncommon, obstruction to translocated coronary arteries can be a significant problem after ASO. Signs of this problem include global myocardial dysfunction, detected clinically and with echocardiography; regional wall motion abnormalities do not appear to be as common in neonates. Ventricular arrhythmias in neonates are uncommon; when these occur after ASO and persist, a coronary artery problem must be ruled out. Neonates with TGA/IVS often undergo rapid deconditioning of the left ventricle after birth, making them intolerant of either excessive afterload or preload. Overdistention of the left ventricle is not tolerated, because excessive myofibril length places them too far to the right on the Starling curve. Increased afterload (hypertension) is also not tolerated. Thus, the hemodynamic goals for the ASO patient post-bypass should be to achieve adequate *CO* with the lowest possible *LAP*. In many patients, an *LAP* of 4–6 mmHg with systolic blood pressure in the 50–75 range achieves these goals. If the LV is overdistended (high and increasing *LAP* in the face of decreasing systemic pressure and *CO*), diuretics can be used, or if hemodynamic deterioration is rapid, removing blood from the central venous catheter until the *LAP* has decreased is effective. Some of these patients are so sensitive to intravascular and intracardiac volume that removing and reinfusing as little as 3–5 $cm^3$ of blood for blood gases may cause significant changes in *LAP* and systemic blood pressure.

Infusion of blood products to achieve hemostasis, hemodynamic instability, and edema of the myocardium and lungs following a long period of CPB can preclude chest closure at the end of the operation. A narcotic infusion may be continued during transport and postoperatively in these neonates as they are not suitable for early extubation.[40] Care should be taken during transport to the intensive care unit to maintain conditions present in the operating room. Specifically, the anesthesiologist should prevent major changes in ventilation, tracheal extubation, interruption of delivery of intravenous inotropes, loss of body temperature, and sudden changes in hemodynamics. Outcome of the ASO in the modern era is

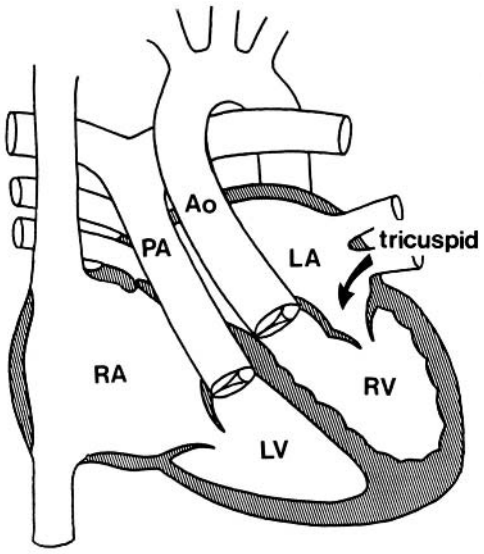


**Fig. 21.4** Congenitally corrected transposition of the great arteries. Ao, aorta; LA, left atrium; LV, left ventricle; PA, pulmonary artery; RA, right atrium; RV, right ventricle; tricuspid, systemic (tricuspid) atrioventricular valve. Reproduced from Karl TR, Weintraub RG, Brizard CP *et al*. Senning plus arterial switch operation for discordant (congenitally corrected) transposition. *Ann Thorac Surg* 1997; **64**: 495–502, with permission from Society of Thoracic Surgeons.

excellent, approaching 100% survival in most experienced centers.

## Congenitally corrected transposition of the great arteries

Congenitally corrected TGA is a rare congenital heart defect. It is a type of TGA with AV discordance in addition to VA discordance; hence it has AV–VA or double discordance. There are three main anatomic types with two ventricles, but this discussion will be limited to the most common anatomic type found in 94% of pathologic specimens.[54] This common anatomic type consists of the usual atrial arrangement (atrial situs solitus), left–right reversal of the AV connection, TGA, and a very high prevalence of Ebstein-like dysplasia of the systemic (tricuspid) AV valve and systemic RV dysplasia (Fig. 21.4). Other terms used to define this lesion include corrected transposition, ventricular inversion, l-transposition, double discordance, physiologically corrected transposition, discordant transposition, and inverted transposition.[55] The terminology atrial situs solitus, AV–VA discordance, and congenitally corrected TGA (ccTGA) will be used here. In the presence of AV–VA discordance, the LV receives blood from the RA then empties into the PA, and the RV receives blood from the LA then empties into the aorta. This provides a physiologic correction so that oxygenated pulmonary venous blood passes to the systemic circulation and deoxygenated systemic venous blood to the pulmonary circulation.[55] Associated malformations occur in up to 98% of patients and include VSD, LVOTO (often multilevel), abnormalities of the systemic (tricuspid) AV valve, abnormalities of the systemic RV, and AV conduction system abnormalities.[54,55]

### Physiology and natural history

The clinical course of patients with ccTGA is determined by the combination and severity of associated cardiac defects. Patients without associated defects are unusual, more likely to survive to adulthood, but often develop systemic (tricuspid) AV valve regurgitation, impaired systemic RV function, and rhythm disturbance after the age of 50 years.[56] Patients with associated defects may die as infants and children or live a shortened lifespan, and exhibit a spectrum of symptoms that ranges from none to cyanosis or heart failure.[56–58] Patients with cyanosis most often have a VSD and LVOTO that cause decreased *PBF* and a right-to-left shunt, and they thus may have undergone a palliative surgical procedure such as placement of an arterial to PA shunt to increase *PBF*. Patients with systemic RV failure tend to become symptomatic earlier, have a VSD with a left-to-right shunt and abnormalities of the systemic (tricuspid) AV valve, or both.[59] Patients may have a combination of cyanosis and heart failure and complete heart block, and are at increased risk to develop infective endocarditis.[58,59]

### Options for surgical correction

The "classical" option for complete surgical repair of patients with ccTGA is to repair the intracardiac associated defects and leave the systemic (tricuspid) AV valve and systemic RV connected to the aorta. Thus surgical procedures include VSD closure, alone or with relief of LVOTO, systemic (tricuspid) AV valve repair or replacement, and pacemaker placement. Perioperative mortality for "classical" repair ranges from 4% to 16%, and the 5- and 10-year survival estimates are 71–85% and 68–85%, respectively.[60–62] Preoperative systemic AV valve regurgitation and associated systemic RV dysfunction, present in many patients, can be an important risk factor for death after "classical" surgical repair.[59,63] Postoperatively, the systemic AV valve often develops regurgitation, even without surgical manipulation. This may be due to a change in geometry or increase in blood flow through the valve following surgical correction of an associated intracardiac defect.[60,63] Right ventricle dysfunction develops postoperatively in up to 55% of these patients, especially in patients with a high preoperative pulmonary to systemic blood flow ratio.[59,60,63] Intrinsic abnormalities of the cardiac conduction system are present in these patients and cause additional postoperative morbidity; specifically, the development of complete heart block in up to 24% of patients.[62]

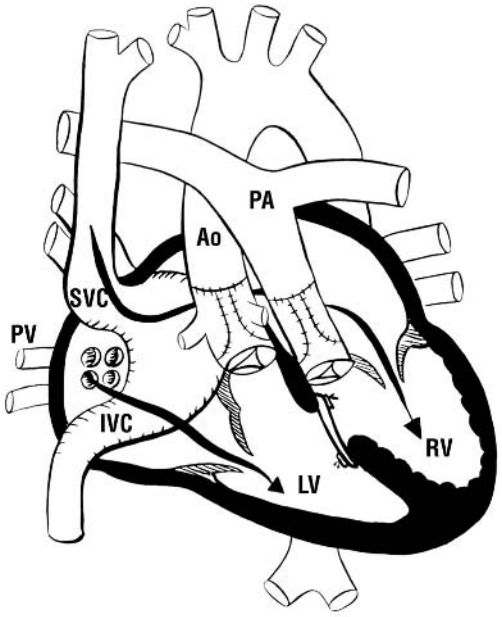


**Fig. 21.5** Senning and arterial switch operation (double switch). Ao, aorta; IVC, inferior vena cava; LV, left ventricle; PA, pulmonary artery; PV, pulmonary valve; RV, right ventricle; SVC, superior vena cava. Reproduced from Lundstrom U, Bull C, Wyse RKH *et al*. The natural and "unnatural" history of congenitally corrected transposition. *Am J Cardiol* 1990; **65**: 1222–9, with permission from Excerpta Medica Inc.

Concern about progressive dysfunction of the systemic AV valve and RV in patients with ccTGA led to the development of anatomic correction for these patients and the "double-switch" operation, i.e. a combination of the Senning and ASO procedures so that the mitral valve and LV become the systemic AV valve and ventricle (Fig. 21.5).[64] Before the LV can become the systemic ventricle, some patients must undergo preoperative placement of a PAB to provide an increase in LV pressure and mass, i.e. "retraining" of the LV. Placement of a PAB is not risk free and may be less successful in patients post-puberty.[65–67] Overall, the Senning and ASO procedures are indicated in patients with systemic RV deterioration and systemic AV (tricuspid) valve regurgitation. Patient selection criteria include a competent mitral valve and good LV function, balanced ventricular and AV valve sizes, no major AV valve straddling, translocatable coronary arteries, LV : RV pressure ratio greater than 0.7, and unobstructed connections to both great vessels.[64,67] A conceptually similar procedure has been performed successfully on patients with ccTGA and VSD with obstructed connection to the PA, incorporating the Senning and Rastelli (insertion of a valved conduit between the RV and PA) procedures.[68] Presently, the perioperative mortality for Senning and ASO procedures is 7–9%, and survival after 2–7 years is 70–91%.[69,70] Postoperative venoatrial obstruction and arrhythmias may limit the application of this procedure, as in prior patients who underwent Senning or Mustard operation for TGA.[69,70] Long-term results of this procedure are unknown but anatomic findings support the opinion that it may be a better surgical option in selected patients.[54] Left ventricle dysfunction may occur because of the new systemic load placed on it, even after a preparatory PA banding, which seldom leaves the LV with systemic pressures. Excessive afterload (hypertension) is not tolerated in these patients, and again the goals should be to achieve adequate *CO* at low left atrial and systemic pressures. The intracardiac Senning baffle may obstruct superior vena cava or inferior vena cava inflow, or may impinge on pulmonary venous orifices, causing pulmonary venous hypertension. Both problems are detectable by TEE and/or direct pressure measurement, and are a cause of low *CO*, and must be corrected immediately. Whether the double switch is the Senning/ASO or the Senning/Rastelli variety, it can be one of the longest and most challenging anesthetics for the pediatric cardiac anesthesiologist.

## Anesthetic considerations

Careful preoperative assessment of these patients includes a thorough history and physical examination and review of baseline cardiac anatomy, presence of associated intracardiac defects, prior surgery performed and residual defects, and evaluation for signs and symptoms of cyanosis and heart failure. It is important to note the presence and degree of systemic (tricuspid) AV valve regurgitation, the status of systemic RV function, and any cardiac conduction system abnormalities. Functional status and mass of the LV must be evaluated in patients who have undergone PAB placement for LV "retraining."

Preoperatively, patients can be quite ill. Some can be dependent on a ventilator and inotropes, while others have complete heart block and are dependent on a pacemaker.[68] Although rare, older patients can have angina and abatement of symptoms with nitrate therapy but normal coronary artery anatomy.[59]

Anesthetic management of the patient with systemic AV valve regurgitation and systemic RV dysfunction is aimed at decreasing RV pressure load by careful control of arterial blood pressure. Care should be taken to prevent sudden increases in arterial blood pressure in response to stimulation from tracheal intubation, placement of invasive monitoring lines, or surgical stimulation.

After completion of the Senning and ASO, TEE is used to detect venoatrial obstruction, assess biventricular function, detect residual defects, assess valvular function, evaluate neo-aortic valve regurgitation, and detect a gradient at the supravalvar anastomotic sites of the great arteries.[51] Intracardiac lines can be used to measure right atrial pressure and *LAP* to evaluate RV and LV function and to deliver inotropes. Bleeding can be brisk and coagulation defects as expected from a long period of CPB. These patients are not candidates for early extubation, and those in whom the LV is unable to

function as well as the systemic ventricle can require extracorporeal support postoperatively.

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# 22 Anesthesia for the patient with a single ventricle

Susan C. Nicolson
James M. Steven

## Introduction

In the early 1970s, Fontan[1] and Kreutzer[2] independently introduced operative treatment of tricuspid atresia that resulted in nearly normal systemic arterial oxygen saturation and normal volume work for the single ventricle. This procedure, subsequently referred to as the Fontan operation, created a series circulation which requires the single ventricle to pump fully saturated blood only to the systemic circulation, thereby reducing the pressure and volume work to that of a normal systemic ventricle. The systemic venous drainage passes directly through the pulmonary vascular bed without benefit of a pumping chamber. The child's pulmonary vascular resistance (*PVR*) must be low to maintain the pulmonary circulation and the cardiac output (*CO*) on which it depends. Since that time, the principle of the Fontan operation has been applied to the full spectrum of cardiac lesions with one functional ventricle. Suitable physiology for ultimate repair by a modification of the Fontan procedure is predicated on carefully planned, appropriately timed and executed palliative operations designed for the specific patient's single ventricle physiology. This chapter will illustrate these principles using hypoplastic left heart syndrome (HLHS), the most common congenital cardiac malformation where there is only one developed ventricle. Hypoplastic left heart syndrome represents the fourth most common defect presenting in the neonatal period and accounts for 7.5% of the newborns with congenital heart disease sufficiently significant to require early therapeutic intervention.

A variety of anatomic lesions may be classified as producing single ventricle anatomy or physiology, also referred to as a univentricular heart (Fig. 22.1). Most of these lesions have both atrioventricular (AV) valves committed to a single systemic ventricular chamber, or atresia/severe stenosis of one of the AV valves. Many of these hearts actually have two ventricles, although one of the ventricles is typically small with minimal contribution to cardiac ejection, thus it is functionally considered a single ventricle. Finally, some patients have two ventricles of normal size which cannot be separated because a ventricular septal defect (VSD) is remote from either great vessel, or because of straddling of the AV valve attachments over the VSD, or very large intraventricular communications that cannot be septated.

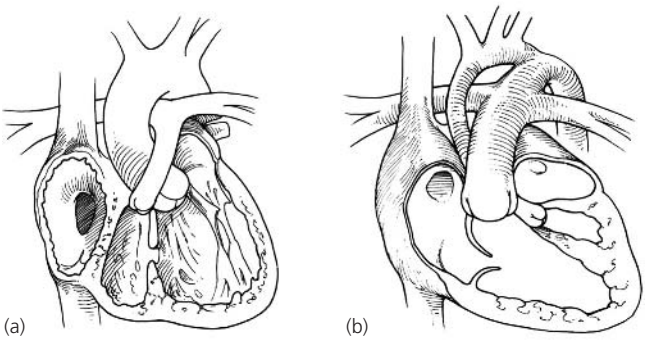


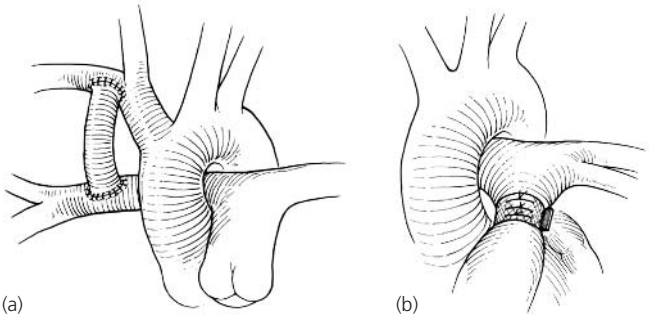

**Fig. 22.1** Basic anatomical features of tricuspid atresia (a) and hypoplastic left heart syndrome (b). In tricuspid atresia, pulmonary blood flow depends on the degree of hypoplasia of the pulmonary valve and artery. In hypoplastic left heart syndrome, there may be atresia or stenosis of the aortic and mitral valves, but all variants have a small or non-existent left ventricle and a hypoplastic ascending aorta. Reproduced with permission from Wernovsky G, Bove EL. Single ventricle lesions. In: Chang C, Hanley FL, Wernovsky G, Wessel DL, eds. *Pediatric Cardiac Intensive Care*. Baltimore, MD: Williams & Wilkins, 1998: 271–87.

After assessment of the details of the cardiac anatomy, the initial approach to the single ventricle patient is to determine the degree of pulmonary blood flow (*PBF*) and whether the pulmonary circulation is dependent on the ductus arteriosus. Patients with ductal dependent circulation will require a reliable source of *PBF*, accomplished by creation of a systemic-to-pulmonary shunt. The most common shunt performed is a modified Blalock–Taussig (BT) shunt, in which a Gortex® tube graft connects the innominate or subclavian to the pulmonary artery (PA) (Fig. 22.2). Some single ventricle patients will have unrestricted flow to both the PA and aorta. Such patients usually develop progressive congestive heart failure as the *PVR* decreases in infancy, and require PA banding to

**Table 22.1** Initial surgical strategy for single ventricle patients.

| Anatomy | Surgical intervention |
|---|---|
| 2 Semilunar valves of adequate size, normal aortic arch | Pulmonary artery band |
| 1 Semilunar valve, normal aortic arch | BT shunt |
| 1 Semilunar valve, hypoplastic aortic arch | Aortic arch reconstruction with BT shunt, or Norwood procedure |
| 2 Semilunar valves, aortic stenosis | Damus, Kaye, Stanzel with BT shunt (possible aortic arch reconstruction) or palliative arterial switch |
| 2 Semilunar valves with pulmonary stenosis | No initial intervention required |

BT, Blalock–Taussig.



(a) (b)

**Fig. 22.2** (a) Right modified Blalock–Taussig shunt. A 3–4 mm Goretex® graft is sewn between the right subclavian or innominate artery and the right pulmonary artery. (b) Pulmonary artery banding. An umbilical tape or similar material is placed around the main pulmonary artery to limit pulmonary blood flow.

limit *PBF* and to protect the pulmonary circulation from high flow and pressure that can eventually cause irreversible pulmonary disease (Fig. 22.2). Finally, an occasional single ventricle patient will have will have a combination of pathologic abnormalities (restrictive VSD, pulmonary stenosis) providing the appropriate amount of *PBF* and obviating the need for immediate surgical intervention (Table 22.1).

## Hypoplastic left heart syndrome—pathophysiology (Fig. 22.3)

The left ventricle is a non-functional structure in the child with HLHS. Pulmonary venous return must be routed to the right atrium through a stretched foramen ovale, an atrial septal defect (ASD), or rarely by total anomalous pulmonary venous connection. Systemic and pulmonary venous returns mix in the right atrium. The right ventricle (RV) supplies both the systemic and pulmonary circulations in a parallel fashion, since the main PA gives rise to the branch pulmonary arteries as well as the systemic circulation via the ductus arteriosus. Blood flows retrograde from the ductus arteriosus through the transverse aortic arch to its branches, and through the ascending aorta to the coronary arteries. Flow to the lower body is antegrade from the ductus arteriosus via the descending aorta. Ductal closure results in inadequate systemic and coronary perfusion, leading to progressive metabolic acidemia, ischemia and death.

Although uncommon, ductal narrowing will result in reduced systemic blood flow. The compensatory increase in right ventricular pressure necessary to provide sufficient systemic perfusion may cause an increased *PBF* ($Q$p) to systemic blood flow ($Q$s) ratio ($Q$p : $Q$s) thereby mimicking the findings of unrestrictive *PBF*.

With the pulmonary and systemic arteries connected in parallel, the $Q$p : $Q$s depends on a delicate balance between the pulmonary and the systemic vascular resistance (*SVR*).

## Stage I reconstruction (Norwood operation)

The basic surgical approach is illustrated in Fig. 22.4.

### Preoperative management

Much of the preoperative management of neonates with HLHS entails optimizing the condition of the cardiovascular and other organ systems. The key to management of HLHS perioperatively rests with the ability to assess and manipulate systemic perfusion and $Q$p : $Q$s. While clinicians have traditionally relied on estimates based upon systemic oxygen saturation, data from Rychik *et al*.[3] comparing accuracy of Doppler flow patterns in the aorta to other methods of estimating $Q$p : $Q$s reveal a weak correlation between systemic oxygen saturation and measured $Q$p : $Q$s. Although cumbersome for routine evaluations, Doppler flow patterns are substantially more accurate and precise in evaluation of $Q$p : $Q$s. When available, the addition of data to quantify systemic output and $Q$p : $Q$s, such as mixed venous oxygen saturation[4,5] or Doppler aortic flow patterns, has greatly improved the assessment and appropriate intervention in neonates with HLHS. This information assumes even greater importance in the volatile physiology exhibited in the early postoperative period.

In the preoperative period, neonates with HLHS who have been stabilized and who are not impaired by other vital organ system dysfunction, are initially assumed to be able to

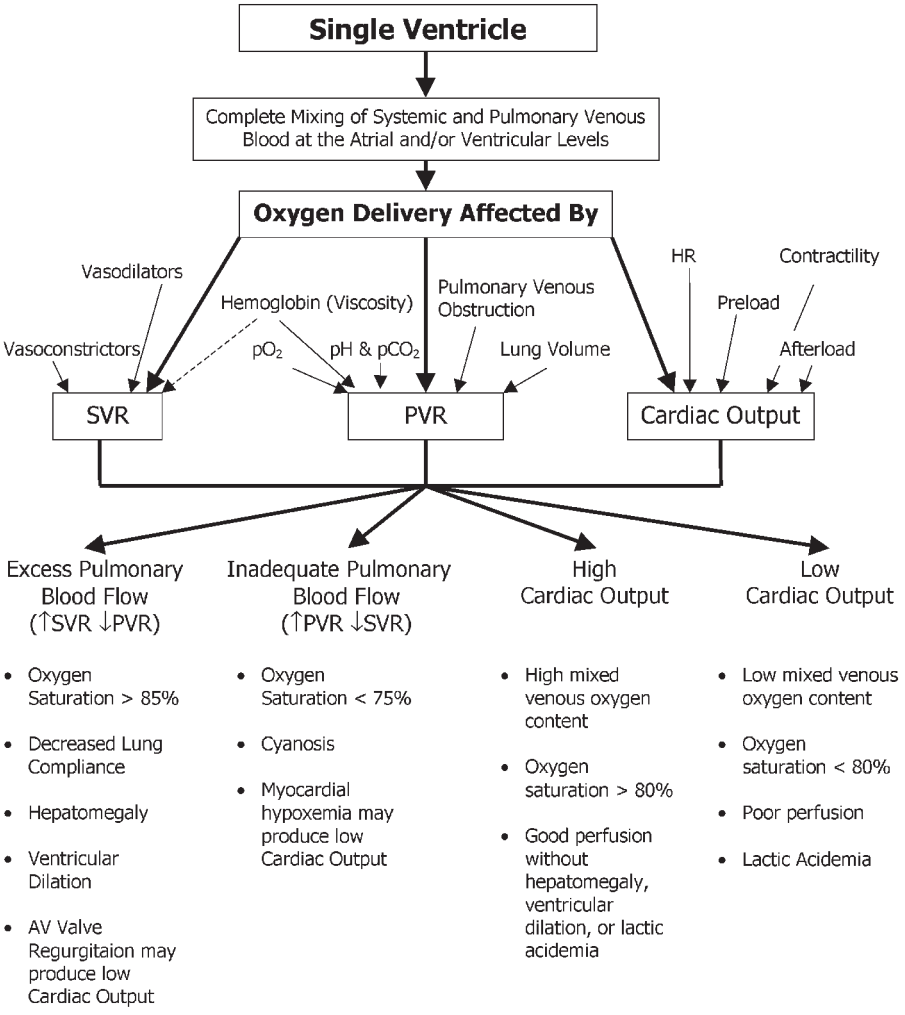



**Fig. 22.3** Single ventricle pathophysiology. There is complete mixing of systemic and pulmonary venous blood in the ventricle, and oxygen delivery is affected by the balance between the systemic vascular resistance (*SVR*), the pulmonary vascular resistance (*PVR*), and the cardiac output (*CO*). Optimal oxygen delivery is provided by a balance between *SVR* and *PVR*, and maintaining good *CO*. AV valve, atrioventricular valve; *HR*, heart rate.

maintain satisfactory balance in *Q*p : *Q*s. The goal for such patients is to allow spontaneous ventilation via a natural airway. The majority of neonates meet this objective.

The most common imbalance of *Q*p : *Q*s typically manifests itself with signs of inadequate systemic output and relative excess in *PBF*. These signs might include hypotension, lactic acidosis, and diminished urine flow in the context of relatively high systemic oxygen saturation. Once assured of an adequate circulating intravascular volume, oxygen carrying capacity, and a non-restrictive patent ductus arteriosus, therapeutic measures are often directed at increasing *PVR*. In order to obtain selective constriction of the pulmonary vasculature, clinicians have employed gas mixtures that either reduced alveolar $P_{O_2}$,[6] promoting hypoxic pulmonary vasoconstriction, or increased alveolar $P_{CO_2}$[7] to achieve constriction via local effects on pH or tissue carbon dioxide.[8] Either of these ambient gas manipulations can be accomplished by placing the infant in a hood supplemented with nitrogen or carbon dioxide, respectively. Controversy persists as to the comparative efficacy of these strategies.[9] Caution must be used when altering the inspired gas mixtures in neonates breathing spontaneously while receiving prostaglandin $E_1$ by infusion. Mild hypoventilation can result in significant hypoxemia in neonates breathing an $F_{IO_2}$ below 0.21. Although increased inspired carbon dioxide has been shown to improve oxygen delivery in the anesthetized neonate under conditions of controlled ventilation,[10] the increased oxygen consumption associated with carbon dioxide induced tachypnea in the spontaneously breathing patient might negate the benefits observed in the anesthetized patient.

Anatomic variables can have a major impact upon the observed physiology. Some restriction to pulmonary venous return, such as occurs with left-to-right flow across the foramen ovale, is desirable as it tends to balance pulmonary and systemic resistance, and thus *Q*p : *Q*s. Infants who lack that restriction, such as those with an ASD or unrestrictive anomalous pulmonary venous return, tend to exhibit high *Q*p : *Q*s. In contrast, those who have severely obstructed pulmonary venous return, such as the few who present with an intact atrial septum and no alternative decompressing vein,

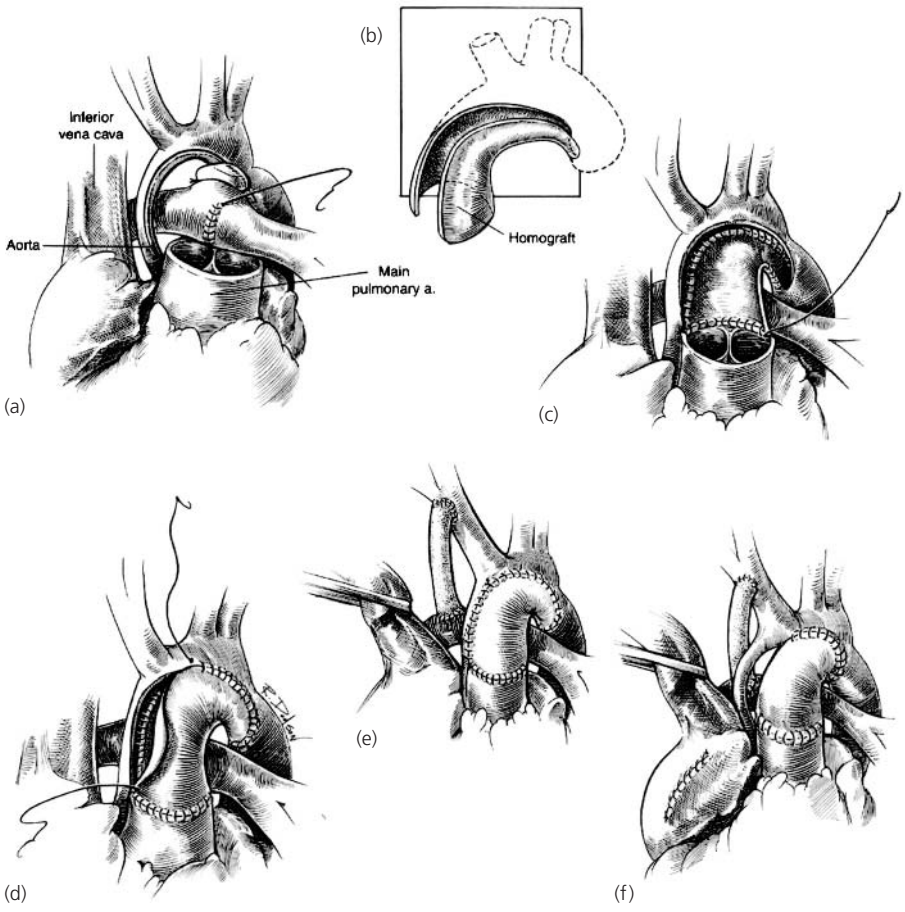



**Fig. 22.4** The Norwood stage I palliation for hypoplastic left heart syndrome. (a) Incision of hypoplastic ascending aorta and preparation of the native pulmonary valve to become the neo-aortic valve. (b) Cutting of a homograft patch to augment the neoaorta. (c,d) Construction of the noe-aorta. (e,f) Completion of the Blalock–Taussig shunt and final anatomy. Reproduced with permission from Casteñeda AR, Jonas RA, Mayer JE, Hanley FL. Hypoplastic left heart syndrome. In: Casteñeda AR, Jonas RA, Mayer JE, Hanley FL, eds. *Cardiac Surgery of the Neonate and Infant*. Philadelphia, PA: Saunders, 1994: 363–85.

have an extremely low *Q*p : *Q*s. Despite therapeutic maneuvers designed to lower *PVR* and promote *PBF*, these infants exhibit marked hypoxemia that requires urgent intervention to decompress pulmonary venous return in order to have any hope of survival.

Preoperative evaluation and stabilization should also include a survey of other vital organ systems for congenital or acquired abnormalities. Our recent series including 102 newborns with HLHS indicates that approximately 15% have some genetic syndrome or significant non-cardiac malformation.[11] The magnitude and distribution of acquired vital organ dysfunction usually relates to circulatory instability at the time of diagnosis. Infants that have suffered a profound or protracted shock state at the time of diagnosis can demonstrate a wide spectrum of injury to renal, central nervous system (CNS), cardiac, gastrointestinal[12,13] or hepatic systems. These derangements may necessitate a delay in operative intervention to permit recovery.

Hypoplastic left heart syndrome is increasingly being diagnosed *in utero* allowing for planned management at delivery suggesting greater stability through more controlled circumstances. A study of patients with critical left heart obstructive lesions (including HLHS) showed greater hemodynamic stability and a lower incidence of preoperative neurologic events in those patients with prenatal diagnosis.[14]

## Intraoperative management

Although the vast majority of neonates presenting for stage I reconstruction (e.g. Norwood or Sano operation) receive an intravenous induction of anesthesia, virtually any anesthetic agent can be used for this purpose with careful attention to the hemodynamic consequences of the technique selected. We prefer the phenylpiperidine-based synthetic opioids (e.g. fentanyl) because they blunt the endogenous catecholamine response to noxious stimuli at doses that are usually tolerated hemodynamically.[15–17] However, even with these hemodynamically "neutral" agents, large doses may result in significant cardiovascular changes, such as bradycardia and hypotension. These observations suggest that the neonate with HLHS requires some endogenous catecholamine release to sustain satisfactory hemodynamics. Unfortunately, this threshold dose that separates "sufficient" from "excessive" varies between patients, necessitating individual titration to arrive at the optimal dose.

Although clinical research conducted more than a decade

ago popularized the view that massive doses of opioid analgesics should be administered perioperatively to effect stress hormone suppression in neonates undergoing cardiac surgery,[18] recent efforts to duplicate these findings have not confirmed the original results.[19] The latter demonstrated that massive doses of fentanyl did not completely suppress release of endogenous catecholamines, even in combination with benzodiazepine infusions. However, outcome measures were no different in any of the study groups. We typically employ total intraoperative fentanyl doses between 50 and 75 μg/kg followed by a fentanyl infusion (2–5 μg/kg/hour) begun postoperatively in the cardiac intensive care unit (CICU).

Management of the airway and ventilation assumes great importance during induction of anesthesia. Given the propensity for the majority of neonates with HLHS to exhibit excessive *PBF*, the anesthesiologist must take care not to employ ventilatory maneuvers that lower *PVR*, such as hyperventilation with high concentrations of oxygen. In an infant with typical HLHS physiology, one might initiate manual ventilation with air or a low concentration of supplemental oxygen. The extent to which the anesthesiologist adjusts $F_{IO_2}$ prior to laryngoscopy would depend upon the magnitude of hemodynamic response to the initiation of controlled ventilation. Infants who demonstrate significant reduction in systemic arterial pressure despite low $F_{IO_2}$ may not tolerate prolonged exposure to high $F_{IO_2}$ without deleterious hemodynamic consequences. Means of increasing *PVR*, as discussed previously, should be available in the operating room. We favor inspired carbon dioxide for several reasons. It tends to augment systemic arterial pressure immediately. Nor does it require neutralization of all safety systems designed to avoid delivery of a hypoxic gas mixture. Finally, as a gas of some historical importance in anesthesia delivery systems, it is available with flow meters in appropriate clinical ranges. Tabbutt *et al*.[10] in a recent clinical comparison of intubated, paralyzed, and anesthetized neonates with HLHS, demonstrated that inspired carbon dioxide proved consistently more effective than hypoxic gas mixtures at increasing indices of systemic output, including systemic arterial pressure and oxygen delivery.

## Hypoplastic left heart syndrome with obstruction of pulmonary venous outflow

Management changes significantly in the context of an infant with extremely high *PVR* and very low *Q*p : *Q*s, such as the infant with an intact atrial septum. Despite transient hemodynamic and metabolic stability that might ensue with aggressive maneuvers designed to lower *PVR* and promote *PBF*, these infants exhibit marked hypoxemia that requires urgent surgical intervention to decompress pulmonary venous return in order to have any hope of survival. Whether this intervention includes the entire stage I reconstruction, or is limited to an atrial septectomy with a planned return following a period of assessment and recuperation, remains a surgical judgement for which little supporting data exist.[20,21] If tolerated hemodynamically, a higher dose of opioid affords the advantage of blunting the response that any noxious stimulus might have on *PVR*. Substantial ventilation with high $F_{IO_2}$ is typically necessary to achieve marginal gas exchange. When systemic oxygenation falls below a threshold value, temporizing measures designed to diminish metabolic demand deserve strong consideration, such as surface cooling of particularly vulnerable organs (e.g. CNS). The use of sodium bicarbonate to address metabolic acidemia in the face of extremely limited *PBF* offers limited benefit, and may even pose hazard. The elimination of carbon dioxide following bicarbonate hydrolysis is severely impaired. Thus, bicarbonate administration will often result in a shift from metabolic to respiratory acidemia with little change in pH and the attendant prospect of highly undesirable increase in *PVR*.

Intraoperative monitoring consists of invasive continuous arterial pressure in addition to standard cardiovascular, respiratory, and temperature monitors. In order to minimize the hazard of thrombosis in the central thoracic veins in all single ventricle patients, we employ direct transthoracic atrial lines in lieu of percutaneous jugular or subclavian central venous pressure catheters. In addition, an umbilical venous catheter positioned in the orifice of the superior vena cava (SVC) at the time of surgery serves as a valuable monitor of mixed venous oxygen saturation, enabling more precise assessment of systemic *CO* and *Q*p : *Q*s.[4,5,10]

At the termination of cardiopulmonary bypass (CPB), the physiologic goals are identical to those expressed preoperatively, although the proclivities are quite different. The pulmonary circulation now resides at either the distal end of a restrictive prosthetic systemic-to-pulmonary shunt or an RV-to-PA tube graft (Sano modification—Fig. 22.5). At our institution, we have far more experience with the systemic-to-PA shunt arrangement. A variety of subtleties in the technical execution of this shunt, relief of atrial obstruction, and pre-existing condition of the pulmonary circulation can render the ultimate physiology somewhat unpredictable. Technical issues of graft insertion, proper graft size, particularly in the neonate under 2.0 kg, and the ability to delineate the etiology of insufficient *PBF* on termination of CPB, introduce additional complexities in a number of patients where a Sano modification has been performed. Given our limited experience managing patients with an RV-to-PA tube graft, subsequent discussion will be limited to patients having their *PBF* provided by a systemic-to-PA shunt, which is far less prone to excessive *PBF* than the native anatomy.

Measures to assure a clear airway and complete re-expansion of the pulmonary parenchyma are performed in the terminal phases of rewarming on bypass. The magnitude of reduction in the mean systemic arterial pressure that occurs with trial opening of the shunt during the terminal

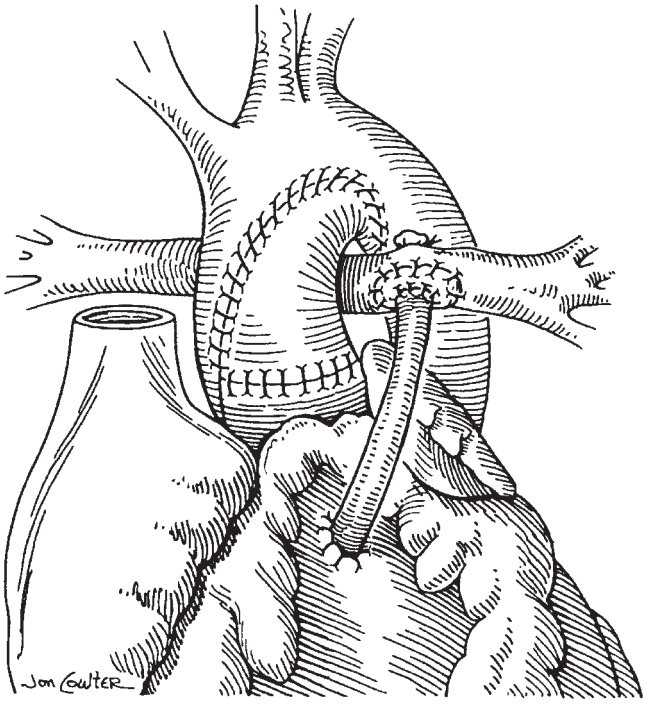


**Fig. 22.5** The Sano modification of the Norwood stage I operation. Instead of a right modified Blalock–Taussig shunt, pulmonary blood flow is provided by a right ventricle to pulmonary artery conduit, usually a 5-mm Goretex® graft. Reproduced with permission from Pizarro C, Malec E, Maher KO *et al*. Right ventricle to pulmonary artery conduit improves outcome after stage I Norwood for hypoplastic left heart syndrome. *Circulation* 2003; **108**: II155–60.

phase on CPB can provide qualitative insights as to what *PVR* one might expect in the early post-bypass period. Initial ventilatory support should be adjusted accordingly. In general, we begin with a pattern of ventilation designed to result in low–normal $P_{ACO_2}$ and a $F_{IO_2}$ between 0.6 and 1.0, recognizing that adjustments become necessary in all patients as indicated by the individual infant's physiology. In addition, the physiology typically demonstrates dynamic change over time, requiring continuous surveillance and further adjustment. Assuming a technically satisfactory repair and no unusual risk factors, *PVR* typically falls in the first few hours after surgery.

Despite a perfect technical result, the Norwood operation does not result in any reduction of the volume or pressure burden placed on the single ventricle, as the physiology of parallel systemic and pulmonary circulations where a $Q_P : Q_S$ of unity remains the objective throughout the postoperative period. Yet the heart incurs the cost of insults related to cessation of coronary perfusion, CPB, and hypothermic circulatory arrest (HCA). This may account for the cardiovascular frailty exhibited by these infants in the early postoperative period. However, in the absence of major deficiencies in myocardial protection or persistent anatomic residua, such as significant arch obstruction, coronary compromise, or valvar insufficiency, this magnitude of myocardial dysfunction can usually be ameliorated with relatively modest doses of inotropic agents (e.g. dopamine at 3–5 μg/kg/minute). In a time course characteristic of many major cardiac interventions in neonates and young infants, myocardial performance may deteriorate in the first 6–12 hours postoperatively before they start to improve. As a result, we routinely take measures to reduce metabolic demands by continuous muscle relaxant (e.g. pancuronium 0.05–0.10 mg/kg/hour) and opioid (e.g. fentanyl 2–5 μg/kg/hour) infusions. Infants demonstrating increased *SVR* during rewarming on CPB often receive a loading dose of milrinone at that time. Zuppa *et al*.[22] recently described the pharmacokinetics of milrinone in 16 neonates with HLHS given a loading dose of milrinone on CPB at the time of rewarming. These investigators recommend a loading dose of 100 μg/kg, followed by initiation of an infusion (0.2 μg/kg/minute) within 90 minutes of the bolus dose to achieve and maintain plasma concentrations similar to those reported in other therapeutic settings. No data exist to guide the bolus and/or infusions doses when milrinone is begun after termination of CPB.

Modified ultrafiltration (MUF) conducted immediately following CPB has been demonstrated to exert beneficial effects upon hematocrit, hemodynamics, hemostasis, pulmonary function, and CNS recovery.[23–27] Perioperative weight gain is reduced significantly as are certain inflammatory mediator levels. Whenever possible, we conduct MUF at the termination of CPB following stage I reconstruction. Occasionally, the position of the bypass cannulae or the continuous flux of blood through the MUF circuit results in unfavorable hemodynamic changes precluding completion of the filtration. In 99 consecutive patients undergoing stage I between September 2000 and August 2002, all tolerated the pertubations of MUF.

Stage I reconstruction requires substantial suture lines in creation of the neo-aorta. Thus, rapid restoration of normal hemostasis represents an important early postoperative objective. Following MUF, once satisfied with the technical and physiologic result of the repair, heparin effect is reversed with protamine. Given the risk factors that jeopardize platelet number and function, including deep hypothermia and profound dilution of circulating volume on CPB,[28] replacement of blood loss with fresh whole blood (< 48 hours old) restores hemostasis more effectively than other blood products.[29] Fresh whole blood replacement also serves to minimize donor exposure to those patients who are anticipated to require three open heart surgical interventions. Should these measures fail to achieve adequate hemostasis despite elimination of all surgical bleeding sites, laboratory testing should be conducted to direct component therapy at those elements of the hemostatic pathway most likely to be impaired: platelet and fibrinogen replacement. Reports of antifibrinolytic therapy in the very young are largely limited to aprotinin.[30,31] The

volume of blood loss can be reduced by high dose aprotinin but it may not be clinically important since donor exposures are not necessarily affected.

Prompt control of hemostasis resulting in reduced transfusion requirement can be associated with a reduced need for re-exploration for bleeding. Re-exploration in patients under 2 years of age undergoing complex surgery at our institution, which includes all patients with a single ventricle, was reduced (from 3.0% to 0.8%) following the adoption of the routine use of fresh whole blood. Cardiac tamponade can easily occur from a small quantity of mediastinal blood accumulated in the early postoperative period before bleeding has completely ceased. Continuous removal is essential because blockage easily occurs in the relatively small mediastinal drainage tubes of these neonates. A technique of active, continuous aspiration of accumulating blood from the mediastinum has virtually eliminated this complication.[32]

## Common problems in the early post-bypass period

Excessive hypoxemia represents one of the more commonly encountered problems in the early post-bypass period. Although inadequate *Q*p : *Q*s becomes the assumed cause, factors that impair systemic oxygen delivery thereby reducing mixed venous oxygen saturation are now known to be more common than previously believed.[3,4,5,33] One typically observes a progressive increase in systemic oxygen saturation during MUF, for example, probably due to the impact that hemoconcentration and the resulting increased oxygen delivery have upon mixed venous oxygen saturation. Thereafter, measures directed at maintaining hematocrit above 40–45% may alleviate excessive demands placed upon the recovering heart to increase systemic output. The distinction between systemic hypoxemia due to low *Q*p : *Q*s, low pulmonary venous oxygen saturation, or low mixed venous saturation is a critical one, as the therapies are diametrically different. Measures designed to reduce *PVR* will impose a further volume load on a heart already struggling to provide marginal systemic perfusion. Patients demonstrating low $Svo_2$ would be better served with therapies that promote systemic output, such as inotropic agents or vasodilators.

Similarly, those with low pulmonary venous oxygen saturation require a strategy of ventilatory support designed to reduce atelectasis and promote gas exchange in impaired alveoli. Unfortunately, the latter diagnosis is rarely made definitively in the OR or CICU, as blood sampling from the pulmonary veins presents logistic challenges. Intraoperatively, expectant measures directed at expansion of the lungs and maintenance of normal functional residual capacity usually suffice to avoid pulmonary vein desaturation. Among the three etiologies of persistent systemic hypoxemia, this was believed to be the least common, but a recent series found pulmonary vein desaturation in as many as 30%.[34]

When systemic hypoxemia occurs due to low *Q*p : *Q*s, other manifestations provide supporting evidence. Trial opening of the systemic-to-PA shunt during the latter phases of rewarming on CPB fails to demonstrate significant drop in the mean systemic arterial pressure. The early post-bypass hemodynamics reveal a relatively narrow pulse pressure and/or high diastolic pressure. A substantial discrepancy exists between arterial and end-tidal carbon dioxide measurements. These suggestive pieces of inferential evidence can be confirmed by aortic Doppler flow analysis or calculation of a Fick ratio using oxygen saturation determinations. Most commonly, diminished *PBF* reflects a subtle technical aspect of the arch reconstruction, innominate artery dimension, or the BT shunt. However, certain patient subsets exhibit profound abnormalities in the pulmonary vasculature that cause excessive *PVR* elevations. Neonates with HLHS routinely demonstrate extremely high and volatile *PVR* when born with extreme pulmonary venous obstruction due to intact atrial septum without alternative decompressing veins. Even the typical HLHS anatomic constellation is associated with marked abnormalities in the number and muscularization of the pulmonary vasculature by pathologic examination.[35] Hypotheses attribute these changes to chronic fetal pulmonary venous obstruction.[36] One can speculate that these changes become more extreme in the context of the marked obstruction caused by HLHS with intact atrial septum. Fetal echocardiography has confirmed alteration in pulmonary venous flow pattern in relation to the magnitude of restriction at the atrial septum.[37]

In the context of hypoxemia due to low *Q*p : *Q*s, interventions fall into three categories: technical, pulmonary vasodilation, and systemic vasoconstriction. In the context of patients expected to have unusually elevated *PVR*, modifications in the surgical technique might entail placement of a larger shunt or interposition between a larger systemic vessel (e.g. aorta) and pulmonary arteries. Pulmonary vasodilator therapy includes the strategies one might employ in any patient demonstrating elevated *PVR*, such as oxygen, moderate hyperventilation, normothermia, alkali, and nitric oxide.[38–40] Should those measures prove insufficient to result in adequate *PBF*, the focus might be expanded to include measures designed to increase the driving pressure across the shunt, using higher doses of inotropic infusions or even vasoconstrictors. The latter necessitates careful monitoring to avoid jeopardizing perfusion to other vital organs.

Depressed myocardial performance represents another potential problem in the early post-bypass period. As mentioned previously, some degree of myocardial dysfunction typically occurs following this procedure as there is no hemodynamic benefit achieved to offset the cost of CPB and an ischemic interval. When this dysfunction becomes more significant than usual, specific causes should be sought. Even in the context of the typical conduct of stage I reconstruction, the consequences of aortic atresia make routine myocardial

protection measures, such as the infusion of cardioplegia solutions, challenging. Thus inadequate myocardial preservation represents one potential cause for persisting or excessive myocardial depression.

Technical considerations represent the predominant cause of myocardial dysfunction following this complex intervention. One of the most intricate aspects of this procedure is the reconstruction of an aortic arch in such a way that the small ascending aorta, which principally serves to provide coronary flow, is not compromised. This subtle finding may not become evident until the cardiac volume is restored in anticipation of terminating CPB. Residual hemodynamic derangement represents another potential cause of myocardial dysfunction. Given that under the best of circumstances, one emerges from the Norwood operation with no appreciable hemodynamic benefit, one would expect a result with newly imposed volume or pressure loads to be poorly tolerated. Examples of such findings would include: residual aortic arch obstruction, AV valve dysfunction, and semilunar valve obstruction or regurgitation.

Metabolic disturbances also result in significant myocardial dysfunction. This fragile RV struggling to cope with significantly increased volume output demands at systemic pressure is perhaps more susceptible to what might otherwise be modest metabolic disturbances. As such, one should track and address those variables that have impact upon myocardial performance, such as ionized calcium and lactic acidosis. The rapid administration of blood products, for example, which contain calcium-binding drugs, high levels of potassium and lactic acid, as well as other vasoactive mediators, can result in an acute, profound deterioration in cardiac performance in the early postoperative period. In our experience, myocardial performance will deteriorate when the arterial pH falls below 7.3 and may contribute to further reduction in *Q*s. The administration of intravenous bicarbonate, calculated to completely eliminate the base deficit, often exerts a beneficial effect on both myocardial performance and *Q*s. In addition to the inherent cardiac sensitivity, inescapable anatomic peculiarities accentuate this vulnerability. Blood carrying the transfused products from the systemic venous circulation enters the RV and is directed immediately to the reconstructed aorta, whereby the first branch is the coronary circulation. Thus constituents of the transfused blood (e.g. citrate, potassium, lactate) infused into the venous circulation arrive at the coronary arteries with greater speed and concentration than might have occurred had they been dissipated over the course of the pulmonary vasculature before entering the aorta. This effect is further accentuated if central venous catheters are employed to infuse the blood product. We abide by a protocol whereby blood transfused via central lines or rapidly through peripheral catheters is either fresh whole or washed packed cells.

Arrhythmias most commonly occur as manifestations of the problems described previously. When they become manifest early in the process of rewarming on CPB, coronary insufficiency represents the most common cause, particularly if the arrhythmia is ventricular in origin. Metabolic disturbances produce the same qualitative rhythm changes seen in normal hearts, although the manifestations might be more extreme. Given the predominantly extracardiac nature of the Norwood procedure, acquired heart block rarely follows this operation, unless it existed preoperatively. On rare occasions, a patient presents with HLHS and a primary arrhythmia, such as Wolff–Parkinson–White syndrome.

Excessive *PBF* may complicate the early postoperative period; however, this diagnosis should be entertained cautiously. In many instances, the apparent excess *PBF* really reflects a relative imbalance with respect to significantly diminished systemic *CO* (*Q*s). The latter should be specifically excluded or addressed before invoking extreme measures to restrict *PBF*. Of course, subtle technical differences in the conduct of the operation can result in an anatomic propensity to an excessive *Q*p : *Q*s, and this can, in turn, jeopardize systemic perfusion. Such patients typically exhibit an extremely wide pulse pressure or low diastolic pressure reflecting pulmonary "runoff". If myocardial performance otherwise appears robust, the specific measures employed to increase *PVR* preoperatively are appropriate in this setting. In most patients, this condition dissipates as the infant recovers from surgery. Should the problem persist beyond the first postoperative day, a cardiac catheterization should be considered to evaluate the need for further surgical intervention aimed at diminishing *PBF*.

The volume work of the single ventricle after stage I reconstruction is equal to the sum of the systemic and *PBF* (*Q*p + *Q*s). After a period of maturation of the pulmonary vasculature, systemic venous return may be directed to the pulmonary arteries, thus placing the two circulations in series. When the Fontan operation was uniformly undertaken 12–18 months after stage I, an operative mortality of 16–40% occurred.[41] The most common cause of early death was low *CO* associated with tachycardia, low systolic and diastolic blood pressures, and high ventricular end-diastolic pressures. The majority of patients with signs of low *CO* demonstrated echocardiographic evidence of an abrupt change in ventricular geometry that resulted in a small, thick-walled cavity with a low diastolic volume when compared to the preoperative state. Although systolic shortening appeared normal, the ventricular compliance was diminished. The physiologic result is impaired diastolic function of the ventricle resulting in increased end diastolic pressure. The resulting increase in pulmonary venous pressure impeded *PBF* thereby reducing systemic output. Retrospective analysis of the data available preoperatively proved insufficient to predict those children who would develop physiologically important reduction of ventricular compliance associated with rapid contraction of end diastolic volume following single stage Fontan.

## Initial management for other univentricular heart malformations

Although HLHS represents the most common anatomic constellation resulting in a single functional ventricle, many other forms exist (e.g. tricuspid atresia). In fact, these malformations may have appeared more common than HLHS because they survive without the need for complex reconstructive surgery in the neonatal period. Hence these variants were much more prevalent during childhood before stage I reconstruction was developed as a viable option for neonates with HLHS.

The management of other single ventricle malformations strives for the same physiologic goals as stage I: balanced *Q*p : *Q*s, unobstructed flow from the single ventricle to the systemic circulation, and conditions in the pulmonary circulation that promote the fall in *PVR* that normally occurs with maturation. The latter typically entails assurance that no resistance to pulmonary venous return exists and pulmonary arterial flow is subjected to an anatomic restriction that limits *Q*p : *Q*s ratio to unity. For example, tricuspid atresia variants may require a range of interventions in the neonatal period, depending on their anatomy. Those with ductal-dependent *PBF* will require a systemic-to-PA shunt to provide a balanced *Q*p : *Q*s. Variants with associated VSD may have adequate *PBF* without a shunt. A small subgroup with tricuspid atresia and a large VSD may exhibit excessive *PBF* requiring a PA band to achieve a *Q*p : *Q*s of 1.

## Evolution of staged approach to Fontan

Many have adopted a systematic staged approach to the Fontan operation for all patients with univentricular hearts in an effort to reduce the volume load of the ventricle as early as possible and to minimize the impact of rapid changes in ventricular geometry and diastolic function that accompany primary Fontan.[42] Two options have gained acceptance as the first step of the staged Fontan: bidirectional Glenn[43] or hemi-Fontan.[44] The SVC is divided and anastomosed to the undivided pulmonary arteries, creating a bidirectional cavopulmonary (Glenn) shunt (Fig. 22.6). This source of *PBF* may be exclusive if the previous shunt is ligated, or additive if it is not. When previous sources are occluded, it provides the same physiologic benefit as hemi-Fontan and can be performed without bypass. During hemi-Fontan, all systemic-to-PA shunts are ligated, and *PBF* is achieved exclusively via an SVC-to-PA anastomosis. Certain technical features of the hemi-Fontan make it, in our opinion, a more logical step in the process of eventual completion of the Fontan. First, it enables elimination of stenosis or distortion of the branch pulmonary arteries and their confluence. Second, the normal relation of the SVC to the right atrium is preserved. As bypass is needed, other coexisting anatomical risk factors can be addressed. Thirdly, it simplifies execution of the Fontan itself.

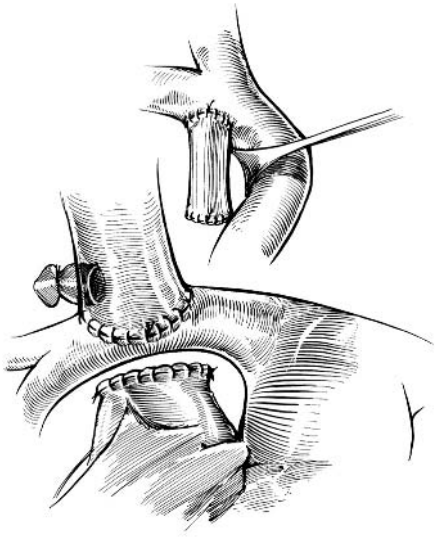


**Fig. 22.6** Bidirectional cavopulmonary anastomosis (or bidirectional Glenn shunt). Top, the previous right modified Blalock–Taussig shunt is divided and ligated, and (bottom) the superior vena cava is anastomosed to the right pulmonary artery. Reproduced with permission from Casteñeda AR, Jonas RA, Mayer JE, Hanley FL. Single-ventricle tricuspid atresia. In: Casteñeda AR, Jonas RA, Mayer JE, Hanley FL, eds. *Cardiac Surgery of the Neonate and Infant.* Philadelphia, PA: Saunders, 1994: 249–72.

### Superior cavopulmonary anastomosis

#### Preoperative assessment

The conversion from a circulation based upon complete mixing and parallel perfusion of both the systemic and pulmonary vascular beds via an arterial shunt to a "series" circulation where *PBF* becomes a diversion of systemic venous return requires certain preconditions. In essence, the flow of blood through the pulmonary circulation must be free of significant impediments in order that systemic venous pressure does not reach physiologically unacceptable levels. These potential impediments take three forms: elevated *PVR*, AV valve dysfunction, and diminished ventricular compliance. Elevated *PVR* encompasses two distinct mechanisms: the size of the major branches or the state of the arteriolar resistance vessels. In patients with HLHS, one must also confirm that no obstruction to flow exists at the remnant of the atrial septum. With the caveat that systemic venous pressures of 16 mmHg or less are generally tolerated without significant sequelae, while those 20 mmHg and over are associated with a variety of morbidities, very small differences distinguish those who do well with the operation from those who have a poor outcome. Contemporary non-invasive methods

of assessing the anatomy and physiology of candidates for superior cavopulmonary anastomosis (SCPA) are not capable of distinguishing such small physiologic differences. Thus, we perform cardiac catheterization on all HLHS patients who are considered candidates for SCPA in order to quantitate *PVR*, ventricular end-diastolic pressure, AV valve function, and obstruction at the atrial septum remnant. In addition, anatomic information about the PA architecture is obtained in conjunction with injections to evaluate the presence of accessory venous communications between the superior venous drainage and the heart or inferior vena cava (IVC) (e.g. left SVC to coronary sinus). Postoperatively, such vessels could serve as a mechanism by which upper body venous return is diverted to the heart without passing through the pulmonary circulation, thereby resulting in unanticipated levels of hypoxemia.

These data can be used to estimate the SVC pressure on completion of SCPA. Recognizing that this formula requires several assumptions that render it an oversimplification, one can estimate the postoperative SVC pressure as follows:

$$P_{svc} = \left\{ \frac{(P_{PA} - P_{PV})(Q_{PA} : Q_{SA})}{Q_{PB} : S_{PB}} \right\} + P_{LA}$$

Where $P_{SVC}$ and $P_{LA}$ represent the pressure determinations in the SVC postoperatively, and the left atrium, respectively

Where $P_{PA}$ and $P_{PV}$ are the preoperative pressures in the PA and vein, respectively

Where $Q_{PB} : Q_{SB}$ and $Q_{PA} : Q_{SA}$ are the $Q$p : $Q$s ratios before and after SCPA, respectively

In infants approximately 6 months of age, we estimate the proportion of venous return coming from the upper body to be roughly equal to that from the lower body, although SVC flow may comprise as much as 60–70% of the total venous return in some. In other words, $Q_{PB} : Q_{SB}$ approximates 0.5–0.7. With this assumption, we estimate the change in $P_{PA} - P_{PV}$ that is proportional to the reduction in flow ($Q_{PB} : Q_{SB}/Q_{PA} : Q_{SA}$). For example, assuming the following hemodynamics measured preoperatively:

$P_{PA} = 17$, $P_{PV} = 8$, $Q$p : $Q$s = 1.5, and $P_{LA} = 8$,
the $P_{SVC}$ postoperatively = $((17 - 8)(0.5)/1.5) + 8 = 11$.

Unfortunately, several of the assumptions limit this sort of calculation to the level of a crude estimate. $P_{PA}$ is notoriously difficult to measure accurately when the only source of *PBF* is a systemic–pulmonary shunt. Catheters placed across the shunt probably alter *PBF* while they are present, while PV wedge pressures to estimate $P_{PA}$ have a variety of limitations, particularly if *PVR* is elevated. The ventricular compliance is dynamic as well, particularly in the context of significant changes in ventricular volume and pressure loading conditions. In addition, the imposition of CPB and an ischemic interval have a negative impact on ventricular compliance, albeit a transient one if the operation proceeds according to plan. Finally, the $Q$p : $Q$s determinations depend upon *PVR* which might be altered by the medications employed to sedate an infant for catheterization. Despite all the limitations, however, this estimate does help to predict problem patients as well as the type of problem they might encounter, whether *PVR*, ventricular compliance or AV valve function.

Preoperative assessment should also incorporate an evaluation of other vital organ systems with a history of primary or secondary dysfunction. For patients receiving anticoagulant or functional platelet inhibitors, plans for the cessation of those therapies must be formalized. Careful history regarding the child's response to sedative medications should be elicited.

### Intraoperative management

Infants typically return for SCPA between 5 and 8 months of age. Given their developmental stage and prior hospital experiences, many will manifest separation anxiety when taken from the parents. Thus, unless they have some contraindication, sedative premedication is administered orally prior to surgery. Although a variety of sedative potions are available, we prefer pentobarbital 4 mg/kg p.o. because of its potency and duration of action. When administered 45–60 minutes in advance, a high proportion of patients will be sleeping. This serves to allay the parental anxieties to some extent and also facilitates induction with a volatile inhaled anesthetic agent, if that is the planned technique.

Anesthesia can be induced with a variety of intravenous or inhaled agents. Unless the preoperative evaluation has revealed myocardial dysfunction or significant unusual hemodynamic loading conditions (e.g. arch obstruction, AV valve insufficiency), these infants generally tolerate nearly normal doses of anesthetic agents without manifesting untoward cardiovascular effects. We usually employ a combination of inhaled anesthetic, opioid, and muscle relaxant. Most commonly, the total opioid administered for the case is the equivalent of 50 μg/kg of fentanyl. Our goal is sufficient emergence from the anesthetic effect to permit tracheal extubation within a few hours of arrival in the CICU. This period of stabilization enables the infant to thoroughly rewarm, recover from CPB, and demonstrate that bleeding has subsided.

Although these infants at the time of induction have the same anatomy and physiology as the newborn following stage I, subtle changes occur in the interval that make them significantly more resilient. Maturation and compensatory mechanisms in myocardial development render the heart more capable of managing the excess volume load of a parallel circulation. In addition, through differential growth, the shunt is more restrictive, protecting the infant from excessive

acute volume loads irrespective of manipulations that lower *PVR* significantly. Finally, the baseline *PVR* is low, so even extreme measures cannot produce a substantial reduction in *PVR* from baseline values, therefore any *Q*p : *Q*s change is comparably small. Nevertheless, we try to minimize any additional volume burden that might be placed on the ventricle prior to CPB and planned ischemia by minimizing supplemental oxygen delivery and ventilating to normocapnea.

All standard non-invasive monitors are applied for induction. An intra-arterial catheter is placed for continuous monitoring following tracheal intubation. The site selected for this catheter varies according to a variety of considerations related to congenital or acquired vascular anomalies. The placement of a BT shunt may have compromised the ipsilateral subclavian artery. In addition, previous monitoring and catheterization sites may not be viable. There are also a variety of aortic arch branching patterns some of which result in stenosis of the subclavian supply. Non-invasive arterial pressure measurement on all four extremities provides the data necessary to identify the appropriate site(s). Cannulation of the central veins via the jugular or subclavian is avoided out of concern for the implications of thrombosis in those vessels.

Unlike stage I, the SCPA provides significant hemodynamic benefit. With occlusion of the shunt, the circulations are no longer connected in parallel, thereby reducing the volume output demands for the RV to that which is necessary to perfuse the systemic circulation alone. Pulmonary blood flow becomes a diversion for venous return from the upper body, in effect a "series" circulation of a pump and two resistors. Since the volume of blood flow to the upper body is at least as great as that to the lower body at 6 months of age, the mixture of oxygenated and deoxygenated blood remains 1 : 1, or higher. Thus the expected systemic oxygen saturation tends to increase slightly, but the heart need only accomplish half the volume work (*Q*s) to do so. Most patients exhibit robust hemodynamics on completion of this procedure. Although we usually infuse a low dose of dopamine (3 μg/kg/minute) in the atrial catheter, it may not be necessary in many. Infants exhibiting substantial diastolic dysfunction or valve regurgitation may benefit from an inodilator such as milrinone. When anticipated on the basis of preoperative information, a loading dose will be administered during rewarming on CPB.

The strategy for managing *PVR* changes dramatically as well. With *PBF* now relying upon "passive" venous return (i.e. no pump to propel blood through the pulmonary circulation), measures designed to minimize the impediments to *PBF* assume paramount importance. Since medical therapies are limited in their capacity to produce reliable, substantial improvement in ventricular compliance or AV valve function, attention is focused on minimizing *PVR*. Shortly before the termination of CPB, the tracheal tube should be cleared of secretions and the lungs completely re-expanded, as *PVR* will be minimized at normal functional residual capacity (*FRC*). Both atelectasis and alveolar overdistension increase *PVR*. A tidal volume designed to achieve a low–normal $PaCO_2$ at a respiratory rate no greater than 20 is selected. Doppler flow studies have demonstrated that *PBF* occurs preferentially during the expiratory phase of positive-pressure ventilation in patients following cavopulmonary anastomosis, thus we strive to limit rate and inspiratory time to no greater than 1 second.[45,46] Positive end-expiratory pressure (*PEEP*) is only applied judiciously to preserve normal *FRC*, based upon investigations in Fontan patients demonstrating significant reduction in cardiac index mediated by an increase in *PVR* at *PEEP* values over 6 mmHg.[47]

Immediately following termination of CPB, MUF is instituted. Modified ultrafiltration offers significant benefit to patients following cavopulmonary anastomosis.[48] Postoperative blood loss and the proportion of patients demonstrating significant pleural and pericardial effusions are both significantly reduced. Other investigators have shown benefits in pulmonary function across a wider spectrum of patients that may prove particularly crucial in this population.

Infants for SCPA represent a high-risk group for postoperative hemorrhage. They have several risk factors which tend to exacerbate bleeding, including age (< 2 years), reoperation, hypoxemia, and deep hypothermic bypass management. Upon completion of MUF, heparin effect is rapidly reversed with protamine. Fresh whole blood comprises the preferred product for blood replacement following protamine administration. As described previously, this product provides restoration of all hemostatic elements, including platelets, and thereby limits donor exposures as well. In the vast majority, SCPA can be performed while limiting patient exposure to a single blood donor.

### Specific problems in the immediate postoperative period

Hypoxemia of greater magnitude than anticipated represents the most common postoperative problem encountered by patients following SCPA. In some instances, this may represent a manifestation of hypovolemia and diminished *PBF*, while in others it might reflect the mechanical ventilation strategy. In the latter circumstance, $PaO_2$ may rise as ventilatory support is tapered. In the absence of improvement with manipulation of intravascular volume or ventilation, diagnostic evaluation is indicated to search for connections that enable venous return from the upper body to bypass the pulmonary circulation and enter the heart or lower body venous system (e.g. an unrecognized left SVC draining to the coronary sinus). Often these collateral vessels can be occluded using transcatheter coil embolization, but the hemodynamic impact of occlusion should be tested with a balloon catheter prior to definitive embolization.

Although the incidence of myocardial dysfunction is significantly lower following SCPA, it does occur. In the absence of significant hemodynamic causes (e.g. aortic arch obstruction, AV valve regurgitation), one must suspect an issue with myocardial protection or coronary perfusion. Despite their youth, some infants have developed extremely thick ventricular walls, particularly in the context of a high *Q*p : *Q*s and residual aortic arch obstruction. Adequate protection for these ventricles requires meticulous technique. Even under optimal circumstances, the compliance of these hearts may not return to normal for an extended period postoperatively. While dysfunctional dilated hearts seem to respond to increasing inotropic support, no medical regimen has proven consistently beneficial to the thick-walled ventricle operating at low end-diastolic volume.

Sinus node dysfunction represents the most common rhythm disturbance following SCPA. Approximately 15% of infants will have periods of junctional rhythm in the early postoperative period. Over 80% return to sinus rhythm in the ensuing days or weeks. Temporary epicardial pacing is employed when the hemodynamics appear impaired by heart rate or rhythm.

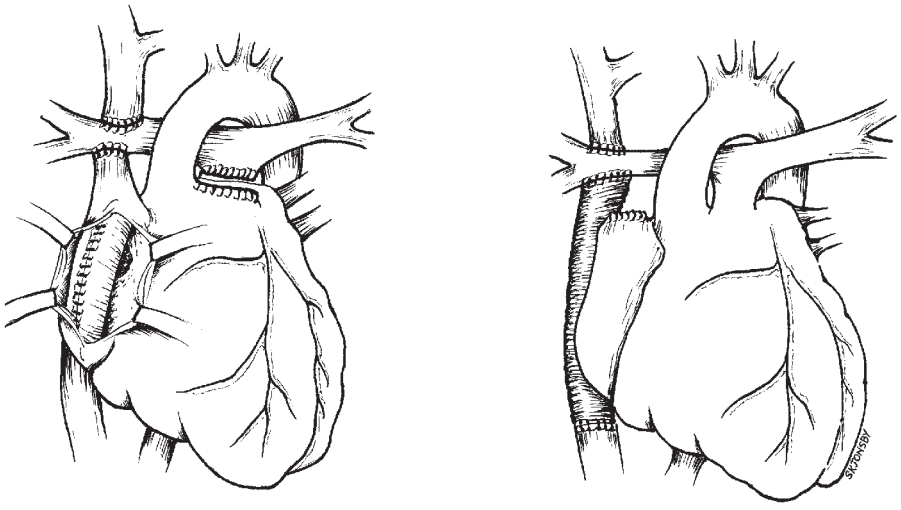
## Fontan completion

The basic surgical approach is illustrated in Fig. 22.7. Precise timing of the completion requires weighing several considerations, each of which is incompletely understood. At a minimum, the interval between the two stages of the Fontan must permit restoration of optimal ventricular compliance at the new end-diastolic dimension. In the absence of a diagnostic tool sensitive or specific enough to evaluate this process, many have arbitrarily established a minimal interval of 9–12 months. Despite its hemodynamic resilience, hemi-Fontan anatomy and physiology does pose risks that may provide compelling reasons not to extend this interval inordinately. These children are subject to the risk of paradoxical emboli returning via the IVC, as well as the consequences of hypoxemia, which accelerate with age. Diversion of the IVC blood away from the pulmonary circulation may predispose the child to development of pulmonary arteriovenous malformations.

### Preoperative assessment

In preparation for the Fontan operation, the same considerations apply as discussed for SCPA; however, the implications are more significant. Unlike the patient following SCPA, the Fontan operation leaves the child's *CO* nearly totally dependent upon *PBF*. Whereas impediments to *PBF* following SCPA might result in lower systemic oxygenation, they produce low *CO* after Fontan operation. Clinical experience suggests that infants and young children are far more tolerant of hypoxemia than diminished *CO*.

Candidates for Fontan operation usually undergo cardiac catheterization preoperatively. One can use the data gathered to predict systemic venous pressure following Fontan operation in much the same way we described for SCPA. In our series, a fenestration is created connecting systemic and pulmonary venous return, in order to ameliorate early postoperative morbidity and provide a pathway that sustains ventricular preload under conditions that might impede *PBF*.[49,50] Apart from coronary sinus return and whatever flow might cross the fenestration that is usually made in the IVC to PA pathway, all systemic venous return traverses the pulmonary circulation. Thus, one would estimate the *Q*p : *Q*s following Fontan operation to reach 0.9 or higher. As an



(a) (b)

**Fig. 22.7** Modern variations of the Fontan operation. (a) The lateral tunnel Fontan, where a conduit is fashioned inside the right atrium. (b) The extracardiac Fontan, where a Goretex® tube is used to connect inferior vena cava and hepatic venous blood to the pulmonary artery. A fenestration can be created with both modifications. Modified with permission from Stayer SA, Andropoulos DB, Russell IA. Anesthetic management of the adult patient with congenital heart disease. *Anesthesiol Clin North America* 2003; **21**: 653–73.

example, given a child catheterized in preparation for Fontan operation, the following determinations were made:

$Qp : Qs = 0.6, P_{PA} = 12, P_{LA} = 8.$

Estimation of the systemic venous pressure (which should equal the PA pressure) would be calculated as:

$P_{SVC} = P_{IVC} = P_{PA} = ((12 - 8)(0.9)/0.6) + 8 = 14$ mmHg.

An interval assessment should include both cardiac and non-cardiac problems and interventions. Previous experience with sedation and anesthesia exerts significant influence on management options. Finally, a plan should be devised in conjunction with the patient's cardiologist for the perioperative management of any cardiac drugs, anticoagulants or other medical regimens.

### Intraoperative management

Patients most commonly present for Fontan operation between 15 months and 2 years of age. At this developmental age, they will demonstrate significant separation anxiety. We prefer to alleviate their anxiety with a potent premedication consisting of either pentobarbital (4 mg/kg p.o) with or without supplementary meperidine (3 mg/kg p.o.). The history of each child's response to previous sedatives assumes importance in governing the decision as to which regimen to employ.

As with infants for SCPA, anesthesia for Fontan operation can be induced with a variety of intravenous or inhaled agents. Unless the preoperative evaluation has revealed myocardial dysfunction or significant unusual hemodynamic loading conditions (e.g. arch obstruction, AV valve insufficiency), these infants generally tolerate the qualitative hemodynamic effects of anesthetic agents in a manner that is virtually indistiguishable from normal children. We usually employ a combination of inhaled anesthetic, opioid, and muscle relaxant. Most commonly, the total opioid administered for the case is the equivalent of fentanyl 50 µg/kg. Our goal is sufficient emergence from the anesthetic effect to permit tracheal extubation within a few hours of arrival in the CICU. This period of stabilization enables the infant to thoroughly rewarm, recover from CPB, and demonstrate that bleeding has subsided.

All standard non-invasive monitors are applied for induction. The considerations for invasive arterial monitoring site selection remain as described for the SCPA. Similarly, the philosophy regarding systemic venous pressure monitoring and postoperative transthoracic monitoring catheters in the PA and common atrium remains consistent.

The immediate benefits from Fontan operation are limited to improved systemic oxygenation at the expense of higher IVC pressure. Volume and pressure loading conditions for the single ventricle do not change in response to this procedure. Nevertheless, this relatively brief operation is well tolerated by the majority of infants, particularly the intracardiac lateral tunnel technique. The details of immediate post-bypass management are identical to those following SCPA. Management includes meticulous ventilation designed to minimize *PVR*, low dose inotropic support, MUF, and rapid restoration of hemostasis with protamine and fresh whole blood. As noted previously, *PEEP* is employed only as necessary to preserve normal *FRC*.

### Specific problems in the immediate postoperative period

Unlike the manifestations of diminished *PBF* following SCPA anastomosis, in which reduction in systemic oxygen saturation occurs, the same phenomenon after Fontan operation will cause reduced *CO*. The signs of the latter tend to be far more insidious and ambiguous. These patients require the utmost vigilance to maintain adequate intravascular volume during the process of rewarming and blood loss in the early postoperative period. Conduit or baffle fenestration tends to ameliorate some of the early postoperative hemodynamic instability. When fenestrated, the IVC conduit allows some blood to shunt from the systemic venous to pulmonary venous system, acting to preserve ventricular preload despite diminished *PBF*.[49,50]

Hypoxemia usually indicates some communication from the systemic venous system to the atrium. A modest degree of hypoxemia frequently occurs related to flow through a planned fenestration and the coronary sinus, which normally enters the atrium on what is functionally the pulmonary venous side. Systemic oxygen saturation less than 85–90% suggests more flow across the fenestration than usual, extremely low mixed venous oxygen saturation, or an additional venous channel diverting blood around the pulmonary circulation. Alternatively, pulmonary arteriovenous malformations, such as those described following Glenn operation, may account for the hypoxemia. Distinguishing these prospects may require catheterization.

Myocardial dysfunction typically follows the same differential described previously for SCPA. In the absence of a hemodynamic cause, one must conclude that it reflects inadequate myocardial preservation, coronary perfusion, or a metabolic process. In the absence of remediable causes (e.g. hypocalcemia), supportive measures represent the mainstay of therapy.

Arrhythmias can arise immediately following Fontan operation. While heart block is uncommon, junctional rhythms occur in a quarter of the patients. If the escape rate is sufficiently low to have a deleterious impact on overall hemodynamics, epicardial atrial or AV pacing usually proves beneficial. In the current era, tachyarrhythmias are less common in the early postoperative period, but more likely to have a significantly negative hemodynamic impact when

they occur. Doppler interrogation of *PBF* patterns suggest that flow is most brisk during diastole under normal circumstances,[51] perhaps explaining the intolerance of tachyarrhythmias. Alternatively, unfavorable hemodynamics may serve to provoke tachyarrhythmias.

## Anesthesia for patients with a single ventricle for non-cardiac surgery

Throughout their lives, a substantial portion of children with single ventricle will require non-cardiac surgical interventions. These procedures span a wide range of complexity and urgency. As such, this section cannot serve as a comprehensive guide to all possible scenarios. Rather, it outlines some general concepts to serve as a framework.

It is our impression that a carefully administered anesthetic, appropriate for age and surgical procedure, is tolerated provided the unique ventilatory and circulatory requirements of these patients are consistently met. When possible, one might defer elective major non-cardiac surgery until the infant has recovered from SCPA. At this stage of the reconstructive sequence, hemodynamic performance tends to be most resilient, as the single ventricle is no longer operating with the excess volume load ($Qp + Qs$) required to sustain a parallel circulation, nor is the *CO* entirely dependent upon *PBF*, as occurs following completion of the Fontan.[44,52,53] An additional consideration arises when major blood loss is anticipated. Both the SCPA and Fontan operation result in significant increases in venous pressure, potentially promoting blood loss. One has to weigh the risks entailed in managing such a patient functioning with the volume load of a parallel circulation against the impact that elevated venous pressure would have on blood loss. Unfortunately, many interventions will not wait for optimum hemodynamic stability. Urgent and emergency surgery often transpires when hemodynamics are least favorable. Whatever the timing, a clear understanding of each patient's anatomy and physiology constitutes the foundation of any perioperative plan. These details can usually be obtained most succinctly from the child's cardiologist. When a considerable interval has elapsed since the cardiologist has evaluated the patient, they must be included in the preoperative assessment plans.

Between July 2000 and June 2003, 363 infants and children with HLHS and comparable single venticle lesions underwent non-cardiac surgery at the Children's Hospital of Philadelphia. While non-cardiac surgery had to be performed at every stage of care, including nine with native anatomy prior to stage I, the majority of these interventions took place between SCPA and Fontan operation. Procedures ranged in complexity from simple, superficial procedures (n = 247; 68%) to highly complex (e.g. major intracavitary, CNS, craniofacial, or orthopedic procedures; n = 116 (32%)). Emergency surgery accounted for 10% of the cases.

### Intraoperative management

Anesthetic management varies depending upon the physiologic state of the patient and the magnitude of the planned intervention. As a starting point, the perioperative plan entails the same components that would be included for any child undergoing the same intervention. The plan is modified according to the cardiac physiology and constraints it imposes. For superficial procedures in a hemodynamically sound patient, no special monitoring is necessary. On the other hand, a neonate with single ventricle and a perforated viscus requires invasive monitoring to track hemodynamic, ventilatory and metabolic changes and all the therapies available as outlined previously to manipulate cardiac function and the vascular beds.

Similarly, induction and maintenance of anesthesia is governed by perioperative expectations, the qualitatively predictable hemodynamic effects of anesthetic agents, and the cardiovascular state of the child. For superficial procedures in a well compensated child with one ventricle, short-acting agents that enable a prompt recovery are appropriate. The plan needs to be adjusted in response to more extensive interventions or hemodynamically compromised patients.

### Postoperative management

Postoperative surveillance also ranges from that which would be used for any child of similar age having a given procedure through admission to an ICU. While some added degree of caution is warranted, patients with one ventricle can have outpatient surgery when they are healthy and the procedure permits. If, however, any aspect of the child's condition would render them vulnerable to the routine consequences of anesthesia and surgery, hospital admission should be considered. These include, but are not limited to, nausea, vomiting, pain, and inability to take fluids or medications orally. If one could envisage a dramatic or life-threatening physiologic change, surveillance in a CICU is advisable. In the Children's Hospital of Philadelphia series discussed above, 55% of the children had day surgery; another 17% had "same day" surgery in which they were admitted from home on the day of their procedure.

## Outcomes

Over the last two decades, considerable progress has been forged in the treatment of HLHS. In a review of 158 patients who underwent stage I reconstruction at Children's Hospital of Philadelphia between January 1998 and June 2001,

operative survival was 77%;[11] in the cohort that had no associated risk facts, operative survival was 88%, compared to 63% with one or more risk factors. These risk factors included low birth weight (< 2.5 kg), associated cardiac and non-cardiac malformations, and prolonged extracorporeal support (e.g. ventricular assist devices or extracorporeal membrane oxygenation). Infants with HLHS now reach the threshold of SCPA in a condition virtually indistinguishable from other forms of single ventricle.[54] Early and intermediate term outcomes rival those of other complex congenital heart malformations. The factors that contribute to sudden death in the late postoperative period following stage I but prior to SCPA require further delineation.[55] Modification of the surgical technique using the Sano modification (Fig. 22.5) offers the prospect of adequate *PBF* without necessitating the low diastolic pressure that potentially jeopardizes coronary and systemic perfusion following stage I with a modified BT shunt.

Routine staging of the Fontan procedure, baffle fenestration and use of MUF results in both low mortality (< 1% for both SCPA and Fontan completion) and morbidity for all patients regardless of anatomic subset of univentricular heart.

## Heart transplantation for single ventricle malformations

Although cardiac transplantation has been performed in selected patients with single ventricle malformations in late childhood and adolescence for progressive ventricular dysfunction, this strategy gained widespread notoriety when it was advocated for neonates with HLHS. In 1986, Bailey *et al*.[56] described successful allotransplantation methods for HLHS. Despite immediate-term reports indicating 70% 7-year survival of recipients,[57] two major limitations arise when contemplating adopting this strategy widely: donor organ availability and long-term transplant outcome. At present, fewer than 70 infants receive heart transplants annually for all indications,[58] while in excess of 1000 children are born with HLHS in the USA.[59] For the relatively small proportion of neonates with HLHS who are currently listed for transplantation, the waiting period can extend as long as 6 months and the mortality is as high as 30% during that interval.[60] Extending this therapy generally would likely result in an increase in both the waiting time and pretransplant mortality. Consideration needs to be given to the long-term impact of this decision. Chronic immunosuppression and rejection limit 12-year survival to 50% in all pediatric heart recipients.[60] Infants with congenital heart malformations fare even less well. Beyond the initial year, mortality in pediatric transplant recipients fall to approximately 3% per year, whereas comparable mortality following Fontan operation is less than 1% per year.[60,61]

## Summary

The anesthesia management for patients with single ventricle encompasses a wide spectrum of care. Careful assessment and planning entails a comprehensive understanding of the typical physiology at each stage of the reconstructive sequence, the specific condition of each patient with respect to that physiology, and the impact that the proposed procedure will likely have. Armed with that knowledge, an anesthesiologist can design a plan taking into account the qualitatively predictable effects of anesthetic agents, airway and ventilatory manipulations, and cardiovascular drugs. This plan is titrated to achieve the desired effects in each patient. No absolute formulas exist. Rather, absolute needs, expectations, capabilities and goals vary between institutions, clinicians, and patients. Optimal results entail carefully orchestrated interactions among anesthesiologists, surgeons, cardiologists, and intensivists.

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# 23 Anesthesia for miscellaneous cardiac lesions

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## Introduction

This chapter will discuss the anatomy, pathophysiology, surgical approach, and anesthetic management of two groups of rare lesions: vascular rings and anomalies of the coronary arteries. Mitral regurgitation (MR) and anesthetic considerations for pericardial effusion and tamponade will then be reviewed.

## Vascular rings

Vascular rings are a variety of anomalies of the aortic arch and its branches, which result in compression of the trachea and/or esophagus. These lesions are rare, accounting for less than 1% of all congenital heart defects.

### Anatomy

Vascular rings were first described in 1737 by Hommel who described a double aortic arch.[1] Bayford[2] reported the first case of retroesophageal right subclavian artery in 1794. However, it was not until 1945 that a vascular ring was successfully divided by the pioneering efforts of Robert Gross.[3]

Vascular rings[4,5] encompass many different vascular anomalies, all of which result from the abnormal regression of the aortic arch complex. The majority (60%) of all vascular rings are of the double aortic arch variety, which results from the persistence of the fourth aortic arch. Many variations in the arrangement of the aorta and its branches exist, and can result in complete or partial rings.

Of the many different anatomies, (i) double aortic arch and (ii) right aortic arch with aberrant left subclavian artery are the most common. In double aortic arch, the right aortic arch passes to the right of the esophagus to join the left-sided descending aorta, thus completing the vascular ring (Fig. 23.1). Two other varieties of vascular ring include (iii) right aortic arch with mirror image branching and left ligamentum arteriosus, and (iv) left aortic arch with retroesophageal right subclavian artery.

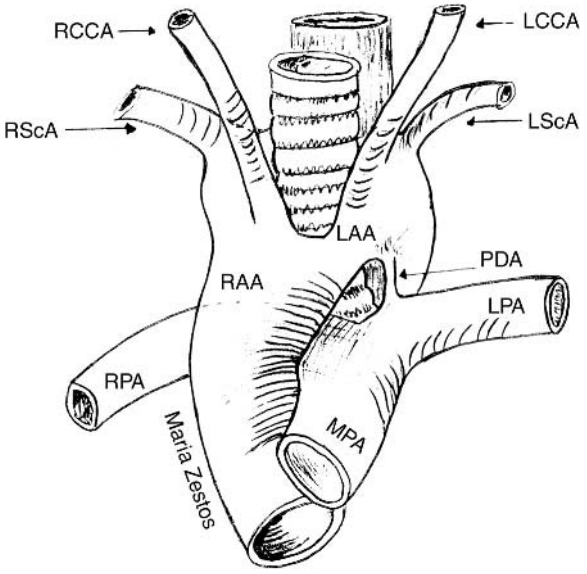


**Fig. 23.1** Drawing of a double aortic arch with the trachea and esophagus encircled by the vascular ring. LAA, left aortic arch; LCCA, left common carotid artery; LPA, left pulmonary artery; LScA, left subclavian artery; MPA, main pulmonary artery; PDA, patent ductus arteriosus; RAA, right aortic arch; RCCA, right common carotid artery; RPA, right pulmonary artery; RScA, right subclavian artery.

Intracardiac lesions are rarely seen with double aortic arch but are often present in cases of (v) left aortic arch with right descending aorta. The left arch crosses behind the esophagus, and a right ligamentum arteriosus completes the ring.

Partial vascular rings or "slings" may also occur. For example, (i) an aberrant right subclavian artery of an otherwise normal arch may pass to the right behind the esophagus with resultant dysphagia. Other partial rings that have been described include (ii) ductus arteriosus sling and (iii) compression of the lower trachea from severe malrotation of the heart. In the latter two, dividing the ductus arteriosus relieves the compression.

Finally, with the pulmonary artery sling, the left pulmonary artery arises from the proximal right pulmonary artery, and passes behind the trachea.[6] The ligamentum arteriosum completes the vascular ring by compressing the trachea anteriorly.

## Pathophysiology and natural history

Symptoms are usually prominent in patients with a tightly obstructed ring as is seen in double aortic arch. Infants often present with respiratory distress, stridor, and swallowing difficulties within the first 6 months of life. Subcostal retractions can be seen in severe obstruction. Recurrent respiratory difficulty or dysphagia in a young infant should raise the question of the presence of a vascular ring. However, the diagnosis of vascular ring in infants without associated anomalies is often delayed months to years after onset of symptoms.[7] Partial vascular rings may be asymptomatic if there is little tracheoesophageal compression. Older infants and adults with undiagnosed vascular rings have presented with acute esophageal foreign body impaction,[8] unsuccessfully treated asthma,[9] and progressive dyspnea on exertion.[10]

Radiographic studies play a crucial role in delineating vascular causes of airway obstruction.[11] A plain chest radiograph may show the presence of a right-sided aortic arch, a retrotracheal opacity, tracheal narrowing, or tracheal compression. The combination of frontal and lateral views shows at least one abnormality in every patient.[12] A barium esophagram is the most useful study, revealing indentation and is usually diagnostic.[5] The filling defects vary with the different anatomies. Bronchoscopy or esophagoscopy, though unnecessary and rarely done, may reveal a pulsating mass compressing the esophagus or trachea. Computed tomography (CT) and magnetic resonance imaging (MRI) have been shown to be diagnostically accurate, eliminating the need for aortography. Some centers advocate routine use of MRI to identify anatomic details of structures not seen with angiography.[13,14] Echocardiography is used liberally by some centers to evaluate the presence of a congenital heart anomaly, which may be present in up to 20% of children with symptomatic vascular rings.[15]

## Surgical approaches

Delayed treatment may result in tracheobronchial damage in symptomatic patients. Surgery, however, is not indicated if symptoms are mild or absent. Best exposure is provided by the left thoracotomy approach through the fourth intercostal space.[4] If coexisting cardiac anomalies require repair, a median sternotomy may be used. The arch, including the retroesophageal component is dissected out completely. Care must be given to the identification and division of the ring without compressing blood flow to the descending aorta or carotid arteries. In double aortic arch, the non-dominant arch is divided and sutured at its distal end close to the junction with the descending aorta. The ligamentum arteriosus is also divided in all cases. The trachea and esophagus are dissected and freed of all strands or bands of tissue that may add to the constriction. On occasion, the descending aorta is suspended to the rib periosteum to keep it away from the esophagus. If the vascular ring is of the right aortic arch type, the division of the left ligamentum arteriosus opens the ring and relieves the constriction.

On rare occasion, right thoracotomy may be indicated. This is the case in double aortic arch with a smaller non-dominant right aortic arch, as well as the case of left aortic arch with a retroesophageal subclavian artery and right ligamentum arteriosus.

Video-assisted thoracoscopic division of vascular rings has been described.[16] This approach is limited by decreased vascular exposure and the reduced ability for direct vascular control. The safety of the thoracoscopic approach is increased if there is an absence of blood flow and atresia of the ring structure undergoing division.

The pulmonary artery sling is usually repaired via median sternotomy with cardiopulmonary bypass (CPB).[6] The left pulmonary artery is removed from its origin on the right pulmonary artery, brought in front of the trachea, and reimplanted on the main pulmonary artery.

## Anesthetic considerations and approach

With any surgery involving dissection and ligation of large vascular structures, there is a potential for significant and rapid blood loss, necessitating adequate and reliable intravenous access. Induction of anesthesia is straightforward in the less symptomatic patient. However, children with significant airway compression are at risk for complete airway obstruction and benefit from an inhalation induction with the maintenance of spontaneous ventilation. In these symptomatic patients, paralysis should be administered only after the ability to assist with positive pressure ventilation has been ascertained. These patients may also require a smaller than expected endotracheal tube size. Neuraxial opioids and/or local anesthetics, either by single shot caudal, or continuous techniques, may greatly facilitate pain relief, early extubation, and pulmonary toilet. In addition to standard monitors, an arterial catheter should be placed in most of these patients because of the potential for hemodynamic and respiratory instability. In the case of an aberrant subclavian artery, the site of the arterial catheter should be chosen after discussion with the surgeon of the surgical approach. Central venous catheterization should be considered for extensive surgery, poor vascular access, or anticipated hemodynamic instability. Consideration should also be given to monitoring the cerebral circulation with near infrared spectroscopy and/or transcranial Doppler ultrasound in cases where cerebral blood flow may be compromised, e.g. clamp-

ing and reimplantation of a carotid artery that arises from an aberrant subclavian artery. Finally, some of these operations may be facilitated by single lung ventilation to improve surgical exposure and lessen movement of vascular structures with ventilation. See Chapter 16 for a discussion of the available techniques.

### Postoperative airway management and pain control

Asymptomatic patients can be extubated at the end of the case. Respiratory symptoms may worsen in symptomatic patients during the first postoperative week, occasionally necessitating intubation for adequate pulmonary toilet. For these infants, continuous positive airway pressure with humidified gas via nasal prongs may also be helpful. Good postoperative analgesia is essential to encourage deep breathing and lung expansion. This can be facilitated with epidural analgesia, intercostal rib blocks or adequate intravenous opioid administration.

## Anomalies of the coronary arteries

Abnormalities can exist in the number, origin, and termination of the coronary arteries. The number of coronary arteries can vary from one to four, often occurring in association with other congenital defects. A single coronary artery may be associated with myocardial ischemia, myocardial infarction or sudden death. Coronary arteries may have an anomalous origin from the aorta, the innominate artery, the carotid artery, the left anterior descending artery or, most commonly, from the pulmonary arteries.[17–19]

### Anatomy

#### Anomalous origin from the aorta

If the left main coronary artery arises from the right aortic sinus, it courses between the ascending aorta and the pulmonary artery where compression can occur, leading to myocardial infarction or sudden death. Variations in the aortic origin of the coronary arteries often occur in association with congenital heart defects. In 7% of patients with tetralogy of Fallot, the left anterior descending artery originates from the right coronary artery, crossing over the right ventricular outflow tract where it can easily be injured. In patients with transposition of the great arteries, the right coronary artery and the circumflex artery often originate from the posterior sinus.

#### Anomalous origin from the pulmonary artery

When both coronary arteries originate from the pulmonary artery in an otherwise structurally normal heart, survival is rare beyond the first few months of life. The presence of intracardiac or extracardiac lesions that increase pulmonary artery pressure and oxygen saturation may increase the survival.

Anomalous origin of the left anterior descending coronary artery, or the circumflex coronary artery from the pulmonary artery has also been reported.[20] Both lesions can result in ischemia and should be surgically repaired with aortic reimplantation or aortocoronary bypass graft.

#### Anomalous origin of the right coronary artery from the pulmonary artery

Occasionally, the right coronary artery arises from the pulmonary artery.[21] Blood usually flows via collaterals from the enlarged left coronary artery to the right coronary artery and then into the pulmonary artery, creating a coronary artery–pulmonary artery fistula. Although a relatively benign condition, death from ischemia can occur and surgical correction is recommended. Surgical repair involves aortic reimplantation of the right coronary artery. This repair is straightforward because of the anterior origin of the anomalous artery and its close proximity to the aorta.

#### Anomalous origin of the left coronary artery from the pulmonary artery

Anomalous origin of the left coronary artery from the pulmonary artery (ALCAPA)[22] is the most studied of this class of defects and was first described in 1908. It occurs in 1 in 300 000 live births and usually occurs as an isolated lesion. The left coronary artery usually arises from the left posterior sinus of the pulmonary artery. The right coronary artery is usually enlarged, with a normal origin from the aorta. Numerous collaterals of variable size and number course over the right ventricular outflow tract, or through the interventricular septum, connecting the two coronary arteries. Anomalous origin of the left coronary artery from the pulmonary artery is one of the most common causes of myocardial ischemia and infarction in children. The left ventricle is usually enlarged and hypertrophied. Endocardial fibrosis and scarring may occur in infancy. Fibrosis may also involve the papillary muscles of the mitral valve and may cause variable degrees of valvular incompetence.

### Pathophysiology and natural history

The physiologic changes produced by ALCAPA worsen after delivery. *In utero*, when the pulmonary artery pressure and oxygen saturation nearly equal the systemic pressure and oxygen saturation, left ventricular myocardial perfusion and oxygenation are adequate. Myocardial ischemia develops soon after birth as pulmonary vascular resistance (*PVR*) falls, causing a marked decrease in left coronary artery perfusion

pressure. The infant's survival is dependent on the extent of collateral formation from the right coronary artery to the left coronary artery. These intercoronary collaterals, however, also allow the flow of blood from the right coronary artery via the left coronary artery system into the pulmonary artery and are often referred to as coronary artery fistulization. This coronary artery "steal" causes lower perfusion pressure and results in myocardial damage.

Typical presentation includes profuse sweating, tachycardia, tachypnea, dyspnea, coughing, wheezing, pallor, and failure-to-thrive. In some infants atypical chest pain upon eating and crying has been mistaken for colic.[23] One should have a high index of suspicion of ALCAPA in any infant with global myocardial dysfunction. However, about 10% of patients with ALCAPA with good collateral flow do not develop myocardial ischemia until adolescence or adulthood.[24] Adults have presented with malignant ventricular arrhythmias,[25] shortness of breath with exercise,[24] cardiac murmur,[26] and cardiac arrest during exercise.[27] Although the most common cause of sudden death in young competitive athletes is hypertrophic cardiomyopathy; 13% of deaths in these athletes involve anomalous coronary artery origin.[28] All older patients with asymptomatic ALCAPA had multiple unusual color flow Doppler signals within the ventricular septum, representing septal coronary collaterals.[29]

Physical examination reveals evidence of congestive heart failure, cardiomegaly and the murmur of mitral insufficiency. The chest radiograph consistently shows massive cardiomegaly. Bronchial compression by the enlarged heart can result in atelectatic changes in the left lung.

The electrocardiogram (ECG) is abnormal in all patients, showing evidence of ischemia, infarction and left ventricular hypertrophy. Electrocardiogram findings have been described that are present in all patients with ALCAPA but absent from most patients with myocarditis and cardiomyopathy. These ECG criteria are: (i) Q-wave depth greater than 3 mm; (ii) Q-wave width greater than 30 ms; and (iii) a QR pattern in one of the following leads: I, aVL, $V_5$–$V_7$.[30]

Echocardiography can demonstrate the anatomic origin of the ALCAPA and provides an assessment of the degree of left ventricular impairment. Studies show a significant enlargement of the right coronary artery and a dilated left ventricle with global hypokinesia. Pulse and color flow Doppler imaging can directly visualize the anomalous origin as well as the reversal of flow from the ALCAPA into the pulmonary artery.[19] Cardiac catheterization is not routinely performed unless ALCAPA is suspected but cannot be visualized by echocardiography. When performed, aortography can show filling of the left coronary artery through collaterals from the dilated right coronary artery and can exclude other anomalies.

The need for early surgical repair of all infants with ALCAPA is essential in even asymptomatic infants because of the extremely poor survival with medical management. Ninety percent of undiagnosed or medically treated infants die within the first year of life. Sudden death frequently occurs in untreated older children and adults. Thus, surgical correction is indicated in all patients with ALCAPA.

## Surgical approaches

Surgical treatment for ALCAPA is directed towards correcting the "coronary steal" phenomenon, and increasing left ventricular myocardial perfusion and function. This can be accomplished by either reconstituting a two-coronary system or by simply ligating the fistulous flow. Restoring a two-coronary circulation is preferred, and when possible, direct coronary–aortic reimplantation is performed.[31] Scarred myocardium or free wall aneurysm is not addressed at the time of initial surgery.

Simple ligation of the ALCAPA eliminates the "steal" phenomenon, and in the past had been recommended as the procedure of choice in critically ill infants but has a prohibitive mortality rate ranging from 20% to 50%.[32] A single coronary artery system is less physiologic with greater risk of postoperative complications, a higher early postoperative mortality, and a higher potential for atherosclerosis as well as late sudden death.

Surgical reconstitution of a two-coronary artery system results in greater recovery of left ventricular function and is now the standard surgical procedure. Direct coronary aortic reimplantation is an excellent procedure because it is simple, does not require prosthetic material, and is expected to provide excellent late results. However, it often requires creative surgical technique to obtain sufficient length and correct angling of the coronary artery to the aorta (Fig. 23.2). This is difficult when the anomalous vessel originates from the left posterior wall of the pulmonary trunk. If mobilization and reimplantation will compromise the vessel, the left subclavian artery may be anastomosed to the left coronary artery (Fig. 23.3). This procedure may be done without CPB but is not feasible if the left main coronary artery is short in length.[33]

A saphenous vein bypass graft may also be used, but requires deep hypothermia (18°C) with total circulatory arrest. The small vein caliber and the incidence of late graft occlusion limit the utility of the saphenous vein graft in infants. Alternatively, an aortocoronary bypass graft with a free segment of the subclavian artery may be used. An end-to-side retroaortic coronary bypass graft construction with a free segment of the left subclavian artery is applicable in the majority of infants. More recently, the left internal mammary artery (LIMA) has been used but long-term results are lacking with ALCAPA.[34,35]

Newer techniques utilize the pulmonary artery as a conduit graft from the left coronary artery to the aorta. This is useful for cases where the left coronary artery arises from the left posterior sinus.[36] The Takeuchi procedure[37] uses a flap derived from the anterior wall of the pulmonary trunk to

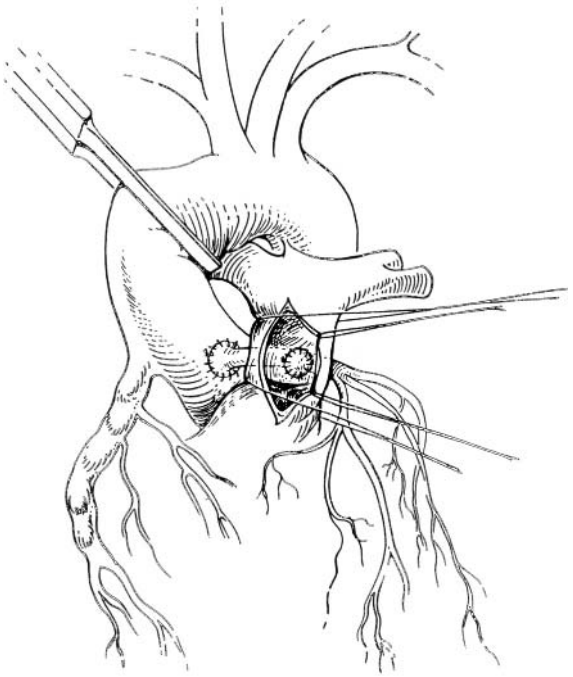

**Fig. 23.2** Direct aortic reimplantation of anomalous left coronary artery from the pulmonary artery. The anomalous ostium is excised with a button of pulmonary artery wall. This button is then implanted into the left lateral side of the ascending aorta. The resulting defect is closed with a pericardial patch. Reproduced with permission from Arciniegas E. Coronary artery anomalies. In: Arciniegas E, ed. *Pediatric Cardiac Surgery*. Chicago: Year Book, 1985: 389–402.

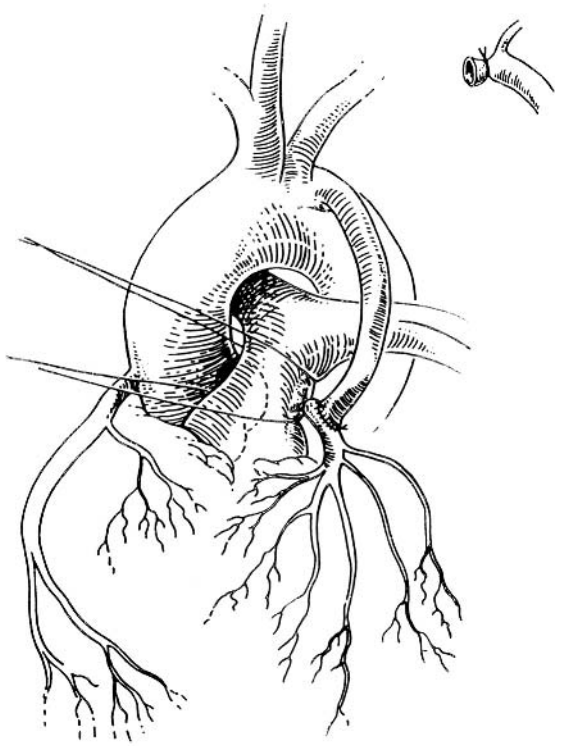

**Fig. 23.3** Left subclavian artery–left coronary artery anastomosis for the management of anomalous origin of the left coronary from the pulmonary artery. The anomalous vessel is also ligated at its origin. Reproduced with permission from Arciniegas E. Coronary artery anomalies. In: Arciniegas E, ed. *Pediatric Cardiac Surgery*. Chicago: Year Book, 1985: 389–402.

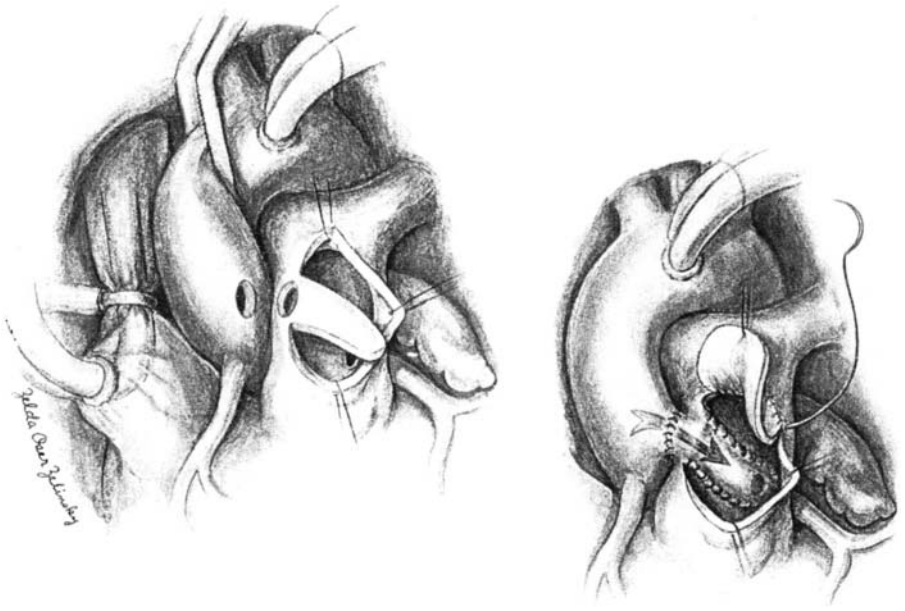

**Fig. 23.4** The Takeuchi procedure is shown through a median sternotomy with cardiopulmonary bypass and cross-clamped aorta. A tunnel for coronary flow (arrow) has been created between the aorta and the anomalous left coronary artery by means of a flap of pulmonary artery wall. The pulmonary wall is then reconstructed with pericardium. Reproduced with permission from Backer CL, Stout MJ, Zales VR *et al*. Anomalous origin of the left coronary artery. A 20-year review of surgical management. *J Thorac Cardiovasc Surg* 1992; **103**: 1049–58.

create a coronary tunnel inside the pulmonary trunk between a surgically created aortopulmonary window and the left coronary ostium (Fig. 23.4). The opening in the pulmonary trunk is then patched with pericardium. Late complications have been reported with the Takeuchi procedure. Tashiro *et al*.[38] has described left coronary angioplasty using pulmonary trunk without prosthetic material, which is expected to yield excellent late results. This procedure combines left coronary

angioplasty, side-to-side anastomosis of the aorta with the newly created left coronary artery and direct anastomosis of the transected pulmonary artery. To date, no difference has been shown in the long-term left ventricular function or late mortality among the various surgical techniques which re-establish a two-coronary circulation.[39]

There have been conflicting opinions as to the necessity for the repair of mitral incompetence in these patients. Some surgeons recommend mitral annuloplasty at the time of the initial operation.[40] However, the vast majority of regurgitant valves gradually improve within 6 months by serial echocardiography without annuloplasty. Even severe MR has been reported to regress fully after reperfusion alone in 62% of cases.[41] Many surgeons now feel that mitral valve repair is not generally necessary at the time of the initial operation.[42] In some patients, the persistence or recurrence of MR may signify a significant coexistent coronary stenosis. Patients who have significant obstruction in their left coronary artery will have residual MR and may require not only mitral valve repair, but also revascularization of the left coronary artery.[42]

### Anesthetic considerations and approach

Infants with ALCAPA are often critically ill with little cardiac reserve and significant ischemia. More severe preoperative MR is associated with increased perioperative mortality.[43] Adequate monitoring, including a multilead ECG, arterial pressure monitoring, and central venous access for drug administration and assessment of volume status are essential. Induction should be a gradual one to avoid major swings in blood pressure. A gentle and rapid laryngoscopy is also critical. Fluid administration is titrated to assure adequate preload for maintenance of cardiac output (*CO*) while avoiding pulmonary edema. Measures to mildly increase *PVR* such as normocapnia and decreasing $F_{IO_2}$ to the lowest level tolerated can help minimize the coronary steal phenomenon. Inotropic agents can improve cardiac function, but can also increase heart rate (*HR*) and myocardial oxygen consumption and worsen the ischemia. The cardiovascular depressant effects of volatile anesthetics are often poorly tolerated, and an opioid technique may be preferred.

If repair requires the use of CPB, significant post-bypass inotropic support may be needed, e.g. dopamine, dobutamine, or epinephrine. Nitroglycerin is often used to improve coronary perfusion. Decreasing the afterload of the left ventricle is also desirable and can be accomplished with an inodilator (milrinone) or a vasodilator (sodium nitroprusside). Mechanical support of the left ventricle with a left ventricular assist device (LVAD) may be required in some patients who are unable to be weaned from CPB.[44] This may be more common in the younger infant with poor collateralization of coronary blood flow and acute myocardial infarction. Postoperative pain control with intravenous narcotic is adequate. Most patients are kept intubated and ventilated postoperatively to allow time for ventricular recovery.

Normalization of LV function occurs substantially after restoration of a two-coronary circulation, although this may take as long as 2 years, and some degree of chronic impairment may persist. Even in the group requiring LVAD support, a high survival rate and good long-term recovery can be achieved.

The optimal follow-up method after ALCAPA repair is controversial, with ECG, Holter monitoring, stress-thallium scanning, and cardiac catheterization all showing equivalent results. Serial echocardiography can be useful to assess the left ventricular function, the severity of mitral insufficiency, and the patency of the revascularized left coronary artery flow. Long-term survivors of ALCAPA repair show regional impairment of myocardial flow reserve which may contribute to impaired exercise performance.[45] However, even under stress testing, the normal growth of the heart has not been found to compromise the anastomosis. Patients with ALCAPA that survive the perioperative period have an excellent prognosis for functional recovery of the left ventricle regardless of their preoperative state.[46]

## Mitral regurgitation

Mitral regurgitation rarely occurs as an isolated lesion in congenital heart disease. Rather, it usually occurs as a component of another lesion, such as complete or partial atrioventricular canal defect, mitral valve prolapse, myocardial or papillary muscle infarction such as that seen with the ALCAPA syndrome (see above), connective tissue disorder such as Marfan's syndrome, rheumatic disease, endocarditis, or Kawasaki disease.[47,48]

### Pathophysiology and natural history

In the normal mitral valve, the leaflets are asymmetric, with the anterior leaflet spanning one-third of the annulus, and the C-shaped posterior leaflet two-thirds. The anterior leaflet inserts into the anterolateral papillary muscle, and the posterior leaflet into the posteromedial papillary muscle. The papillary muscles insert into the left ventricular free wall in the normal mitral valve; the anterior leaflet is normally perfused by the left coronary artery and the posterior leaflet by branches of both left and right coronary arteries.[49] Valve competency depends on the large posterior leaflet overlapping the anterior leaflet during systole, and thus complete coaptation is necessary. Any process interfering with this coaptation, be it a cleft in the posterior leaflet, annular dilation from left ventricular infarction or severe dysfunction, may cause MR.

The clinical severity and symptoms of MR can be classified as mild, moderate, or severe.[50] In the patient with chronic MR, the patient may be asymptomatic. As MR worsens, both

the left atrium and left ventricle dilate, resulting in enlargement of the mitral annulus, and creating a vicious cycle of worsening MR as the annulus dilates. Resting *HR* increases, and as left atrial pressures (*LAP*s) increase, pulmonary venous, capillary, and finally pulmonary artery hypertension can occur. This results in tachypnea, pulmonary edema, poor feeding and diaphoresis in infants, and may result in atrial arrhythmias such as atrial fibrillation. The enlarged left atrium may cause compression of the left mainstem bronchus in infants. Obstructive airways disease and frequent infections occur in infants with moderate to severe MR. Physical examination in moderate to severe MR often reveals a diaphoretic, tachypneic patient, with resting tachycardia and an increased precordial impulse. The left ventricular apex may be displaced laterally, and the second heart sound intensity may be increased with pulmonary hypertension. A holosystolic, high frequency murmur is heard at the apex, radiating to the axilla. A low pitched diastolic rumble is heard with moderate or severe MR. The presence of a third heart sound indicates severe MR. Chest radiograph reveals cardiomegaly, with left atrial and left ventricular enlargement, and varying degrees of increased pulmonary vascular markings. The left lower lobe may have atelectasis due to left atrial enlargement and compression of left sided bronchi. Medical treatment includes the use of diuretics, digoxin, and afterload reduction is provided by angiotensin-converting enzyme inhibitors. Acute MR, such as that seen with acute infarction of a papillary muscle or left ventricle from ALCAPA, is often very poorly tolerated, with rapid development of pulmonary edema and respiratory and circulatory decompensation. Indications for surgical intervention include uncontrolled congestive heart failure resulting in failure to thrive, progressive enlargement of the left atrium and ventricle despite medical management, or atrial arrhythmias or persistent airway symptoms.

Echocardiographic diagnosis is essential to define the anatomy underlying the MR, and its severity. Various schema for grading echocardiographic severity have been devised; generally, when there is flow reversal in the pulmonary veins, the MR is considered significant. A regurgitant fraction can be calculated. Another indicator of severity of MR is the diameter of the regurgitant jet at the level of the orifice.[51] Cardiac catheterization is infrequently required for MR, but a regurgitant fraction can often be calculated angiographically, with a 20% regurgitant fraction considered mild MR, 20–40% moderate, 40–60% moderately severe, and greater than 60% severe. The *LAP* is elevated with a large A wave.[52]

Surgical approaches include annuloplasty with a prosthetic DeVega or Carpentier ring, suturing the cleft in the mitral valve, resection of a portion of the posterior leaflet, repairing or foreshortening a ruptured or damaged chordae tendinae, or mitral valve replacement.[53,54] Mitral valve repair is preferred in most centers in growing children, because of the need for anticoagulation with prosthetic valves, and the need for repeated replacement until growth is complete.[54] The surgery is done via midline sternotomy with CPB, and is often approached through an incision in the left atrium. The exact surgical approach is often not determined until the surgeon inspects the anatomy. After repair of the valve, appropriate annular size may be tested by passing a Hegar dilator of appropriate size for the patient's body surface area, and competence of the valve by injecting saline rapidly through the valve orifice into the left ventricle and noting competence while the heart is flaccid, which often predicts residual regurgitation.

## Anesthetic considerations

The optimal hemodynamic state for a patient with moderate or severe MR consists of afterload reduction, adequate preload and contractility, and high–normal *HR*. Faster *HR*s lead to less diastolic filing time, and less time for ejection, which will lead to a smaller regurgitant fraction, i.e. more forward stroke volume and *CO*. Afterload reduction will encourage forward flow as well, and adequate preload is necessary for forward flow to be normal.[55] Contractility should be maintained at normal levels to ensure ejection of the large stroke volumes seen in this lesion. A number of anesthetic regimens can be used to meet these goals, but high dose synthetic narcotics will need to be combined with a vagolytic agent such as pancuronium to maintain high *HR*s. Ketamine may not be desirable because this agent usually elevates systemic vascular resistance. Volatile agents are acceptable as long as they do not unduly depress contractility and they maintain *HR*; thus isoflurane, desflurane, or sevoflurane may be preferable to halothane in this lesion.[56]

Monitoring consists of standard monitors, arterial and central catheters, and transesophageal echocardiography (TEE), which is critical to reconfirm the preoperative findings, and most importantly, to assess the adequacy of surgical repair.[51] In addition, since the left side of the heart is opened for mitral valve surgery, TEE is critical to assess adequacy of intracardiac de-airing before the aortic cross-clamp is removed and before the patient is weaned from CPB.[57] Carbon dioxide is insufflated into the surgical field in some centers when the left side of the heart is open to air to decrease the number and size of air bubbles in the heart.[58] A left atrial catheter is often placed transthoracically by the surgeon during rewarming on bypass, in order to measure left sided filling pressures after bypass. Transcranial Doppler ultrasound is used in some centers to detect cerebral emboli, along with near infrared cerebral oximetry. Inotropic support is often required after CPB, and phosphodiesterase inhibitors such as milrinone are often used because of their vasodilating effects on both pulmonary and systemic circulations, and effects on both systolic and diastolic ventricular function.

Assessment of the postoperative repair and hemodynamics after bypass includes *LAP* measurement, both the absolute

number (may be elevated in both residual MR, or in mitral stensosis), and the presence or absence of a large V wave (present in MR, not as prominent in mitral stenosis or left ventricular dysfunction), which signifies residual MR. Once again TEE is crucial to determine the presence of residual MR, or the occasional creation of mitral stenosis, signified by elevated mitral valve inflow velocities or abnormal inflow patterns (see Chapter 9). These patients usually are not at great risk for postoperative bleeding because the suture lines are low pressure atrial sutures. Length of postoperative ventilation depends entirely on the patient's pre and postoperative condition; some older patients with preserved ventricular function may be candidates for early extubation.

## Pericardial effusion and tamponade

The pericardium is composed of visceral and parietal layers, and forms a fibroserous sac around the heart and extends a short distance onto the great vessels.[59] Collagen and connective tissue fibers form the fibrosa, and are compliant under normal conditions of low fluid volume and stretch, but when fluid in the pericardial sac increases significantly, the steep portion of the pressure–volume curve may be reached, and intrapericardial pressures increase greatly, and create tamponade physiology. The periocardium is opened and partially removed for most cardiac surgeries, but the closed mediastinal space still has limited reserve to accumulate blood and fluid, especially in small infants.

Symptomatic pericardial effusion and tamponade may be seen in a number of clinical settings, both post-surgical and in medical conditions. Acute postoperative hemorrhagic tamponade is obviously a life-threatening emergency, but mediastinal bleeding and tamponade physiology may develop more slowly, over hours to several days postoperatively. Other causes of pericardial effusion and tamponade include cardiac perforation from cardiac catheterization or central venous catheter placement, chylous pericardial effusion after surgery, acute viral or bacterial infections, trauma, post-pericardiotomy syndrome, malignancy, congestive heart failure, renal failure, and inflammatory and autoimmune disorders.[60]

Cardiac tamponade occurs when fluid, blood, or blood clots fill the pericardial space or mediastinum and increase pressure enough to significantly affect *CO*. Beck's triad consists of hypotension, elevated systemic venous pressure, and a small quiet heart on auscultation.[61] Clinically patients with tamponade physiology have dyspnea, tachycardia, distended neck veins, narrow pulse pressure, and pulsus paradoxus in the presence of a pericardial effusion. Tamponade physiology develops as right and left atrial, and biventricular end-diastolic pressures equalize as the cardiac chambers compete for restricted space.[60] Diastolic filling and thus stroke volume become restricted, and the sympathetic nervous system compensates by increasing the contractile state, ejection fraction, and *HR*. Inspiration lowers intrathoracic pressure and promotes venous inflow into the right ventricle, which fills, but this shifts the interventricular septum to the left, restricting left ventricular filling. The negative intrathoracic pressure also decreases pressure in the pulmonary veins, and in combination with elevated left ventricular diastolic pressure, this also inhibits left ventricular filling, and thus stroke volume decreases greatly during inspiration, creating pulsus paradoxus. Interestingly, pulsus paradoxus detected on the pulse oximeter plethysmographic waveform correlates well with clinical cardiac tamponade in pediatric patients.[62] Of note, positive pressure ventilation, atrial septal defect, severe left ventricular dysfunction, hypertrophic cardiomyopathy, and aortic insufficiency all reduce or eliminate pulsus paradoxus.

Aside from clinical signs and symptoms, echocardiography is the most important diagnostic tool in pericardial effusion and tamponade syndromes.[63] The size and location of the effusion can be defined, as well as its consistency—serous or bloody vs. fibrous or clots. In addition, tamponade physiology can be confirmed by detecting reduced mitral valve and pulmonary vein inflow during inspiration. The echocardiogram can also direct the physician to the best and safest location for pericardiocentesis, or open drainage.

In a patient with tamponade physiology, the induction of general anesthesia, muscle relaxation, tracheal intubation, and positive pressure ventilation are fraught with danger, and cardiac arrest and death may occur in this scenario. The patient is often barely compensating, and only the combination of maximal sympathetic stimulation and negative intrathoracic pressure during spontaneous respiration allow enough stroke volume to maintain barely adequate *CO*. Any upset in this balance can result in cardiac arrest. Anesthetic agents may remove sympathetic stimulation, and the institution of positive pressure ventilation may increase intrathoracic pressure to the point that systemic and pulmonary venous return essentially cease. The ideal situation would be to drain some of the fluid under local anesthesia so that ventricular filling and *CO* can improve to the point that the patient can tolerate anesthetic induction for a definitive procedure. This is often possible in the adult or cooperative older child or teenager, but not in the infant or toddler. In this situation, ketamine, despite its potential for direct myocardial depression, is usually well tolerated, while maintaining spontaneous ventilation until some fluid can be drained.

If general anesthesia must be induced, the cardiologist or surgeon responsible for the drainage of the fluid must be present, prepared to emergently access the pericardial or mediastinal space, either by needle or incision. Echocardiographic guidance is essential for pericardiocentesis, where the pericardial space is not being accessed under direct vision. All equipment and crossmatched blood must also be readily available, and in some instances it is prudent to have

the subxyphoid area sterilely prepared and draped for immediate incision if hemodynamic collapse occurs on induction. An adequate period of preoxygenation is essential. Intravascular volume loading is recommended because it may maximize venous return, and is unlikely to worsen the situation acutely. Etomidate would appear to be the preferable agent for rapid intravenous induction of anesthesia because of its lack of negative inotropic effect on the myocardium.[64,65] Ketamine would be a possible choice, but again has direct negative effects on the myocardium.[66] If the patient is not at high risk for gastric aspiration, it may be preferable to induce anesthesia and keep the patient breathing spontaneously or gently assisted, if possible, until some of the fluid can be drained. Succinlycholine may need to be avoided because of its propensity to cause bradycardia. Tracheal intubation should be rapid, and positive pressure ventilation extremely gentle, or avoided for as long as possible. Preparations should be made for a full resuscitation, including epinephrine and atropine. In the event of hemodynamic collapse, drainage of the pericardial space must proceed immediately while resuscitative efforts are made. Draining the fluid normally allows the patient to recover enough *CO* to continue the procedure at a more controlled pace.

Drainage of the pericardium or mediastinum can be accomplished by pericardiocentesis, where the space is accessed under echocardiographic guidance with a needle, then a guidewire, and finally a catheter is placed for drainage. Injection of agitated saline as echocardiographic contrast medium may assist in localizing the pericardial space.[67] This is normally performed by a cardiologist, and should be performed in a location where full resuscitative resources, including personnel, are available. A subxyphoid pericardial window for drainage is frequently performed by the surgeon, with a mediastinal drain left in place for several days. Occasionally, as in the case of constrictive pericarditis with impending tamponade, a pericardial stripping must be done with full sternotomy. Acute postoperative tamponade from mediastinal bleeding is heralded by low blood pressure and poor systemic perfusion accompanied by elevated central venous and *LAP*s. Mediastinal tube drainage may be increased, or may have decreased greatly, giving the team a false sense of security. A widened mediastinum may be seen on chest radiograph, and this can be confused with low *CO* due to myocardial dysfunction. Echocardiography, if time permits, will exclude the latter diagnosis. The sternum must be reopened immediately at the bedside in the intensive care unit in cases of impending cardiac arrest. A more controlled re-exploration may be undertaken in the operating room if time permits.

Reported complications for pericardiocentesis in pediatric patients range from death from cardiac perforation and tamponade to pneumopericardium, to ST changes from coronary artery lacerations.[68,69] Higher complication rates are seen with younger patients under the age of 2 years, inexperienced operators, and lack of echocardiographic guidance, making the latter essential. Hand-held portable ultrasound technology has progressed to the point where this may be a viable option in any hospital setting.[70]

## Summary of management

### Vascular rings

- Reliable vascular access is essential because of the potential for significant and rapid blood loss. Arterial line for most; also consider central line.
- An inhalation induction should be performed with maintenance of spontaneous ventilation until the ability to assist with positive pressure ventilation has been ascertained.
- Patients may require a smaller-than-expected endotracheal tube size, and single lung ventilation may be desirable.
- Minimally symptomatic patients can be extubated at the end of the case.
- Good postoperative analgesia is essential using epidural analgesia, intercostal rib blocks or adequate intravenous opioids.

### Anomalies of the coronary arteries

- Infants with ALCAPA are often critically ill with little cardiac reserve and significant myocardial ischemia.
- Adequate monitoring, including a multilead ECG, arterial pressure monitoring, and central venous access for drug administration and volume assessment are essential.
- Induction should be gradual to avoid major swings in blood pressure. A gentle and rapid laryngoscopy is also critical.
- Fluid administration is titrated to assure adequate preload for maintenance of *CO* while avoiding pulmonary edema.
- Measures to mildly increase *PVR* such as normocapnia can help minimize the coronary steal phenomenon.
- Inotropic agents can improve cardiac function, but can also increase *HR* and myocardial oxygen consumption and worsen the ischemia.
- The cardiovascular depressant effects of volatile anesthetics are often poorly tolerated, and an opioid technique may be preferred.
- After CPB, significant inotropic, inodilator, and coronary and systemic vasodilator support may be needed.
- Most patients are kept intubated and ventilated postoperatively to allow time for ventricular recovery.
- Mechanical support of the left ventricle with a LVAD may be required in some patients who are unable to be weaned from CPB.
- Severe preoperative mitral insufficiency and ventricular dysfunction often result in postoperative hemodynamic instability and increased perioperative mortality.

## Mitral regurgitation

- The optimal hemodynamic state for a patient with moderate or severe MR consists of afterload reduction, adequate preload and contractility, and high–normal *HR*.
- High dose synthetic narcotics will need to be combined with a vagolytic agent such as pancuronium.
- Volatile agents are acceptable as long as they do not unduly depress contractility and they maintain *HR*; halothane may not be desirable.
- TEE and *LAP* monitoring are crucial to determine the presence of residual MR, or the occasional creation of mitral stenosis.

## Pericardial effusion and tamponade

- Patients with tamponade physiology have dyspnea, tachycardia, distended neck veins, narrow pulse pressure, and pulsus paradoxus.
- Induction of general anesthesia, muscle relaxation, tracheal intubation, and positive pressure ventilation may precipitate cardiovascular collapse.
- Drainage of a small amount of the pericardial fluid with sedation (ketamine) and local anesthesia should be performed if possible.
- Etomidate is the preferred drug for induction of general anesthesia.
- Personnel and equipment for immediate drainage and resuscitation must be immediately available.
- Echocardiographic guidance is essential for closed procedures not under direct vision, e.g. periocardiocentesis.

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# 24 Anesthesia for cardiac and pulmonary transplantation

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## Heart transplantation

The first human heart transplant was performed by Christian Barnard on December 3rd, 1967,[1] and 3 days later Kantrowitz completed the first pediatric heart transplant on a 16-day-old infant with Ebstein's anomaly and pulmonary atresia.[2] Unfortunately, during the first decade of heart transplantation, outcome was poor and very few pediatric heart transplants were performed until the 1980s, when cyclosporine became available and transplantation was proposed for neonates with complex congenital heart lesions such as hypoplastic left heart syndrome (HLHS) (Fig. 24.1).[3] Since the mid-1990s, the number of reported pediatric recipients has remained stable despite improved survival, underlining the rate-limiting step of donor organ availability.[4]

Organ transplantation in the USA is sanctioned by congressional mandate through the Nation Organ Transplant Act (NOTA). An Organ Procurement and Transplant Network (OPTN) was created and is administered by the United Network for Organ Sharing (UNOS). Donation of organs is voluntary and is managed by government-regulated local agencies called organ procurement organizations. Equitable allocation of a scarce life-saving resource is challenging. The UNOS has three recipient status categories—status IA, IB, and II, with status IA indicating the sickest patients who are in urgent need of heart transplantation for survival.

### Indications for heart transplantation

Heart transplantation is generally indicated when expected survival is less than 1 or 2 years and/or when there is unacceptable quality of life secondary to irreparable cardiac diseases.[5] Survival rates have increased as management and immunosuppressive techniques have improved and absolute contraindications for transplantation have now become more relative. Often the dilemma is no longer whether to transplant or not, but rather when to do it. However, heart

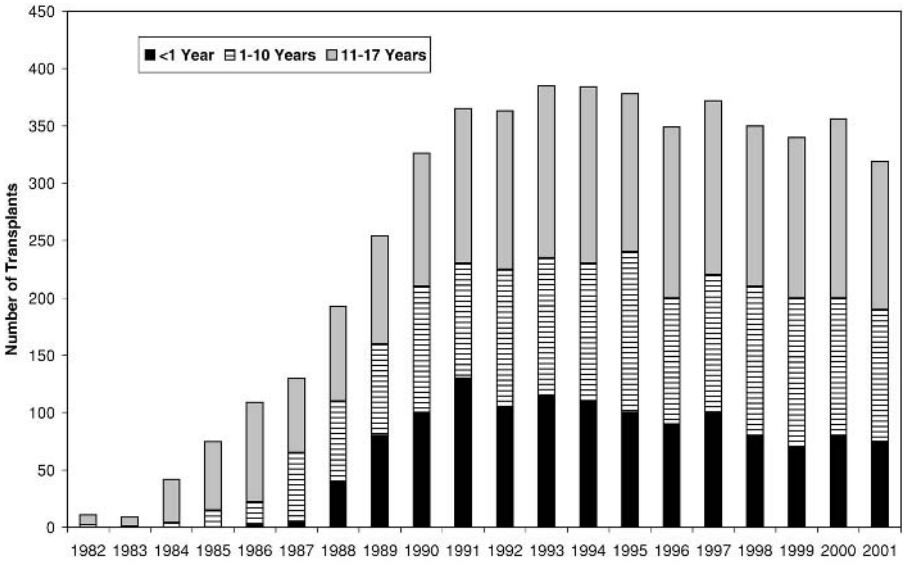


**Fig. 24.1** Age distribution of pediatric heart transplant recipients by year of transplant. Reproduced with permission from Boucek MM, Edwards LB, Keck BM *et al*. The Registry of the International Society for Heart and Lung Transplantation: Fifth official pediatric report—2001 to 2002. *J Heart Lung Transplant* 2002; **21**: 827–40.

transplantation remains a palliative procedure at present.[6] Pediatric indications for heart transplantation vary with age and include cardiomyopathy, congenital heart disease (CHD) and retransplantation (Fig. 24.2). The majority of transplantations in infants are for CHD, whereas cardiomyopathy is the predominant indication in older children.[4]

## Cardiomyopathy

### *Dilated cardiomyopathy*

The etiology is diverse and incompletely understood but includes viral myocarditis, drugs (e.g. adriamycin), abnormalities of fatty acid, amino acid, glycogen and mucopolysaccharide metabolism, mitochondria and genetic disorders, chronic arrhythmia, and coronary artery abnormality.[5] Predictors of a poor outcome are a family history of cardiomyopathy, syncope, ventricular arrhythmia or near-death episode, left ventricular end-diastolic pressure greater than 25 mmHg, and left ventricular ejection fraction less than 30%.

### *Hypertrophic cardiomyopathy*

A number of genotypes are known. Risk factors for sudden death include marked left ventricular wall thickness, family history of sudden death, and non-sustained ventricular tachycardia.

### *Restrictive cardiomyopathy*

These uncommon disorders with diastolic dysfunction generally have a poor prognosis and are associated with myocardial infiltrative processes such as amyloidosis, hemochromatosis, glycogen storage disease, mucopolysaccharidosis, sarcoidosis, and endomyocardial fibrosis. Elevated pulmonary vascular resistance (*PVR*) is often present.

## Congenital heart disease

This group of patients include children with "failed" Fontan or equivalent palliation of single ventricle physiology, patients with end-stage failure after surgical repair of congenital defects, HLHS, and complex congenital heart variants with no option of palliative surgery.

One-year survival rates after surgery in excess of 80% have been achieved for infants with HLHS, irrespective of whether primary transplantation or staged reconstruction (Norwood approach) was performed.[7] Most centers opt to perform staged reconstruction, partly because of the desperate paucity of donor organs and the significant mortality (up to 30%) while waiting for transplantation.[8]

## Other indications

Although rare, there are children who may require cardiac transplantation for unresectable cardiac tumors and other diseases such as Kawasaki's syndrome.

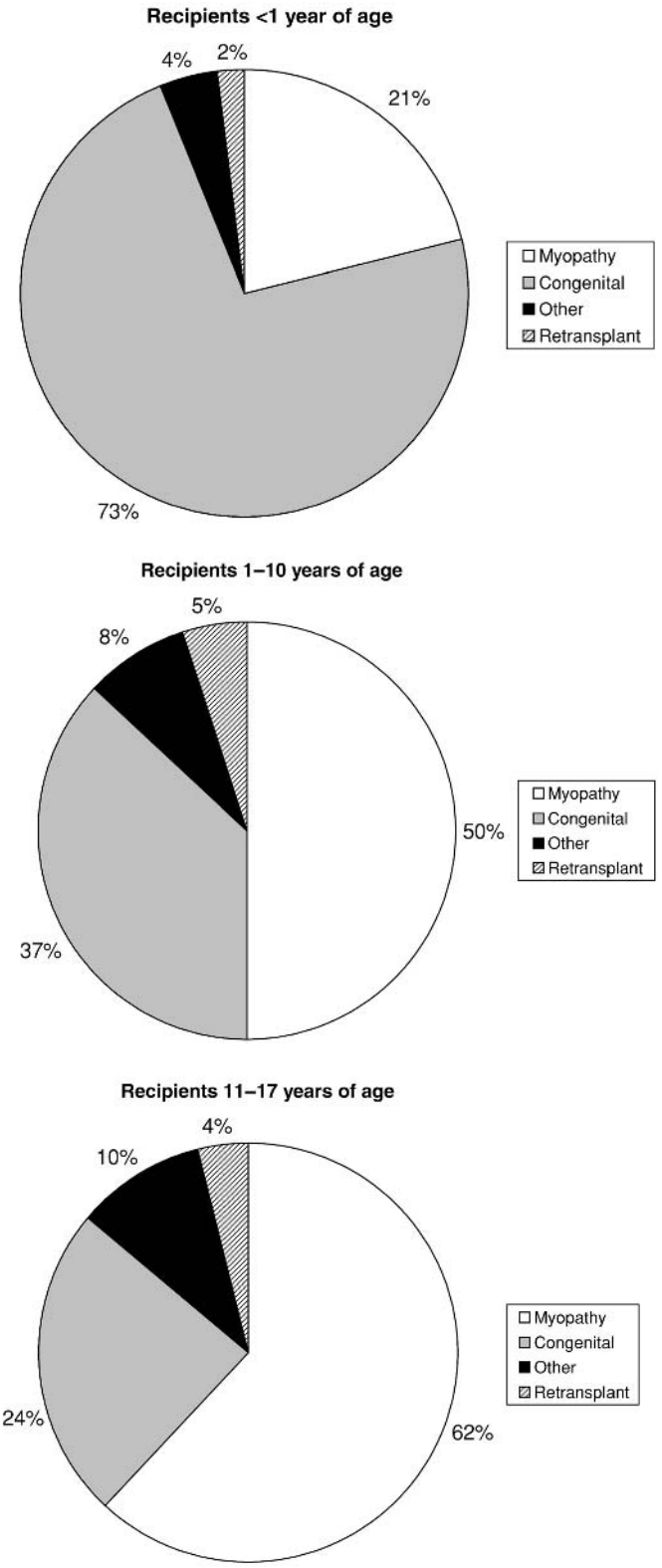


**Fig. 24.2** Diagnoses of pediatric heart transplant recipients of differing ages. Reproduced with permission from Boucek MM, Edwards LB, Keck BM *et al*. The Registry of the International Society for Heart and Lung Transplantation: Fifth official pediatric report—2001 to 2002. *J Heart Lung Transplant* 2002; **21**: 827–40.

## Recipient evaluation

A detailed assessment of patients is required to determine their suitability for heart transplantation (Table 24.1). Factors that may exclude patients from consideration for transplantation include severe central nervous system, liver or kidney dysfunction, pulmonary infarction, pulmonary hypertension, morbid obesity, and some infections, malignancies or chromosomal abnormalities.

Assessment of cardiopulmonary function usually includes cardiac catheterization and angiography. The recipient's cardiac anatomy has to be accurately delineated as abnormal cardiovascular anatomy influences surgical technique during harvesting and transplantation. Hemodynamic measurements are required, especially determination of *PVR*. Transplantation in patients with *PVR* in excess of 5 Wood U/m$^2$ or a transpulmonary gradient greater than 15 mmHg is potentially contraindicated because it is associated with acute right heart failure and increased mortality.[9] The upper limit of *PVR* associated with successful cardiac transplantation has not been established in children.

All patients with pulmonary hypertension have *PVR* measured at baseline conditions and during administration of oxygen, nitric oxide and/or other pulmonary vasodilator therapy. When the response is marginal, repeat values after 1–2 weeks of inotropic support, afterload reduction, and pulmonary vasodilation may demonstrate improvement (see Chapter 14 for management of pulmonary hypertension). Experienced institutions may accept children with *PVR* as high as 8–12 Wood U/m$^2$ if it is reactive. Patients whose *PVR* does not respond to therapy may be candidates for heterotopic heart transplantation, heart–lung transplantation, or lung transplantation. Children with restrictive cardiomyopathy are particularly prone to marked elevation of *PVR*, which may contribute to the poor prognosis in these patients and potentially make cardiac transplantation problematic. Nitric oxide appears to be a good agent to demonstrate reversibility of *PVR* in these patients.[10]

Radionuclide angiography is useful for assessing systemic ventricular dysfunction in patients with complex cardiac morphology. Endomyocardial biopsy can identify acute myocarditis and myocardial infiltrates. Pulmonary function tests (PFTs) may be indicated for older children with chronic lung disease. Evaluation of patients with cardiomyopathy should include a metabolic work-up because potential etiologic factors include mitochondrial disorders, and genetic studies if indicated by phenotypic appearance or family pedigree.

Infectious disease and immune system evaluation are important. The child's immunization status should be updated if necessary. Tests are performed for latent infections such as cytomegalovirus or Epstein–Barr virus that may become clinically significant during immunosuppression. Donor matching is based on ABO typing. The candidate's

**Table 24.1** Routine pre-transplant evaluation.

| |
|---|
| *History and physical examination* |
| Age, height, weight, body surface area |
| Diagnoses |
| Past medical history |
| Medications |
| Allergies |
| Immunization record |
| |
| *Laboratory data* |
| Liver and kidney function tests |
| Urine analysis |
| Glomerular filtration rate |
| Prothrombin time/INR/partial thromboplastin time |
| Complete blood count and differential |
| PPD skin test |
| Serologies for human immunodeficiency virus, hepatitis, cytomegalovirus, Epstein–Barr virus, *Toxoplasmosis gondii*, syphilis |
| ABO type |
| Panel reactive antibody |
| |
| *Cardiomyopathy work-up* |
| Thyroid function tests |
| Blood lactate, pyruvate, ammonia, acyl carnitine |
| Urine organic acids, acyl carnitine |
| Skeletal muscle biopsy |
| Karyotype |
| |
| *Cardiopulmonary data* |
| Cardiac catheterization |
| Echocardiogram |
| Radionuclide angiography |
| Endomyocardial biopsy |
| Electrocardiogram |
| Chest radiograph |
| Pulmonary function tests |
| $Vo_{2max}$ |
| |
| *Psychosocial evaluation* |
| Possible relocation |
| Long-term supportive care |
| Parental substance abuse |
| History of neglect or abuse |
| |
| *Consultations as required* |
| Dental services |
| Other services |

INR, international normalized ratio; PPD, purified protein derivative.
Adapted from Boucek MM, Shaddy RE. Pediatric heart transplantation. In: Allen HD, Gutgesell HP, Clark EB, Driscoll DJ, eds. *Moss and Adams' Heart Disease in Infants, Children, and Adolescents Including the Fetus and Young Adult*, 6th edn. Philadelphia, PA: Lippincott, Williams & Wilkins, 2001: 395–407.

blood is also screened for antibodies against sera of random blood donors and, if reactive, a serum crossmatch with the donor is performed. Although human lymphocyte antigen (HLA) compatibility may improve graft survival, HLA matching is not routinely performed because of time constraints and the limited availability of donor organs. Panel reactive antibodies (PRA) are preformed circulating HLA alloantibodies that, in high titers, are associated with reduced allograft survival.[11] Therapies to reduce PRA levels have included intravenous immunoglobulin, plasmapheresis, and cyclophosphamide. Homologous blood products can increase antibody titers and should be avoided if possible during the pre-transplant period.

Heart transplantation requires long-term immunosuppression, frequent invasive procedures, and lifelong medical care. Patients have to live close to the hospital during the initial months after surgery and temporary relocation of the family may be necessary. Prolonged periods of stressful hospitalization are likely. A stable social situation is essential for success and psychosocial evaluation is an important aspect of the pre-transplantation process.

## Recipient pre-transplant management

Mean waiting period from acceptance for heart transplantation to actual surgery currently is about 3 months but varies with the child's age, blood group, and list status. Approximately 20% of children with cardiomyopathy and 30% of those with end-stage CHD die waiting for a donor heart.[12,13]

Aggressive medical management to achieve stabilization is required and includes supplemental oxygen, diuretics, inotropic support (e.g. dobutamine, dopamine, phosphodiesterase inhibitors), arrhythmia therapy, and mechanical ventilation. Children with chronic heart failure often receive digoxin, diuretics including spironolactone, and angiotensin-converting enzyme inhibitors. Studies of β-blockade therapy (e.g. metoprolol, carvedilol) have been limited in children but are encouraging.[14] Patients with severe left ventricular dilation may need anticoagulation, preferably coumadin, to prevent the development of intracardiac thrombi and systemic embolization. Amiodarone is often chosen for treating arrhythmia. Implantable defibrillators have been effective in pediatric patients large enough for these devices. Biventricular pacing is an experimental modality showing promise.

Patients with refractory myocardial failure require mechanical circulatory support as a bridge to cardiac transplantation. Extracorporeal life support is the only modality currently available for small children and can be used for at least 2 weeks with acceptable survival and hospital discharge rates. Renal insufficiency requiring dialysis decreases the likelihood of survival.[15] Other complications include sepsis, bleeding, and neurologic injury. Ventricular assist devices and intra-aortic balloon pumping are usually reserved for older adolescents but have been employed successfully in younger children weighing about 15 kg.[16,17] Partial left ventriculectomy has been used to improve clinical status and acts as a biological bridge to heart transplantation in children with end-stage dilated cardiomyopathy.[18] Congenital heart disease is the main indication for heart transplantation in children less than 1 year of age. Many of these infants have HLHS and are managed invasively in an intensive care setting. Patency of the ductus arteriosus is maintained initially by prostaglandin $E_1$ ($PGE_1$) infusion and may require stenting later. Restriction of flow across the atrial septal defect is addressed by interventional catheterization techniques. Balance between systemic and pulmonary blood flow is necessary, and occasionally may require pulmonary artery banding.

## Donor management

Once the diagnosis of brain death is established and parental/guardian consent obtained, the donor's specifics are checked for possible match with patients listed by UNOS for transplant. Because of the shortage of suitable organ donors and the high morality rate on the waiting list, most centers use a liberal donor screening strategy. The age distribution of pediatric heart donors is similar to that of heart recipients.[4] Echocardiography is useful for assessment of donor heart function. Widespread malignancy or infection in the prospective donor are exclusion criteria, but cardiac resuscitation and chest trauma are not necessarily contraindications provided the donor's hemodynamics have been stabilized and inotropic agents are no longer needed or are at minimal doses. Usually the donor should be 80–160% of the recipient's weight, but the upper limit may be extended for neonates or for recipients with pulmonary hypertension.[19] Attempts to limit donor heart ischemia time are important but may be hampered by transport issues. Many centers prefer the period to be less than 6 hours, especially if the recipient has increased *PVR* although successful outcomes after graft ischemia times of up to 9 hours have been reported.[19] The anesthetic management of a pediatric organ donor is beyond the scope of this chapter and has been reviewed elsewhere.[20]

## Surgical technique

There are two methods for performing heart transplantation—orthotopic, in which the recipient heart is excised and replaced in the correct anatomical position by the donor heart, and heterotopic, in which the donor heart is placed in the right side of the chest alongside the recipient organ and anastomosed so as to allow blood flow through either or both hearts. The majority of transplants in children have been of the orthotopic type.

The orthotopic approach first described by Lower and Shumway[21] has been employed for many years in cases where anatomy is straightforward. This technique avoids individual systemic and pulmonary venous anastomoses but results in capacious atrial chambers, comprising donor and recipient components, which contract asynchronously. It has been suggested that atrial contribution to cardiac output (*CO*) may be superior with near to total cardiac transplantation.[22] A small cuff of left atrial tissue is left in place, incorporating all pulmonary veins, and the entire right atrium is removed. Bicaval anastomoses are then performed. This technique results in more normal anatomical result. It has been suggested that it improves sinus nodal function, invokes less tricuspid regurgitation, and improves exercise performance.[23] However, there are only preliminary data in children to demonstrate that outcomes are improved.[24]

Cardiac transplantation for children with congenital malformations can require surgery of greater complexity. Deep hypothermic circulatory arrest may be employed in patients requiring extensive vascular reconstruction; for example, Bailey's technique for transplantation in infants with HLHS.[25]

## Anesthetic management

### Pre-cardiopulmonary bypass period

Children listed for heart transplantation have little or no cardiac reserve and can be extremely sensitive to the perturbations induced by anesthesia and surgery. For children with CHD, the pre-cardiopulmonary bypass (pre-CPB) anesthetic management for heart transplantation differs little from that for non-transplant cardiac surgery and requires a good appreciation of the patient's particular pathophysiology. The physiological consequences of cardiac failure are discussed in Chapter 3. In brief, children with end-stage cardiac dysfunction have a chronically activated sympathetic nervous system and an impaired response to β-agonists. Reduced renal perfusion triggers the renin–angiotensin system, which leads to increases in vasoconstriction, venoconstriction, and intravascular volume. These compensatory mechanisms increase preload and afterload and perpetuate congestive heart failure. Plasma norepinephrine levels are about three times normal, while myocardial norepinephrine concentrations are reduced. Cardiac $\beta_1$-receptors are downregulated and there is a partial uncoupling of cardiac $\beta_1$-receptors for adenylate cyclase. Additionally, altered ratios of inhibitory/stimulatory signal transduction proteins decrease $\beta_1$-receptor sensitivity. These factors contribute to reduced levels of cyclic adenosine monophosphate with reduced movement of calcium into myocytes. The contractile response to direct β-adrenergic inotropes is impaired. Since tissue norepinephrine levels are decreased, indirect-acting agents such as ephedrine are also less effective.

A dysfunctional, dilated heart is exquisitely sensitive to changes in preload, afterload, heart rate (*HR*), and contractility. Systolic and diastolic function is impaired and high mean atrial pressure is required to ensure adequate filling. Elevated left atrial pressure results in elevated *PVR* and right ventricular dysfunction. Because these patients have exhausted their preload reserve, reduction in *HR* results in a decline in *CO*. Conversely, an increase in *HR* decreases the diastolic filling time which reduces end-diastolic volume and stroke volume. Small increases in afterload result in comparatively large increases in end-systolic volume leading to a large decrease in stroke volume and *CO*.

Prior to surgery, young infants and children with uncompensated heart failure are usually already in intensive care, and may have invasive lines *in situ* and be on ventilator support. More stable patients may have been called in from home for the transplantation surgery and could have eaten recently. Several hours usually elapse before surgery but therapy to modify gastric pH and volume and the application of continuous cricoid pressure during induction is reasonable. Good communication between the transplant surgeons, anesthesiologists, operating room staff, and donor procurement team is vital in order to coordinate care and ensure graft ischemia time is minimized. The advisability of premedication and the method of anesthesia induction depend upon the patient's age, cardiac lesion, and cardiopulmonary function. Establishing invasive hemodynamic monitoring prior to induction of anesthesia may not always be feasible and so it is imperative to institute non-invasive patient monitoring prior to the administration of medications that alter hemodynamic and/or respiratory function. Meticulous airway management is vital as hypoxia and hypercarbia aggravate *PVR* and may further depress *CO*. Similarly, anesthesia or surgery-induced changes in *HR*, preload, afterload or contractility may precipitate hemodynamic decompensation. Rapid sequence induction may be poorly tolerated in patients with a minimal cardiorespiratory reserve. A wide variety of anesthetic agents have been used successfully. The desirable and detrimental cardiovascular effects of anesthetic agents are reviewed in Chapter 4. In children with CHD, a fentanyl/midazolam/muscle relaxant anesthetic technique was reported to preserve cardiac index better than volatile agents, provided *HR* was maintained.[26] Etomidate has minimal effect on hemodynamics; propofol decreases systemic vascular resistance.[27] Nitrous oxide has myocardial depressant and pulmonary vasoconstrictor properties and is best avoided. Ketamine supports the circulation by indirectly stimulating catecholamine release. This may be blunted in children with dilated cardiomyopathy and impaired β-agonist responses and the drug's direct myocardial depressant effects may then predominate.

Monitoring during surgery does not differ from that used for pediatric open heart surgery. Some authorities avoid inserting catheters into the right internal jugular vein because


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the vessel will later be accessed repeatedly for endomyocardial biopsies. Transesophageal echocardiography (TEE) is useful for evaluation of heart anatomy and function, mural thrombus, and intracardiac air. Many experienced institutions do not use pulmonary artery catheters because the value of information gained does not warrant the additional risk. The prophylactic use of antifibrinolytics should be considered. Aprotinin has been reported to diminish blood loss in children during heart transplantation if they have previously undergone median sternotomy.[28] The value of antifibrinolytics for primary heart transplantation is uncertain.

### Cardiopulmonary bypass period

Ultrafiltration during CPB may benefit the patient by removing excess free water, hemoconcentrating red cells and coagulation factors, and modulating the inflammatory response. Diuretic therapy may be required. Methylprednisolone is administered to attenuate any hyperacute immune response; the timing and dose is institution-specific.

### Post-cardiopulmonary bypass period

Issues of concern include denervated donor heart, global ischemia–reperfusion injury, elevated *PVR*, arrhythmia, hemostasis, and hyperacute rejection.

The transplanted heart is functionally denervated.[29] The recipient atrial remnant remains innervated but no electrical impulses cross the suture line so the donor atrium is responsible for the patient's *HR*. There are two P waves on the electrocardiogram (ECG), representing activity of the transplanted and native sinoatrial nodes. Resting *HR* is higher than normal because vagal tone is absent and the normal beat-to-beat variations in response to respiration are lost, as are the normal responses of the heart to alterations in body position and carotid body massage. The donor heart cannot abruptly increase *HR* and *CO* in response to stress because the baroreceptor reflex is disrupted. The attenuated *HR* response to stress means the anesthesiologist must be particularly vigilant to ensure the child does not become too lightly anesthetized. With the loss of the baroreceptor reflex, the patient with a denervated heart may initially show an exaggerated response to hypovolemia with a marked decrease in mean blood pressure, and then a delayed exaggerated hypertensive and tachycardia response, due to endogenous catecholamine release. The Frank–Starling (pressure–volume) relationship remains intact and compensates for hypovolemia and hypotension by increasing stroke volume secondary to an increased venous return. Therefore, it is important to maintain adequate preload, especially if vasodilators are administered. Innervation of the peripheral vasculature is preserved, and changes in peripheral vascular resistance may still occur in response to alterations in sympathetic outflow from the vasomotor center due to signals from stretch receptors in the great vessels.

Drugs such as atropine, glycopyrrolate, neostigmine and pancuronium that act on the heart through vagal or sympathetic neuromechanisms will no longer affect *HR*. Alpha- and beta-adrenergic receptors remain intact and inotropes such as epinephrine and isoproterenol will cause appropriate responses from the heart.

The donor organ is subjected to ischemia–reperfusion injury and patients usually require inotropic support for separation from CPB. Left-ventricular diastolic dysfunction is common and characterized by a restrictive ventricular filling pattern, with a reduced preload reserve and a relatively fixed stroke volume. Sinoatrial node dysfunction is relatively common. Dopamine or isoproterenol are often selected and epicardial atrioventricular pacing can be instituted if necessary to achieve the desired *HR*. Temporary pacing wires are placed in all patients. Arrhythmias are quite common in the early postoperative period, usually premature atrial or premature ventricular contractions. Compression of intrathoracic structures may be problematic during closure of sternotomy, particularly if the donor heart is relatively oversized.[30]

It is important to minimize *PVR*. Catecholamine release is reduced by ensuring the patient remains adequately anesthetized. Ventilation management is facilitated by muscle relaxants. Prior to separation from CPB, toilet of the airway should be performed and the lungs inflated with an inspiratory hold maneuver to eliminate atelectatic areas. Metabolic acidosis is corrected and a blood pH of 7.45–7.48 achieved by ventilating to moderate hypocapnia (30–32 mmHg) with 100% oxygen. Lung overdistension and positive end-expiratory pressure (*PEEP*) are avoided because *PVR* is lower when lung volumes are at functional residual capacity.

Elevated pulmonary artery pressures can be discerned by echocardiography and measured by the surgeon (catheter or palpation). Right ventricular failure may develop without manifesting increased pulmonary artery pressure because the "untrained" right ventricle may dilate and fail when posed with the increased work of high *PVR*. This situation can be recognized echocardiographically or with invasive monitoring: the CVP will rise as the left atrial pressure decreases and *CO* falls. Additional measures to control *PVR* may be necessary, including pulmonary vasodilator therapy such as nitric oxide, nitroglycerine, nitroprusside; and $PGE_1$, prostacyclin, phosphodiesterase inhibitors, and isoproterenol. More extreme hypocapnia may help, but also causes cerebral vasoconstriction and leftward shift of the oxygen dissociation curve. If the patient's *CO* remains inadequate despite maximal drug therapy, mechanical right ventricular assist or extracorporeal membrane oxygenation (EMCO) may be employed.[31]

Blood loss during heart transplantation can be considerable and is associated with increased morbidity and mortality. Coagulation management is no different from that for other open heart surgeries in children (see Chapter 10).

Packed red blood cells are cytomegalovirus-matched, leukoreduced, and irradiated. For infants, some centers wash packed red blood cells to reduce the potassium load. Citrate-induced hypocalcemia impairs contractility and coagulation; this may be minimized by initiating a calcium infusion (calcium chloride 10–30 mg/kg/h). Rapid platelet transfusion may aggravate *PVR*.

## Immunosuppression

Pediatric heart transplant provides a unique immunological opportunity because the development of the immune system extends not only into infancy, but continues throughout childhood. For example, cytokine production and the cytokine profile mature after birth. The absolute number of mature T cells and killer T cells is lower in the infant, naïve T cells are greater than in the adult, and the lymphocyte surface receptor repertoire is age-dependent. T-cell responses and phenotype are naïve, compared with adults, with decreased expression of integrins and adhesion molecules.[32] Younger age at time of transplantation is associated with better long-term survival and lower frequency of rejection compared with older children.[33] Infants apparently lacking significant anti-ABO antibody can safely undergo transplantation across ABO barriers, thus expanding the pool of donor hearts available to infants.[34]

Immunosuppressive therapies can be categorized by their actions into: (i) broad spectrum immunosuppressants: corticosteroids; (ii) calcineurin inhibitors: cyclosporine and tacrolimus; (iii) antiproliferative agents: mycophenolate mofetil (MMF) and azathioprine; (iv) antibodies against interleukin-2: basiliximab and daclizumab; (v) target of rapamycin inhibitors: sirolimus; (vi) mono- and polyclonal T-cell antibodies: OKT3, antithymocyte gamma globulin (ATGAM), thymoglobulin; and (vii) non-drug therapies: total lymphoid irradiation, photopheresis and plasmapheresis.

Typical clinical use of these agents has been summarized as follows:[35]

1 *Induction therapy*: Antibodies are used at the time of transplantation to reduce early rejection and diminish dose requirements for calcineurin inhibitors and corticosteroids. Data demonstrating improved survival are currently limited. T-cell-depleting antibodies include polyclonal rabbit antithymocyte globulin (thymoglobulin), equine ATGAM, and monoclonal murononab-CD3 (OKT3). The latter has neurologic effects, prominent first dose "cytokine release syndrome" and may increase the risk of lymphoproliferative disorders. Interleukin-2 blockers (basiliximab and daclizumab) are well tolerated.
2 *Maintenance therapy*: The choice and number of maintenance agents is largely guided by institutional experience and the recipient's clinical profile, rejection history, and comorbid associations. The objective is to prevent acute and chronic rejection while minimizing the adverse effects of immunosuppression. All regimens involve a calcineurin inhibitor. Many patients receive adjunct therapy with an antiproliferative agent or sirolimus. Often, corticosteroids are also administered, although many programs attempt to limit or avoid their long-term use.

### Calcineurin inhibitors

Cyclosporine (Sandimmune, Neoral) is the most commonly used immunosuppressant following pediatric heart transplantation. It binds to cyclophilin within the cytoplasm of T cells; this complex inhibits calcineurin phosphatase, thus interfering with the transcription of key cytokines required for T-cell activation and proliferation. Adverse effects may be dose related and include toxicity of renal, hepatic and neurologic systems, hypertension, hyperlipidemia, hirsutism, and gingival hyperplasia. Therapeutic drug monitoring is mandated because the therapeutic window is narrow and many other drugs influence drug levels. Cyclosporine trough levels are usually maintained in the range of 100–300 ng/mL.

Tacrolimus (Prograf, FK506) has a mode of action and spectrum of side effects that are very similar to cyclosporine. The choice of calcineurin inhibitor depends on institutional experience and drug side effects. Efficacy does not differ between the two agents but there may be less rejection (controversial)[36] and fewer side effects with tacrolimus (no hirsutism or gingival hyperplasia, less hypertension). Tacrolimus has been reported to allow more rapid weaning from corticosteroids. Like cyclosporine, the therapeutic window is narrow and blood levels can be affected by other medications. Trough levels are maintained in the range of 5–15 ng/mL.

### Antiproliferative agents

Antiproliferative agents such as azathioprine (Imuran) and MMF inhibit lymphocyte proliferation and one of these agents is often added to calcineurin inhibitor therapy. Azathioprine is a purine antagonist that inhibits T and B cells. Bone marrow depression is common and dosing is guided by the white blood cell count. Mycophenolate mofetil (CellCept) converts to mycophenolic acid, an inhibitor of purine synthesis. Lymphocytes are suppressed because they lack a salvage pathway. Absorption is variable and dosing may be guided by blood levels. Gastrointestinal side effects rather than bone marrow depression are the usual dose-limiting factor.

### Sirolimus

Sirolimus (rapamycin) is a macrolide antibiotic that blocks nuclear transcription of cytokines and can act synergistically with cyclosporine or tacrolimus. It is usually used to reduce calcineurin inhibitor dosing but its indications remain undefined. Sirolimus may inhibit the process of coronary

arteriopathy. Hyerlipidemia may occur and drug interactions are a concern.

### Corticosteroids

Corticosteroids are non-specific anti-inflammatory agents that were widely used in the pre-cyclosporine era. Nowadays, they are used mainly as triple therapy (steroid + calcineurin inhibitor + antiproliferative agent or sirolimus). Many centers try to minimize the dose and duration of corticosteroid therapy. Side effects are myriad and include higher infection risk, diabetes mellitus, bone demineralization, and coronary artery disease. Rejection risk may increase when steroids are withdrawn.

### Acute rejection therapy

High dose corticosteroid, usually methyl prednisolone, is first line therapy for acute rejection. Other agents are reserved for refractory or recurrent severe rejection and for rejection with severe hemodynamic compromise. These include monoclonal and polyclonal anti-T antibodies. Recurrent moderate rejection can usually be controlled with enhanced maintenance therapy (tacrolimus, sirolimus and corticosteroids).

Use of non-pharmacologic therapies for resistant or recurrent allograft rejection has been reported. Total lymphoid irradiation is given as an inverted Y-shaped mantle biweekly for 10 treatments. Bone marrow depression and development of lymphomas are concerns. Plasmapheresis is used to temporarily remove anti-donor antibodies in highly sensitized recipients. Photopheresis is a technique of immune modulation by reinfused lymphocyes from patients pretreated with psoralen and exposed to ultraviolet-A light *ex vivo*. No experience in children is reported.

### Chronic rejection therapy

Chronic rejection is manifest as coronary vasculopathy. There are no proven therapies that can halt or reverse this process and retransplantation is the most suitable option for advanced diffuse disease.

## Outcome following heart transplantation

Data from the International Society for Heart and Lung Transplantation show the actuarial 10-year survival for all pediatric heart recipients exceeds 50% (Fig. 24.3).[4] Review of long-term survival of children who had undergone heart transplantation at Stanford showed, with the assumption of survival to 10 years, cumulative survival was 79% at 14 years and 53% at 20 years.[37] Infants less than 1 year of age had a statistically lower 1-year survival than adolescents.[4] This

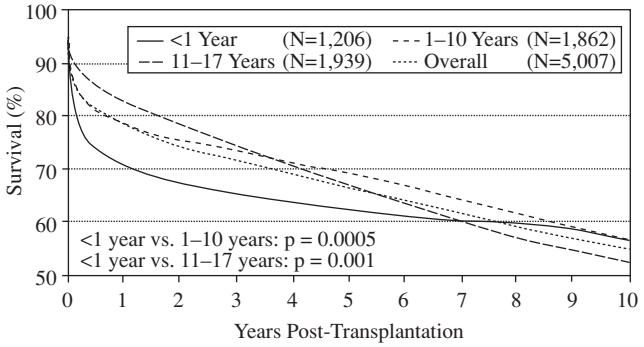


**Fig. 24.3** Actuarial survival after pediatric heart transplants between 1982 and 2001. Reproduced with permission from Boucek MM, Edwards LB, Keck BM *et al*. The Registry of the International Society for Heart and Lung Transplantation: Fifth official pediatric report—2001 to 2002. *J Heart Lung Transplant* 2002; **21**: 827–40.

early infant mortality, usually within the first 30 days after transplantation, has decreased in recent years and is most likely from graft failure. Hemorrhage, infection and other causes only account for a small percentage of deaths.[38] Once beyond the first year post-transplant, infants fare better than older children, perhaps reflecting the impact of immunolgic aspects of development on transplant survival. Conditional 3-year actuarial survival was greater than 95% for infants and 80% for adolescents, and incremental yearly mortality between 4 and 10 years post-transplant was less than 2% for infants and 4% for adolescents.

Risk factors for 1-year mortality were (in order): CHD, mechanical ventilation at time of transplantation, non-cardiac disease, ventricular assist device, and donor cause of death; and for 5-year mortality were: history of previous transplant and inotropic support at time of transplantation. Acute rejection was the leading cause of death during the first 3 years post-transplant but was displaced thereafter by coronary artery vasculopathy, which accounted for 40% of all deaths beyond 3 years.[4]

## Rejection

Rejection is defined by the Pediatric Heart Transplant Study Group as the clinical decision to intensify immuosuppression in association with either histopathology or dysfunction.[39] Pediatric heart transplant recipients experience an average of about two rejection episodes in the first 3 years after transplantation.[39] Approximately one-third of patients are rejection-free. Rejection that occurs more than 2 years after transplantation has been linked to poor compliance with therapy. Acute cellular rejection is fatal in less than 10% of episodes. Clinical evidence of rejection ranges from no symptoms to tachycardia, tachypnea, lethargy, irritability, poor feeding, fever, hepatomegaly, new murmur, gallop rhythm, and supraventricular and ventricular tachycardia.

Endomyocardial biopsy remains the "gold standard" for the diagnosis of acute allograft rejection. The numbers of infiltrating lymphocytes and the presence of myocyte injury are used to grade rejection and to guide rejection therapy. A histologic classification system is used to grade the biopsy between 0 and 4. Current practice is to intensify immunosuppression if the biopsy score is 3 or greater. The use of echocardiography as a non-invasive method of diagnosing acute rejection is unresolved. Indices of systolic dysfunction reportedly have high specificity but low sensitivity—systolic dysfunction is a late finding. Diastolic dysfunction indices have high sensitivity but low specificity because diastolic parameters are load-dependent and abnormal in a significant number of recipients in the absence of rejection. Surveillance for late rejection is controversial. Some centers use clinical and echocardiographic parameters for screening and reserve endomyocardial biopsy for selected cases. Hyperacute rejection is a rare syndrome mediated by preformed recipient cytotoxic antibodies against donor heart antigens and leads to intractable heart failure and death unless mechanical support is instituted.

### Graft atherosclerosis

The long-term decline in patient survival is primarily due to accelerated coronary vasculopathy involving intramyocardial and epicardial coronary arteries and veins.[38] It is an immune-mediated disease and interacts with non-immune risk factors such as dyslipidemia and hypertension.[40] The incidence of graft atherosclerosis is about 15% at 5 years post-transplant. Currently, there is no known treatment.

### Infection

Infection is a significant cause of morbidity and mortality, particularly in the first 6 months after transplantation when immunosuppression is greater. The most common types of serious infection are bacterial (60%), cytomegalovirus (18%), other viral (13%), fungal (7%), and protozoal (2%).[41] Bacterial, protozoal, and fungal infections commonly involve the respiratory tract or sternal wound. Viral infections increase the risk of graft rejection. Ebstein–Barr virus is associated with lymphoproliferative disease.

### Malignancy

Although there is an increased risk of malignancy in children after heart transplantation, the risk is extremely low.[4] The majority of these neoplasms are lymphoproliferative disorders that often respond to reduction in immunosuppression and are Ebstein–Barr virus driven. When primary Ebstein–Barr virus infection develops, antiviral therapy with acyclovir should be considered.

### Other complications

Children with CHD who required extensive reconstruction of vessels during transplantation may develop stenoses at anastomotic sites (e.g. aorta, pulmonary veins). This can usually be relieved by interventional catheterization techniques but some cases may require surgery. Endomyocardial biopsy procedures should be minimized because there is some risk, including trauma to veins, tricuspid valve and heart muscle, air emboli, arrhythmia, and infection.

## Quality of life

Approximately 50% of children do not require hospitalization in the first year after transplantation. By 3 years, this percentage had increased to 72%.[38] Rejection and infection are the major causes for hospitalization. The functional status of survivors is excellent. The percentage of survivors without functional limitation was 93% at 1 year and 95% at 5 years. Less than 1% required total assistance. Pre-adolescent children exhibited "catch-up" growth in height and weight after transplantation, with a height mean at approximately the 40th percentile. Older children failed to demonstrate any increase in linear growth post-transplant but did increase in weight. Failure of linear growth is correlated with steroid requirements.[4]

Over 90% of patients are discharged home after transplantation with good cardiac function (New York Heart Association class I). Ventricular growth is in proportion with growth of the recipient. Some hypertrophy of the muscle wall is common, but cardiac function is normal with high–normal end-diastolic pressures. Coronary autoregulation is normal. Pulmonary vascular resistance usually becomes normal but may remain elevated in some children with congenital heart defects. Pulmonary arteriovenous malformations regress after transplantation.[42] Reduced exercise tolerance has been reported.[43]

The cumulative incidence of post-transplant morbidities at 5 years for survivors of heart transplantation was: hypertension (60%), hyperlipidemia (17%), coronary vasculopathy (11%), renal dysfunction (6%), and diabetes mellitus (5%).[4] Chronic hypertension was associated with steroid therapy.

A retrospective analysis of 104 children who underwent heart transplantation noted serious gastrointestinal complications in 18% of patients (median post-transplant follow-up was 3 years). Complications included (in order) pancreatitis, cholecystitis, recurrent abdominal infection, malignancy, and intestinal pneumatosis. Half of the patients with complications required abdominal surgery.[44]

A review of cognitive and psychological outcomes after pediatric heart transplantation found that children and adolescents generally functioned within the normal range on most measures of cognitive function post-transplant. However, a

complicated transplant course may place these recipients at increased risk for cognitive difficulties post-transplant. Approximately 20% of recipients experienced significant symptoms of psychological distress (e.g. anxiety, depression, behavior problems) during the first year after transplantation.[45] There is evidence that children with CHD should be considered separately because those who have undergone surgical palliation or repair have significantly lower scores on IQ and achievement tests, delays in reaching motor milestones, and higher frequencies of learning disabilities, use of special services, and speech, language, and behavioral abnormalities when compared with a normative sample.[46] A study of developmental outcomes of patients with HLHS after heart transplantation reported cognitive deficits and adaptive/behavioral abnormalities. Mean scores of cognitive ability were 1 standard deviation below expected values, and the median Full Scale IQ was 89.[47] Interestingly, the test scores were remarkably similar to those published for patients with HLHS after the Fontan operation, despite differences between these treatment strategies in duration of hypoxemia, number of surgical procedures, and long-term medical management. The similarities in neurological outcome suggest that genetic factors, congenital brain abnormalities, and ischemia/reperfusion injury may be more important than the type of surgery performed. As an aside, post-traumatic stress disorder seems to be relatively common in parents of pediatric heart transplant recipients.[48]

### Heterotopic and heart–lung transplantation

Potential recipients with elevated fixed *PVR* may be eligible for heterotopic heart transplantation or heart–lung transplantation. Actuarial survival rates of 83% (1 year) and 66% (5 year) have been reported, however experience is limited.[49] Heart–lung transplantation experience is also limited, but survival rates reported are 67% (1 year) and 41% (5 year), equivalent to those of adults.[50]

### Retransplantation

Retransplantation accounts for less than 5% of heart transplantations, despite the large number of infants who undergo transplantation and who potentially need retransplantation in the next decade.[38] Indications for retransplantation are (in order) coronary vasculopathy, acute rejection, chronic rejection, and intraoperative graft failure.[51] An ethical dilemma exists whether it is appropriate to use scarce donor organs for retransplantation when the long- and short-term outcomes are not as good as with other potential candidates.[52]

### Anesthetic management of children who have undergone heart transplantation

Patients may present for surgery because of complications from cardiac transplantation (e.g. infection, malignancy, drug adverse effects), or the indication for surgery may be unrelated to heart transplantation. Successful anesthetic management requires consideration of the patient's medical status, the physiology of the transplanted heart, and the implications of immunotherapy. These have been discussed above.

### Future prospects

Currently, heart transplantation cannot be regarded as a "cure." While new immunosuppressive agents have been introduced in the last decade, progress on induction of graft tolerance remains at a relatively preliminary stage. Transplantation tolerance implies the patient will indefinitely accept their allograft but without the need for chronic immunosuppressive therapy. Such a state would leave the patient immunocompetent against all non-donor antigens and, thus, at no increased risk for infection or malignancy.[53] Controversy exists on the best manner to monitor rejection. Controversy has also arisen as to the appropriateness of fetal listing for transplantation. Currently, fetuses can be placed on a waiting list for cardiac transplantation once they reach 36 weeks gestation. The debate about management of HLHS continues to evolve. Donor shortage remains a frustrating problem. The role of options such as a totally implantable pediatric artificial heart, xenotranplantation, clinical application of stem cell biology, and transplantation across ABO barriers remain frontiers in pediatric heart transplantation.[3]

## Lung transplantation

In the last decade, lung transplantation has been accepted as a treatment modality for adult patients with end-stage lung disease. In spite of concerns regarding growth of the implanted lungs, technical difficulties, and lack of well-defined indications, lessons from adult lung transplantation have been extended to children with end-stage lung disease. More than 600 such procedures have been performed around the world in patients below 18 years of age. This, however, represents less than 5% of the cumulative total of 14 000 lung transplantations reported by the registry of International Society of Heart and Lung Transplantation (ISHLT).[4] Even though survival after lung transplantation in children approaches or may even exceed adult lung transplantation, occasionally it is still described as an "experimental" procedure.[54] Since the inception of pediatric lung transplantation program in 1990, more than 260 such procedures have been performed at St Louis Children's Hospital (SLCH).

These children undergo a number of surgical interventions before and after lung transplantation, thus it is important to be familiar with the anesthetic implications of end-stage lung diseases in childhood, conduct of lung transplant surgery, and management of a child after lung transplantation.

## Donor pool

Donor availability remains a major obstacle to expanding the indications and viability of lung transplantation as a treatment modality for a vast list of childhood diseases causing irreversible lung damage. After an initial increase, the number of pediatric lung transplants performed each year has remained constant. This observation has been made by most of the institutions offering pediatric lung transplant surgery. Longer waiting lists with an ever-increasing number of children suggest that this plateau is caused by lack of potential donors. The average time from listing to transplantation at SLCH currently stands at an average of 225 days (range 1–1484). Approximately one third of the children on the waiting list die before transplantation.[55] According to the data from US Department of Health and Human Services,[56] there are more donors (> 15% of total donors) under the age of 18 years than recipients (< 5% of total recipients). It suggests that some of the lungs from donors under the age of 18 years are being used for adult patients. As the outcome from pediatric lung transplantation improves, the list of indications is expected to expand. This will further increase the time a child has to wait before receiving matching donor lungs. Current criteria for donor selection are listed in Table 24.2. These criteria are used with reasonable flexibility.

Various strategies are being evaluated to increase the size of the potential donor pool. Aggressive measures such as improving ventilation and treatment with diuretics may improve gas exchange of otherwise borderline donor candidates. Starznicka and colleagues[57] studied survival in lung transplant recipients from borderline donors who had been aggressively treated with steroids, diuretics, inotropes, fluid restriction, and central venous pressure monitoring. Survival at 30 days and 1 year after surgery was no different from patients receiving lungs from donors who met standard criteria. Currently ischemic times of 6–8 hours are considered acceptable for donor lungs. Better understanding of the mechanisms of ischemia and reperfusion injury may lead to improvement of preservation techniques, longer acceptable ischemic times, and retrieval of potential donors from longer distances. Clinically it appears that methods like infusion of donor lungs with prostaglandins and the use of better preservative solution have reduced the incidence of acute graft failure.

**Table 24.2** Selection criteria for pediatric lung transplantation donors.

| |
|---|
| ABO blood group compatibility |
| Reasonable size match |
| HIV negative serology |
| Less than 55 years of age |
| $Pao_2$ > 300 mmHg at an $Fio_2$ 1.0 |
| No active pulmonary infection |

HIV, human immunodeficiency virus.

The technique of transplanting mature lobes from two voluntary living related donors has been used in children. As morbidity accompanying donor lobectomy is significant,[58] this option is often reserved for critically ill children with little chance of surviving until cadaveric lungs become available. The need for retransplantation is also considered an indication for living related lung transplantation. Since the availability of cadaveric lungs is unpredictable, some institutions offer living related lung transplantation as a primary procedure.[59]

Recently, following successful animal experiments, Steen *et al*.[60] successfully transplanted lungs from a non-heart beating donor. The impact of these strategies on long-term survival, early graft dysfunction, and incidence of bronchiolitis obliterans (BO) is still not known. Until the supply of donor lungs increases, a significant number of children will continue to die while waiting for lung transplantation.

## Indications, contraindications and listing criteria for lung transplantation

Pediatric lung transplant recipients consist of a heterogeneous mix of age groups and disease diagnoses. Data from registry of ISHLT indicate that most pediatric lung transplant recipients are between 11 and 17 years of age with a second smaller group of children less than 2 years of age.[4] This distinction is significant as the disease profile and physical status at the time of transplantation is remarkably different between the two groups. Indications for lung transplantation are listed in Table 24.3.

Cystic fibrosis and pulmonary hypertension remain the most frequent indications for lung transplantation in older children. Infant recipients are usually full-term babies, presenting with respiratory distress that rapidly progresses to end-stage pulmonary failure, secondary to a variety of rare diseases such as surfactant B deficiency, primary alveolar proteinosis, and pulmonary vascular disease.[55] Unlike older recipients who present with chronic pulmonary insufficiency and minimal oxygen supplementation, most of the infant

**Table 24.3** Common indications for lung transplantation in children.

| Pre-transplant diagnosis | Number (%) Total = 207 |
|---|---|
| Cystic fibrosis | 89 (42%) |
| Pulmonary vascular disease | 44 (21%) |
| Bronchiolitis obliterans | 21 (10%) |
| Primary alveolar proteinosis | 12 (6%) |
| Pulmonary fibrosis | 15 (7%) |
| Miscellaneous | 26 (12%) |

Adapted with permission from Huddleston CB, Bloch J, Sweet S *et al*. Lung transplantation in children. *Ann Surg* 2002; **236**: 270–6.

candidates at SLCH were mechanically ventilated with a significant number on ECMO at the time of surgery. Lung transplantation is still considered a palliative surgery but an increasingly large number of children are listed for repeat transplantation as a treatment option for terminal BO.

The criteria for listing patients for lung transplantation are based on the natural history of the disease, functional status, hemodynamic parameters, and overall medical judgment. The generally acceptable principle is that children should be listed when they have less than a 50% chance of surviving for another 2 years. However, the natural history of rare diseases leading to end-stage respiratory failure may not be fully understood. In a retrospective analysis by Kerem *et al.*,[61] cystic fibrosis patients with forced expiratory volume in first second ($FEV_1$) of less than 30%, $PaO_2$ of less than 55 mmHg, or a $PaCO_2$ of greater than 50 mmHg, were observed to have more than 50% mortality in 2 years, which is the average time a cystic fibrosis patient waits before lung transplant surgery. Patients with pulmonary hypertension usually deteriorate rapidly.

Most centers consider patients infected or colonized with panresistant bacteria like *Burkholderia cepacia* as an absolute contraindication. Children with coexisting severe hepatic and renal dysfunction, family history of poor medical compliance, or severe psychiatric ailments are also not usually considered for this surgery. Many children with cystic fibrosis have significant hepatic dysfunction. These patients can be candidates for simultaneous lung and liver transplants. Combined simultaneous liver and lung transplantation have been carried out successfully in five cystic fibrosis patients at SLCH.

## Use of cardiopulmonary bypass

Use of CPB is an issue of much debate in adult lung transplant surgery. Unlike the surgical technique in adults, most pediatric lung transplant surgeries are carried out with the assistance of CPB. There are several reasons for using CPB in children. In children with cystic fibrosis, risk of cross contamination is minimized by simultaneous removal of both native lungs. Most children are physically too small to accommodate a double lumen endotracheal tube. Pediatric patients with severe pulmonary hypertension and infants are often too unstable to tolerate one-lung ventilation. Cardiopulmonary bypass also assists in improving surgical exposure by providing stable hemodynamics. Consequently use of CPB greatly simplifies anesthetic and surgical management and helps to minimize ischemic times of donor lungs.

Use of CPB, however, comes with its own risks and potential for complications. Generation of inflammatory mediators and activation of complement cascade may contribute to ischemic–reperfusion injury of the donor lungs. Systemic anticoagulation may increase intraoperative bleeding and accrue the need for blood products. The data from adult patients suggest a higher incidence of graft dysfunction associated with use of CPB. This observation may reflect the fact that CPB was more often used in patients with pulmonary hypertension, a pre-transplant diagnosis associated with higher mortality.[62] Moreover in children, early as well as long-term survival after lung transplantation is either similar to or better than those in adults suggesting a minimal impact of CPB on the outcome.

## Surgical technique

Pediatric lung transplantation is performed using a bilateral anterolateral trans-sternal clamshell incision. Though single lung transplantation has been performed in a few patients, most children undergo bilateral sequential lung transplantation. Maximal exposure and dissection is carried out before instituting CPB. Lung transplant is initiated by performing end-to-end bronchial anastomosis. Since the bronchial circulation is not reestablished, peribronchial tissue is wrapped around the anastomotic suture line. This measure is considered sufficient to ensure adequate blood supply to an otherwise ischemic tissue. This is followed by anastomosis of pulmonary artery. The donor atrial cuff is attached to the recipient's left atrium to avoid individual pulmonary vein anastomoses, reducing the risk of a potentially serious complication of pulmonary vein stenosis. Smaller donor lungs can expand to fill a relatively large recipient chest cavity. In case donor lungs are too large, volume reduction has to be carried out in order to remove areas of atelactasis.

## Preoperative evaluation

Children listed for lung transplantation at SLCH visit the preoperative anesthesia clinic and undergo an extensive evaluation, including ECG, echocardiogram, PFTs, arterial blood gas analysis, and complete metabolic panel. Children with pulmonary hypertension and associated cardiac defects are also subjected to cardiac catheterization, where *PVR* and its response to 100% oxygen or nitric oxide right ventricular function are evaluated, and cardiac anatomy is defined.

Children are at various degrees of end-stage respiratory failure at the time of transplantation. A large number of children, especially cystic fibrosis patients, are living at home with minimal oxygen supplementation. On the other hand, infants and small children are critically ill at the time of surgery. Almost all of the infants we have transplanted required mechanical ventilation or may be supported on ECMO.

When the notification of a potential donor arrives, the time until surgery is often short. Anesthesiologists are usually required to evaluate, anesthetize, and obtain adequate vascular access in these critically sick patients in a short period of time. There is evidence to suggest that longer ischemic time may correlate with increased incidence of BO.[55]

Most children and parents carry a hospital given pager and have been anticipating the transplant for a long period of time. They are often excited and frightened at the same time. Anxiolytics such as midazolam can be safely given to most patients either orally or intravenously. However, one must be cautious in administering sedatives to patients with severe pulmonary hypertension without adequate hemodynamic monitoring. In children with Eisenmenger's complex, intravenous or intramuscular ketamine is a reasonable choice as a premedicant.

## Anesthetic management

Standard NPO guidelines are followed to minimize the risk of aspiration and contamination of new lungs. The choice of induction agent and muscle relaxants is largely guided by the patient's condition. Propofol and etomidate are safe in patients with cystic fibrosis but ketamine may be preferred in patients with Eisenmenger's complex and those with pulmonary hypertension. Unlike its effects in adults, ketamine does not cause a significant increase in *PVR*.[63]

Anesthesia is maintained with opioids like fentanyl and benzodiazepines, and can be supplemented with inhalational agents like isoflurane if permitted by the hemodynamics of the child.

Anesthesiologists must ensure that non-anesthetic drugs, including preoperative antibiotics and immunosuppressants, are administered on time. Some patients require continuous delivery of prostacyclin, a pulmonary vasodilator, which must be maintained. Prostacyclin must be administered through a separate lumen and should be given through a central line, as it tends to precipitate when given in combination with other drugs.

Since pediatric lung transplant surgery is carried out with assistance of CPB, patients are intubated with standard endotracheal tubes. The extensive nature of surgery and use of CPB mandates invasive monitoring of arterial and central venous pressure in all patients. Intraoperative and postoperative monitoring of pulmonary artery pressures is most beneficial in patients with primary or secondary pulmonary hypertension. The pulmonary artery catheter is advanced from the superior vena cava into the pulmonary artery. In smaller children, the surgeons can place a catheter directly into the pulmonary artery under direct vision. Intraoperative TEE provides valuable information about right ventricular function, post-bypass pulmonary artery pressures, and residual cardiac defects.[64] Intraoperative TEE can be used to evaluate flow patterns in the pulmonary artery and pulmonary veins to rule out any stenosis.

Repeated suctioning of the endotracheal tube is required to effectively ventilate cystic fibrosis patients. Maintaining adequate gas exchange and oxygenation in the pre-bypass period is a challenge for the anesthesiologist. High $P_{aCO_2}$ (high 60s) values are common and permissive hypercapnia and mild respiratory acidosis is acceptable. Overzealous correction of hypercarbia, particularly during CPB, can lead to significant respiratory alkalosis and reduced cerebral blood flow that may produce to cerebral ischemia. A normal pH with elevated $P_{CO_2}$ should therefore be maintained through the entire intraoperative period.

Perioperative bleeding is a common and serious problem. Dense lung adhesions develop from previous chest surgeries and are often seen in cystic fibrosis patients; the dissection is time consuming and involves significant blood loss. Aortopulmonary collaterals are common in patients with chronic hypoxemia and contribute to bleeding in the pre-bypass period. Aprotinin, a serine protease inhibitor is routinely used to decrease perioperative bleeding in most institutions. In a retrospective review, Spray[28] observed that the use of aprotinin is beneficial in reducing bleeding in children with a history of previous thoracotomy and those undergoing repeat sternotomy. Aprotinin also has the potential advantage of reducing the production of inflammatory mediators responsible for reperfusion injury; however, its impact on early graft function has not been evaluated. Repeat use of aprotinin carries a small but definite risk of anaphylactic reaction. Incidence of anaphylactic reaction after repeat dose has been reported to be low in pediatric patients (1.2%) compared to adult patients (6%). Also, the incidence of adverse reactions to repeat dose of aprotinin is higher when the re-exposure interval is less than 200 days.[65]

During CPB, the patient is usually cooled to 32°C. Cardioplegic arrest of heart and aortic cross-clamp is required in patients who require simultaneous intracardiac repair. All cystic fibrosis patients are colonized with bacteria and, after excision of both native lungs, the tracheal stump is irrigated with concentrated tobramycin to reduce contamination of donor lungs. After the first lung is implanted, a small amount of blood is allowed to eject into the pulmonary artery while the second lung is being anastomosed. This maneuver reduces the ischemic times for the first lung. At the conclusion of all the anastomoses, before weaning from CPB, ventilation is resumed. In most children, minimal inotropic support is needed to wean the patient off CPB. In children with pulmonary hypertension and those who undergo simultaneous repair of congenital heart defects, more than one inotropic drug is often required to improve myocardial contractility. Careful adjustment in tidal volumes and airway pressure are necessary to remove all visible atelectatic areas. A flexible bronchoscopy may be done to rule out any narrowing at the site of bronchial anastomosis and to evaluate any airway leak, which should be immediately repaired.

## Primary graft failure

Persistent hypoxemia after weaning from CPB often signals the onset of acute graft dysfunction. Unlike other organs, vascular endothelium makes up a vast portion of lung


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parenchyma, and oxygen is readily available to the metabolically active endothelium, producing free radicals both during reperfusion as well as during the ischemic phase. Inflammatory mediators like tumor necrosis factor, interleukins, and platelet-activating factors generated during preservation can trigger a cascade of events leading to increased permeability and movement of fluid into interstitial as well as alveolar space.[66] Clinically, reperfusion injury presents as hypoxemia despite adequate ventilation and the production of pink frothy secretions from the endotracheal tube. Before attributing low $PaO_2$ values to ischemic reperfusion injury, other reversible causes such as inadequate ventilation, right ventricular dysfunction with paradoxical right to left shunting, and atelectasis, must be ruled out.

In an effort to reduce reperfusion injury, $PGE_1$ infusion at 0.025 µg/kg/minute is routinely started before establishing circulation to the first lung and is continued for 48 hours after the surgery. Prophylactic use of nitric oxide to prevent reperfusion injury remains controversial. Nitric oxide is a potent smooth muscle relaxant in vascular muscle cells. In a small group of adult patients, Thabut *et al*.[67] were able to demonstrate a marked decrease in the incidence of allograft dysfunction with the prophylactic administration of nitric oxide and pentoxyfylline. In this study, prophylactic nitric oxide–pentoxifylline significantly improved hemodynamics and reduced the duration of postoperative mechanical ventilation as well as early mortality. In another prospective study in adult patients, Ardehali *et al*.[68] concluded that prophylactic inhaled nitric oxide improved gas exchange and reduced pulmonary arterial pressures in all patients including those with established reperfusion injury. Prophylactic administration of nitric oxide, however, did not reduce the incidence of reperfusion injury. Nitric oxide is expensive and is associated with platelet dysfunction, bleeding and methemoglobinemia. Currently prophylactic use of nitric oxide to reduce the incidence of acute graft dysfunction is not indicated until further studies establish its role. Other pulmonary vasodilators such as inhaled prostacyclin (Iloprost) have been shown to be efficacious and safe for treatment of severe pulmonary hypertension.[69] Some patients with severe reperfusion injury and high pulmonary pressures are not responsive to nitric oxide and require ECMO support to allow recovery of donor lungs.

## Postoperative course

The postoperative course and duration of stay in intensive care varies by age group and by pre-transplant diagnosis. Older children with cystic fibrosis require mechanical ventilation for an average of 3 (1–47) days and their average stay in the intensive care unit is 5 (1–53) days.[70] On the other hand, infants and smaller children require prolonged mechanical ventilation (24 ± 19 days) and a longer intensive care unit stay (56 ± 33 days).[71] This difference in their postoperative course can be explained by small size, poor preoperative status, airway complications, and associated cardiac defects. Children with pre-transplant diagnosis of pulmonary hypertension manifest significant hemodynamic instability in the immediate postoperative period, are kept sedated and paralyzed for the first 48 hours after the surgery.

In the immediate postoperative period, pain relief is accomplished by narcotic infusions and patient-controlled analgesia. Regional analgesia with an epidural catheter has been frequently used in adult patients but systemic heparinization required for CPB and the emergent nature of surgery add difficulty to the preoperative placement of an epidural in pediatric patients. Many small children require mechanical ventilation and sedation for a period lasting more than 72 hours. Post-surgical placement of an epidural catheter in these younger patients is of minimal value. Epidural analgesia on the day before the surgery may be planned for older children undergoing elective living related donor transplantation. Older patients who may be extubated within 12–24 hours may be candidates for preoperative placement of a thoracic epidural catheter, or in the immediate postoperative period. Careful attention to the coagulation status and the risk–benefit ratio with systemic heparinization must be considered.

## Surveillance

These children are monitored very closely for infection, rejection and the development of BO. Pulmonary function tests are performed at regular intervals to monitor function and growth of transplanted lungs. Older children can easily perform spirometric tests such as $FEV_1$, forced vital capacity (*FVC*), and flow volume loops. Since standard PFTs require the patient's cooperation, these tests cannot be performed in infants and younger children. Instead, expiratory flow rates at functional residual capacity are measured by applying rapid thoraco-abdominal compressions at the end expiration. Any deterioration in these values is further investigated by invasive tests such as bronchoscopies, lung biopsy, computed tomography (CT) scan, and open lung biopsy.

## Changes in transplanted lungs

### Physiological changes

Transplantation surgery produces denervation of donor lungs, producing only minimal consequences on airway reflexes, mucociliary movement, and bronchial hyperactivity.[72,73] Denervation also leads to the loss of afferent stimuli to the respiratory center; and loss of coordination between thoracic and abdominal respiratory muscles is sometimes obvious in the immediate postoperative period. Adult lung transplant patients have a subnormal carbon dioxide response curve,[74] and increased sympathetic and reduced parasympathetic activity. Loss of lymphatics in transplanted lungs makes

them more susceptible to pulmonary edema in the initial post-operative period, and increased vasculature and water content result in lower compliance.[75]

### Growth of transplanted lungs

Somatic growth in lung transplant recipients lags behind normal children, with height and weight staying between the fifth and tenth percentiles. However, based on PFTs, radiological and histological evidence, it appears that lungs continue to grow after transplantation. Cohen *et al*.[76] showed that increases in functional reserve capacity accompanying somatic growth, which is comparable to normal subjects. This simultaneous increase in functional reserve capacity and $FEV_1$ suggests an increase in number of alveoli rather than overdistension of the alveoli. Histological studies have supported the assumption that number of alveoli increase after transplantation of immature cadaveric lungs. Transplanted mature lobes of living related donors also continue to grow. These lobes are able to accommodate the entire *CO* without an increase in pulmonary artery pressures suggesting growth in the pulmonary vasculature. On postoperative chest radiograph, transplanted mature lobes expand and fill the entire chest cavities. Morphometric studies suggest that this increase is a result of distension of alveoli rather than an increase in number of alveoli.[77] The growth of larger airways is also suggested by the ability to tolerate larger flexible bronchoscopes with the passage of time. Ro *et al*.[78] using CT imaging in a small group of patients were able to demonstrate near normal growth pattern in the trachea and both donor and native segments of bronchi.

### Airway complications

Dehiscence of the bronchial anastomosis is rarely seen today. However, bronchial stenosis and tracheomalacia still develop frequently in adult as well as pediatric lung transplant recipients. Huddleston *et al*.[55] reported 16% incidence of airway stenosis in patients less than 18 years of age, an incidence similar to that reported in adults. The underlying mechanism of airway stenosis is thought to be relative ischemia at the bronchial anastomosis. Other factors like high doses of corticosteroids and frequent infection also contribute to the development of airway stenosis. Usually airway complications are diagnosed within the first month after transplant. Initial treatment of stenosis at the bronchial anastomosis involves repeated balloon dilation using a rigid bronchoscope under fluoroscopic guidance. Mechanical stents are placed across the stenosis for a period of 6–8 months in patients with recurrent stenosis unresponsive to repeated dilations. Younger age is not considered a risk factor for developing narrowing at the site of bronchial anastomosis.[79,80] However, infants may have a higher incidence of tracheomalacia and dynamic obstruction of their airways. This occasionally complicates weaning from mechanical ventilation. Most of these infants with dynamic obstruction improve over a period of time without any surgical intervention.

### Vascular complications

Vascular complications are rare, and most commonly mechanical obstruction to blood flow develops from redundant tissue of the pulmonary artery or the left atrial cuff. Stenosis of either pulmonary artery or pulmonary vein usually manifests with symptoms similar to those of reperfusion injury, such as increased pulmonary artery pressures with pink frothy secretions and hypoxemia. Pulmonary artery or vein stenosis can be diagnosed with intraoperative TEE, and all patients undergo a routine lung perfusion scan within the first 24 hours as a screening tool. Cardiac catheterization with angiography can confirm the diagnosis and a mechanical stent can be placed if a significant pressure gradient is measured across the anastomotic site.

### Nerve injuries

Injury to the phrenic, recurrent laryngeal and vagus nerves are common after lung as well as heart and lung transplant surgery. Huddleston[79] reported a 22% incidence of phrenic nerve injury in children, and the resulting diaphragmatic paralysis is a transient phenomenon but can prolong the need of mechanical ventilation and postoperative intensive care. Injury to the vagus nerve leads to gastroparesis and gastroesophageal reflux. In a small retrospective study, delayed gastric empting times were reported in 83% of adult patients following combined heart and lung transplantation.[81] Severe gastroparesis affects absorption of immunosuppressant drugs. Delayed gastric emptying may also predispose these patients to silent aspiration of gastric contents resulting in recurrent pneumonia. The incidence of severe gastroesophageal reflux is as high as 50% after lung transplantation. Infants are especially susceptible and most of them require surgical interventions such as Nissen fundoplication. Injury to the recurrent laryngeal nerves leading to vocal cord paralysis is seen in 10% of children, most commonly affecting the left vocal cord, and most recover.[79]

## Medical complications

### Graft rejection

Recurrent graft rejections are common after lung transplantation. Rejection tends to occur less frequently in infants compared to older children and adults. This discrepancy may be explained by their relatively immature immune system.[71,82] The clinical picture of rejection is usually non-specific, and therefore any deterioration in clinical status or PFT measurements are investigated with a lung biopsy to rule out acute

rejection. Such episodes are aggressively treated with intravenous methylprednisolone followed by newer immunosuppressant drugs such as antithymocyte globulin, tacrolimus, and MMF.

Immunosuppression, abnormal mucociliary movement in transplanted lungs, and frequent hospitalizations contribute towards an increased risk of serious infections. Prophylactic antibiotics and antifungal medications are routinely given to these patients.

### Bronchiolitis obliterans

Bronchiolitis obliterans remains the Achilles heel of lung transplantation. The histological features of BO include scar formation and fibrosis of small airways with thickening of blood vessels. Clinically, BO presents as progressive deterioration of airflow and limitation in activity. The $FEV_1$ is a reliable indicator of graft function, and BO is diagnosed by a greater than 20% deterioration from the previous values of $FEV_1$. The overall incidence remains about 50% at 5 years. Prolonged ischemic time, age more than 3 years, and more than two episodes of rejection have been identified as risk factors for developing BO in children.[55] The incidence of BO was only 20% in patients with ischemic time of less than 2 hours compared to 52% incidence seen in patients where ischemic time was more 6 hours. Three patients receiving mature donor lobes were perceived to be immune to developing BO. This observation may, however, reflect the shorter ischemic times seen during living related lung transplantation. The incidence of BO also seems to be low in infants, probably because they have lower incidence of rejection. Infants had an average of 0.2 episodes of acute rejection. This is significantly lower when compared to older children who had an average of 1.95 rejection episodes.[55,82] Other factors like pre-transplant diagnosis, early graft dysfunction, and presence of cytomegalovirus do not affect incidence of BO. Retransplantation remains the only option for children with BO resulting in severe pulmonary insufficiency.

### Side effects from immunosupressive drugs

Lung tissue is more susceptible to graft rejection than other organs because of a large endothelial surface and the presence of large number of immunologically active cells. Therefore immunosuppressive drugs are used in higher doses and for a longer duration after lung transplant surgery. Most lung transplant centers use a triple drug (cyclosporine, azathioprine, and steroids) regimen. Each drug used in this combination may have multiple side effects and toxicities. Cyclosporine plasma levels must be closely monitored in cystic fibrosis patients due to unreliable absorption and variable hepatic clearance. In fact, an increased incidence of central nervous system complications like seizure, headache, and stroke in cystic fibrosis patients has been attributed to high plasma levels of cyclosporine.[84,85] More than one third of children develop hypertension at 1 year after lung transplantation due to immunosuppressive therapy, and this number increases to 71% after 5 years. A significant number of patients develop chronic renal insufficiency occasionally requiring renal transplantation.

A number of malignancies including post-transplant lymphoproliferative disease (PTLD) and hepatic sarcoma have been reported in lung transplant recipients. The greatest risk factor for PTLD is a pre-transplant diagnosis of cystic fibrosis. In patients with cystic fibrosis, the only risk factor associated with PTLD was two or more episodes of acute rejection within 3 months after transplantation.[85]

### Intestinal obstruction

The incidence of intestinal obstruction is high after lung transplantation in children with cystic fibrosis. A significant number of children undergo laparotomy for procedures like gastrostomy, jeunostomy, and meconium ileus. In one series, 10% of patients required laparotomy for bowel obstruction after lung transplantation. Previous laparotomy is identified as a risk factor.[86]

### Arrhythmias

The left atrial suture line is a potential source of abnormal depolarization and repolarization.[87] Clinically significant atrial flutter is seen in 11% of pediatric lung recipients. In most cases arrhythmias are persistent and require treatment with antiarrhythmic drugs like procainamide and amiodorone.[79]

## Mortality and long-term survival

The overall first year survival rate is reported to be 77%. Survival declines to 63% at 3 years, and only 54% are alive at 5 years after transplantation. Primary graft failure is the leading cause of early mortality accounting for 62% of deaths.[55] Infants also have very high (25%) early mortality.[71] Bronchiolitis obliterans, infection, and malignancies are the leading causes of death in the late period. Patients with pre-transplant diagnoses such as pulmonary hypertension and repeat transplant surgery appear to have relatively poor outcome.

## Summary

Lung transplantation has become a viable option to prolong life in children with end-stage lung disease. A large number of children still die prematurely because of lack of suitable donor organs. Improving techniques of organ preservation may help reduce the incidence of fatal complications like primary graft failure and BO.

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# 6 Anesthesia outside the cardiac operating room

# 25 Anesthesia for the cardiac catheterization laboratory

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## Introduction

The use of catheters to investigate cardiac function dates back to the 19th century. Three early 20th-century pioneers in cardiac catheterization won the Nobel Prize for Medicine in 1956 (Werner Forssman, Andre Cournand, and Dickinson Richards). Forssman's efforts cost him his job at the time, but Cournand and Dickinson went on to use right heart catheterization in a systematic effort to understand cardiac function. For many years diagnostic cardiac catheterization was the primary method for delineating the anatomy in congenital heart disease (CHD) as well as providing physiological data.

Interventional catheterization was first described in 1953 by Rubio-Alvarez[1] to treat pulmonary stenosis. In 1968 Rashkind and Miller[2] described balloon atrial septostomy for palliation of transposition of the great arteries, and in the last few years the number of transcatheter interventions has increased dramatically.

The history of anesthetic involvement in cardiac catheterization dates to the early 1950s. In 1953 anesthesia for angiocardiography at the Brompton Hospital was described using thiopentone and succinylcholine. The use of rectal thiopentone and intravenous meperidine, and rectal and intramuscular barbiturates were described in 1956. In 1958 Smith[3] described the "CM3" mixture for sedation (chlorpromazine, demerol, and promethazine), which was widely used until recently.

Indications for diagnostic catheterization have become more limited in the last decade as other less invasive imaging techniques have become available. However, diagnostic catheterization is still required in selected cases to resolve the anatomy in complex patients and to make hemodynamic measurements. As the number of diagnostic catheterizations has diminished, the use of cardiac catheters for therapeutic purposes has increased.[4,5] At the Hospital for Sick Children (HSC) in Toronto, interventional catheterizations currently outnumber diagnostic studies by two to one. Interventional procedures are used to avoid surgery, for lesions not amenable to surgical treatment (e.g. peripheral pulmonary artery [PA] stenosis) or to palliate patients and postpone surgical repair. As opposed to diagnostic catheterization the focus is on treatment, not precise diagnosis, and maintenance of baseline hemodynamics is less critical. Some procedures are performed in high-risk patients with the potential for serious complications, and are associated with major hemodynamic disturbances. Another group, electrophysiology (EP) procedures, include delineation and transcatheter ablation of abnormal conducting pathways and implantation of pacemakers. Anesthetic and sedative drugs have effects on cardiac conduction, and particular agents should be chosen to minimize this effect.

## Environment

The cardiac catheterization laboratory is an inhospitable environment for the anesthesiologist (Fig. 25.1). It is often remote from the operating room, frequently undersized, of necessity not brightly illuminated, and filled with equipment that makes access to the patient difficult. Patients are frequently transferred some distance to recovery or intensive care facilities, and during transport the anesthesiologist must be satisfied that the patient is in a stable condition. The patient should be transferred with suitable monitoring, appropriate personnel and oxygen, resuscitation equipment, and drugs.

Radiation exposure is a hazard to both the patient and staff during cardiac catheterization. Non-stochastic effects such as erythema and cataracts are a direct result of cellular injury and are dose related. Stochastic effects are the result of injury to DNA. The risk of injury is increased with increasing dose (amount of energy absorbed); however, the magnitude of effect is not dose related. Exposure is measured in rem (radiation equivalent in man) or Sieverts (100 rem = 1 Sievert). Background exposure is 0.1 rem/year. The risk of a fatal cancer is increased by 0.04% per rem of life-time exposure, and thus no level of radiation exposure can be considered

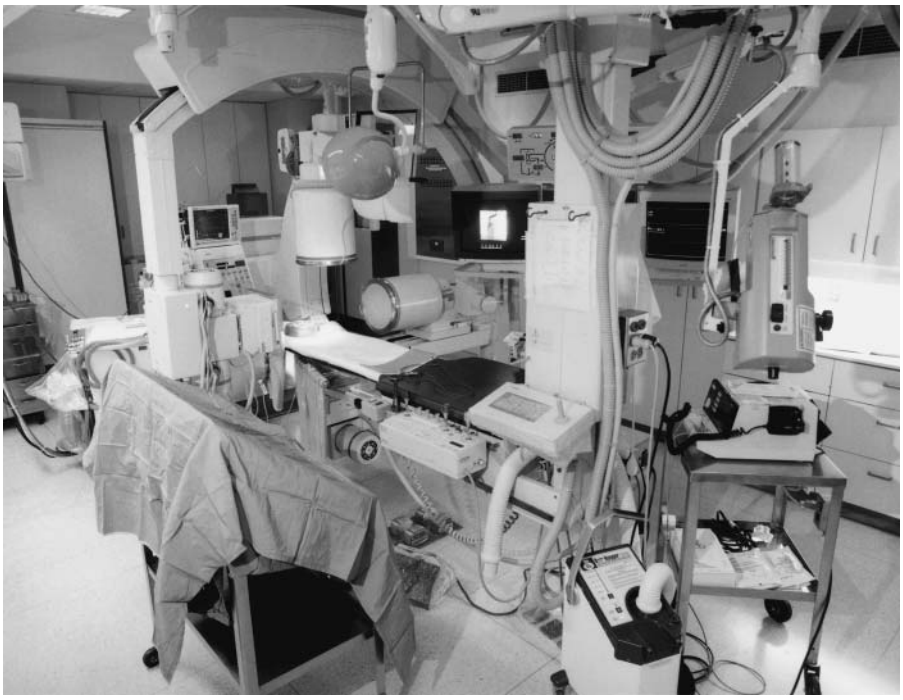

**Fig. 25.1** The catheter laboratory can be an inhospitable place for both the anesthetist and patient. X-ray and hemodynamic monitoring equipment limits access to the patient.

safe.[6] The patient is inevitably exposed directly to X-rays. The total dose should be limited and sensitive tissues such as the gonads and the eyes protected. Exposure during cinefluoroscopy is as high as 10–20 rem/minute. Newer digital technologies, collimation, and limitation of fluoroscopy time allow reduction of dose; however, staff are also unavoidably exposed to radiation. Exposure of anesthesiologists may be as high as 0.17 rem/month.[7] The maximum radiation exposure recommended for medical workers is 5 rem/year. Ideally exposure should be much lower than this (0.12 rem/year). Limitation of the dose relies on time, distance, and barriers. Radiation dose is reduced with distance from the source according to the inverse square law. Barriers include protective clothing ("lead" aprons, thyroid collar, and protective eye glasses) and screens. In many cases the patient and monitors can be observed from the safety of the control room.

## Anesthetic considerations

As early as 1958, a satisfactory state for pediatric cardiac anesthesia was described: (i) freedom from pain; (ii) absence of restlessness; (iii) no respiratory depression; and (iv) sedation light enough to allow a normal response to a selective ether test.[3] While selective ether tests are no longer conducted, the requirements for cardiac catheterization at present are broadly similar. General anesthesia is not essential to achieve these aims; in adult patients it is routine to conduct cardiac catheterization with minimal or no sedation. However, cardiac catheterization is different in children. Procedures are longer, more complex and more likely to involve interventions. Most children will not tolerate this without some pharmacological suppression of consciousness. The benefits of general anesthesia or sedation should be considered in relation to the individual patient and procedure.

Sedation may be administered without the presence of an anesthesiologist. Recognition that adverse events occur in association with this practice has lead to a series of guidelines being produced.[8] The most recently revised (and most applicable) guidelines are those of the American Society of Anesthesiologists (ASA).[9] Four levels of sedation and anesthesia are recognized: minimal, moderate, or deep sedation; and general anesthesia. A purposeful response to verbal stimulation can be produced during moderate sedation. During deep sedation only painful or repeated stimuli elicit a purposeful response. Sedation to a depth that no response or only reflex withdrawal can be produced is defined as general anesthesia. The distinction between deep sedation and anesthesia is often arbitrary, and in the UK, no distinction is made between the two.[8]

The ASA guidelines specify that the individual supervising the sedation must be able to rescue the patient if the level of sedation enters the next level. To ensure that a potentially uncooperative child remains still during cardiac catheterization, deep sedation or general anesthesia is required. Therefore the individual supervising the sedation must have the skills to manage general anesthesia, to support the airway, ventilation, and cardiovascular system. The risk of major complications during cardiac catheterization and the physiological

status of the patients require the presence of an individual who is skilled in resuscitation other than the operator. Deep sedation supervised by a non-anesthesiologist sometimes occurs, but this situation does not provide optimum care for children.

Inadequate preoperative assessment and inadequate monitoring contribute to poor outcome during sedation. Assessment and monitoring of patients undergoing cardiac catheterization, whether under sedation or general anesthesia, should be comparable to that of a patient undergoing any other operative procedure. A means of monitoring adequacy of ventilation and the airway is mandatory; oxygen masks or nasal cannulae can be adapted to allow monitoring of end-tidal carbon dioxide.[10]

The risk of airway obstruction increases as the level of consciousness decreases. Access to the airway is limited during the procedure, and intubation of the trachea and control of ventilation provide the safest option in most patients, unless it is desirable to avoid positive pressure ventilation (e.g. during diagnostic procedures in some patients with Fontan physiology). Total intravenous anesthesia can be achieved in many patients without specific support of the airway, although care and very close observation is required. In patients who develop airway obstruction, the laryngeal mask airway (LMA) is well tolerated and allows maintenance of the airway. In spontaneously breathing patients, intubation of the trachea requires deeper anesthesia and produces higher arterial carbon dioxide concentration and greater depression of the cardiovascular system. Patients at increased risk of airway obstruction, such as those with Down's syndrome, and patients at risk of ventilatory failure, including neonates of low birth weight, should have their airway secured by endotracheal intubation.[11] Endotracheal intubation is usually advisable if transesophageal echo is required. Continuous monitoring of the airway and ventilation is mandatory with any of these techniques.

Vascular access is most commonly achieved via groin vessels, although vessels in the neck, umbilical vessels and the arms may also be used. Observation of the patient is further limited by sterile drapes and by reduction in lighting levels. Reliance on electronic monitoring is normal and monitoring devices should be positioned out of the way of the radiological view.

Analgesia for cardiac catheterization can be provided by infiltration of local anesthetics at vascular access sites. It is simple and if performed correctly should not complicate vascular access. When performed prior to cannulation the need for deepening of sedation or anesthesia is minimized.

## Complications

Care should be taken in positioning the patient since neuropathy due to traction on the brachial plexus has been reported.[12] When biplane fluoroscopy is used it is common to position the patient's arms above the head. Such patients may require intubation and positive-pressure ventilation. Children with congestive heart failure, pleural effusions, or airway anomalies may not tolerate the supine position while awake. Temperature should be monitored and devices such as forced air warmers may be used for smaller patients.

Major complications are rare (2%) except during interventional procedures.[13,14] Serious complications include arrhythmias, vascular damage at access sites, bleeding, perforation of vessels or the heart, cardiac tamponade, vascular thrombosis, air embolus, catheter fragment embolus, valvular incompetence, allergy to contrast medium or drugs, and stroke. Risk factors for complications include lower patient age or size (less than 5 kg) and the particular intervention performed. The overall mortality rate is 0.14% (0.28% for interventional procedures) and is most often due to either perforation of the heart and great vessels or due to the patient's underlying disease.

Arrhythmias are the most common complication, occurring in 2.6% of all procedures. Arrhythmias, including heart block caused by mechanical stimulation, are usually transient and respond to withdrawal of the catheter. Contributory factors such as electrolyte disturbance, hypercarbia and excessive catheter manipulation within the heart should be minimized. Equipment for defibrillation should be immediately available. Pacing can be instituted to treat heart block or supraventricular tachycardia (SVT). Other causes of arrhythmias must be considered including cardiac ischemia, coronary air embolus and direct damage to the myocardium or conducting system.

Catheters used for interventional procedures have a larger diameter than those used during diagnostic studies, and the risk of vascular damage at the site of insertion is increased, as is the risk of damage to heart structures. Complications such as perforation of the heart or vessels or valvular incompetence may require urgent surgical intervention. Blood should be immediately available and interventional procedures in children should only be conducted in hospitals where facilities for cardiac surgery exist.[6,15,16] In the event of sudden blood loss, rapid transfusion and arterial monitoring is possible via the vascular access sheaths placed for the procedure. During balloon angioplasty it may be possible for the cardiologist to tamponade a rupture by reinflation of the balloon. However, emergency surgical repair will often be required.

Thrombosis and thromboembolism may occur at any site where the vascular endothelium is disrupted. Heparin is given in a dose of 50–150 U/kg prior to arterial cannulation, when the systemic circulation is entered, and during procedures that inevitably cause damage to the vascular endothelium. The use of anticoagulants will increase the likelihood of hematoma formation at vascular access sites. Protamine may be used to reverse heparinization but caution must be exercised due to the risk of adverse reactions.

Serious complications occur in 0.7–3.3% of EP studies in children.[14,17] Complications are related to vascular access, catheter manipulation, or the use of radiofrequency energy. The Radiofrequency Ablation Registry provides data on complication rates for radiofrequency ablation. This includes a mortality rate of 0.2%, complete heart block in 1%, and valvular regurgitation in 0.5% (G. Van Hare, pers. comm., PAPCA registry data). Complications are higher in patients with CHD and heart block is more common when the abnormal pathway is close to the normal conducting system. Coronary artery injury has been demonstrated in animal models of radiofrequency ablation (G. Van Hare, pers. comm., PAPCA registry data).

## Diagnostic catheterization

Advances in other imaging techniques, most notably echocardiography and magnetic resonance imaging, have provided less invasive methods for demonstrating cardiac and vascular anatomy and reduced the need for diagnostic cardiac catheterization. These modalities are less successful to date in assessing physiological parameters, although this may change. Careful consideration is given to the indications for diagnostic catheterization due to the invasive nature of the procedure and the inevitable radiation exposure. Current indications can be summarized as follows:

1. To measure central and peripheral intravascular pressures and derive hemodynamic information such as pulmonary and systemic vascular resistance (*SVR*), shunt fractions, and cardiac output (*CO*). The most common situation for this type of investigation is in preparation for the Fontan procedure.
2. To define cardiac and vascular anatomy: poor windows can defeat the most expert echocardiographer and certain anatomical features are difficult to visualize. This occurs in a minority of cases and usually implies either complex anatomy or complicating factors in the patient such as lung disease.
3. To evaluate myocardial function and to assess the effects of drugs and respiratory interventions on the cardiovascular system; for example, during investigation of patients with pulmonary hypertension.

Endocardial biopsies, coronary artery angiography and assessment of myocardial function are part of the routine surveillance of patients following heart transplantation. Endocardial biopsy is also diagnostic in cases of cardiomyopathy and viral myocarditis. Diagnostic studies are also an integral part of transcatheter interventional procedures.

### Anesthetic considerations

The anesthesiologist's role during diagnostic catheterization is to provide care so that the patient emerges from the procedure with minimal psychological or physiological trauma, and the cardiologist derives meaningful data on which to base decisions about the child's future treatment. All sedative and general anesthetic agents have hemodynamic effects and all depress respiration; this in turn influences the results of the investigation. It is important that the anesthesiologist has a clear understanding of the information being sought in the investigation, and that the cardiologist has some understanding of the effects of sedatives on the cardiovascular system.

More than 30% of children with CHD have reparative surgery in the neonatal period and more than 50% are operated on in the first year of life. The majority of children come to surgery without cardiac catheterization; the necessary information is acquired by echocardiography. A majority of patients presenting for diagnostic cardiac catheterization are either infants presenting with some complexity of their condition or as postoperative patients. Preoperative assessment should include a careful review of the child's medical history, current symptoms, and any available diagnostic tests. Appropriate laboratory investigations will depend on the child's physical condition and any medications prescribed. As a minimum, a hemoglobin level should be measured and blood group ascertained.

Particular concerns during cardiac catheterization of neonates and small infants include airway management, limited cardiovascular reserve, hypothermia, and changes in intravascular volume. Hypovolemia can arise from extensive blood sampling during the procedure or as a result of blood loss during catheter placement or exchange. It is difficult to monitor as bleeding is hidden on the drapes, therefore serial hematocrit measurements are helpful. The use of check-flow valves markedly reduces bleeding from the sheath. Hypervolemia is also a concern as fluid is routinely administered through the sheath and catheters. Extensive angiographic studies result in the administration of significant amounts of contrast and this should be limited. The use of low osmolarity non-ionic contrast has reduced the number of side effects, but the total volume of fluid can still be considerable.

Postoperative patients are often understandably anxious when returning to hospital. There are benefits from premedication even with parental presence at induction of anesthesia.[18] Midazolam 0.25–0.75 mg/kg is a safe and effective oral premedication for children with CHD and has the advantage of a rapid onset.[19,20] These children are unlikely to have normal hemodynamics and may have severely limited cardiovascular and respiratory reserve. The most common cardiac sequelae of surgery for CHD are arrhythmias and myocardial dysfunction. Recurrent laryngeal and phrenic nerve palsy are recognized complications of cardiac surgery and result in limited respiratory reserve, as does congestive heart failure. Vascular access can be extremely difficult in children who have had prolonged hospitalization. Venous

thrombosis (and the attendant complications) is being increasingly recognized as a source of morbidity in children, thus increasing the difficulty of cardiac catheterization.[21]

In addition, 25% of children with CHD have other congenital anomalies. Craniofacial, airway, and intrathoracic anomalies are a major cause for concern. The combination of a patient with a challenging airway, limited cardiac reserve, and difficult vascular access in an area of the hospital often some distance from colleagues, epitomizes the challenge for the pediatric anesthesiologist in the cardiac catheterization laboratory.

## Procedure

The routine approach to diagnostic catheterization is via the femoral vein and/or artery using the Seldinger technique. It is common to elevate the pelvis to facilitate venepuncture. Following cavopulmonary connection, subclavian or internal jugular vein cannulation is required to study the pulmonary vascular bed. After dilation and placement of an appropriate sheath, the catheter is advanced through the circulation; pressure and oxygen saturation measurements are then made in sequence. Oxygen saturation measurements allow the calculation of shunts, and in combination with measurements or estimates of oxygen consumption, allow calculation of *CO* and pulmonary blood flow (see Tables 25.1 and 25.2 for normal data and calculations). The use of a high inspired concentration of oxygen at this stage will introduce errors due to dissolved oxygen and pulmonary vasodilation. Whenever possible 21% oxygen should be administered and normocapnia achieved. Cardiac output can be measured using thermodilution techniques in patients without shunts.

## Anesthetic techniques

It has been common to provide sedation for cardiac catheterization with large single doses of oral or intramuscular sedation. Regimens include a mixture of meperidine, promethazine, and chlorpromazine (DTP) and large doses of oral chloral hydrate. The limitations of such techniques are considerable, as the dose cannot be titrated to response and the duration of action may be greatly prolonged in infants.[22] Periods of either excess sedation or inadequate sedation are common. These techniques have been rightly superseded by use of shorter acting agents with rapid onset.[23] Table 25.3 summarizes agents in common use.

Many of these agents have steep dose–response curves and need to be carefully titrated to achieve a predetermined endpoint. The results of excess sedation are predictable: loss of airway reflexes, respiratory depression, and cardiovascular compromise. Specific antagonists exist for opioids and benzodiazepines; however, initial management should be support of the airway and ventilation. In an analysis of critical incidents due to sedation, no correlation could be found between particular agents or mode of administration and outcome.[22,24] In specific situations combinations of two agents may be useful: opioids and sedatives may be of value for painful procedures and benzodiazepines reduce the incidence of hallucinations when ketamine is used.

The effects of sedative and analgesic drugs on the heart are variable. Inhalational anesthetics cause peripheral vasodilation, varying degrees of myocardial depression, and affect sinus node function and cardiac conduction tissue. Sevoflurane has a less direct myocardial depressant effect than halothane: in normal children sevoflurane produces a fall in

**Table 25.1** Normal cardiac catheterization data.

| | Pressure in mmHg | | Oxygen saturation (%) |
|---|---|---|---|
| | Newborns | Older children | |
| Right atrium | | | 60–80 |
| a wave | 3–8 | 5–10 | |
| v wave | 2–6 | 4–8 | |
| Mean | 0–4 | 2–6 | |
| Right ventricle | | | 65–75 |
| Systolic | 65–80 | 15–25 | |
| End-diastolic | 2–7 | 3–8 | |
| Pulmonary artery | | | 65–75 |
| Systolic | 65–80 | 15–25 | |
| Diastolic | 35–50 | 8–12 | |
| Mean | 40–70 | 10–16 | |
| PA wedge | | | 95–100 |
| a wave | 6–10 | 8–14 | |
| v wave | 7–11 | 10–17 | |
| Mean | 5–8 | 7–13 | |
| Left atrium | | | 95–100 |
| a wave | 4–7 | 6–12 | |
| v wave | 6–12 | 8–15 | |
| Mean | 3–6 | 5–10 | |
| Left ventricle | | | 95–100 |
| Systolic | 65–80 | 90–120 | |
| End-diastolic | 3–7 | 2–5 | |
| Aorta | | | 95–100 |
| Systolic | 65–80 | 90–120 | |
| Diastolic | 45–60 | 60–75 | |
| Mean | 55–65 | 70–90 | |
| Flows | L/min/$m^2$ BSA | | |
| Pulmonary (*Q*p) | 3.5–5.0 | 3.5–5.0 | |
| Systemic (*Q*s) | 3.5–5.0 | 3.5–5.0 | |
| Resistances | Woods units × $m^2$ BSA | | |
| Pulmonary (*R*p) | 8–10 | 1–3 | |
| Systemic (*R*s) | 10–15 | 15–30 | |

BSA, body surface area; PA, pulmonary artery.

**Table 25.2** Hemodynamic calculations performed during cardiac catheterization.

| | | |
|---|---|---|
| *Flows* | | |
| Pulmonary: | $\dot{Q}_p = \frac{VO_2}{(S_{PV}O_2 - S_{PA}O_2) \times Hgb \times 1.34 \times 10}$ | |
| Systemic: | $\dot{Q}_s = \frac{VO_2}{(S_{Ao}O_2 - S_{MV}O_2) \times Hgb \times 1.34 \times 10}$ | |
| Effective pulmonary: | $\dot{Q}_{EP} = \frac{VO_2}{(S_{PV}O_2 - S_{MV}O_2) \times Hgb \times 1.34 \times 10}$ | |
| *Resistances* | | |
| Pulmonary: | $R_P = \frac{\overline{PAP} - \overline{LAP}}{\dot{Q}_P}$ | |
| Systemic: | $R_S = \frac{\overline{AoP} - \overline{RAP}}{\dot{Q}_S}$ | |
| *Shunts* | | |
| Pulmonary to systemic: | $\frac{\dot{Q}_P}{\dot{Q}_S} = \frac{S_{Ao}O_2 - S_{MV}O_2}{S_{PV}O_2 - S_{PA}O_2}$ | (a flow ratio) |
| Left to right: | $\dot{Q}_P - \dot{Q}_{EP}$ | (absolute flow) |
| Right to left: | $\dot{Q}_P - \dot{Q}_{EP}$ | (absolute flow) |

Ao, aorta; *AoP*, aortic pressure; Hgb, hemoglobin; *LAP*, left atrial pressure; MV, mixed venous; PA, pulmonary artery; *PAP*, pulmonary artery pressure; PV, pulmonary vein; $\dot{Q}_{EP}$, effective pulmonary flow; $\dot{Q}_P$, pulmonary flow; $\dot{Q}_s$, systemic flow; *RAP*, right atrial pressure; $R_P$, pulmonary vascular resistance; $R_S$, systemic vascular resistance; *S*, saturation.

**Table 25.3** Suitable agents for sedation during cardiac catheterization.

| Agent | Suggested dose | Comments |
|---|---|---|
| Midazolam | Oral 0.25–1.0 mg/kg<br>i.v. bolus 50–150 µg/kg<br>Infusion: 1–2 µg/kg/min | After i.v. bolus 4 min before peak effect<br>Steeper dose–response curve than diazepam |
| Ketamine | 1–2 mg/kg<br>Infusion 50–75 µg/kg/min | Psychic disturbances in 5–30%<br>Prolonged recovery time |
| Propofol | 1–2 mg/kg<br>Infusion: 100–200 µg/kg/min | High risk of loss of airway reflexes |
| Nitrous oxide | Up to 50% | Seldom adequate as sole agent, useful adjunct during skin infiltration |
| Morphine | 0.05 mg/kg | Risk of respiratory depression and nausea<br>Prolonged action |
| Fentanyl | 1 µg/kg | |
| Alfentanil | 20 µg/kg then 0.5 µg/kg/min | Much smaller doses required after Fontan procedure |
| Remifentanil | 0.05–0.15 µg/kg/min | High potential for apnea |
| Etomidate | 0.1–0.3 mg/kg i.v. bolus then 25–50 µg/kg/min infusion | Transient adrenal suppression, pain and thrombophlebitis; excellent maintenance of baseline hemodynamics |

*SVR* without an increase in heart rate (*HR*) resulting in no change in cardiac index.[25] Isoflurane preserves contractility in children with CHD,[26] yet produces greater myocardial depression in infants.[27]

Intravenous agents such as propofol, midazolam and ketamine are all used for sedation and general anesthesia. Propofol has been studied in children with intracardiac shunting undergoing cardiac catheterization; it decreases *SVR* resulting in significant decreases in the ratio of pulmonary to systemic flow ($Q$p : $Q$s).[28] In patients with elevated pulmonary vascular resistance (*PVR*), propofol caused pulmonary vasodilation[29] and varying degrees of bradycardia.[30] When a combination of oral midazolam and ketamine was used for cardiac catheterization, patients often required intravenous supplementation and developed airway obstruction.[23] Ketamine causes sympathetic stimulation, salivation and bad dreams. It has negative inotropic effects on isolated myocardium, but this is masked in the intact patient due to the sympathomimetic effects. Ketamine increases oxygen consumption ($V\text{O}_2$), leading to a potential source of error in hemodynamic calculations unless $V\text{O}_2$ is actually measured. There are conflicting reports on the effects of ketamine on *PVR*. Etomidate maintains CV stability and has been used for induction of anesthesia in children with CHD and end-stage cardiomyopathy. There are few reports of its use for cardiac catheterization, but baseline hemodyamics are preserved during procedures lasting up to several hours.[31,32]

The use of short acting intravenous narcotics such as alfentanil and remifentanil for sedation of spontaneously breathing children has also been reported.[33,34] These drugs generally produce good hemodynamic stability. The problems of respiratory depression (apnea and airway obstruction) and vomiting limit the usefulness of these agents unless the airway and ventilation are controlled. In addition the use of remifentanil with sevoflurane and positive pressure ventilation is associated with a decrease in *HR* and arterial blood pressure.[35]

Respiratory manipulations also affect hemodynamics. A switch from positive to negative pressure (cuirass) ventilation increased *CO* by 11% in healthy children, 28% in postoperative cardiac patients, and 54% in patients with a Fontan circulation.[36,37] A similar increase in *CO* has been demonstrated on extubation of postoperative Fontan patients.[38] If the child has a large left-to-right shunt then the effect of breathing high concentrations of oxygen are twofold: first, it is necessary to consider the contribution of dissolved oxygen when calculating pulmonary blood flow using the Fick equation; secondly, high oxygen levels decrease *PVR* thereby increasing $Q$p : $Q$s. Similarly, changes in arterial carbon dioxide tension or pH will affect pulmonary blood flow. From the perspective of deriving the best hemodynamic data, the ideal situation is a patient spontaneously breathing room air; however, airway obstruction, carbon dioxide retention, or atelectasis also produced potential sources of error in the study.[39]

## The patient with pulmonary hypertension

Primary pulmonary hypertension is rare in children, as in adults. However, children with CHD and large left-to-right shunts are at risk of acquired pulmonary hypertension if their cardiac anomaly is not dealt with in a timely fashion. Infants with outflow obstruction to the pulmonary vascular bed (e.g. mitral stenosis or pulmonary vein obstruction) are also at risk.

When surgery is planned for children with pulmonary hypertension it is important to carefully assess pulmonary vascular reactivity, in order to decide if the lesion is operable. These investigations require teamwork on the part of the anesthesiologist and cardiologist. Children with severe pulmonary hypertension are at risk of sudden death, and require careful anesthetic management, and children whose pulmonary vascular bed is labile can appear inoperable if improperly managed.

Pulmonary hypertension causes right ventricular failure. The thin-walled right ventricle (RV) responds to pressure loading by dilating and becoming hypertrophied. This reduces right coronary blood flow rendering the subendocardial region vulnerable to ischemia. The dilated RV interferes with left ventricular geometry and function causing increased left ventricle (LV) end-diastolic pressure and decreased stroke volume. Tricuspid regurgitation can also occur. Acute increases in PA pressure and *PVR* are poorly tolerated, reducing *CO*, which may lead to arrhythmias and death.

The intimate relationship between *PVR*, alveolar oxygenation, and carbon dioxide means that the first principle of anesthetic management of the child with pulmonary hypertension is meticulous attention to the airway and to the gas exchange. Hypercarbia or hypoxia will cause an elevation in *PVR*, which in turn has been shown to cause bronchospasm resulting in greater difficulties with oxygenation and ventilation, inducing a rapid downward spiral.[40] Ineffective bag and mask ventilation, or too large a leak around the endotracheal tube can result in life-threatening acute increases in PA pressure in vulnerable children and is particularly important if there is no intracardiac shunt (e.g. patent foramen ovale or atrial septal defect), because the RV fails and *CO* is significantly reduced.

The rationale behind the management of children undergoing investigation of pulmonary hypertension is to establish the baseline hemodynamic values and then to intervene to assess the reactivity of the pulmonary vascular bed. This also provides data against which the effects of therapy can be measured, and decisions are based on the lowest value of *PVR* that can be attained.

For such studies at HSC, all children receive general anesthesia with muscle relaxants and endotracheal intubation. Premedication with oral midazolam is routine. Cautious inhalation induction with sevoflurane has been used if

vascular access is difficult, and avoids the inevitable agitation due to multiple attempts at obtaining intravenous access. A bolus (0.5–1.0 μg/kg) of remifentanil followed by an infusion at doses of 0.25 μg/kg/minute is started and titrated to effect. Atropine can be given if the *HR* slows significantly. Isoflurane 0.5% or small doses of midazolam are given intravenously to induce amnesia. The patient is ventilated with air and oxygen and the pH and $P_{CO_2}$ are maintained within normal limits while intracardiac pressures and saturation are measured, and calculations of *PVR* and the *PVR* index are made. The patient is then hyperventilated until the $P_{CO_2}$ is 30 mmHg on 100% oxygen after which all measurements are repeated. Patients who do not respond to hyperoxia and hypocarbia are given 40 p.p.m. nitric oxide and the study repeated. In selected patients the study is used to assess the effects of therapy such as inhaled or intravenous prostacyclin, or oral sildenafil.

## Endocardial biopsy

Endocardial biopsy is used in three patient groups: the routine surveillance of patients post-cardiac transplant, the assessment of patients with suspected rejection of the transplanted heart, and the diagnosis of myocarditis. The latter two groups are more likely to have myocardial dysfunction. When seen preoperatively all patients should be questioned as to symptoms of heart failure or arrhythmia, and reports of preoperative echocardiograms and electrocardiograms (ECGs) inspected. The procedure is usually performed by cannulation of the right internal jugular or femoral vein. The biopsy catheter is passed into the heart and samples of endocardium taken for histology. Stress testing, coronary angiogram, and ultrasound examination of the coronary arteries may be performed during the same procedure.

## Interventional cardiology

### Anesthetic considerations

Patients presenting for interventional procedures range from healthy children with asymptomatic lesions presenting as day-case patients to critically ill neonates undergoing procedures associated with marked hemodynamic disturbance (Table 25.4).[15] The anesthetic approach should be tailored to the individual patient; it is important that the anesthesiologist appreciates the nature of the procedure to be performed. Sedation may be appropriate on occasion; however, transcatheter interventions raise a number of specific concerns. The airway should be controlled during procedures associated with a significant risk of hemodynamic instability or serious complications likely to require further interventions or resuscitation. Aortic valvotomy, dilation of severe pulmonary stenosis, and closure of ventricular septal defect (VSD) should be considered absolute indications for general anesthesia and tracheal intubation. Transesophageal echo is used during many procedures and usually necessitates tracheal intubation.

Patient movement or coughing during device or balloon placement may have disastrous consequences, and some interventions, e.g., pulmonary angioplasty, may induce coughing. Movement at other times, however, may only have effects on the demeanor of the cardiologist. A combination of sedation techniques with an additional bolus of an intravenous anesthetic, such as ketamine, to ensure stillness during interventions has been described.[41] It is not clear what advantage is offered by this technique over general anesthesia with control of the airway.

## Interventional cardiology techniques

### Valvotomy

The technique used for balloon dilation of any stenotic valve (aortic, pulmonary, mitral, or bioprosthetic) is essentially similar. A catheter is introduced past the stenosis and pressures are measured proximal and distal to the lesion. A wire is positioned across the valve and the catheter withdrawn. The wire is used to guide a balloon catheter into position across the stenotic valve and to stabilize the balloon. The size of balloon used is dictated by the size of the valve annulus, because the purpose of the procedure is not to dilate the valve annulus but to separate the fused valve leaflets. Larger balloons reduce the gradient, but increase the risk of regurgitation. During inflation the valve is completely obstructed; for this reason, sustained single inflations are avoided. When a balloon is inflated across a stenotic valve, a "waist" is seen at the site of stenosis, and short inflations are repeated until this waist disappears.[42]

### Angioplasty

Vascular angioplasty involves the inflation of a balloon across an area of vascular stenosis using a similar technique to balloon valvotomy. It results in tearing of the endothelium and subsequent healing by scar formation and re-endothelialization. The technique may be applied to native blood vessels or to surgical conduits. Established indications are recurrent aortic coarctation, systemic venous stenosis and PA stenosis. Complications include rupture of the vessel, dissection, late aneurysm formation, thrombosis, and restenosis.

### Endovascular stents

Modification of balloon angioplasty by the placement of endovascular stents has been applied to PA stenosis, systemic

**Table 25.4** Indications for transcatheter interventional procedures from American Heart Association Scientific Statement.

| | Class I: Generally agreed indication | Class II: May be indicated | Class III: Not indicated |
|---|---|---|---|
| Balloon dilation of cardiac valves | Pulmonary stenosis<br>Congenital aortic stenosis<br>Rheumatic mitral stenosis | Discrete subaortic stenosis<br>Dysplastic pulmonary valve<br>Congenital mitral stenosis<br>Prosthetic conduits<br>Pulmonary stenosis with complex heart disease | Infundibular pulmonary stenosis<br>Fibromuscular subaortic stenosis<br>HOCM<br>Supravalvular aortic stenosis |
| Balloon angioplasty | Recoarctation of aorta<br>Systemic venous stenosis<br>Pulmonary artery stenosis | Systemic-to-PA shunts<br>Native coarctation (> 7 months)<br>PDA | Pulmonary vein stenosis |
| Stent placement | PA stenosis<br>SVC/IVC stenosis<br>Baffle obstruction following atrial switch | Stenotic RV-to-PA conduit<br>Stenotic AP collaterals<br>Coarctation of aorta<br>PDA | Pulmonary vein stenosis |
| Balloon atrial septostomy | TGA<br>TAPVC<br>Tricuspid atresia<br>Mitral atresia<br>Pulmonary atresia (IVS) | HLHS with highly restrictive ASD | Interrupted IVC<br>Infants older than 6 weeks |
| Blade atrial septostomy | As above in infants > 6 weeks old | As above > 6 weeks<br>Pulmonary hypertension with increased RAP | Interrupted IVC |
| ASD closure devices | Secundum ASD or PFO < 20 mm, rim of > 5 mm<br>Fenestrated Fontan | None | Primum ASD<br>Sinus venosus ASD |
| Other closure devices | Symptomatic PDA<br>Asymptomatic PDA with heart murmur<br>AP collaterals | "Silent" PDA | PDA with irreversible pulmonary obstructive disease |
| Coil occlusion | AP collaterals (dual supply)<br>Small PDA (< 4 mm)<br>Surgical shunts<br>Pulmonary AV fistula<br>Venovenous connections | Moderate PDA (4–7 mm)<br>Coronary AV fistula | AP collaterals (without dual supply)<br>PDA > 7 mm |

AP, aortopulmonary; ASD, atrial septal defect; AV, arteriovenous; HLHS, hypoplastic left heart syndrome; HOCM, hypertrophic obstructive cardiomyopathy; IVC, inferior vena cava; IVS, intact ventricular septum; PA, pulmonary artery; PDA, patent ductus arteriousus; PFO, patent foramen ovale; RAP, right atrial pressure; RV, right ventricle; SVC, superior vena cava; TAPVC, total anomalous pulmonary venous connection; TGA, transposition of the great arteries.
Data from Allen HD, Beekman RH IIIrd, Garson A, Jr *et al*. Pediatric therapeutic cardiac catheterization: A statement for healthcare professionals from the Council on Cardiovascular Disease in the Young, American Heart Association. *Circulation* 1998; **97**: 609–25.

venous stenosis, and to coarctation of the aorta (Fig. 25.2).[43] The placement of endovascular stents improves the initial success of angioplasty, reduces the incidence of recurrence and may reduce late aneurysm formation. The stents used are deployed over a balloon that is positioned and inflated to dilate the stent and the vessel, then withdrawn, leaving the stent *in situ*.

The technique is limited by the large size of catheters required to deploy stents and a failure of the stents to grow with the patient; however, newer designs of stents that allow redilation reduce this limitation. Large catheters increase the risk of damage to vascular and cardiac structures, especially thrombosis of the femoral vessels. Further complications are malposition or embolization of the stent.

## Closure of shunts

A number of devices are available to close intravascular

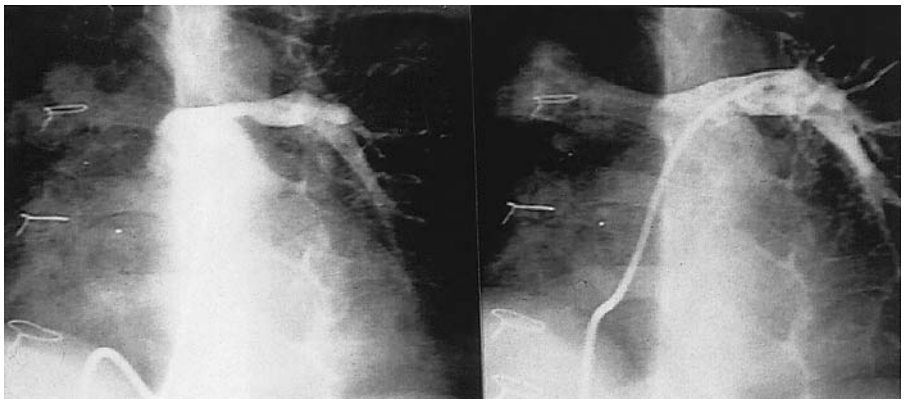

**Fig. 25.2** In the left-hand image contrast has been injected into the left pulmonary artery to demonstrate a profound stenosis. In the right-hand image the stenosis has been dilated and an endovascular stent deployed.

shunts. For smaller shunts the most common are helical wire coils, which are available in different diameters and lengths. More complex devices are required for larger vessels and for closure of intracardiac connections. The most commonly used devices have a double "umbrella" design. They are deployed with the two sides of the "umbrella" on either side of the shunt. Complications are malposition or embolization of the device, vascular occlusion, myocardial perforation, hemolysis, and vascular trauma. The larger devices require large catheters to deploy them and may not be suitable for use in infants.

## Treatment of specific lesions

### Pulmonary stenosis

Percutaneous balloon pulmonary valvotomy has now been performed for over 20 years. It is indicated when the transvalvular gradient is greater than 50 mmHg with a normal *CO* and is the treatment of choice for isolated pulmonary valve stenosis. Immediate results are good, and in a series of 533 patients, 77% had an adequate result at follow-up (average interval 33 months).[44,45] Pulmonary regurgitation is common following the procedure but is generally well tolerated in young children.

Neonates with critical pulmonary stenosis are critically ill and profoundly cyanotic. The pulmonary circulation is dependent on flow from the ductus arteriosus (DA). The majority of infants require mechanical ventilation because of profound hypoxia and the use of prostaglandin ($PGE_1$) infusion to maintain patency of the DA. Because there is minimal flow through the pulmonary valve and an open DA, inflation of the balloon often does not cause further hemodynamic compromise. Acute complications occur in 10–30% of patients.[46,47] Pulmonary stenosis causes pressure overload of the RV, which does not immediately recover with relief of the outflow obstruction, and continuation of the $PGE_1$ infusion maintains pulmonary flow during this period. The size of the valve annulus, tricuspid valve size, and ventricular volume are predictors of outcome.[48]

In older infants, in whom the DA is closed, there is no alternative route for pulmonary blood flow; therefore, inflation of the balloon leads to greater hemodynamic upset. Cardiac output decreases dramatically, resulting in significant hypotension. This usually improves on deflation of the balloon, but if ventricular dilation develops the blood pressure may not recover promptly. Bolus doses of epinephrine and occasionally more prolonged inotropic support may be required.

A modification of the technique is used for treatment of pulmonary atresia with intact ventricular septum in which radiofrequency energy is used to perforate the membrane at the pulmonary annulus. Because the pulmonary valve leaflets are absent and the membrane destroyed, pulmonary insufficiency is inevitable, and the risk of inadvertent perforation of the right ventricular outflow tract is higher during this procedure.

### Pulmonary artery stenosis

Pulmonary artery stenosis may be congenital or acquired, often following surgery. Congenital stenosis is associated with three conditions: reduced pulmonary blood flow (such as tetralogy of Fallot), branch stenosis in association with Williams' syndrome or congenital rubella, or as an isolated stenosis at the site of insertion of the DA. Stenosis may occur after any surgery involving manipulation of PAs, particularly creation of shunts or PA banding. Stenosis can arise at any point in the pulmonary vascular bed and multiple sites are not uncommon. Two thirds are confined to proximal vessels. The right ventricular pressure is raised when the main PA is affected or when multiple peripheral stenoses are present. If only one branch PA or the peripheral PAs are affected, then the PA pressure may be normal at rest.

Surgery is the treatment of choice for proximal PA stenosis but surgical treatment of peripheral PA stenosis is difficult. Transcatheter angioplasty is initially successful in 50% but restenosis is common and long-term benefits are seen in less than 35% of patients.[49,50] In a large series published in 1992, the mortality was 1–2% and the risk of serious complications

5%. Complications include vessel rupture, hemoptysis, paradoxical embolism, balloon rupture, aneurysm formation, air embolism, and unilateral pulmonary edema.

The outcome of PA stenosis is improved with the use of endovascular stents, which reduce the incidence of initial failure, and restenosis. The large catheter positioned in a stenotic PA increases the degree of obstruction resulting in worsening hypoxia and right ventricular failure. The use of extracorporeal membrane oxygenation has been described in high-risk patients.[51]

Patients with cavopulmonary shunts have a limited capacity to tolerate obstruction to pulmonary blood flow. Obstruction can occur at the site of the superior vena cava to PA anastomosis, at the site of previous surgery, or at a remote site. Angioplasty, commonly with placement of stents, may be used to relieve the obstruction; however, when required in the early postoperative period, the patient's condition is often poor.

Patients with Williams' syndrome may have multiple peripheral stenoses of the PAs, associated supravalvular aortic stenosis and coronary artery stenosis. In a series of 39 procedures the mortality rate was 7.7%,[52] and high right ventricular pressure was a predictor of mortality. Three out of 22 patients initially managed with deep sedation required intubation.

### Aortic valvotomy

Balloon dilation of isolated aortic valve stenosis is indicated when the transvalvular gradient is greater than 70 mmHg, or is greater than 50 mmHg with symptoms, or when ECG evidence of ischemia is seen. Neonates have much smaller gradients despite severe stenosis, as flow across the aortic valve may be minimal. Untreated severe stenosis carries a 19% risk of sudden death.[42,45]

In a series of 630 dilations, the immediate outcome was less than optimal (failure or major morbidity) for 17% of patients and procedural mortality was 1.9%.[53] Major complications, including aortic regurgitation, vascular damage, and perforation of the heart or great vessels, occurred in 6.3% of patients. Age less than 3 months, high gradient, the use of small balloon sizes, and the presence of an aortic coarctation predicted poor outcome,[54,55] and outcome improved with greater experience of the technique. The procedure is essentially palliative, with 50% of patients requiring further interventions within 8 years.

Damage to the aortic valve is a major concern and severe aortic insufficiency occurs in 1.6% of cases. The valve may be damaged by use of an oversized balloon causing dilation of the valve annulus or by inadvertent puncture of the valve leaflet. The latter complication may be reduced by use of an antegrade approach to the valve via the atrial septum (either puncturing the septum or through the foramen ovale). This approach also eliminates the risk of damage to the femoral artery, the passage of the wire across the stenotic valve is simplified and less hemodynamic compromise occurs. If severe aortic insufficiency occurs then coronary blood supply is compromised and urgent surgical repair may be required, which is associated with high mortality, especially in the neonatal age group.[56]

The most difficult patients are neonates with critical aortic stenosis. The incidence of major complications in this age group is 16.7% and procedural mortality is 8.3%. There is a risk of sudden death from myocardial ischemia and arrhythmia. The systemic and coronary circulations are dependent on right-to-left flow through the DA, and the LV is greatly hypertrophied with poor compliance. Initial resuscitation includes mechanical ventilation, $PGE_1$, and cautious use of inotropes. Inflation of the balloon across the aortic valve causes complete obstruction of coronary flow. A narcotic based anesthetic technique reduces cardiac work, and minimizes afterload reduction and tachycardia. Care must be taken to maintain preload as any reduction in *CO* leads to further ischemia. Inotropes, vasopressors, and a defibrillator should be immediately on hand.

Older infants may present with severe degrees of aortic stenosis. They have heart failure and are at risk of ischemia and arrhythmias. Cardiovascular compromise during balloon inflation is inevitable but on deflation of the balloon prompt return of *CO* is to be expected. The incidence of arrhythmias is higher than during other interventional procedures. As with neonates there is a risk of arterial damage and of aortic regurgitation, which may require surgical intervention. It has been suggested that these patients may be managed safely with sedation.[41] However, the patient needs to be still during positioning of the balloon and there is risk of hemodynamic compromise or complications, and at the HSC it is normal to provide general endotracheal anesthesia for this group. Older patients may present with progressive aortic stenosis or with restenosis.

### Coarctation of the aorta

Balloon angioplasty is used for both native and recurrent coarctation of the aorta.[57] The indications are resting hypertension proximal to the coarctation with a gradient of greater than 20 mmHg or the presence of multiple collaterals (Fig. 25.3). The best results are obtained when there is a short discrete coarctation with an otherwise normal aortic arch. Initial success with native coarctation is greater than for recurrent coarctation; however, there is a high incidence of late aneurysm formation (2–6%) and of restenosis (7–12%). In neonates recurrence rates are high and angioplasty is not indicated. In older children with native coarctation the role of angioplasty is controversial.[18] Surgery for recurrent coarctation is more difficult and recoarctation is an accepted indication for transcatheter angioplasty. Use of endovascular stents may reduce both restenosis and aneurysm formation, but the risk of damage to the femoral artery and the failure of stents to grow with the patient limit the use of this technique.

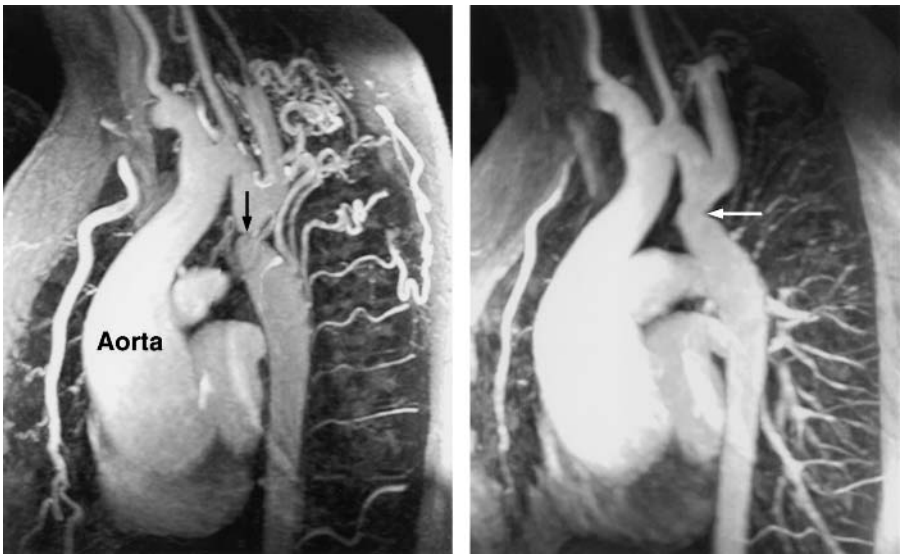


**Fig. 25.3** On the left side is an magnetic resonance image of a coarctation of the aorta prior to dilation. There is a tight narrowing of the aorta (arrow) and numerous collaterals. Post-balloon dilation (right-hand image) the degree of narrowing is reduced and the collaterals are no longer present.

The procedure is generally well tolerated but the risk of serious sequelae is significant. Older patients often have significant collaterals and this reduces the incidence and severity of hemodynamic compromise during balloon inflation. Complications occur in 15% of procedures and include aortic rupture or dissection, stroke, femoral artery damage, thrombosis, and late aneurysm formation[54] with a 0.7% mortality. As with surgical repair, postoperative hypertension should be anticipated.

### Closure of atrial septal defect and ventricular septal defect

Selected atrial septal defects can be closed with a device. The technique is unsuitable for ostium primum defects or for large defects. A rim of septal tissue is required to allow the device to be anchored. At 1 year, 5–10% of patients have significant residual leaks.[58,59] Complications are uncommon and include embolization of the device, encroachment on atrioventricular (AV) valves, obstruction of pulmonary or systemic veins, perforation of the heart or great vessels and air embolus. Generally the procedure is well tolerated. The procedure is usually performed with general endotracheal anesthesia due to the use of transesophageal echo and the need for a still patient.

Transcatheter closure of a VSD is a more complex procedure with a greater risk of serious complications.[60] A wire is placed across the defect from the left side. This wire is then snared from the right heart and brought out of the femoral vein so that a continuous connection is made from the venous system and right heart, through the VSD into the LV and out through the aortic valve and arterial system. The device is then deployed via the right heart, avoiding passage of a large catheter through the femoral artery and aortic valve. Complications include blood loss, arrhythmias, atrioventricular or aortic valve regurgitation, and cardiac arrest. In one series, 50% of patients were admitted to intensive care following the procedure.[61] General anesthesia and control of the airway is required due to the high risk of cardiovascular instability, the length of the procedure, and the use of transesophageal echocardiography. The precise role of this procedure has yet to be defined, though with greater experience and improved technology the incidence of complications is likely to be reduced.

### Closure of extracardiac connections

Connections between the systemic and pulmonary circulations may occur in isolation (patent ductus arteriosus [PDA], in association with CHD (aortopulmonary connections with pulmonary atresia), as a complication of cyanotic heart disease (venovenous connection after cavopulmonary connection) or through surgically created shunts.[62]

Usually these lesions are closed by embolization with helical wires. The choice of anesthetic technique will depend on the patient's physiology. Cyanotic patients with a cavopulmonary connection and multiple collaterals may not tolerate positive pressure ventilation. Older patients presenting with large PDAs may have significant pulmonary hypertension and be at risk of right heart failure. Embolization of the device into the pulmonary or systemic circulation may cause vascular occlusion and infarction. Often the device can be retrieved via the catheter but open retrieval may be required.

### Atrial septostomy

Balloon atrial septostomy was first described in 1966. The objective is to open a non-restrictive connection between the left and right atria to allow bidirectional mixing of blood. It has most widely been used for the initial palliation of

transposition of the great arteries, and in this situation the improvement in the patient's condition may be dramatic. Other indications are total anomalous pulmonary venous drainage, atrioventricular valve atresia, and pulmonary atresia with intact ventricular septum.

The technique involves the passage of a balloon tipped catheter across the foramen ovale into the left atrium. The balloon is inflated and withdrawn across the septum, tearing the atrial septum. This procedure is repeated until the inflated balloon can be withdrawn without resistance. The procedure can be performed at the patient's bedside using echocardiographic guidance. A modification of the procedure is applied to older infants, because by 1 month of age the atrial septum is too thick to be torn by the balloon alone. A catheter with a retractable blade is used to initiate the tear.

Complications include arrhythmias, perforation of the heart, balloon rupture, and embolization and damage to heart structures. Patients are often extremely hypoxic, acidotic and may have pulmonary edema. Ventilation and $PGE_1$ infusion are the first priorities and resuscitation should continue through the procedure. The effect of successful septostomy is dramatic with a rapid increase in oxygenation and in end-tidal carbon dioxide from improved pulmonary blood flow.

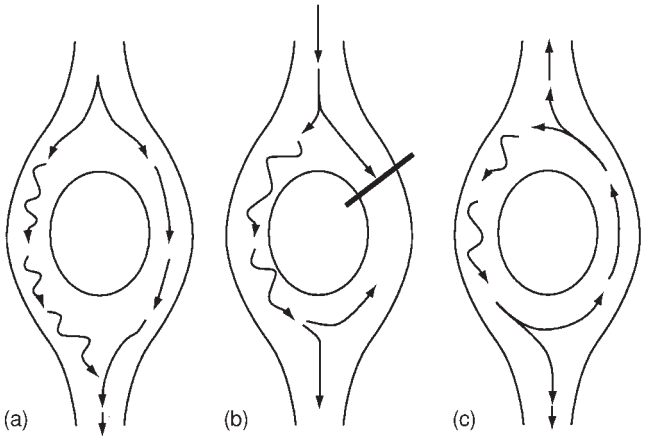


**Fig. 25.4** Re-entry tachycardia requires a circuit with two limbs of different conduction velocities and refractory periods. The left-hand limb of the circuit in the figures has a shorter refractory period and slower conduction velocity (curved arrows). In (a) neither pathway is refractory and the impulse is conducted over both limbs. In (b) a premature impulse travels over the left-hand pathway; however, the right-hand pathway is refractory from previous conduction. If the right-hand pathway is no longer refractory by the time the impulse reaches the distal end of the circuit it is conducted in a retrograde fashion via the right-hand pathway and the re-entry rhythm is perpetuated (c).

## Electrophysiology studies and radiofrequency ablation

The purpose of an EP study is to identify the mechanism of the patient's arrhythmia by recording signals from electrodes placed within the heart. Use of fluoroscopy and reference to anatomic landmarks allows localization of the abnormal pathways and foci responsible for the arrhythmia. Ablation of the abnormal pathway is initially successful in 91% of patients with a recurrence rate of 23%.[17,63]

The majority of children presenting for EP investigation and treatment are otherwise healthy, have functionally normal hearts, and present with well-tolerated SVT. A minority have either a life-threatening arrhythmia, or an arrhythmia complicating CHD. This is in contrast to the adult population, who more frequently present with ventricular arrhythmias complicating ischemic heart disease. Anesthetic concerns include the length of the procedure, poor access to the patient, and the possibility of anesthetic agents altering the EP of the heart. The effect of anesthetic agents on the ability to study the arrhythmia depends upon the mechanism of the arrhythmia.

### Pathogenesis of arrhythmia

The most common mechanism of tachycardia is re-entry. This requires a circuit composed of connected pathways with different conduction velocities and refractory periods (Fig. 25.4). Pre-excitation syndromes occur in a subgroup of patients with re-entry tachycardia. One arm of the circuit is the patient's atrioventricular node and the other is a congenital muscular pathway between the atrium and ventricle. Tachycardia arises when depolarization occurs in the circuit while one limb is refractory and the other is able to conduct. The depolarization continues around the circuit and reaches the previously refractory pathway, which is now able to conduct, and the circle is therefore perpetuated (Fig. 25.4).[64]

A second mechanism is altered automaticity. During normal sinus rhythm only the sinoatrial node independently generates rhythmic impulses through spontaneous depolarization of the basement membrane. Other cells demonstrate this activity but at a slower rate, and only control the *HR* if the sinus node is not functioning or conduction is blocked. When cells are damaged and subjected to extrinsic factors (electrolyte disturbance, hypoxia, hypercarbia, high wall tension, ischemia, and high catecholamine levels) spontaneous depolarization may be accelerated. This leads to rapid repetitive depolarization of a single focus: ectopic tachycardia.

### Electrophysiology techniques

Figure 25.5 demonstrates the typical electrode catheter position during an EP study for investigation of SVT. The catheters have multiple electrodes along their length. An electrode placed across the tricuspid valve can be positioned to record an ECG from the His bundle. Further electrodes are typically placed high within the right atrium, at the apex of the RV, and "roaming" electrodes can be placed elsewhere in the right heart. Potentials from the left heart can be recorded

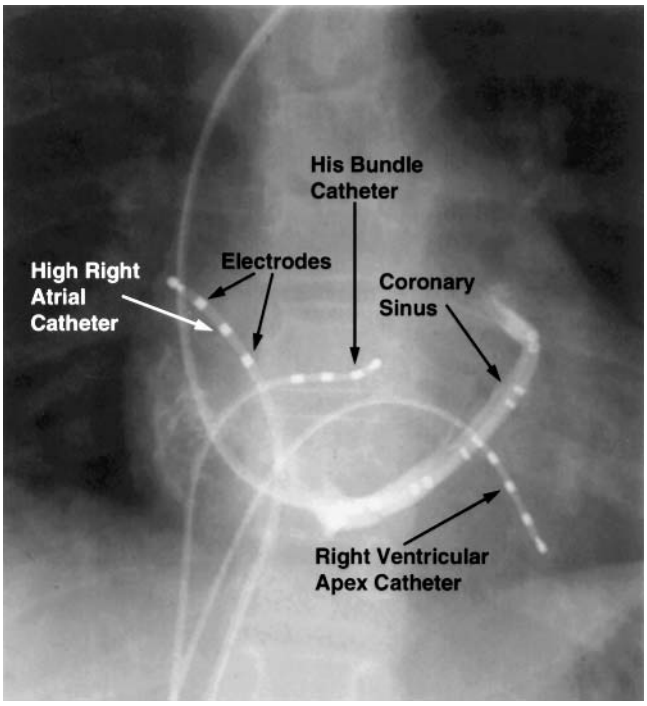


**Fig. 25.5** Typical catheter position during electrophysiology study for investigation of supraventricular tachycardia. Catheters have multiple electrodes along their length. Catheters are positioned across the tricuspid valve to record the signal from the His bundle, in the ventricular apex, in the high right atrium, and within the coronary sinus. In this image contrast has been injected into the coronary sinus.

via an electrode within the coronary sinus or from electrodes placed directly within the left heart (via puncture of the atrial septum or retrograde passage through the aortic valve).

Figures 25.6 and 25.7 demonstrate typical ECGs recorded during an EP study. In order to identify the mechanism of the arrhythmia periods of pacing and programmed stimulation are undertaken. Pacing, commonly via the high right atrium and ventricular apex, allows arrhythmias to be provoked or terminated, permits measurement of EP properties of the conduction system and allows for ventricular pacing should complete heart block occur (a rare complication). Drugs may be used to further refine the study. Adenosine blocks normal AV conduction exposing a concealed abnormal pathway. Isoproterenol increases sinoatrial rate, speeds AV node conduction, reduces refractory periods, and increases automaticity of other contractile tissue.

## Radiofrequency ablation

Destruction of abnormal pathways and automatic foci abolishes the arrhythmia. This is most often accomplished by delivering radiofrequency energy to ablate the area. In the treatment of pre-excitation syndromes a specialized catheter is positioned along the AV ring then adjusted to record the earliest conduction via the abnormal pathway. When delivering radiofrequency energy, the size of lesion created is controlled by measurement of the temperature generated at

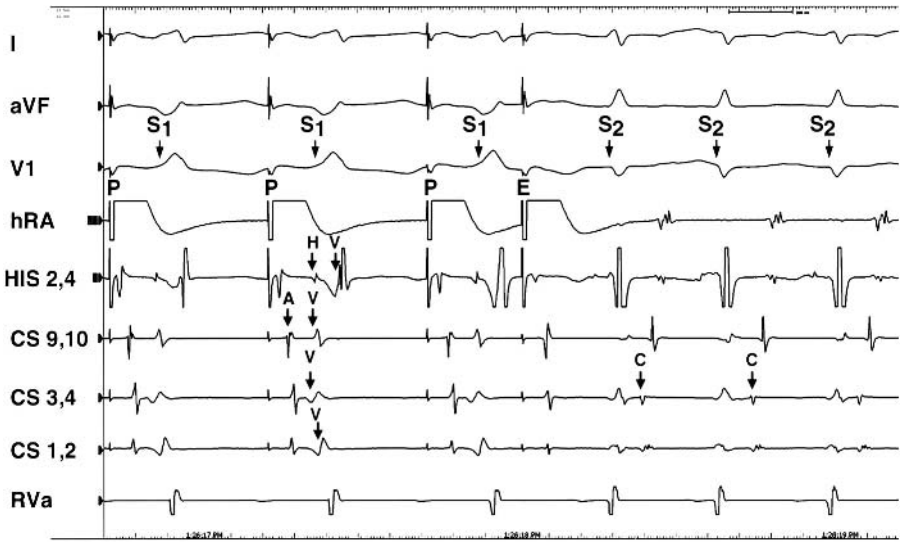


**Fig. 25.6** Simultaneous surface and intracardiac electrocardiograms (ECGs) are shown. Three paced beats (P) are delivered via the high right atrial catheter followed by a premature stimulus (E) resulting in supraventricular tachycardia (SVT). For each beat the CS 9,10 lead demonstrates three signals: an artifact corresponding to the pacing stimuli; a signal from depolarization of adjacent atrial muscle (A); followed by a signal from the adjacent ventricle (V). The His-bundle depolarization (H) coincides with depolarization of the ventricular septum adjacent to the electrode. During paced rhythm ventricular depolarization (V) occurs earliest in the CS 3,4 electrode (an electrode in the center of the coronary sinus catheter), indicating proximity to the accessory pathway. The pre-excitation (delta wave) seen on the surface ECG ($S_1$) is confirmed by depolarization of CS 3,4 prior to His-bundle depolarization (H). Following initiation of SVT the morphology of the surface QRS becomes normalized indicating activation via the normal conducting system ($S_2$). Earliest retrograde activation of atrial muscle is seen on the CS 3,4 electrode confirming the position of the accessory pathway.

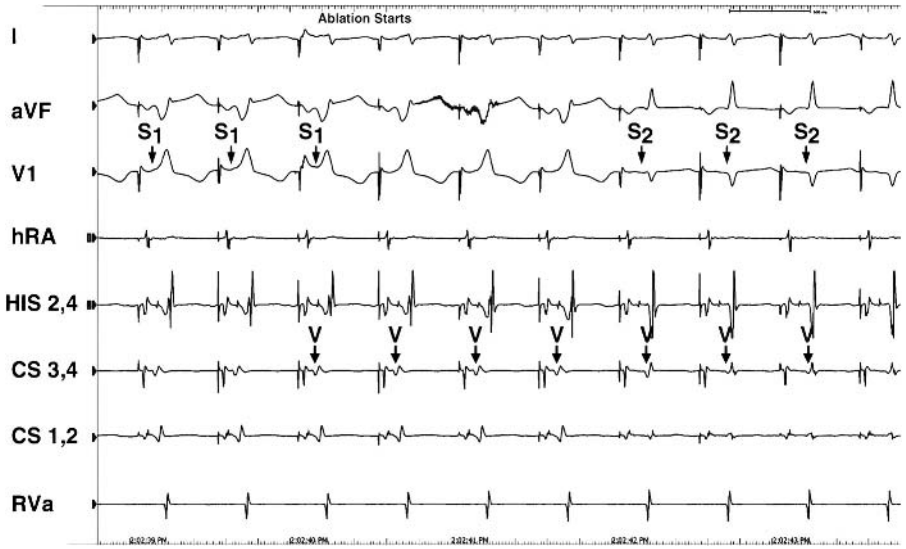


**Fig. 25.7** Surface and intracardiac electrocardiograms (ECGs) are shown from the same patient as in Fig. 25.6. Ventricular depolarization (V) is earliest in CS 3,4 and pre-excitation is demonstrated on the surface ECG ($S_1$). As radiofrequency energy is delivered pre-excitation is lost with normalization of the surface QRS morphology ($S_2$) and ventricular depolarization on CS 3,4 occurs later in the cardiac cycle.

the catheter tip and time of exposure. A further EP study is conducted following attempted ablation to test for residual or additional pathways. The ablation of an abnormal atrial focus is potentially more difficult, as reference to anatomical landmarks and obtaining a stable electrode position is less certain.

Indications for radiofrequency ablations have recently been discussed.[17] Arrhythmias may resolve spontaneously in patients less than 4 years old without CHD; and indications are thus limited to life-threatening arrhythmias not controlled by antiarrhythmic drugs. A small series has described the successful use of radiofrequency ablation to treat life-threatening tachycardia in children less than 18 months old; however, the risks in this group are higher.[65] Arrhythmias in older children are less likely to resolve and the indications for ablation are wider. Indications include failure of medical treatment, risk of sudden death, and a patient's preference for ablation rather than long-term treatment with antiarrhythmic drugs.

## Arrhythmia in patients with congenital heart disease

Patients with CHD may present with arrhythmia in a number of circumstances.[66] Some lesions, such as Ebstein's anomaly are associated with accessory pathways and pre-excitation; atrial dilation is often associated with arrhythmia, and suture lines or scars can act as substrates for re-entry or automatic arrhythmia. The latter is especially true following extensive atrial surgery, such as the Mustard procedure or classical Fontan. These patients may not tolerate tachycardia and the placement of intracardiac electrodes may be complex. In a series of 139 patients, radiofrequency ablation was possible in 66% of studies, with a recurrence of 11% at 2 years without significant morbidity.[66]

## Anesthetic considerations

As with other catheter procedures it is possible to conduct EP studies in conscious patients or with minimal sedation. At the HSC in Toronto it is common to use general anesthesia for procedures in children and adolescents. Though only vascular access is painful, the procedures are often prolonged, multiple venous and arterial access points are required, and periods of arrhythmia are inevitable. Arrhythmias are unpleasant for the patient and urgent interventions are facilitated by anesthesia. Deep sedation offers no advantage to anesthesia and the additive effect of repeated doses of sedative drugs over a period of time must be considered. When vascular access sheaths are placed within the thorax in a spontaneously breathing patient greater care is required to reduce the risk of air embolus.

Preoperative considerations include the presence of CHD, cardiomyopathy, or familial conditions associated with arrhythmia (long QT syndrome and arrhythmogenic right ventricular dysplasia). The patient should be questioned to the frequency of arrhythmia, factors that precipitate the arrhythmia, their symptoms during the arrhythmia, and whether treatment is required to terminate the arrhythmia. Arrhythmias associated with fainting or collapse of the patient are likely to be associated with greater hemodynamic compromise. If anxiety precipitates the arrhythmia, preoperative anxiolysis is indicated. Antiarrhythmics are usually stopped prior to the procedure unless the arrhythmia is frequent and poorly tolerated. The majority of patients are adolescents and discreet questioning as to risk of pregnancy (especially in view of X-ray exposure) and substance abuse is appropriate.

The likely mechanism of arrhythmia is often known from surface ECG (e.g. the presence of delta waves indicates

Wolff–Parkinson–White syndrome) or from a holter recording of the arrhythmia. This allows the anesthetic technique to be adapted to avoid suppression of the arrhythmia and to have minimal effects on the patient's EP. Specific agents may suppress abnormal pathways or foci to a point where their detection and the induction of the arrhythmia is not possible. This leads to false negative studies and failure of the procedure.

Other considerations are the length of the procedures, poor access to the patient, and the potential for hemodynamic compromise. X-ray tables are very firm and patient positioning can be awkward. Care needs to be taken to avoid injury to nerves and pressure areas and large adolescent patients are particularly difficult to position.

Access to the patient is reduced from the use of the subclavian or internal jugular veins for vascular access for some procedures. The need to have X-ray and EP equipment close to the patient further reduces access to the patient, and intravenous lines, ventilator tubing, and anesthetic machines should be positioned accordingly.

Periods of very rapid *HR* and rhythm are to be expected during an EP study and healthy patients tolerate this well. Studies in patients with atrial arrhythmias often fall into this category, and beat-to-beat monitoring of arterial pressure may not be necessary. Greater hemodynamic compromise occurs when the ventricular rate is very high, when the focus is ventricular, or when the patient has reduced cardiac reserve. Continuous arterial pressure monitoring via a femoral artery catheter should be considered in these patients. Vasopressors may be required to improve perfusion pressure though α-adrenergic agonists have reflex effects on the EP of the heart. Discussion with the cardiologist prior to and during the procedure is vital in the management of more difficult patients. Most arrhythmias can be terminated rapidly by overdrive pacing. Drugs (other than adenosine) or external cardioversion are rarely required and may force the cancellation of the procedure.

## Anesthetic drugs and the cardiac conduction system

Anesthetic agents influence the EP of the heart. Effects are mediated via the sympathetic and parasympathetic systems or via the cardiac conduction system and myocardium. The significance of these effects depends upon the mechanism of the tachycardia.

### Anesthetic drugs and pre-excitation syndromes

Supraventricular tachycardia due to pre-excitation syndromes requires conduction of impulses in a circuit involving the functional atrioventricular node and accessory pathway. Effects upon the accessory pathway are most critical and can be characterized by two EP variables: the accessory pathway effective refractory period (APERP) and the coupling interval.[67] The APERP is the minimal time between two impulses that are still conducted by the accessory pathway. The coupling interval is the maximal time between two impulses able to precipitate a SVT. A false negative EPS due to suppression of conduction via the accessory pathway is most critical following radiofrequency ablation, because it may lead to recurrence of SVT.

Enflurane, isoflurane and halothane at 1 minimum alveolar concentration (*MAC*) have been shown to cause prolongation of the APERP in both adults and children.[67,68] It has been suggested that these agents be avoided during ablation of accessory pathways. Enflurane has a greater effect than other agents. However a further study of isoflurane and a study of sevoflurane failed to demonstrate significant electrophysiological effects at 1 *MAC*.[69,70] Conversely, isoflurane and halothane prolong the coupling interval, potentially increasing susceptibility to SVT.[67] From animal studies it is clear that inhalational agents do have a number of electrophysiological effects when administered in sufficient dose; however, the clinical significance of this may be limited.

A number of clinical studies have demonstrated no direct effect of propofol on conduction at doses of 100–150 μg/kg/minute other than slight prolongation of atrial refractory period.[69,71,72] In studies on isolated hearts, significant electrophysiological effects are apparent only at concentrations unlikely to be achieved clinically. Midazolam and alfentanil in combination do not have direct effects on cardiac conduction.[73] Droperidol produces a marked prolongation of APERP and should be avoided.[74] Sufentanil in very high doses produces a slowing of cardiac conduction, though it is not clear if this is true of other opiates. Vecuronium has no EP effects but other neuromuscular blocking agents have not been studied.

Despite the electrophysiological effects of volatile agents, it is possible to induce SVT due to re-entry in most patients. A technique utilizing opioids, nitrous oxide, and a low concentration of volatile is acceptable,[71] and sevoflurane may be preferable to isoflurane in this circumstance. The successful use of propofol for maintenance of anesthesia during EP studies for re-entry tachycardia has been described, but it remains uncertain whether the risk of false negative studies is reduced in comparison to volatile anaesthetics.[75]

### Anesthetic drugs and automatic tachycardia

Ectopic arrhythmias resulting from increased automaticity behave differently under anesthesia. Many of the extrinsic factors, which promote automaticity, are minimized during steady state anesthesia. Typically, catecholamine levels are low and cardiac work is decreased.

The direct effects of inhalational anesthetics on automaticity are complex. As described above, the abnormal behavior of these foci is related to an acceleration of spontaneous depolarization of the cell membrane. Halothane reduces the

rate of depolarization in sinoatrial cells producing a predictable reduction in *HR*.[76] However, when uninjured Purkinje cells exposed to epinephrine are exposed to halothane, the rate of spontaneous depolarization is increased.[77] The most likely substrate for ectopic tachycardia is injured Purkinje cells already demonstrating increased automaticity. Volatile agents do not affect these cells or their response to epinephrine.[77] In intact hearts, halothane decreased the ability to induce ventricular tachycardia in dogs though enflurane had no effect on the ability to induce ventricular tachycardia during human EP studies.[78,79]

In a series of 150 patients with SVT, anesthetized with propofol infusions, seven patients had arrhythmias due to increased automaticity.[75] The arrhythmia could not be induced in four of these patients despite the infusion of isoproterenol, though EP studies were successful in all of the 143 patients with re-entry tachycardia. In a further case report an incessant SVT due to increased automaticity was terminated by propofol.[80]

Given this data it is difficult to suggest a best anesthetic technique for EP studies in patients with ectopic tachycardia. Propofol should be avoided, as should higher doses of narcotics. Limiting the dose of volatile anesthetics during attempts to induce the tachycardia and the replacement of endogenous sympathetic activity with sympathomimetic drugs such as isoproterenol is one approach. The avoidance of general anesthesia can be considered in older patients; however, EP studies for automatic tachycardia are feasible in anesthetized patients. In a series of 12 children with automatic tachycardia, anesthesia did not appear to add to the difficulties in studying the arrhythmia.[81]

## Implantation of pacemakers and defibrillators

Pacemaker implantation is less common in children than in adults.[82] It is indicated for complete heart block (congenital or acquired) or for sinus node dysfunction leading to symptomatic bradycardia. Bradycardia may complicate CHD or be surgically produced. Innovative indications include antitachycardia pacing of SVT and implantation of defibrillators.

In cooperative older patients the procedure can be performed awake, but for small children general anesthesia is required. Anesthesia may be associated with worsening of bradycardia. Treatment with atropine (not effective for complete heart block) and isoproterenol may be instituted followed by the rapid placement of a temporary pacemaker wire, or the use of transthoracic or esophageal pacing. Transthoracic pacing requires a general anesthetic and possibly muscle relaxation; however, placement of pacing pads prior to induction of anesthesia facilitates treatment.

There are practical problems associated with placement of pacemakers in small children. Wires must be sufficiently long to accommodate patient growth and subcutaneous placement of the pacemaker may be impossible (the abdomen is a commonly used site). Epicardial wires are required in small infants and when access to the heart via the venous system is not possible (post-Fontan).

Implantation of defibrillators is a rare procedure in children and is indicated for life-threatening ventricular arrhythmias.[83] Implantation is similar to implantation of pacemakers; however, it is usual to test the defibrillator by induction of ventricular fibrillation which is unpleasant for a conscious patient. Indications include isolated arrhythmias associated with long QT syndromes and patients with hypertrophic cardiomyopathy or arrhythmogenic right ventricular dysplasia who may have more general myocardial disease.[84–86] Often, patients present after "near miss" sudden death or death of a close family member, and they and their families are often extremely anxious. Preoperative anxiety can be sufficient to induce arrhythmia and premedication with an anxiolytic is advisable.

## Conclusion

The trend toward more invasive therapeutic cardiac catheterization procedures in younger, smaller, and sicker patients increases the potential for hemodynamic and respiratory instability. As such, preparation and vigilance for these procedures by the anesthesiologist is essential. Approaching these procedures as if the patient were undergoing surgery will help ensure the best outcome. Indeed, in the future an increasing number of combined surgical and catheter interventions may be performed at the same setting, in a modified catheterization laboratory that is fully equipped for surgery.[87]

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# 26 Anesthesia for non-cardiac surgery and magnetic resonance imaging

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## Introduction

In the USA each year nearly 32 000 children are born with congenital heart disease (CHD).[1] Many of these children require the care of an anesthesiologist within the first year of life, as extracardiac anomalies are seen in up to 30% of infants with CHD[2,3] and may necessitate surgical intervention in the neonatal period prior to repair or palliation of their cardiac lesion. As a result of continuing advances in prenatal diagnosis, interventional cardiology, pediatric cardiac surgery, anesthesia, and critical care nearly all these children will survive to adulthood. These patients will subsequently return for additional palliative or reparative cardiac surgeries as well as more routine general surgeries.

Caring for children with underlying cardiac disease presents a unique set of challenges. Studies of morbidity and mortality in general pediatric anesthesia indicate that a greater risk of anesthesia exists for healthy infants and children, particularly those under 1 year of age, when compared with adults.[4,5] Studies of closed malpractice claims in pediatric anesthesia also represent infants as a particularly high-risk group, with claims involving children less than 6 months of age accounting for 20% of all pediatric claims, more than any other age group.[6] The Pediatric Perioperative Cardiac Arrest (POCA) Registry, formed in 1994, has evaluated 289 cases of perioperative cardiac arrests in children, with 150 of these arrests determined to be anesthetic related in origin. Patients less than 1 year of age accounted for more than half the reported arrests. In 18 cases a cardiovascular cause of the arrest was ascertained, and of that number, ten had underlying CHD. Additionally, four patients arrested due to difficulty with tracheal intubation. All were under 4 months of age and all had significant underlying disease, two with CHD. Overall, CHD was present in 15 of the 39 patients who died and three additional patients were later found to have previously undiagnosed cardiomyopathies.[7]

Several studies have specifically examined the influence of CHD on patient outcome after non-cardiac surgery. A review of 191 261 inpatient anesthetics administered to children less than 18 years of age revealed an increase in both short-term and 30-day mortality rates for major or minor surgical procedures among those patients who had CHD. In patients with major cardiac anomalies the observed 30-day mortality rate was nearly twice that of patients with minor cardiac anomalies. A twofold increase in mortality was noted in neonates and infants with CHD when compared to children of similar age without heart disease.[8] A 10-year study of patients with CHD undergoing inpatient and outpatient general surgery procedures in a university hospital showed the preoperative American Society of Anesthesiologists (ASA) classification to be the most accurate predictor of postoperative mortality, as no deaths were noted in ASA physical status 1 or 2 patients. Mortality was increased in patients with age less than 6 months, emergency status, complex cardiac lesions, and those undergoing major surgical procedures.[9] In another retrospective study of children and adults with CHD undergoing non-cardiac procedures, those patients with pulmonary hypertension, cyanosis, congestive heart failure (CHF), inpatient hospital status or age less than 2 years were found to have an increased risk of perioperative morbidity.[10]

Several common factors emerge from these studies. Although physiologically well-compensated patients may undergo non-cardiac surgery with minimal risk, certain patient groups have been identified as high risk: children less than 1 year of age, especially premature infants; patients with severe cyanosis, poorly compensated CHF or pulmonary hypertension; patients for emergency surgery and patients with multiple coexisting diseases.

A joint task force of the American College of Cardiology (ACC) and the American Heart Association (AHA) has formulated practice guidelines for the perioperative care of adult patients with heart disease presenting for non-cardiac surgery.[11] With increasing numbers of children and adults surviving after palliative or reparative surgeries for CHD it will be important to develop similar strategies for their care.

**Table 26.1** American Heart Association guidelines for bacterial endocarditis prophylaxis in patients with cardiac conditions.

| Endocarditis prophylaxis recommended | Endocarditis prophylaxis not recommended |
|---|---|
| *High-risk category* | *Negligible-risk category* |
| Complex cyanotic congenital heart disease | Physiologic, functional or innocent heart murmurs |
| Single ventricle physiology | Surgical repair without residua beyond 6 months |
| Transposition of the great vessels | Atrial septal defect |
| Tetralogy of Fallot | Patent ductus arteriosus |
| Surgically created systemic-to-pulmonary shunts or conduits | Ventricular septal defect |
| Prosthetic cardiac valves | Cardiac pacemaker or implanted defibrillator |
| Bioprosthetic valves | Isolated secundum atrial septal defect |
| Homograft valves | Mitral valve prolapse without valvar regurgitation |
| Previous bacterial endocarditis | Previous coronary artery bypass surgery |
| | Previous Kawasaki disease without valvar dysfunction |
| *Moderate-risk category* | Previous rheumatic heart disease without valvar dysfunction |
| Other congenital cardiac anomalies | |
| Acquired valvar dysfunction | |
| Hypertrophic cardiomyopathies | |
| Mitral valve prolapse with valvar regurgitation | |

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## Endocarditis prophylaxis

The goal of prophylaxis for infective endocarditis is to provide appropriate antibiotic therapy to protect against organisms known to cause endocarditis during a period of time when the patient is at high risk for bacteremia with these organisms. Despite published guidelines for the use of antibiotic prophylaxis, an increasing incidence of bacterial endocarditis has been noted in the pediatric population over the past three decades. Several factors have been implicated in this trend. Children and adults with CHD are a steadily growing group of patients whose incidence of bacterial endocarditis is nearly 35-fold that of the population-based rate.[12] In a review of 62 cases of infective endocarditis occurring in children between 1977 and 1992, more than 50% were in patients with CHD. Children with complex cyanotic heart disease were at particular risk and constituted more than 33% of the reported cases.[13] In addition, each year larger numbers of patients have indwelling prosthetic materials or central access catheters that can serve as a focus for infection, and the number of children receiving immunosuppressive therapy continues to increase as well. Advances in echocardiography and new diagnostic criteria have resulted in earlier detection of infective endocarditis and fewer missed diagnoses.[14]

The first recommendations for antibiotic prophylaxis against endocarditis were the result of the studies of Northrop and Crowley[15] in 1943, which showed a decrease in the incidence of bacteremia during dental extractions when the patients were given sulfathiazole prior to the procedure. Recommendations by the AHA for antibiotic prophylaxis prior to procedures likely to cause bacteremia followed several years later and have been regularly updated since. The most recent recommendations by the AHA for the prevention of bacterial endocarditis were issued in 1997, and three separate risk groups were established (Table 26.1).[16] Patients with complex cyanotic heart disease, systemic-to-pulmonary artery (PA) shunts, or conduits fall into the highest risk group along with patients who have had prosthetic heart valves or a previous history of endocarditis. The highest annualized risk for endocarditis has been found in children who have undergone repair or palliation of cyanotic heart disease.[17] Moderate risk patients include those with uncorrected patent ductus arteriosus (PDA), ventricular septal defects (VSDs), coarctation of the aorta, biscuspid aortic valve, or acquired valvar dysfunction. Patients with atrial or VSDs 6 months beyond surgical repair with no residual defect, unrepaired secundum atrial defects, pacemakers, defibrillators, and coronary artery disease are considered to be at no greater risk for the development of endocarditis than the general population. At this time no data exist to support recommendations for prophylaxis for patients who have received heart transplants; however, due to the immunosuppressed status of these patients, most physicians recommend the use of antibiotic prophylaxis.

A rising rate of endocarditis in patients with mitral valve prolapse accompanied by mitral insufficiency has also been observed. Other lesions associated with infective endocarditis include Marfan's syndrome with aortic valve disease, hypertrophic obstructive cardiomyopathy (HOCM), and any lesion producing high velocity turbulent flow resulting in damage to the endocardial endothelium.[18] High velocity flow lesions include VSDs, PDA, aortic stenosis, and coarctation of

**Table 26.2** American Heart Association guidelines for antibiotic prophylaxis: dental, oral, respiratory tract and esophageal procedures.*

| | | |
|---|---|---|
| Standard prophylaxis | | Amoxicillin 1 h before procedure<br>Children: 50 mg/kg p.o.<br>Adults: 2.0 g p.o. |
| Unable to take oral medications | | Ampicillin within 30 min before procedure<br>Children: 50 mg/kg i.m. or i.v.<br>Adults: 2.0 g i.m. or i.v. |
| Allergic to penicillin | | Clindamycin 1 h before procedure<br>Children: 20 mg/kg p.o.<br>Adults: 600 mg p.o. |
| | OR | Cephalexin or<br>cefadroxil 1 h before procedure<br>Children: 50 mg/kg p.o.<br>Adults: 2.0 g p.o. |
| | OR | Azithromycin or<br>clarithromycin 1 h before procedure<br>Children: 15 mg/kg p.o.<br>Adults: 500 mg p.o. |
| Unable to take oral medications AND allergic to penicillin | | Clindamycin within 30 min before procedure<br>Children: 20 mg/kg i.v.<br>Adult: 600 mg i.v. |
| | OR | Cefazolin within 30 min before procedure<br>Children: 25 mg/kg i.m. or i.v.<br>Adults: 1.0 g i.m. or i.v. |

* Total pediatric dosage should not exceed adult dosage; cephalosporins should not be used in patients with immediate-type hypersensitivity reaction to penicillins.
Reproduced with permission from Dajani AS, Taubert KA, Wilson W *et al*. Prevention of bacterial endocarditis. Recommendations by the American Heart Association. *Circulation* 1997; **96**: 358–66. See also AHA website: www.americanheart.org.

the aorta. Interestingly, high-velocity regurgitant flow across a systemic atrioventricular (AV) or semilunar valve is considered a high-risk substrate while high-velocity regurgitant flow across a tricuspid or pulmonary valve is of negligible risk.[19]

Some patients may already be taking antibiotics for other infections such as otitis media or may be on chronic antibiotic therapy for conditions such as asplenia. It is recommended that an antibiotic of a separate class be chosen for endocarditis prophylaxis for these patients because their flora may be relatively resistant to ampicillin or amoxicillin. Current AHA guidelines emphasize the judicious use of antibiotics when bacteremia with high-risk organisms is suspected (Tables 26.2 & 26.3). Prolonged use of broad-spectrum antibiotics is discouraged in order to avoid the development of resistant organisms.

## Preoperative preparation and evaluation

### Preoperative assessment

The spectrum of congenital and acquired cardiac lesions is so varied and the type of non-cardiac surgeries performed so diverse that formulating one set of rules for evaluation and perioperative care of these patients is extremely difficult. One may begin by asking: Is the child's cardiac disease the primary consideration in his or her perioperative care, one of several considerations, or a relatively minor consideration? A premature newborn with single ventricle physiology presenting for repair of a tracheoesophageal fistula is representative of an unrepaired, critically ill patient whose cardiac disease will directly impact anesthetic and postoperative management. A 6-year-old child with Down's syndrome, repaired AV canal defect and obstructive sleep apnea requiring tonsillectomy and adenoidectomy presents both cardiac and airway management issues, while a child who has previously undergone successful closure of an atrial septal defect (ASD) does not even require endocarditis prophylaxis. Children with unrepaired or palliated heart disease, children requiring surgery as a result of their cardiac disease, and children undergoing emergent surgery tend to be more critically ill and require more intensive preoperative preparation and assessment. An understanding of the child's underlying

**Table 26.3** American Heart Association guidelines for antibiotic prophylaxis: genitourinary/gastrointestinal procedures.*

| | | | |
|---|---|---|---|
| *High-risk patients* | | | |
| Adults | Within 30 min of starting procedure:<br>Ampicillin 2.0 g i.m./i.v. and<br>Gentamicin 1.5 mg/kg i.m./i.v. | | Six hours later:<br>Ampicillin 1.0 g i.m./i.v. OR<br>Amoxicillin 1.0 g p.o. |
| Children | Within 30 min of starting procedure:<br>Ampicillin 50 mg/kg i.m./i.v. and<br>Gentamicin 1.5 mg/kg i.m./i.v. | | Six hours later:<br>Ampicillin 25 mg/kg i.m./i.v. OR<br>Amoxicillin 25 mg/kg p.o. |
| *High-risk patients: allergic to ampicillin/amoxicillin* | | | |
| Adults | Complete infusion within 30 min of starting procedure:<br>Vancomycin 1.0 g i.v. over 1–2 h<br>Gentamicin 1.5 mg/kg i.m./i.v. | | |
| Children | Complete infusion within 30 min of starting procedure:<br>Vancomycin 20 mg/kg i.v. over 1–2 h<br>Gentamicin 1.5 mg/kg i.m./i.v. | | |
| *Moderate-risk patients* | | | |
| Adults | One hour before procedure:<br>Amoxicillin 2.0 g p.o. | OR | Within 30 min of procedure:<br>Ampicillin 2.0 g i.m./i.v. |
| Children | One hour before procedure:<br>Amoxcillin 50 mg/kg p.o. | OR | Within 30 min of procedure:<br>Ampicillin 50 mg/kg i.m./i.v. |
| *Moderate-risk patients: allergic to ampicillin/amoxicillin* | | | |
| Adults | Complete infusion within 30 min of starting procedure:<br>Vancomycin 1.0 g i.v. over 1–2 h | | |
| Children | Complete infusion within 30 min of starting procedure:<br>Vancomycin 20 mg/kg i.v. over 1–2 h | | |

* Total pediatric dose should not exceed adult dose; maximum dose gentamicin 120 mg; no second dose of gentamicin or vancomycin recommended.
Reproduced with permission from Dajani AS, Taubert KA, Wilson W *et al*. Prevention of bacterial endocarditis. Recommendations by the American Heart Association. *Circulation* 1997; **96**: 358–66. See also AHA website: www.american heart.org.

lesion, the residua and sequelae of any reparative or palliative surgeries he or she has undergone, and his or her current functional status will aid in determining whether the patient requires a cardiology consultation before proceeding with surgery or whether information from the parents and records of previous hospitalizations and clinic visits will suffice.

A thorough history is essential, including both details of the present indication for surgery and the past history of cardiac disease (Table 26.4). While details of previous surgeries or catheterizations may be obtained from old medical records, it is equally important to obtain information from the parents regarding the patient's current state of health, activity level, growth and development, exercise tolerance, and any recent changes from his or her baseline condition. In infants the ability to appropriately feed and gain weight usually indicates adequate cardiac reserve. Observation of the child during the preoperative interview often provides valuable information to supplement the verbal history: Is the child active, playful and age appropriate, or is he/she lethargic and failing to thrive compared to his/her peers? It is important to use as many sources of information as possible to assess the child, because the history obtained from a parent may not always be a reliable indicator of cardiac function. Parents may unwittingly minimize the child's symptoms or lack an adequate frame of reference for comparison with other children. In addition to the cardiac history, details of other medical problems must be solicited. Certain syndromes, such as Goldenhar's (hemifacial microsomia or facio-auriculovertebral syndome), may include both cardiac and airway malformations and because airway management may be challenging in such patients, it is helpful to review any previous anesthetic records for problems with tracheal intubation. Details regarding feeding disorders, gastroesophageal reflux, frequent respiratory infections, reactive airway disease, seizure disorders or developmental delay should also be sought.

Recent illnesses should be noted, particularly respiratory tract infections. Upper and lower respiratory tract infections

**Table 26.4** Preoperative evaluation of the congenital heart disease patient.

- Review underlying anatomy and physiology of cardiac lesion:
  - (a) Previous cardiac surgeries: palliative vs. reparative
  - (b) Evaluate existing residua or sequelae
- Assess other pre-existing diseases or congenital anomalies
- Review information from last cardiology examination:
  - (a) Recent cardiac catheterization, echocardiography or MRI
  - (b) Functional status and reserve at time of last examination
  - (c) Presence of high risk factors:
    - Congestive heart failure
    - Dysrhythmias
    - Pulmonary hypertension
    - Cyanosis
- Review changes since last cardiology examination:
  - (a) History and physical examination
  - (b) Laboratory data
  - (c) Current medications
- Review proposed surgical procedure:
  - (a) Elective vs. emergent
  - (b) Expected length and invasiveness
  - (c) Need for endocarditis prophylaxis
- Plan treatment of potential complications:
  - (a) Dysrhythmias
  - (b) Pulmonary hypertension
  - (c) Ventricular dysfunction
- Plan postoperative care:
  - (a) Monitoring
  - (b) Pain management
  - (c) Cardiology follow-up as needed
- Discuss anesthetic plan and risks with parents and/or guardians

MRI, magnetic resonance imaging.

can cause changes in airway reactivity and pulmonary vascular resistance (*PVR*) which may be poorly tolerated in children with decreased pulmonary compliance or pulmonary hypertension. In particular, patients with bidirectional cavopulmonary shunt (Glenn) or total cavopulmonary anastomosis (Fontan) physiology may be compromised by changes in *PVR*. While studies suggest that active or recent upper respiratory infections (URIs) carry no increase in long-term morbidity or mortality,[20] the increased likelihood of reversible morbidities such as laryngospasm, major desaturation events or breath-holding may pose an unacceptable risk in cardiac patients presenting for elective surgeries. In a recent study of 713 children undergoing cardiac surgery, children with URIs had a significantly higher incidence of respiratory and postoperative complications when compared to children without URIs.[21] The risk must be balanced against the possible benefit of surgery in patients who have frequent upper respiratory tract infections. This situation is most often observed in children presenting for ear, nose and throat surgeries, because chronic otitis, sinusitis, or tonsillitis may be unresponsive to repeated courses of antibiotics and may require surgical intervention in order for improvement to occur.

Children with congenital cardiac lesions are often receiving numerous medications, including antiarrhythmics, angiotensin-converting enzyme (ACE) inhibitors, digitalis, and diuretics. Our practice is to continue cardiac medications throughout the perioperative period with as little interruption as possible, with the possible exception of diuretics. Patients who have had cardiac transplants should have arrangements made to assure continuance of their immunosuppressants throughout the perioperative period. Children on daily medications for reactive airway disease, severe gastroesophageal reflux and seizure disorders should also have these medications continued with as little interruption as possible.

Patients may be receiving chronic aspirin therapy for a variety of reasons, including the presence of systemic-to-PA shunts, treatment of Kawasaki disease, and the presence of risk factors for thromboembolic events. The antiplatelet effects of aspirin therapy are a result of the inhibition of cyclo-oxygenase and occur even at very low daily doses.[22] In addition, aspirin-induced platelet inhibition is irreversible and thus persists for the life of the platelet (10–14 days). No specific guidelines exist for the discontinuation of aspirin therapy prior to elective surgery. During preoperative evaluation the surgeon or cardiologist may request that aspirin therapy be stopped a week prior to elective surgery, but this allows for only partial reversal of the antiplatelet effect. We advocate awareness of aspirin's antiplatelet effect by avoidance of nasotracheal tubes and discussion regarding possible platelet transfusion with the patient's family prior to surgeries where significant blood loss is anticipated. In patients who are dependent on a systemic-to-PA shunt for pulmonary blood flow (*PBF*), particularly patients who are exhibiting increasing levels of cyanosis, we do not routinely stop aspirin therapy preoperatively as the risk of increased bleeding is less severe than the risk of a thrombosed shunt.

The physical examination should include a detailed evaluation of the airway, chest, and heart, with any change from the child's baseline status carefully noted. Wheezing, retractions, increased work of breathing or change in a cardiac murmur may require further work-up. If new onset arrhythmias are suspected, a 12-lead electrocardiogram (ECG) should be obtained along with a cardiology consultation prior to surgery. Examination of the extremities for cyanosis, edema, adequacy of perfusion, and possible vascular access sites is also important. Vital signs should include blood pressure measurements in all four extremities in patients with a history of coarctation of the aorta or aortic arch reconstruction. Height, weight, and baseline hemoglobin–oxygen saturation should be recorded in all patients.

Recent chest radiographs should be reviewed for the presence of cardiomegaly, increased pulmonary vascular

markings and other abnormalities. A new chest radiograph should be obtained in any patient exhibiting new onset of cardiac or lower respiratory symptoms. Electrocardiogram may reveal ventricular hypertrophy or strain, residual bundle-branch block and other rhythm disturbances.

While preoperative lab work is not universally required, a hematocrit is useful as an index for evaluating the degree of chronic hypoxemia among patients with cyanotic CHD. Severely cyanotic patients with hematocrits greater than 60% may have clotting factor abnormalities and/or thrombocytopenia.[23] Phlebotomy is not advocated for patients, however, unless they are experiencing severe symptoms of hyperviscosity syndrome (headache, dizziness, impaired mentation, visual disturbances, muscle weakness, or paresthesias) in the absence of dehydration. Symptoms of hyperviscosity syndrome with a hematocrit less than 65% may be due to iron deficiency,[24] and consultation with the patient's cardiologist prior to elective phlebotomy is recommended. Preoperative evaluation of serum electrolytes, particularly potassium, is recommended for patients receiving digoxin, ACE inhibitors, or diuretic therapy.

A review of all available information from previous surgeries, cardiac catheterizations, and cardiology clinic visits is imperative. Recent echocardiographic assessments of anatomy and ventricular function should be sought, and if the child's symptoms appear to be worsening, a cardiology consultation and follow-up echocardiogram may be advisable. Cardiac catheterization data are useful for reviewing intracardiac and PA pressures, saturations, and shunting. Whenever possible the patient's current physical status, anatomy and physiology should be reviewed with his or her cardiologist in order to optimize anesthetic management and reassure parents who have frequently established a strong relationship with their child's cardiologist.

Emergency surgery presents additional management issues and often adds risk in several areas. Patients who have not been appropriately fasted or who present with bowel obstruction may be at increased risk for aspiration events. There may be little time preoperatively to optimize the patient's cardiac condition, along with difficulty obtaining complete cardiology and surgical records prior to the administration of an anesthetic. In these cases the preoperative evaluation must be distilled into the most important factors: the nature and duration of the present illness, and the child's underlying cardiac disease, baseline status, and medications. Fasting status and the need for a rapid sequence induction must be considered in light of the child's cardiac lesion. A patient who depends on a shunt for *PBF*, cyanotic patients, and patients who have undergone total cavopulmonary anastomosis (Fontan procedure) require intravenous hydration prior to induction of anesthesia if they are hypovolemic. Based on the child's condition and the nature of the emergency, a decision can be made as to whether to proceed with the case with no further work-up and a review of available old records, or whether new consultations and studies should be obtained preoperatively. It should be recognized that in extreme cases the child's clinical status will make the decision for the anesthesiologist: the critically injured trauma patient cannot wait for a consultation with a cardiologist prior to entering the operating room. In many centers such patients are brought directly to the operating room for their initial resuscitation. In this situation maintaining preload, judiciously using inotropes to support ventricular function, and promptly treating acidosis are most important until more information can be obtained.

### Fasting guidelines

Although a 6-hour fast from solid foods is still recommended, in recent years NPO guidelines have been modified to allow ingestion of clear liquids until 2 hours prior to surgery. Studies in children undergoing cardiac surgery have shown no increase in gastric volume or acidity with this practice.[25] In addition to improved patient and parental satisfaction, these guidelines offer clinical advantages to cyanotic and shunt-dependent patients who would be adversely affected by prolonged periods of fasting and possible dehydration. It remains important to verify NPO times with parents prior to surgery as surgical delays can still occasionally result in patients who have been fasted for prolonged periods of time. These patients are best served by offering them clear liquids if time permits, or by starting an intravenous infusion prior to the induction of anesthesia if significant dehydration is suspected.

### Premedication

Anesthetic care of the pediatric patient with heart disease begins with psychological preparation of the patient and his or her family for the proposed anesthetic and surgical procedure. Developing a rapport with the child and his or her family is often as effective as a pharmacologic premedication in allaying anxiety prior to surgery. It is important to discuss the available alternatives for induction and maintenance of anesthesia and postoperative pain management so that both the child and the family feel comfortable with the proposed plans. Many of these patients have had previous heart surgeries or cardiac catheterizations and their questions and concerns may be different than those of the family who has never visited the hospital before. Children who have had multiple surgical procedures have often developed strong personal preferences regarding the method of induction of anesthesia and whenever possible these preferences should be respected.

There are multiple benefits to premedication for children with CHD. Certainly one of the major reasons for administering a pharmacologic premedication is to ease the child's separation from his or her parents. Even older children and teenagers often feel significant anxiety when the moment of

separation arrives although they may have maintained a calm facade until that time. Premedication may also facilitate the induction of anesthesia by decreasing the amount of inhalation or intravenous agents necessary for induction. Additionally it is safer and easier to induce a calm, cooperative child than an anxious, crying toddler or a combative older child. In cyanotic patients the use of appropriate premedication may decrease their oxygen consumption, thereby increasing their oxygen saturation as they become calm and sedated. A study of children with CHD receiving intramuscular scopolamine/morphine/secobarbital showed the effects of this premedication on $SaO_2$ in cyanotic children to be variable. Although the mean $SaO_2$ of the group increased, significant decreases in $SaO_2$ were noted in several individual patients.[26] Monitoring with continuous pulse oximetry and intermittent blood pressures is recommended after the administration of premedication. Personnel trained in airway management and necessary drugs and equipment for resuscitation should also be readily available.

In the pediatric cardiac population, the primary goals of premedication are to achieve sedation and anxiolysis with minimal hemodynamic or respiratory effects. A premedication that will not delay time to discharge is also desirable for patients undergoing outpatient surgery. The use of intramuscular injections has been largely abandoned as oral premedications have been shown to be equally efficacious[27] and are better accepted by children. Intranasal midazolam provides effective anxiolysis and sedation with stable hemoglobin–oxygen saturations and hemodynamic parameters but is poorly tolerated by children due to its bitter taste.[28] Intranasal administration of sufentanil, although better accepted than intranasal midazolam, was shown to have an unacceptably high incidence of desaturation and decreased chest wall compliance.[29] Oral transmucosal fentanyl citrate (Fentanyl Oralet) provides a pleasant vehicle for administration with a rapid onset of sedation but unfortunately is associated with a high incidence of undesirable side effects such as pruritus, vomiting, and occasional hypoxemia in children with CHD.[30]

Midazolam has been used as an oral premedication by mixing the intravenous midazolam product with a variety of additives to enhance patient acceptance. Studies have shown a dose of 0.5 mg/kg will reliably produce sedation and anxiolysis at the time of separation from parents with no observed changes in heart rate (*HR*), systolic blood pressure, hemoglobin–oxygen saturation, or respiratory rate. In addition, no increase in the incidence of postoperative vomiting or increase in time-to-discharge was noted. Although doses of 0.75 mg/kg and 1 mg/kg were also efficacious in providing sedation and anxiolysis, an increase in loss of balance, blurred vision, and dysphoric reactions were observed at these higher doses.[31] Midazolam syrup (2 mg/mL, Roche Laboratories, Inc., Nutley, NJ) has recently become available in a cherry flavored commercial preparation. In a comparison of ASA physical status 1–3 children receiving either 0.25 mg/kg, 0.5 mg/kg or 1 mg/kg of the commercially prepared midazolam syrup, the smallest dose was found to be equally effective in providing sedation and anxiolysis, though a faster onset of sedation was noted with the larger doses. This is in contrast to previous studies utilizing non-standard preparations, suggesting more consistent bioavailability of the commercial preparation.[32] For those children presenting with an intravenous line in place midazolam 0.05–0.2 mg/kg provides an effective premedication with minimal hemodynamic effects.

In patients who are unable or unwilling to accept an oral premedication and who have no intravenous access, intramuscular ketamine provides a rapid and effective means of premedication. Ketamine 2–4 mg/kg i.m. will facilitate the acceptance of an inhalation induction of anesthesia within several minutes. With the lower dose of 2 mg/kg excessive salivation has not been observed and the routine administration of an antisialogogue may not be necessary.[33]

The risks of premedication include oversedation, which can result in airway obstruction, hypoxia, and hypercarbia. A statistically significant increase in $PETCO_2$ and decrease in $SaO_2$ was observed in children after they received either intramuscular morphine and scopolamine or oral midazolam as premedication before cardiac surgery. Clinically significant changes in $SaO_2$ were seen both in children with and without pre-existing pulmonary hypertension or cyanosis.[34] Care in avoiding hypercarbia is particularly important in patients with pulmonary hypertension because these patients have increased pulmonary vascular reactivity and are at risk for pulmonary hypertensive crises. These risks can be minimized by careful attention to patient selection and drug dosage along with appropriate monitoring after the premedication is administered. Often patients presenting for emergency surgery have received sedatives or narcotics in the Emergency Department and this should be taken into account before additional medications are given.

## Monitoring

Once in the operating room standard non-invasive monitors are placed prior to induction of anesthesia. Occasionally a crying patient will resist the placement of monitors, in which case a precordial stethoscope and pulse oximeter are applied and the remainder of the monitors are added as the child is going to sleep. Standard non-invasive monitors include pulse oximetry, oscillometric blood pressure measurement, precordial stethoscope, ECG, capnography and temperature monitoring. An additional pulse oximeter probe should be placed to assure continuous monitoring of hemoglobin–oxygen saturation particularly for infants, cyanotic children, or cases expected to be of long duration. In patients with vasoconstriction due to hypothermia or poor peripheral perfusion a pulse oximeter may be placed on an ear lobe, the tongue, or the buccal mucosa.[35] Not only will a centrally located pulse oximetry

probe function more effectively during periods of hypothermia or vasoconstriction but it will also reflect periods of desaturation and recovery more quickly than peripheral sensors.[36] In the neonate, a pulse oximeter that "suddenly" stops working should warn of hypotension or poor peripheral perfusion. At these times a second pulse oximetry probe is extremely useful to differentiate between failure of an individual probe vs. a true inability of the oximetry probe to obtain a signal from the patient. Additional information to corroborate any acute changes in the patient's condition can be gained from examining trends in the patient's *HR*, blood pressure, and capnography tracing. Direct observation of the patient is also a critical source of monitoring information. Important information regarding blood pressure, the quality of peripheral perfusion, and an indirect assessment of fluid balance can be obtained by palpating arterial pulses, checking capillary refill, and feeling an infant's anterior fontanelle.

Depending on the duration and magnitude of the planned surgical procedure, as well as the child's cardiac lesion and preoperative condition, more invasive monitoring may be useful. Preoperative consultation with the surgeon can be helpful to discuss his or her expectations regarding the planned duration of surgery, potential blood loss, and the need for invasive monitoring intraoperatively and/or postoperatively. It is important to remember that many of these children have previously had arterial or central venous lines placed for cardiac procedures and that accessing these vessels again may be difficult. Cardiac catheterization diagrams often yield useful information regarding previously occluded vessels. Should arterial or central venous line placement prove excessively difficult, the relative importance of such monitoring should be weighed against the risks and delays involved in multiple attempts. In cases where large fluid shifts or blood loss are expected the placement of a urinary catheter is helpful to assess urine output and fluid balance.

The presence of a classic or modified Blalock–Taussig (BT) shunt (systemic-to-PA shunt, often utilizing the subclavian artery), coarctation of the aorta, or previous radial artery cutdowns should be noted prior to attempting placement of a radial arterial line. Often this assessment may be more easily accomplished once anesthesia has been induced. When a BT shunt is present or a subclavian flap repair of coarctation of the aorta has been performed, the contralateral radial artery should be used for monitoring. The pulse oximeter probe should also be placed on the opposite side from the previous surgical intervention.

Central venous lines may be placed after reviewing the child's specific anatomy. In small infants with single ventricle physiology it is usually advisable to avoid the right internal jugular vein if possible, because any stenosis of the superior vena cava would prove extremely detrimental to these children as they undergo their staged bidirectional cavopulmonary shunt (Glenn) and total cavopulmonary anastomosis (Fontan) procedures. Small (3 Fr) single lumen catheters may be placed if necessary. In placing a central venous line in a child, the use of audio Doppler or ultrasound guidance is very helpful in facilitating cannulation of small vessels. Careful attention to positioning of internal jugular or subclavian venous lines is warranted as perforation of the heart with resultant pericardial tamponade is a devastating and potentially fatal complication.[37,38] A simple formula utilizing the child's height as a guide for depth of insertion has been studied in infants and children. Using this formula:

[height in centimeters/10] – 1 for patients < 100 cm and
[height in centimeters/10] – 2 for children > 100 cm

yields placement of the central venous line above the right atrium in 97% of patients.[39] Pulmonary artery catheters are only rarely used in children and the utility of the information to be gained must be measured against the difficulty and risk of placing such a line.

Transesophageal echocardiography (TEE) can be used during major non-cardiac surgeries and often proves helpful in evaluating ventricular filling and function. A prospective study of pediatric patients undergoing scoliosis surgery in the prone position found TEE to be more useful than central venous pressure monitoring in determining cardiac volume and function.[40]

### Monitoring considerations in cyanotic patients

Studies of children with cyanotic CHD have demonstrated that pulse oximetry is less accurate below an $Spo_2$ reading of 80% and may overestimate the actual hemoglobin–oxygen saturation of the patient. Should extreme or prolonged desaturation occur, it is best to measure arterial blood gases to confirm the patient's actual $Pao_2$.[41] Alternatively, the arterial hemoglobin–oxygen saturation may be measured by analysis of an arterial blood sample in a laboratory co-oximeter. It is also noteworthy that at lower saturations a higher degree of accuracy was noted when the sensor was placed on an ear rather than a finger.[42]

Arterial desaturation due to intracardiac shunting is also associated with an increased arterial-to-end-tidal ($Paco_2$ to $PETco_2$) difference, as a portion of mixed venous blood returning to the heart will bypass the lungs, adding blood that is low in oxygen and rich in carbon dioxide to the systemic circulation. Studies comparing acyanotic and cyanotic children with CHD have shown that $PETco_2$ may significantly underestimate $Paco_2$ in cyanotic children.[43] Individuals with unrepaired tetralogy of Fallot (TOF) (VSD, right ventricular outflow tract [RVOT] obstruction, overriding aorta and right ventricular hypertrophy) may have varying degrees of right-to-left shunting depending on the degree of dynamic infundibular narrowing occurring and the resultant obstruction to *PBF*. In these patients the relationship between $PETco_2$ and $Paco_2$ will also fluctuate, thus $PETco_2$ will not reliably estimate $Paco_2$ during surgery in this group of patients.[44]

### Special considerations for patients with pacemakers and implanted cardioverter-defibrillators

In patients with pacemakers or automatic implantable cardioverter-defibrillators (AICDs) it is important to monitor not only electrical but also mechanical evidence of cardiac activity. While the ECG gives electrical indication of heart function, it does not guarantee that mechanical systoles are actually being generated with each QRS complex. Manual palpation of the pulse, auscultation of heart sounds, pulse oximetry, plethysmography, and direct monitoring via arterial line are all useful methods to verify mechanical function of the heart. Continuous arterial pressure monitoring is recommended for pacemaker-dependent patients with poorly tolerated escape rhythms. Back-up methods to increase the *HR* or provide pacing should be available in the event of an emergency. External pacing systems should be in place for patients who have hemodynamic compromise without proper pacemaker function, but it is important to remember that only ventricular contractions will be generated. Patients who are dependent on atrial function, such as those who have undergone total cavopulmonary anastomosis (Fontan procedure), may remain hemodynamically compromised during external pacing.

Recently published guidelines from the ACC/AHA advocate preoperative and postoperative interrogation of permanent pacemakers if at all possible.[11] Previous recommendations to use a magnet to convert a pacemaker to asynchronous mode during surgery are no longer universally valid as most modern pacemakers are programmable and may be unpredictably affected by the placement of a magnet over the pacemaker, especially in the presence of electrocautery. Unipolar devices should be programmed to an asynchronous mode, and rate-responsive pacemakers should have the rate-responsive modes deactivated prior to surgery.[45] Implanted cardioverter-defibrillators should have their antitachycardia and arrhythmia therapies disabled preoperatively by a cardiologist or other knowledgable individual and external methods of cardioversion or defibrillation should be available. Postoperatively, pacemakers and implantable cardioverter-defibrillators should be reinterrogated and re-enabled (Table 26.5).[46]

Electrocautery may inhibit or cause permanent changes in pacemaker function. Converting the pacemaker to the asynchronous mode will eliminate electrocautery-induced inhibition but circuit damage may still occur.[47] Bipolar electrocautery should be utilized whenever possible in the patient with a pacemaker or implantable cardioverter-defibrillator. If monopolar electrocautery is used, the electrocautery return pad should be placed as far away from the pacing generator as possible, and additionally the pacemaker generator/leads axis should not be located between the operative site and the grounding pad. If the pacemaker cannot be placed in an asynchronous mode and electrocautery adversely affects it, cautery current should be applied for no more than 1 second at a time with 10 seconds between bursts of current to allow for maintenance of cardiac output (*CO*).[46]

**Table 26.5** Evaluation and care of the patient with a pacemaker or automatic implantable cardioverter-defibrillator.

- History
  - (a) Indication for placement of device
  - (b) Type of device
  - (c) Date device placed
  - (d) Date of last evaluation
- Physical examination
  - (a) Evaluate underlying rate, rhythm and hemodynamic stability
  - (b) Review recent ECG
- Interrogation of device by a trained individual
  - (a) Evaluate lead integrity
  - (b) Obtain current programming information
  - (c) Determine frequency of initiated therapies with AICDs
  - (d) Consult pacemaker representative if questions arise
  - (e) Reprogram device if necessary prior to surgery
  - (f) Disable antitachycardia therapies on AICDs preoperatively
  - (g) Disable rate responsive modes preoperatively
- Intraoperative management
  - (a) Ensure electrical activity is converted to mechanical systole
  - (b) Have temporary pacing support available
- Postoperative interrogation and reprogramming of device

AICD, automatic implantable cardioverter-defibrillator; ECG, electrocardiogram.

## Intraoperative management

The anesthetic plan should be formulated prior to entering the operating room, taking into account the child's preoperative condition, the anticipated duration of surgery, the possible hemodynamic consequences of surgery, and the expected length of postoperative recovery.

Goals of anesthetic management include optimizing oxygen delivery and ventricular function within the range expected for an individual patient according to their preoperative assessment and underlying cardiac physiology. For most patients a euvolemic state should be maintained. In general, efforts should be made to avoid increases in oxygen demand, *HR* or contractility. Maintenance of normal sinus rhythm is especially important in patients with single ventricle physiology. Emergency cardiac resuscitation drugs should be immediately available for all patients; if complications arise due to hypotension or arrhythmias, immediate pharmacologic intervention is critical.

### Induction

Induction of anesthesia may be accomplished in several ways. Many children will present without intravenous access

prior to surgery and prefer not to have an i.v. started while awake. Hensley *et al*.[48] studied the effects of an inhalation induction with halothane and nitrous oxide in 25 children with cyanotic heart disease and found that oxygen saturation increased with induction, especially in those patients with dynamic RVOT obstruction. With the introduction of sevoflurane, an alternative to halothane now exists for inhalation induction and recent studies suggest that sevoflurane provides improved hemodynamic stability in children with CHD. Russell *et al*.[49] compared the safety and efficacy of sevoflurane and halothane in 180 infants and children with CHD. Anesthesia was induced with either sevoflurane to a maximum of 8% or halothane to a maximum of 4%, with delivered concentrations decreased by half in children with CHF. Although episodes of hypotension were noted in both groups, patients receiving halothane experienced nearly twice as many episodes of severe hypotension. Moderate bradycardia and emergent drug use were also more prevalent in the group receiving halothane, indicating that it may be more difficult even for the experienced practitioner to maintain hemodynamic stability as effectively with halothane as compared to sevoflurane.

The presence of right-to-left shunting can slow the inhalation induction of anesthesia by decreasing the available blood flow to the lungs and therefore decreasing the rate of rise of inhaled anesthetic concentrations in the arterial blood. Not only does the shunted blood not absorb any inhaled agent but it also dilutes the concentration of agent in systemic arterial blood as the two mix. This effect is more dramatic with poorly soluble agents such as sevoflurane and nitrous oxide in contrast to the more soluble agents, halothane and isoflurane. A computer model demonstrated little effect on the speed of induction with left-to-right shunts or mixed right-to-left and left-to-right shunting.[50]

For children presenting with existing intravenous access, or those desiring an intravenous induction, several alternatives exist. Propofol, a sedative-hypnotic, is a rapidly acting intravenous agent that can be utilized for both induction and maintenance of anesthesia. Its short half-life and antiemetic properties make it an ideal drug for day surgery patients. Doses ranging from 2.5 to 3.5 mg/kg are recommended for induction of anesthesia in pediatric patients.[51] Propofol does have significant hemodynamic effects, which must be considered carefully in more fragile patients. Williams *et al*.[52] compared the hemodynamic effects of propofol in 30 children with CHD. Sixteen patients had no intracardiac shunt, six had left-to-right shunts and eight had right-to-left shunts. Propofol was initially given as a 2 mg/kg bolus and then continued as an infusion. Both systemic mean arterial pressure and systemic vascular resistance (*SVR*) decreased significantly while systemic blood flow increased. In patients with cardiac shunts this yielded an increase in right-to-left shunt flow, resulting in clinically important decreases in $Paco_2$ and $Spo_2$ in cyanotic patients. Two patients with unrepaired TOF and left-to-right shunting exhibited reversal of shunt flow after administration of propofol. Propofol should be used with caution in patients whose *PBF* depends on balancing their systemic and *PVR*s and in patients who cannot tolerate systemic afterload reduction.

Etomidate, an imidazole derived sedative-hypnotic agent, is short-acting and has minimal cardiovascular effects, making it an extremely useful agent in critically ill patients undergoing short procedures. Due to its side effects of pain on injection, myoclonus, high incidence of postoperative nausea and vomiting, and possible adrenocorticoid suppression, its use has remained selective rather than widespread. Although prolonged use or multiple doses of etomidate may cause adrenal suppression, single doses of 0.3 mg/kg in children have not been shown to decrease cortisol levels below the lower limits of normal.[53] In a study examining the effects of etomidate on failing and non-failing human cardiac tissue it was shown that etomidate does not cause myocardial depression at clinically relevant concentrations.[54] For children with marginal cardiac reserve etomidate provides an excellent alternative to propofol for the intravenous induction of anesthesia.

Ketamine is a versatile drug that may be used for premedication, induction or maintenance of anesthesia. It is most commonly used via the intramuscular or intravenous routes for induction of anesthesia. Intramuscular ketamine still proves useful for induction in severely developmentally delayed or autistic children who are unable to cooperate with an inhalation induction or placement of an i.v. preoperatively. When used intramuscularly for induction, doses of 4–10 mg/kg should be combined with an antisialogogue in order to avoid excess oral secretions. Ketamine has not been shown to increase *PVR* in children, even those with pre-existing elevations in *PVR*, as long as the airway and ventilation are adequately maintained.[55] While ketamine is a direct myocardial depressant, this effect is clinically manifest only in the catecholamine depleted patient.[56]

In critically ill patients fentanyl and midazolam may be used for induction of anesthesia, particularly when tracheal extubation is not anticipated at the conclusion of surgery. Patients with poorly compensated CHF may not tolerate the myocardial depressant effects of inhaled agents and an opioid–benzodiazepine anesthetic is more likely to provide hemodynamic stability during induction of anesthesia.

## Maintenance of anesthesia

Newer, shorter-acting muscle relaxants and narcotics have provided enhanced flexibility in planning an anesthetic without exclusive reliance on inhaled agents. In recent years fentanyl has been the "gold standard" of narcotic anesthesia for pediatric cardiac patients. In a study of infants who had recently undergone congenital heart surgery, the administration of fentanyl 25 μg/kg over 1–2 minutes resulted in no

significant changes in *HR*, mean PA pressure, *PVR* index or cardiac index.[57] With the introduction of remifentanil, a non-specific esterase metabolized synthetic opioid, an anesthetic technique that combines the hemodynamic stability of a high dose opioid technique yet allows tracheal extubation at the conclusion of surgery has become possible. Pharmacokinetic studies of remifentanil in ASA 1–4 pediatric patients ranging in age from 5 days to 17 years show a consistent half-life with means from 3.4 to 5.7 minutes.[58] Remifentanil's non-specific esterase-based metabolism allows its elimination to be independent of *CO*, renal or hepatic function;[59] in addition, it is not subject to the genetic variability and drug interactions seen with drugs that are dependent on plasma cholinesterase for clearance.[60] A bolus of 1 μg/kg followed by an infusion of 1 μg/kg/minute was shown to provide cardiovascular stability during strabismus surgery in children.[61] As remifentanil alone cannot reliably assure amnesia, the concomitant use of an inhaled agent, propofol infusion or a benzodiazepine is important. Remifentanil is well-suited for short procedures with intense stimulation followed by minimal postoperative pain such as bronchoscopy or foreign body removal. For procedures where significant postoperative pain is anticipated plans should be made for the provision of postoperative analgesia prior to discontinuation of remifentanil in order to avoid the acute onset of pain in the post-anesthesia care unit (PACU).

Many choices exist when considering the use of a neuromuscular blocking drug. For routine or rapid sequence induction of anesthesia rocuronium 0.5–1.2 mg/kg may be used in place of succinylcholine.[62] Generally, the length of the surgical procedure and the cardiovascular profile of the individual drug will dictate the choice of blocking drug. Although patients may breathe spontaneously for short procedures, controlled ventilation is optimal for most patients undergoing longer or more invasive procedures. Many patients with CHD cannot tolerate the high concentration of inhaled agent that is required during spontaneous ventilation. Appropriate mechanical ventilation can also help prevent the atelectasis and hypercarbia that often result from spontaneous ventilation while anesthetized. Postoperative ventilation should be considered for patients whose lungs were ventilated preoperatively, patients with poorly controlled CHF who have undergone major procedures, and patients who have had an unexpectedly complicated intraoperative course.

Regional anesthesia is a useful adjunct to general anesthesia in children and may assist in providing both intraoperative and postoperative pain relief. Caudal blocks with bupivacaine or ropivacaine provide excellent postoperative pain relief for children undergoing lower extremity or urologic procedures.[63] Preservative free morphine (Duramorph™, Astromorph™) may be added for those children undergoing more extensive procedures who will have appropriate in-hospital monitoring postoperatively.[64] Preoperative coagulation studies should be obtained for severely cyanotic children who may be at risk for coagulation abnormalities if placement of an indwelling lumbar or thoracic epidural catheter is planned.

## Emergence and postoperative management

Residual neuromuscular blockade should be reversed prior to tracheal extubation in patients who have received muscle relaxants. Adequate return of neuromuscular function should be assured prior to tracheal extubation by monitoring peripheral nerve stimulation, as well as by clinical observation of respiratory pattern, depth of respirations and muscle tone.

Once tracheally extubated and transferred to the PACU, patients should be continuously monitored for adequacy of oxygenation and ventilation; it is important to remember that a pulse oximeter reading of 100% does not assure appropriate ventilation. Postoperative fluid management is especially important in patients with passive *PBF* (Glenn or Fontan physiology) and patients being treated for CHF. Control of postoperative nausea and vomiting allows patients to resume their oral medications as soon as possible. Postoperative pain may be controlled with incremental doses of fentanyl or morphine, and ketorolac 0.5 mg/kg may be utilized in patients without renal dysfunction or concerns regarding postoperative bleeding.

## Considerations for outpatient surgery

Outpatient surgery provides many advantages to children and families and the presence of CHD need not exclude children from consideration for day surgery. Even ASA physical status 3 patients may qualify for outpatient surgery if their cardiac disease is stable, their current condition optimized, and appropriate preoperative consultation with the child's cardiologist has occurred. In a series of 25 children with CHD undergoing outpatient surgery, including four with compensated CHF, only two adverse occurrences were noted in 27 anesthetics with neither occurrence related to the child's underlying heart disease.[65] It should be recognized, however, that children with chronic disease processes have limited physiologic reserve, and even when well-controlled may be adversely affected by seemingly minor surgery. Prior to surgery, agreement should be reached between the family, surgeon, and anesthesiologist ensuring that arrangements can be made for overnight observation should the surgery be protracted in length, blood loss more than minimal, or issues arise in postoperative management.

Children who have pacemakers or implantable cardioverter-defibrillators should not be cared for at freestanding surgery centers if personnel are not available to provide device

interrogation and reprogramming. Outpatient surgery should not include intrathoracic, intracranial or major abdominal procedures, and the intraoperative blood loss and risk of postoperative hemorrhage should be minimal. No particular activity restriction or special care should be needed postoperatively, and the child's parents should be able to follow care instructions and seek appropriate medical help if needed. Same day discharge should be discouraged if the child cannot resume his or her home medications postoperatively or if the child will not have ready access to medical care once he or she has returned home. Families who live in remote areas several hours from the hospital are encouraged to stay overnight for observation at the hospital or to stay close to the hospital for the first postoperative night before returning home. It is also preferable for the outpatient surgery facility to be hospital-based or affiliated in the event that it is necessary to admit the child unexpectedly.

Upper respiratory tract infections occur frequently in children and can increase the risk of adverse respiratory events. Consequently, children with CHD should be evaluated with particular care prior to clearance for outpatient surgery. Factors to be considered include the child's overall appearance, activity level, and appetite; the onset and duration of symptoms; any fever or increase in white blood cell count; and the nature of the child's cough or nasal drainage. Children who snore, are exposed to passive smoke, have nasal congestion or a productive cough, or whose parents report they have a cold have been shown to have a higher probability of anesthetic complications than other children.[66] It is best in younger children or those requiring endotracheal intubation to reschedule surgery unless the symptoms are clearly non-infectious and related to seasonal or vasomotor rhinitis.

In order to be discharged home after same-day surgery specific criteria must be met. Vital signs including hemoglobin–oxygen saturation must be stable and at baseline levels and the child must be in no respiratory distress. An appropriate level of consciousness should be attained, pain well-controlled, and age appropriate ambulation possible. Opinions vary on the advisability of forcing children to tolerate liquids prior to discharge from day surgery, as recent studies suggest that requiring children to drink in the PACU may increase the incidence of early vomiting and prolong their hospital stay.[67] If children are not willing to take oral liquids prior to discharge, they should receive appropriate intravenous fluid replacement to compensate for their hourly maintenance requirements during fasting, surgical, and PACU time. In addition, if nausea or vomiting has occurred it should be adequately treated and resolved prior to discharge. Children who are more compromised by their cardiac disease warrant more conservative treatment and should be able to tolerate oral fluids and take any necessary cardiac medications prior to discharge. The parents' comfort with the child's condition and readiness for discharge should be noted and written instructions provided for the child's care after leaving the hospital.

## Anesthetic management of specific lesions

A thorough understanding of the pathophysiology of each cardiac lesion is essential in order to provide optimal perioperative care for pediatric cardiac patients. Within each category of lesions there exists a spectrum of severity and a variety of surgical treatments, resulting in varying pathophysiology even for children with the same anatomic diagnosis.

Paradoxical emboli are possible in any patient with a septal defect and care should routinely be exercised to avoid air bubbles in intravenous tubing in any patient with CHD.

### Tetralogy of Fallot

#### Tetralogy of Fallot with pulmonary atresia/tetralogy of Fallot with absent pulmonary valve syndrome/tetralogy of Fallot with complete atrioventricular canal defect

***Anatomy/pathophysiology***

Tetralogy of Fallot consists of an overriding aortic root, RVOT obstruction, a malalignment VSD or multiple VSDs, and right ventricular hypertrophy. The RVOT obstruction may be valvar, subvalvar or supravalvar. Both fixed and dynamic components of the RVOT obstruction may exist.

***Variations/associated lesions***

Absent pulmonary valve variant usually includes aneurysmal dilation of the pulmonary arteries with resultant airway compression and tracheo/bronchomalacia. Patients who have TOF with pulmonary atresia require a systemic-to-pulmonary shunt in the newborn period to provide *PBF*. Tetralogy of Fallot may also be associated with complete atrioventricular canal, and may be seen in patients with CHARGE (coloboma, heart anomaly, choanal atresia, retardation, and genital and ear anomalies) association, velocardiofacial syndrome, DiGeorge syndrome, and Goldenhar's syndrome.

***Issues in unrepaired patients***

Symptomatology correlates with degree of RVOT obstruction. Dynamic obstruction results in hypercyanotic or "tet" spells with right-to-left shunting of blood. Children commonly receive β-blockers to decrease infundibular spasm. Treatment of a hypercyanotic spell includes oxygen, sedation or deepening of the anesthetic level, augmentation of preload, and the use of phenylephrine to increase the *SVR* : *PVR* ratio. Abdominal compression may also result in increased venous return and an increase in *SVR* via compression of the aorta.

***Issues in palliated patients***

Modified BT (innominate or subclavian artery-to-PA) shunts are sometimes used to palliate children prior to definitive repair. Blood pressure monitoring may not be as accurate in the upper extremity ipsilateral to the shunt. The amount of *PBF* through a systemic-to-pulmonary shunt is directly related to the radius of the shunt and the pressure gradient between the systemic and PA pressures. If systemic blood pressure decreases, *PBF* will also decrease leading to hypoxemia. While a shunt that is too small will result in cyanosis, one that is too large can result in pulmonary edema and CHF.

***Issues in repaired patients***

Residual RVOT obstruction, residual VSD and pulmonary insufficiency may exist postoperatively. Right bundle branch block is commonly seen on ECG. An increased prevalence of significant ventricular arrhythmias has been demonstrated in patients with severe pulmonary regurgitation and right ventricular dysfunction.[68] Children who underwent repair later in life also have a higher risk of postoperative atrial and/or ventricular arrhythmias and sudden cardiac death.[69] Patients with ventricular arrhythmias may require electrophysiologic studies and placement of an implantable cardioverter-defibrillator.

Children with pulmonary atresia typically have right ventricle-to-pulmonary artery (RV-to-PA) conduits placed as part of their repair, and these may later become stenotic or regurgitant. Children with absent pulmonary valve syndrome often continue to have symptoms of tracheo/bronchomalacia and bronchospasm even after repair and plication of the pulmonary arteries.

***Special anesthetic concerns***

Tachycardia, increased contractility and dehydration can result in increased RVOT obstruction and should be avoided, especially in unrepaired patients. Care should be taken to avoid hypovolemia and hypotension in shunt-dependent children. Acute hypercyanotic events may be treated by increasing *SVR* relative to *PVR*. Concerns after surgical repair of TOF include the presence of residual defects and the ability to detect and manage ventricular arrhythmias. New onset of arrhythmias noted prior to surgery requires a cardiology consult and evaluation. If the patient has an implantable cardioverter-defibrillator, preoperative reprogramming is necessary and intraoperative placement of defibrillator and external pacing pads is recommended.

## Atrial septal defects

***Anatomy/pathophysiology***

Left-to-right shunting results in atrial dilation and right ventricular volume overload.

***Variations/associated lesions***

Sinus venosus defects are frequently associated with partial anomalous pulmonary venous connection. Primum ASDs are often associated with a cleft in the anterior leaflet of the mitral valve and resultant mitral regurgitation.

***Issues in unrepaired patients***

Right ventricular volume overload is commonly seen but PA hypertension is rare. Atrial tachyarrhythmias are more common in older unrepaired patients.

***Issues in repaired patients***

Residual defects and atrial dysrhythmias may occur. Sinus node dysfunction is more likely after the repair of a sinus venosus defect, while residual mitral regurgitation is possible after repair of an ostium primum defect.

## Ventricular septal defect

***Anatomy/pathophysiology***

Left-to-right shunting of blood results in ventricular volume overload, increased *PBF* and possible CHF. The degree of shunting is determined by the size and location of the defect, along with the relative resistances of the pulmonary and systemic vascular beds.

***Variations/associated lesions***

Ventricular septal defect may occur as single or multiple defects; they are also associated with TOF, interrupted aortic arch, transposition of the great vessels, coarctation of the aorta and truncus arteriosus.

***Issues in unrepaired patients***

Ventricular septal defects result in increased *PBF*, potentially allowing the development of PA hypertension, pulmonary vascular occlusive disease (PVOD), and eventual Eisenmenger's syndrome. Increased respiratory infections, failure to thrive and CHF may be seen. Aortic regurgitation is possible with subarterial defects.

***Issues in palliated patients***

Patients with multiple VSDs and severe CHF may have a PA band placed to limit *PBF* prior to definitive repair. Baseline preoperative hemoglobin–oxygen saturations should be noted in these patients, as they may be relatively cyanotic due to limitation of their *PBF*.

***Issues in repaired patients***

Residual defects may exist. Right bundle branch block is frequently seen and may be secondary to right ventriculotomy or injury to the right bundle near the VSD.[70] Complete heart block may also occur after surgical repair. Postoperative ventricular arrhythmias are more likely in patients repaired later in life or in patients who have had ventriculotomies.[71]

***Special anesthetic concerns***
Increased work of breathing, decreased pulmonary compliance, and frequent respiratory infections are commonly seen in unrepaired patients. Fluid overload should be avoided. Increasing the child's $F_{IO_2}$ and lowering his or her $P_{CO_2}$ will result in decreased *PVR*, and consequently increase *PBF* at the expense of systemic blood flow.

## Atrioventricular canal defect

***Anatomy/pathophysiology***
An ostium primum defect, common AV valve and an interventricular communication result from failure of fusion of the endocardial cushions with subsequent biatrial and biventricular hypertrophy.

***Variations/associated lesions***
This defect is often seen in children with trisomy 21 (Down's) syndrome. In the "unbalanced" form, hypoplasia of the right or left ventricle may make a two-ventricle repair difficult to achieve and single-ventricle palliation may be required.

***Issues in unrepaired patients***
Increased *PBF*, frequent respiratory infections, failure to thrive, and CHF are seen in these patients.

***Issues in palliated patients***
Pulmonary artery banding may be done on rare occasions prior to complete repair and baseline oxygen saturations should be noted in these patients.

***Issues in repaired patients***
Residual atrial or ventricular defects, tricuspid or mitral valve insufficiency, and ventricular dysfunction may exist. Heart block and residual PA hypertension may also be seen.

***Special anesthetic considerations***
Controlled ventilation is recommended due to decreased pulmonary compliance and possible PA hypertension. Patients with Down's syndrome may also have an increased likelihood of upper airway obstruction.

## Truncus arteriosus

***Anatomy/pathophysiology***
A single arterial trunk arises from both ventricles and supplies the coronary, pulmonary and systemic circulations. A VSD is present. The truncal valve may have a varying number of leaflets and may exhibit both stenosis and regurgitation.

***Variations/associated lesions***
Interrupted aortic arch, coronary artery or PA anomalies and a right aortic arch may be present. Truncus arteriosus is often associated with DiGeorge syndrome or microdeletion of the 22nd chromosome, which can also include hypocalcemia and T-cell deficiency.

***Issues in unrepaired patients***
As *PVR* falls, patients develop pulmonary overcirculation and manifest CHF with early development of PVOD. Truncal valve regurgitation may further worsen heart failure. Coronary ischemia may be seen due to low diastolic pressures. Alternatively, PA stenosis may be present, limiting *PBF*.

***Issues in repaired patients***
Residual ventricular dysfunction, VSDs, and pulmonary hypertension may exist postoperatively. An atrial defect may have been left as a "pop-off." Other possible postoperative sequelae include dysrhythmias and complete heart block. Right bundle branch block is nearly always seen on postoperative ECG due to the right ventriculotomy. The truncal valve may be stenotic or regurgitant, along with the RV-to-PA conduit.

***Special anesthetic considerations***
Neonatal patients with DiGeorge syndrome should have blood products irradiated and serum calcium levels checked. Additionally, they may have associated findings of micrognathia, choanal atresia, esophageal atresia, imperforate anus or diaphragmatic hernia.

## Aortic stenosis

***Anatomy/pathophysiology***
The aortic valve may be unicommissural in neonates with critical aortic stenosis. Older children with aortic stenosis more frequently have a bicuspid aortic valve. Left ventricular pressure load and hypertrophy occur, and endocardial fibroelastosis may also be seen in neonates with aortic stenosis.

***Variations/associated lesions***
Other left-sided obstructive lesions such as mitral stenosis, hypoplastic ascending aorta or hypoplastic left ventricle may also be present. Aortic insufficiency may also be seen.

***Issues in unrepaired patients***
Pulmonary edema and pulmonary hypertension may be seen with severe aortic stenosis. Neonates may be ductal-dependent and can present in shock if ductal closure has occurred. Coronary ischemia may be seen. Older children may be asymptomatic despite moderate to severe aortic stenosis, or they may exhibit symptoms of angina, syncope, or easy fatiguability.

***Issues in repaired patients***
Patients who have undergone balloon valvuloplasty or surgical valvotomy may have resultant aortic insufficiency.

***Special anesthetic considerations***
Tachycardia, hypotension and increased oxygen demand should be avoided along with decreases in *SVR*. Care should be exercised to maintain adequate coronary perfusion.

### Subaortic stenosis, membrane-type/subaortic stenosis, tunnel-type/subaortic stenosis, dynamic/hypertrophic

***Anatomy/pathophysiology***
A discrete membrane or a long segment tunnel-type stenosis may exist beneath the aortic valve resulting in left ventricular hypertrophy and aortic valve insufficiency.

***Variations/associated lesions***
Subaortic stenosis may be associated with coarctation of the aorta, aortic insufficiency, or VSD.

***Issues in unrepaired patients***
Patients with symptoms of chest pain, syncope or new onset arrhythmias should be re-evaluated by their cardiologist prior to elective surgery. A gradient greater than 25 mmHg is considered significant, and patients who are symptomatic or have a gradient greater than 50 mmHg are generally referred for surgical intervention. Patients with dynamic obstruction are often receiving β-blockers.

***Issues in repaired patients***
Patients with a discrete membrane may have resection of the membrane with possible injury to the mitral valve or creation of a VSD. A Konno procedure (aortoventriculoplasty) may be performed for tunnel type stenosis and these patients may develop heart block, residual VSD, RVOT obstruction, and prosthetic valve complications. Recurrence of subaortic obstruction may also occur. Children may also undergo a Ross procedure, which involves replacement of the aortic valve with the native pulmonary valve, translocation of the coronaries to the new aortic valve, and placement of a valved homograft in the pulmonary position. Resultant complications can include coronary ischemia, RVOT conduit obstruction, aortic insufficiency, and ventricular dysfunction.

***Special anesthetic considerations***
It is important to maintain coronary perfusion pressure and normal *SVR*. Tachycardia, hypotension and increased cardiac contractility should be avoided.

### Supravalvar aortic stenosis

***Anatomy/pathophysiology***
Supravalvar aortic stenosis consists of a membranous or tubular supravalvar narrowing of the aorta with possible impairment of coronary filling and resultant left ventricular pressure overload and hypertrophy.

***Variations/associated lesions***
This lesion may be associated with Williams' syndrome, which also includes elfin facies, peripheral pulmonic stenosis, mental retardation, and neonatal hypercalcemia.

***Issues in unrepaired patients***
Patients may have chest pain, syncope and ST–T segment changes on ECG. Sudden death with anesthesia has been reported.

***Issues in repaired patients***
Residual left ventricular outflow tract stenosis, aortic insufficiency, and coronary ischemia may occur.

***Special anesthetic considerations***
Avoid myocardial depressants and maintain coronary artery perfusion pressure.

## Coarctation of the aorta

***Anatomy/pathophysiology***
Coarctation of the aorta is a constriction of the thoracic aorta which may be either discrete or long segment, and usually occurs at the point of ductal insertion into the aorta. Left ventricular pressure overload and hypertrophy result with eventual development of upper extremity hypertension and aortic collaterals.

***Variations/associated lesions***
Coarctation of the aorta may be seen in Turner's syndrome along with webbed neck, short stature, and edematous hands and feet. It can also be associated with other left-sided obstructive lesions such as bicuspid aortic valve, and aortic or subaortic stenosis. Coarctation of the aorta may also be associated with a VSD.

***Issues in unrepaired patients***
Patients with critical coarctation in the neonatal period are dependent on a PDA for distal aortic flow and frequently require a prostaglandin $E_1$ ($PGE_1$) infusion prior to repair in order to maintain ductal patency. Left ventricular overload and pulmonary edema may be evident. In older children left ventricular hypertrophy, systemic hypertension and development of collateral vessels are frequently seen. A blood pressure differential between the upper and lower extremities is usually evident.

***Issues in repaired patients***
Patients may have residual or recurrent coarctation and left ventricular hypertrophy. They may also continue to require antihypertensive therapy post-repair.

***Special anesthetic considerations***
Left ventricular hypertrophy and systemic hypertension

often persist after repair of coarctation. Blood pressures in the left arm may be inaccurate if subclavian flap angioplasty has been performed for repair of the coarctation.

## Single ventricle lesions and physiology

***Anatomy/pathophysiology***

The anatomy of patients classified as having single ventricle physiology may include any lesion or group of lesions in which a two-ventricle repair is not feasible. Generally, either both AV valves enter a single ventricular chamber, or there is atresia of an AV or semilunar valve. Intracardiac mixing of systemic and pulmonary venous blood flow occurs and ventricular output is shared between the pulmonary and systemic circulations. Patients with relative hypoplasia of one ventricle such as unbalanced AV canal defect or severe Ebstein's anomaly may also undergo single ventricle palliation.

The first stage in palliation involves establishing unobstructed blood flow from the systemic ventricle to both the systemic and pulmonary circuits with creation of a controlled source of *PBF*. This is usually accomplished by creating a modified BT shunt, but occasional patients may require PA banding to limit *PBF*. If the atrial septum is restrictive, an atrial septectomy is performed to assume adequate mixing. A bidirectional cavopulmonary shunt, generally performed as the second stage palliative procedure, entails ligation of the systemic-to-pulmonary shunt and anastomosis of the superior vena cava to the pulmonary arteries allowing bidirectional flow. The final palliative procedure for most single ventricle patients is a total cavopulmonary anastomosis, or Fontan procedure, which involves baffling the inferior vena cava flow to the PA–superior vena cava anastomosis, thus directing all venous return to the pulmonary circulation.

***Issues in unoperated patients***

Patients with single ventricle physiology have parallel circulations and care requires appropriately managing systemic and *PVR*s in order to balance systemic and *PBF*. Prostaglandin $E_1$ is generally used to maintain ductal patency prior to first stage palliative surgery. Hemoglobin–oxygen saturations should range between 75% and 85% when systemic and pulmonary circulations are appropriately balanced. In ventilated patients the $P_{CO_2}$ should be 40–45 mmHg. Permissive hypercarbia with $P_{CO_2}$ in the 50s may occasionally be used for patients with pulmonary overcirculation in order to increase their *PVR* and decrease *PBF*. Generally these patients are ventilated with an $F_{IO_2}$ of 0.21 unless other pulmonary issues exist. Patients with persistently high oxygen saturations (> 90%) typically have poor systemic perfusion and develop acidemia. The hematocrit should be kept at 40–45 in order to optimize oxygen carrying capacity.

***Issues in patients after initial palliation***

Patients are frequently dependent on a modified BT shunt for *PBF*. Saturations greater than 85% indicate pulmonary overcirculation and patients may exhibit symptoms of CHF. Once the patient is anesthetized and mechanically ventilated their oxygen saturation often increases, requiring the adjustment of the $F_{IO_2}$ and $P_{CO_2}$ in order to maintain saturations between 75% and 85%. An acute drop in oxygen saturation along with the absence of a murmur indicates loss of shunt flow and is catastrophic.

***Issues in patients after bidirectional cavopulmonary shunt (bidirectional Glenn procedure)***

Oxygen saturations will range from 75% to 85% as patients are still mixing oxygenated and deoxygenated blood for ejection from the systemic ventricle. Ventricular function is generally improved as the volume load has been removed from the heart. Systemic hypertension is frequently seen in these children.

***Issues in patients after total cavopulmonary anastomosis (Fontan)***

Surgeons may choose to place a fenestration in the atrial baffle allowing right-to-left shunting to occur, and these patients often have hemoglobin–oxygen saturations of 80–90%. The presence of aortopulmonary collaterals or baffle leaks may also result in decreased systemic oxygen saturation. Atrial arrhythmias and ventricular dysfunction are frequently seen as late complications. The patient's volume status should be assessed preoperatively and patients who are dehydrated should have an i.v. placed and adequate hydration assured prior to induction of anesthesia. Care should be taken to avoid hypovolemia as *PBF* is dependent on preload. Normal sinus rhythm should be maintained if possible. A cardiologist or pacemaker representative should be available for patients with pacemakers, and external pacing or cardioversion should be available for patients who have a history of arrhythmias. Controlled ventilation is appropriate for most procedures as long as excessive airway pressures are avoided.

## Transposition of the great arteries

### d-Transposition of the great arteries with or without ventricular septal defect

***Anatomy/pathophysiology***

The PA arises from the morphologic left ventricle while the aorta is malpositioned anterior and rightward above the right ventricle. A PDA, ASD, and/or VSD must exist to allow mixing of pulmonary and systemic venous return prior to repair.

***Variations/associated lesions***

Ventricular septal defects, coarctation of the aorta, obstruction to *PBF* and abnormal coronary artery anatomy may be seen with d-transposition of the great arteries (D-TGA).

***Issues in unrepaired patients***
Patients who do not have adequate mixing via an ASD or VSD are dependent on $PGE_1$ to maintain ductal patency prior to repair. If patients do not respond to $PGE_1$ a balloon atrial septostomy may be performed to improve mixing and reduce hypoxemia.

***Issues in patients after atrial switch (Senning or Mustard)***
Atrial arrhythmias, sinus node dysfunction, baffle leak or obstruction and late right (systemic) ventricular dysfunction may be seen.

***Issues in patients after arterial switch***
Arrhythmias may be a marker of coronary ischemia. Supravalvar aortic stenosis or pulmonic stenosis may be seen.

***Issues in patients after Rastelli operation***
The Rastelli operation is performed for children with D-TGA, VSD, and LVOT obstruction. Left ventricular outflow is baffled to the aorta and a RV-to-PA conduit is placed. Late complications include residual VSD, subaortic stenosis, and conduit obstruction.

***Special anesthetic considerations***
Arrhythmias and late ventricular dysfunction are frequently seen in patients who have undergone an atrial switch. Ventricular function appears to be better preserved after an arterial switch operation.

### Congenitally corrected transposition of the great arteries or l-transposition of the great arteries

***Anatomy/pathophysiology***
l-Transposition of the great arteries (L-TGA) or ventricular inversion implies that the morphologic left ventricle is on the right side and the right ventricle is on the left side. Transposition of the great arteries also exists such that the aorta arises from the left-sided, morphologic right ventricle and the PA originates from the right-sided, morphologic left ventricle. If no other defects exist the patient then has a series circulation, albeit with the right ventricle as the systemic ventricle. If no coexisting defects are present this lesion may go undetected for many years.

***Variations/associated lesions***
Ventricular septal defect, LVOT (subpulmonic) obstruction, and tricuspid valve abnormalities may exist. Approximately 5–10% of children are born with complete heart block, and the incidence increases annually by about 2%.[72]

***Issues in unoperated patients***
An increased incidence of complete heart block exists in patients with L-TGA. Depending on the presence or absence of pulmonary obstruction and a VSD the patient may have cyanosis, pulmonary overcirculation, or be asymptomatic.

***Issues in "repaired" patients***
Heart block is common after repair of a VSD. Residual VSD and residual LVOT obstruction may be seen, along with late ventricular dysfunction.

***Issues in anatomically repaired patients***
A combined Senning (atrial switch)–arterial switch may be performed for patients without LVOT obstruction and a combined Senning–Rastelli for patients with LVOT obstruction. These anatomic corrections result in the left ventricle becoming the systemic ventricle. Residual VSD, systemic (tricuspid) valve regurgitation, baffle obstruction, and heart block may occur.

***Special anesthetic considerations***
Patients with pacemakers should be evaluated by the cardiologist or designated representative preoperatively and again postoperatively. The patient's underlying rate and rhythm should be known and pacing capability should be available intraoperatively. Late ventricular dysfunction is often seen in anatomically unrepaired patients.

### Cardiac transplant patients

***Initial etiology of heart failure/date of transplant***
Patients are transplanted due to either cardiomyopathy or CHD.

***Special anesthetic considerations***
Immunosuppressive regimens should be maintained during the perioperative period. Patients on cyclosporine, tacrolimus (FK506) or steroids frequently exhibit hypertension and may be taking ACE inhibitors or calcium channel antagonists. New onset arrhythmias are suggestive of acute rejection or coronary artery disease and should be investigated prior to surgery.

The denervated transplanted heart will not respond to atropine, thus isoproterenol should be available to increase the *HR* if necessary.

## Long-term consequences of congenital heart disease

### Pulmonary hypertension

Constant exposure of the pulmonary vascular bed to high flows due to left-to-right shunting lesions can lead to elevated PA pressures and the development of PVOD. Any prolonged obstruction to pulmonary venous drainage or exposure to high left atrial pressures can also result in increased pulmonary

vascular pressures. The time to development of PVOD is variable according to the amount of flow and pressure the vessels are exposed to. Pulmonary veno-occlusive disease develops earlier in certain lesions, such as D-TGA with VSD, and in certain patient populations, such as children with Down's syndrome.[73] Reversibility of these changes once a defect is repaired is variable as well.

While the structural changes affecting the pulmonary vascular bed may be fixed, a superimposed reactive component of vascular smooth muscle also exists which can be positively or negatively affected by a variety of factors. Increases in *PVR* are seen with acidosis, hypercarbia, hypoxia, hypothermia, increased sympathetic stimulation, and increased airway pressures, and these factors may act alone or in synergistic fashion.[74] Pulmonary vascular resistance can be reduced, right ventricular function improved, and the degree of intracardiac right-to-left shunting minimized by appropriate management of these variables. Conversely, acute increases in *PVR* can result in right ventricular failure, hypoxemia, and death. Morray *et al*.[75] studied the effects of pH and $P_{CO_2}$ on pulmonary hemodynamics in children with CHD, concluding that hypocarbic alkalosis decreases PA pressures and that higher PA pressures exhibit a more dramatic response to alkalosis. They also noted that hydrogen ion concentration, rather than carbon dioxide concentration, seems to be the most important factor mediating the decrease in PA pressures. Lung volumes and airway pressures also affect *PVR*. While lung volumes less than the patient's functional residual capacity can result in higher *PVR* due to hypoxic vasoconstriction, volumes above functional residual capacity can result in compression of intra-alveolar vessels.

Pre-anesthetic assessment should include consultation with the patient's cardiologist and a review of the most recent cardiac catheterization or echocardiographic information in order to obtain a measure of PA pressures, *PVR* and the degree of reactivity noted in the pulmonary vascular bed when exposed to 100% oxygen or other pulmonary vasodilators. The presence of pre-existing cardiac disease and the direction of intracardiac shunting, if present, should be noted. It is important that a frank discussion of the high risk of anesthesia in these patients be held with the patient's family when anesthetic consent is obtained.

Patients with primary pulmonary hypertension may present for a variety of procedures while awaiting lung transplantation. Severely affected patients require a constant intravenous infusion of prostacyclin (Flolan) in order to lower *PVR*. As noted by Burrows *et al*.,[76] anesthetic management should be guided by three considerations: (i) appropriate manipulation of those factors known to affect *PVR*; (ii) the effect of anesthetic agents on *PVR*; and (iii) maintenance of *CO* and coronary perfusion pressure. Adequate depth of anesthesia should be assured prior to any manipulation of the airway to avoid acute increases in *PVR*. Laryngeal mask airways may be useful for shorter procedures in order to minimize airway instrumentation, but in patients undergoing more extensive procedures endotracheal intubation allows optimal control of oxygenation, ventilation, and the ability to aggressively manage a pulmonary hypertensive crisis. Acute increases in *PVR* will lead to oxygen desaturation in patients who are able to shunt right-to-left. In patients with intracardiac shunting, increased *PVR* will cause hypotension secondary to decreased *CO*, and bradycardia. Treatment consists of hyperventilation with 100% oxygen, inotropic support of the right ventricle, and prompt treatment of any acidosis. Inhaled nitric oxide, an endothelium-derived vasodilator, may also be used to decrease *PVR*.

Preload should be maintained and hypotension avoided in these patients in order to provide normal *CO* along with adequate coronary artery flow and oxygen supply to the right ventricle. Dopamine, dobutamine or milrinone should also be available to further improve cardiac function if necessary. Controlled ventilation is recommended in these patients, maintaining lung volumes at or around functional residual capacity with minimal positive end-expiratory pressure (*PEEP*) and avoidance of high inspiratory pressures, hypercarbia or hypoxemia.

## Congestive heart failure

Congestive heart failure is the end product of continued increased pressure or volume load on the heart, resulting in signs and symptoms of jugular venous distention, hepatomegaly, poor peripheral perfusion, tachypnea, tachycardia, and failure to thrive. Patients are generally treated with digoxin, diuretics and afterload reducers such as captopril. Chronic CHF leads to increased work of breathing due to pulmonary congestion. Even after corrective cardiac surgery many children remain on digoxin and diruetics in order to optimize cardiac function.

In children taking anticongestive medications serum electrolytes should be checked prior to surgery. Loop diuretics such as furosemide can result in hypokalemia and hypochloremic alkalosis. Potassium sparing diuretics such as spironolactone and triamterene can result in hyperkalemia. Captopril and enalapril and ACE inhibitors are also potassium sparing. Our practice is to give all cardiac medications on the morning of surgery and resume them as soon as possible after surgery in order to minimally disrupt the child's physiologic balance. Care should be taken to judiciously manage intravenous fluids in order to avoid electrolyte imbalance or fluid overload. When surgery is necessary for a patient with poorly controlled chronic CHF, consideration should be given to placing an arterial line for blood pressure and blood gas monitoring. For surgeries with significant anticipated blood loss or fluid shifts, central venous pressure monitoring is useful, along with placement of a urinary catheter for precise measurement of urine output. Transesophageal echocardiography may be considered for continuous

monitoring of ventricular filling and function, and may provide better information for optimal intraoperative management of ventricular function than a PA catheter.[77] Dopamine may prove helpful intraoperatively to support *CO* and enhance renal blood flow. Mechanical ventilation should be utilized throughout surgery in patients with CHF and may also be necessary afterwards in poorly compensated patients. Afterload reduction therapy should be reinstituted as soon as possible after surgery is completed.

## Cyanosis and polycythemia

Cyanosis in patients with CHD can be the result of either right-to-left shunting with inadequate *PBF* or admixture of oxygenated and deoxygenated blood into the systemic circulation. Severe, longstanding cyanosis causes a variety of systemic derangements and hematologic, neurologic, vascular, respiratory, and coagulation abnormalities can all result.

One of the initial responses to cyanosis is an increase in erythropoietin levels with a subsequent increase in hemoglobin and hematocrit. Once the increase in red cell mass and hemoglobin is adequate to allay tissue hypoxemia the erythropoietin levels return to normal.[78] At hematocrit levels greater than 65% increased blood viscosity can result in a decrease in the delivery of oxygen to tissues; this is especially true if iron deficiency is present, as it causes an increase in rigidity of the red cells which further increases the blood viscosity.[79] Hyperviscosity syndrome is characterized by symptoms of headache, dizziness, fatigue, visual disturbances, paresthesias, myalgias, and reduced mentation.[80] Increases in *PVR*, *SVR*, and a decrease in coronary blood flow can also be seen as blood viscosity increases. Preoperative phlebotomy is recommended only in patients who have hematocrits greater than 65%, are experiencing symptoms of hyperviscosity, and are not dehydrated. Acute onset of symptomatic hyperviscosity syndrome can be seen in cyanotic patients whose hematocrit abruptly increases due to dehydration. In these patients rehydration is recommended rather than phlebotomy. Cerebrovascular accidents occur with greater frequency in cyanotic patients, particularly children under 4 years of age. Erythrocytosis alone is not felt to be a risk factor for cerebral arterial thrombosis, but dehydration in younger cyanotic patients can predispose to intracranial venous thrombosis with devastating consequences.[81]

Increased bleeding tendencies and a wide variety of associated laboratory abnormalities have long been noted in cyanotic patients. When compared to acyanotic children a disproportionate number of cyanotic children are thrombocytopenic, with the degree of thrombocytopenia directly related to the severity of polycythemia. Abnormalities in prothrombin time, partial thromboplastin time, and individual factor deficiencies have also been described[82] and defy simple classification. Although these deficiencies may cause no symptoms other than easy bruising, severely cyanotic patients should have clotting studies prior to surgery. In surgeries expected to involve more than minimal blood loss fresh frozen plasma and platelets may be necessary to treat non-surgical bleeding.

Cyanotic patients also exhibit respiratory abnormalities of importance to the anesthesiologist. The ventilatory response to hypoxia is significantly decreased in cyanotic children and directly proportional to the degree of cyanosis. This abnormality in ventilatory drive normalizes after surgical correction of cyanotic heart disease.[83] Patients with cyanotic heart disease also display chronic alveolar hyperventilation with abnormally high minute ventilation for a given amount of carbon dioxide production,[84] therefore the metabolic and respiratory cost of eliminating carbon dioxide is very high in these children.[85]

It is important that cyanotic children remain well hydrated throughout the perioperative period to avoid symptoms of hyperviscosity syndrome or thrombosis. This is particularly critical in those children who are dependent on a systemic-to-pulmonary shunt for their *PBF*. Children should be encouraged to take clear liquids until 2 hours prior to surgery, and an i.v. should be started on arrival to the hospital for provision of maintenance fluids until surgery. Due to their repeated need for intravenous access during hospitalizations and the tendency for neovascularization, these children often have small, tortuous veins. A 24 g i.v. may prove adequate for preoperative hydration and induction of anesthesia and a larger i.v. may be placed after the child is anesthetized. During preoperative evaluation, the child's baseline range of hemoglobin–oxygen saturation, *HR*, and blood pressure should be noted. Any history of stroke, seizure, or pre-existing neurologic defects should also be documented. Care should be taken during the anesthetic to maintain normal fluid balance and cardiac function. The use of air filters in intravenous lines and meticulous attention to air in volume lines without filters is essential as paradoxical emboli may occur in children with right-to-left shunts. Controlled ventilation is recommended for all but the shortest procedures due to the ventilatory abnormalities in these patients. It is important to remember that end-tidal carbon dioxide monitoring underestimates $P_{ACO_2}$ in cyanotic children and that this relationship may vary during surgery in those children whose cyanosis is due to mixing of oxygenated and deoxygenated blood.[86]

Postoperative concerns include assurance of adequate respiratory drive, hemostasis, and control of nausea and vomiting. Intravenous fluids should be continued until the child's oral intake is adequate.

## Arrhythmias

Many children who have undergone surgery for CHD are at increased risk for arrhythmias, particularly those who have had surgeries involving extensive atrial suture lines

or ventriculotomies. Patients on medications for control of chronic arrhythmias should have these medications continued up to the time of surgery and restarted as soon postoperatively as feasible. Concerns have been raised regarding the safety of amiodarone in patients undergoing anesthesia,[87] but given the extremely long elimination half-life of this drug it is not usually appropriate to discontinue it prior to surgery, as it would cause an unreasonable delay and possibly place the patient at risk for life-threatening arrhythmias. Preoperative consultation with the child's cardiologist is essential and a plan should be formulated for intraoperative monitoring and management of arrhythmias and potential hemodynamic complications.

Atrial arrhythmias are commonly seen in patients who have previously undergone surgery involving the atria or AV valves. Those who have had Mustard or Senning (atrial switch) procedures or a Fontan procedure (total cavopulmonary anastomosis) are at increasing risk for atrial dysrhythmias with each passing postoperative year. Ventricular dysrhythmias are more frequently seen in patients who have undergone ventriculotomies or had RV-to-PA conduits placed. Any new onset of arrhythmias, particularly those causing dizziness, syncope or chest pain, should be investigated by the child's cardiologist prior to the induction of anesthesia.

In the rare patient with congenital complete heart block, the child's underlying rate, rhythm, and hemodynamic stability should be assessed with exercise studies or Holter monitoring prior to surgery.[88] The advisability of temporary transvenous pacing or the availability of intraoperative transcutaneous pacing should be discussed with the patient's surgeon and cardiologist preoperatively.

## Anesthesia for magnetic resonance imaging

Magnetic resonance imaging (MRI) in pediatric patients is being used with increasing frequency as it provides excellent images of brain, spine, and soft tissue lesions without the use of ionizing radiation. Magnetic resonance (MR) is also becoming an important modality for evaluation of patients with cardiac and vascular disease. Because all images are obtained in one time interval and because image quality depends on patient immobility to reduce motion artifact, pediatric anesthesiologists are frequently asked to provide sedation or general anesthesia for children undergoing MR scans.

Magnetic resonance scanners utilize high strength magnetic fields and radiofrequency (RF) pulses to create tomographic images of the body. Patients are exposed to a static magnetic field, time-varying magnetic fields, and RF pulses. The patient is placed in a static magnetic field, typically at 1.5 Tesla (approximately 30 000 times the intensity of the earth's magnetic field), and rapid minor variations of the magnetic field are then induced via the transient application of magnetic field gradients during imaging. The static magnetic field causes a net orientation of protons along the long axis of the patient's body; when RF pulses are applied, the protons deviate away from the direction of the static magnetic field. When the transient RF pulse is removed the protons "relax" back to their original positions, resulting in the emission of a RF signal, which is then detected by a receiving coil. The necessary time for this realignment is known as the relaxation time and is specific for a given tissue. Evaluation of the varying rates of return of the different nuclei to their original alignment creates contrast between different tissues in the image. Any movement of the patient during this process results in artifact and blurring of the desired images. Gadolinium, a contrast agent, is a paramagnetic substance used to enhance proton relaxation, thus allowing improved image contrast between two adjacent tissues with differing amounts of perfusion. Although allergic reactions are rare, anaphylactoid reactions and death have been reported after use of gadolinium.[89]

Due to the strength of the magnetic field and its ability to interfere with the function of implanted devices certain contraindications exist for MR scanning (Table 26.6). Absolute contraindications include electrically, magnetically or mechanically activated implants such as pacemakers, implantable cardiac defibrillators, cochlear implants, neurostimulators, bone growth stimulators, and implantable drug infusion pumps. Patients with external pacing wires, PA catheters or other conductive wires should not undergo MRI due to the risk of the wire acting as an antenna and inducing burns or fibrillation.[90] Many aneurysm clips are ferromagnetic; if insufficient information regarding the nature of the clip is unavailable the patient should not undergo an MRI. Most prosthetic heart valves have been tested and found to safely tolerate MR scanning. Coils or stents placed in the catheterization laboratory should be attached sufficiently into the vessel wall after 6 weeks to make MR scanning possible without undue risk, although they can cause significant artifact on future scans. Nickel, stainless steel, titanium and alloys are safe metals and may enter the scanner. A comprehensive list of materials, devices and implants that have been tested for ferromagnetic properties and deflection force may be found in Shellock and Kanal's chapter "Bioeffects and safety of MR procedures."[89]

**Table 26.6** Contraindications to magnetic resonance imaging.

| |
|---|
| Intracranial aneurysm clips |
| Cardiac pacemakers or defibrillators |
| External pacing wires or pulmonary artery catheters |
| Cochlear implants |
| Implanted drug infusion pumps |
| Neurostimulators |
| Bone growth stimulators |
| Recently (< 6 wks) implanted endovascular or intracardiac implants |

## Considerations for sedation and general anesthesia with magnetic resonance imaging

The MR scanner is one of the most challenging environments anesthesiologists face, as it renders monitoring difficult and direct patient observation nearly impossible. Multiple hazards exist in providing anesthesia for MR scanning, among them field avoidance, movement of the patient from the induction area to the scanner, hypothermia, possible injury from projectile objects in the scanner, and the administration of contrast material. Despite the complications of inducing anesthesia in a remote location and the difficulties in monitoring imposed by the magnetic field, the same standards of care apply as in the operating room. Patients requiring anesthesia for an MR scan should be given appropriate instructions for pre-anesthetic fasting and may be admitted through the ambulatory surgery area on the day of the procedure. Preoperative assessment should note the reasons for the scan, the information to be obtained and any recent changes in the child's condition. After discussion of the anesthetic plan with the parents, an informed consent for sedation or general anesthesia should then be obtained and signed. In many institutions, consent is not obtained for the scan itself; it is incumbent on the anesthesiologist to be sure the appropriate documents have been signed and witnessed for provision of anesthesia. After completion of the scan, children return to the PACU for recovery and eventual discharge by the anesthesia staff.

Although MR scanning is not painful, it does require immobility for the duration of the scan and tolerance of a noisy, claustrophobic environment. For most infants and children, deep sedation or general anesthesia is necessary in order to obtain a successful scan. The partial or complete loss of airway reflexes that accompanies deep sedation, coupled with the anesthesiologist's lack of immediate access to the patient, may make general anesthesia a safer alternative for patients with poorly controlled CHF, pulmonary hypertension, airway obstruction, or gastroesophageal reflux. Cardiac MR places additional demands on the anesthesiologist as the scans tend to be longer in duration and often require periods of apnea during certain scan sequences. Depending on the number and length of breath-holding episodes necessary, general endotracheal anesthesia with controlled ventilation is often the only reasonable option.

Although rectally and orally administered drugs have been used for sedation, intravenous agents offer the advantage of increased flexibility should the scan take more time than originally anticipated or should the patient cough or move. Propofol is well suited for use in the MR scanner as it is easily titratable, does not require an MR compatible anesthetic machine or scavenging of gases, and allows the patient to ventilate spontaneously and awaken promptly at the conclusion of the procedure. Although the Medfusion 3010 pump is Food and Drug Administration (FDA) approved for use in the MR scanning room, it must still be bolted down. The Medrad Continuum™ is currently the only MR compatible intravenous infusion system available and may be used in scanners up to and including 1.5 Tesla in strength. Frankville *et al*.[91] studied thirty ASA physical status 1 and 2 children undergoing MRI and found that after halothane induction and a propofol bolus of 2 mg/kg, a continuous infusion of propofol at 100 μg/kg/minute provided good scanning conditions in all children with no episodes of desaturation noted during the scanning process. All children received supplemental oxygen by mask, remained breathing spontaneously throughout the study, and were able to maintain a patent airway with no intervention other than slight neck extension. It is important to note, however, that propofol may produce apnea after bolus doses and has a dose-dependent depressant effect on ventilation;[92] appropriate equipment to assist or control ventilation must always be readily available.

Barbiturates may also be successfully used for deep sedation and may be administered either intravenously or rectally. A single dose of rectal thiopental (dosage range 35–50 mg/kg) was found to provide good imaging conditions in 79 of 83 children with CHD. No respiratory depression was noted in any patient.[93] Recently, intravenous pentobarbital was used by Galli *et al*.[94] for MR of the brain in infants less than 6 months of age who had recently undergone surgery for CHD. All infants breathed spontaneously throughout the study and no episodes of acute desaturation were noted. Median time to first feeding after the study was 30.2 minutes. Careful titration of intravenous pentobarbital is advised, however, as other studies have noted periods of severe, prolonged desaturation with its use when compared to chloral hydrate or intramuscular pentobarbital.[95]

Many practitioners induce sedation or general anesthesia on the detachable scanner table outside the MR scanner room, which provides better proximity to an anesthesia cart and drugs, and also allows the use of a metal laryngoscope and a conventional ferromagnetic stethoscope. Should resuscitation of the patient be necessary at any point, the child is brought out of the scanner so that standard equipment may be freely used without interference from the magnet. Once induction is complete and the patient is stable, the table is rolled into the scanner room and locked into place. Special attention is paid to positioning in order to optimally maintain the airway in patients whose tracheas have not been intubated. In smaller patients a rolled sheet is often placed under the shoulders and rolled sheets on either side support the head. A variety of MR compatible anesthesia machines are now available with pneumatically or electronically driven ventilators capable of ventilating even premature infants. Alternatively an MR compatible Siemens 900C Servo ventilator (Siemens–Elema AB, Solna, Sweden) provides an effective means of ventilation for infants and children. Non-invasive (oscillometric) blood pressure monitoring, ECG, pulse oximetry, and capnography via endotracheal tube or nasal cannula

are utilized. All MR scanners do not operate at the same frequency and therefore it is essential not only that monitoring equipment be MR compatible, but also that it has been tested to assure its proper functioning within each individual MR scanner.[96] The pulse oximeter probe should be placed as far from the scan site as possible, avoiding any loops in the cable which may act as an antenna and either absorb signal from the MR receiver or burn the patient due to induced current in the loop. Electrocardiogram electrodes should be nonferromagnetic and positioned in a straight line parallel to the magnetic field lines. Electrocardiogram wires should be braided to avoid looping of cables and brought down the center of the table with a towel or blanket between the wires and the patient in order to protect against burns.[97] Remote visual monitoring via a television camera provides some opportunity to observe the patient should the anesthesiologist elect not to stay in the scanner with the patient. As noise levels in the scanner can reach 95–110 dB, earplugs should be placed in order to protect the patient's hearing during the scan, and should the anesthesiologist elect to stay in the scanner room during the study, he or she should wear protective earplugs as well. Temperature monitoring may be achieved by using liquid crystal temperature monitoring strips (CliniTemp, Hallcrest, Glenview, IL). Warm blankets and thermal packs are used to maintain body temperature, as the room must be kept cool to accommodate the magnet.

At the conclusion of the procedure the patient is brought out of the scanning room on the scanner table and transferred to a PACU bed. Unless children are returning to an intensive care unit, those who have received a general anesthetic may be extubated at this time. Depending on the proximity of the recovery area to the radiology suite, essential equipment for transport includes oxygen, a transport monitor for ECG and pulse oximetry, a "tackle box" with emergency drugs and airway equipment, and elevator override keys to ensure rapid, uninterrupted transport.

## Cardiac magnetic resonance imaging

Magnetic resonance imaging in the evaluation of CHD has evolved tremendously since its introduction in the 1980s. As technology continues to improve, MR can provide considerable advantages over cardiac catheterization and transthoracic echocardiography for many patients. Although expensive, MR is less costly and invasive than cardiac catheterization and does not require exposure to ionizing radiation. In children who will require multiple surgeries, the ability to conserve vascular access is an important consideration. Compared to transthoracic echocardiography, MR does not rely on the need for certain acoustic windows, has superior ability to evaluate extracardiac thoracic anatomy and can achieve three-dimensional imaging of cardiovascular anatomy.[98] Disadvantages of cardiac MR include difficulty in obtaining scanner time, the long examination times required (usually an hour or more), and the need for sedation or general anesthesia in most pediatric patients, especially those in whom breath-holding techniques will be used. The portability of echocardiography will continue to make it a valuable tool in assessing patients who are too critically ill to be transported to the MR scanner.

Once the patient is sedated or anesthetized, ECG leads are placed in a cluster on the anterior chest to allow synchronization of the acquisition of data with the R wave from the ECG signal. A coil is then positioned around the chest as snugly as possible in order to serve as the receiver. Examinations begin with localizing images in the axial, coronal, and sagittal planes. Depending on the information being sought, a variety of techniques may then be utilized, including cine-MR, phase-encoded velocity mapping, and gadolinium enhanced angiography.[99] Electrocardiogram-gated spin echo yields basic anatomic and morphologic information and is well-suited to analyze the segmental anatomy of the heart, including evaluation of atrial situs, atrioventricular, and ventriculoarterial connections. Gradient reversal or "cine" imaging looks at changes in the size and shape of the atria and ventricles, intracardiac and extracardiac shunts, and abnormal flow patterns in the cardiac chambers, valves, and great vessels. It is useful in assessing ventricular shortening, regional wall motion abnormalities, ejection fraction, and cardiac index. Because cardiac MR can measure indices of ventricular geometry in multiple planes, it is extremely useful in gathering data regarding ventricular volume and performance in single ventricle patients.[100] Cine phase contrast can measure flow volumes and characteristics, estimating pressure gradients across valves and stenotic regions.

Magnetic resonance imaging is an excellent tool for evaluating the aorta and characterizing the precise anatomy of coarctation, arch anomalies, dilation of the aortic root, and vascular rings. In addition, the caliber of the trachea and bronchi in relation to a vascular ring can be clearly delineated, defining areas of vascular compression. Postoperative imaging of the reconstructed aorta can be useful in patients who have undergone a Norwood procedure (reconstruction/augmentation of a hypoplastic aorta, atrial septectomy, and systemic-to-pulmonary shunt) for hypoplastic left heart syndrome.[101]

Pulmonary arterial and venous anatomy is also well demonstrated with MR (Fig. 26.1). Magnetic resonance is superior to echocardiography in defining the subpulmonary region, delineating main and branch PA anatomy, PA continuity, and assessing aortopulmonary shunts.[102] The presence of aneurysmal pulmonary arteries and resultant bronchial compression may be seen in TOF with absent pulmonary valve syndrome. The patency of systemic-to-PA shunts, size and confluence of pulmonary arteries and anatomic variations of anomalous pulmonary venous return may all be well defined with MR.[103] Sources of collateral blood flow to the lungs can also be identified (Fig. 26.2).

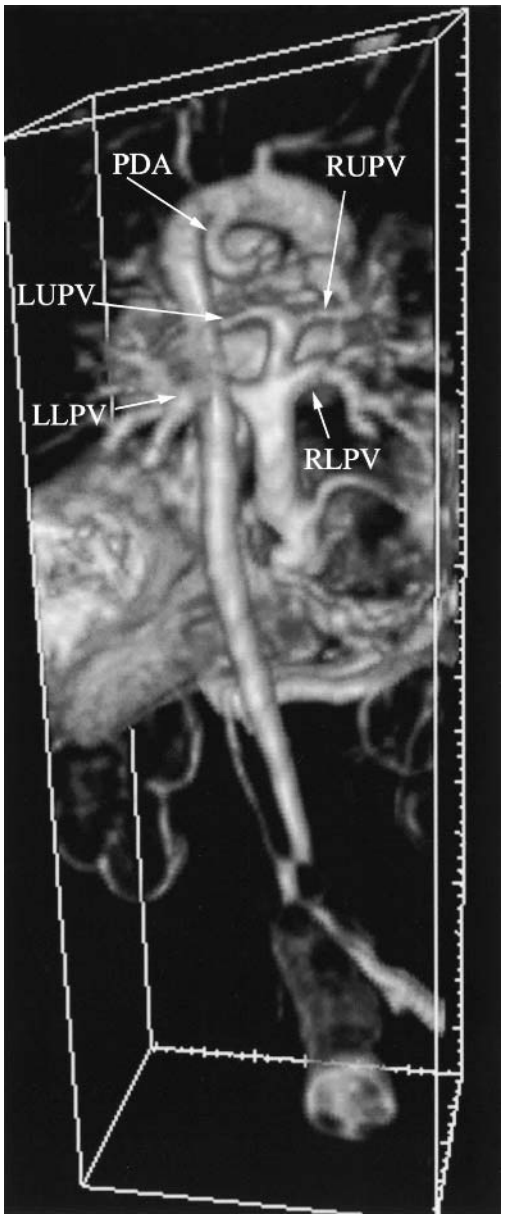


**Fig. 26.1** A neonate with infradiaphragmatic total anomalous pulmonary venous return. LLPV, left lower pulmonary vein; LUPV, left upper pulmonary vein; PDA, patent ductus arteriosus; RLPV, right lower pulmonary vein; RUPV, right upper pulmonary vein. Also reproduced in color, facing p. 146.

New generations of MR scanners with advanced technology will allow faster image acquisition, new imaging strategies and move towards "real-time" evaluation of patients.[104] *In utero* evaluation of cardiac anomalies with MRI has also been described.[105] As the utility of this non-invasive modality in diagnosing cardiac disease continues to grow, anesthesiologists will increasingly be called upon to assist in providing sedation and general anesthesia for these children in order to safely obtain the best possible scans.

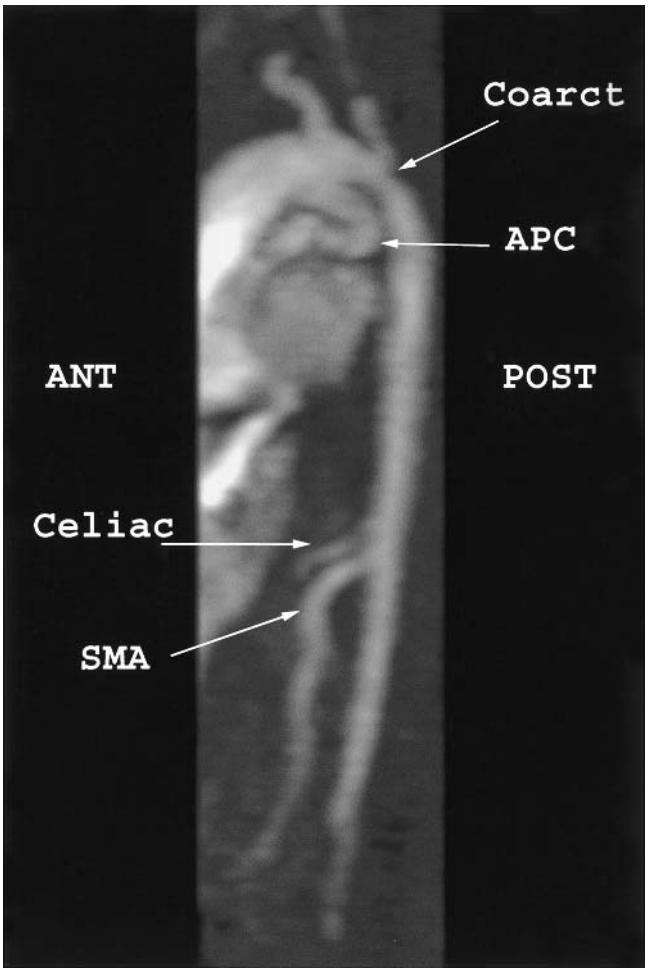


**Fig. 26.2** A 4-day-old infant with pulmonary atresia and ventricular septal defect. ANT, anterior; APC, aortopulmonary collateral vessel; Celiac, celiac axis; Coarct, coarctation of aorta; POST, posterior; SMA, superior mesenteric artery.

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# 27 Cardiac intensive care

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## Introduction

The primary aims of treatment strategies for managing children with congenital cardiac defects are to promote normal growth and development and to limit the pathophysiologic consequences of congenital cardiac defects such as volume overload, pressure overload, and chronic hypoxemia. As a result, there has been a distinct change in management philosophy over the past 10–20 years towards performing reparative operations on neonates and infants, rather than initial palliation and later repair.[1] However, because of a limited physiologic reserve and the complications associated with cardiopulmonary bypass (CPB) and open heart surgery, the risk for cardiorespiratory dysfunction in neonates and young infants in the immediate postoperative period may be increased.

The successful management of congenital heart defects requires detailed knowledge, experience, and technical expertise because of the significant heterogeneity in patient age, structural disease, and cardiorespiratory physiology. The range of operative procedures performed at Children's Hospital Boston during calendar year 2001 is shown in Chapter 1, Table 1.1. Many of the postoperative management problems are therefore quite different from those experienced in adults in the intensive care unit (ICU) following surgery for acquired heart disease. The wide age range of patients undergoing congenital cardiac surgery is another factor that has had a substantial bearing on postoperative management. The age ranges for patients undergoing general anesthesia for cardiac surgery at Children's Hospital Boston in the calendar year 2002 are shown in Fig. 27.1. Patients at the extremes of this age spectrum—the low birth weight and premature newborns at one end and adults with congenital cardiac disease at the other end—are providing new challenges for postoperative management and resource management in the ICU.

Virtually all congenital cardiac defects are now amenable to either an anatomic or functional repair, but "corrected" may not be "cured." The optimal postoperative management of patients with congenital heart disease (CHD) requires a multidisciplinary approach, combining the disciplines of cardiology, cardiac surgery, anesthesia, critical care, and nursing. A thorough understanding of the precise anatomic diagnosis, pathophysiology, and details of the surgical technique, including the potential for residual defects, is necessary when managing pediatric cardiac patients in the ICU.

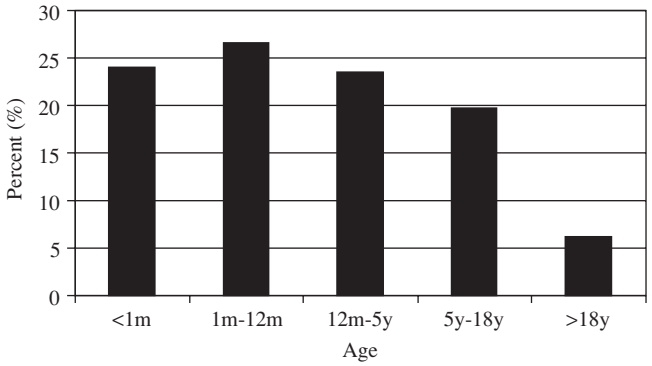


**Fig. 27.1** Cardiac surgery procedures performed according to age at the Children's Hospital Boston in 2002.

For most patients, postoperative recovery is uncomplicated, reflecting the improvements in preoperative diagnosis and stabilization, surgical techniques and, in particular, CPB management. In general, when the patient's clinical progress or postoperative cardiorespiratory function does not follow the expected course, the accuracy of the preoperative diagnosis should be questioned and the adequacy of the surgical repair investigated, either with echocardiography and/or cardiac catheterization.

## Pathophysiology of congenital cardiac defects

A thorough understanding of the pathophysiology of

congenital cardiac defects is essential when managing these patients in the ICU. Not only will this influence preoperative management strategies for stabilization and/or resuscitation prior to surgery, but the effects of pre-existing cyanosis and pressure and volume overload may have a substantial impact on myocardial performance and recovery after surgery. Further, if there are hemodynamically significant residual intracardiac lesions or defects after surgery, the accompanying alterations in pulmonary blood flow, systemic perfusion and ventricular compliance may significantly affect recovery in the ICU.

## Mixing

Intra-atrial mixing of pulmonary and systemic venous return is essential for maintenance of cardiac output (*CO*) in defects with severe right or left atrioventricular valve stenosis or atresia, e.g. hypoplastic left heart syndrome (HLHS) or tricuspid atresia, those with an anatomically parallel pulmonary and systemic circulation, such as d-transposition of the great vessels (D-TGA), and postoperative patients who have undergone a Norwood-type procedure. If complete mixing occurs, the systemic arterial oxygen saturation ($Sa_{O_2}$) should be approximately 85% in room air, although this can be highly variable depending on the amount of pulmonary blood flow. Inadequate mixing across a restrictive atrial septal defect (ASD) can cause significant systemic desaturation secondary to reduced pulmonary blood flow and/or pulmonary edema from pulmonary venous hypertension. The septal defect can be enlarged either by catheter balloon septostomy, balloon dilation or atrial stent; or surgically by atrial septectomy.

## Shunts

Shunting between the pulmonary and systemic circulations can be intracardiac occurring between the atria or ventricles (e.g. across an ASD or ventricular septal defect [VSD]), or extracardiac occurring between the pulmonary arteries and aorta (e.g. across a patent ductus arteriosus [PDA], aortopulmonary window or an aortopulmonary artery collateral vessel in patients with tetralogy of Fallot [TOF] and pulmonary atresia). Depending on the size of the communication and the pressure and resistance differences between the systemic and pulmonary circulations, patients may have an increased or decreased amount of pulmonary blood flow and be either acyanotic or cyanotic.

### Increased pulmonary blood flow

Shunts that increase pulmonary blood flow may occur either between the ventricles, atria, or great arteries, and can be described as "simple" (either unrestricted or restricted) or "complex."

**Table 27.1** Simple shunts: defects or surgical procedures contributing to an increased *Q*p : *Q*s.

| | Acyanotic | Cyanotic |
|---|---|---|
| Two ventricles | ASD<br>VSD<br>CAVC<br>DORV | D-TGA/VSD<br>PA/VSD |
| Single ventricle | | TA ± TGA<br>HLHS<br>DORV/MA<br>Norwood procedure<br>BT shunt |
| Aortopulmonary connection | PDA<br>Truncus arteriosus<br>AP window | PA/MAPCA |

AP, aortopulmonary; ASD, atrial septal defect; BT, Blalock–Taussig; CAVC, complete atrioventricular canal; DORV, double outlet right ventricle; D-TGA, d-transposition of the great arteries; HLHS, hypoplastic left heart syndrome; MA, mitral atresia; MAPCA, multiple aortopulmonary collateral arteries; PA, pulmonary atresia; PDA, patent ductus arteriosus; *Q*p, pulmonary blood flow; *Q*s, systemic blood flow; TA, tricuspid atresia; VSD, ventricular septal defect.

#### *Simple shunt*

The amount of flow across a "simple" left-to-right shunt depends on the size of the defect and balance between pulmonary and systemic vascular resistance. It is important to understand that this is a physiologic term and has no direct relationship to specific diagnoses (Table 27.1). Therefore, patients who have a simple shunt may have:

1. A normal $Sa_{O_2}$ with two ventricles, such as in a large VSD, complete atrioventricular canal (CAVC) defect, and large PDA.
2. A normal $Sa_{O_2}$ with single ventricular outflow trunk and two ventricles, such as in truncus arteriosus.
3. A low $Sa_{O_2}$ and two ventricles, such as in patients with D-TGA and VSD.
4. A low $Sa_{O_2}$ and a single ventricle, such as in atrioventricular valve atresia (tricuspid or mitral) and following placement of a systemic-to-pulmonary artery shunt as in the Norwood-type procedure.

If the simple shunt is "unrestrictive," the physiologic consequence for all the above diagnoses will be the same, i.e. excessive pulmonary blood flow and volume overload to the systemic ventricle. The clinical manifestation will also be the same, i.e. congestive cardiac failure and pulmonary hypertension, although some patients will be cyanotic and others acyanotic depending on the amount of intracardiac mixing.

On the other hand, for a simple "restrictive" shunt, the orifice or size of the defect is small, and the pressure gradient across this now determines the magnitude of shunting rather

than relative vascular resistances.[2] In this circumstance, there is less systemic ventricle volume overload and the pulmonary circulation is protected to some extent from excessive pressure and flow; as a result patients may be relatively asymptomatic and continue to thrive or present later for management.

***Complex shunt***

In the presence of additional pulmonary or systemic outflow obstruction, the ratio of pulmonary (*Q*p) to systemic (*Q*s) blood flow (*Q*p : *Q*s) is determined by the size of the orifice, the outflow gradient as well as the resistance across the pulmonary or systemic vascular bed. The obstruction may be fixed as with valvular stenosis, or dynamic as in subvalvar stenosis (some forms of TOF).

### Clinical consequence of increased *Q*p : *Q*s

If the increase in pulmonary blood flow and pressure persists over months to years, structural changes occur within the pulmonary vasculature, until eventually pulmonary vascular resistance (*PVR*) becomes irreversibly elevated.[2–4] The time course for developing this pathology, termed pulmonary vascular occlusive disease (PVOD), depends on the amount of shunting, but changes may be evident by 4–6 months of age in some lesions. The progression is more rapid when both the volume and pressure load to the pulmonary circulation is increased, such as with a large VSD or CAVC defect. When pulmonary flow is increased in the absence of elevated pulmonary artery pressure, as with an ASD, persistently elevated *PVR* develops much more slowly, if at all.

As *PVR* decreases in the first few months after birth, and the hematocrit falls to its lowest physiologic value, the increased left-to-right shunt, and therefore volume load on the systemic ventricle, can lead to congestive cardiac failure and failure to thrive. A typical pressure–volume loop for a volume-loaded ventricle is shown in Fig. 27.2.[5,6] The end-diastolic volume is increased, and the end-systolic pressure–volume line displaced to the right indicating reduced contractility. The time course over which irreversible ventricular dysfunction develops is variable, but if surgical intervention to correct the volume overload is undertaken within the first 2 years of life, residual dysfunction is uncommon.[6] The volume load on the systemic ventricle and increased end-diastolic pressure contributes to increased lung water and pulmonary edema by increasing pulmonary venous and lymphatic pressures. Compliance of the lung is therefore decreased, and airway resistance increased secondary to small airway compression by distended vessels.[7–9] Lungs may feel stiff on hand ventilation and deflate slowly.

Besides cardiomegaly on chest radiograph, the lung fields are usually congested as well as hyperinflated. Ventilation/perfusion mismatch contributes to an increased alveolar-to-systemic arterial oxygen ($A–aO_2$) gradient, and dead space ventilation.[10] Minute ventilation is therefore increased, primarily by an increase in respiratory rate. Pulmonary artery and left atrial enlargement may compress mainstem bronchi causing lobar collapse.

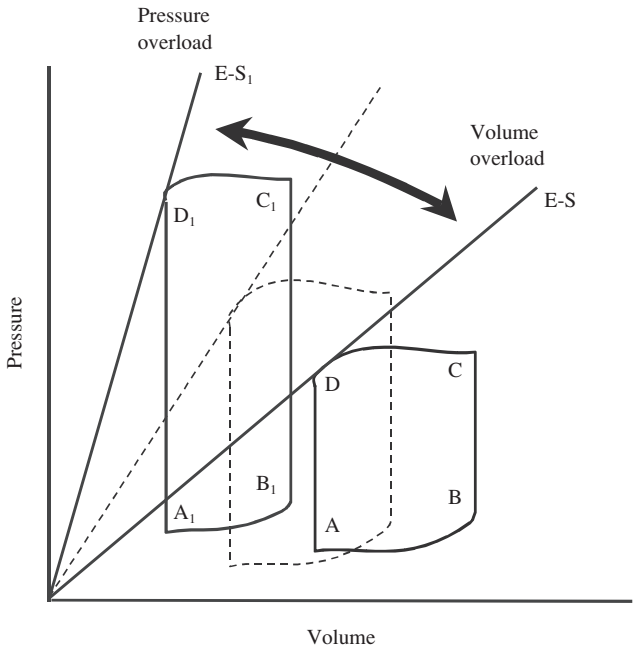


**Fig. 27.2** Comparison of pressure–volume loops between ventricles with a volume load (*ABCD*) or pressure load ($A_1B_1C_1D_1$). The end-systolic pressure–volume line is displaced to the right in a volume-loaded ventricle (*E–S*) reflecting decreased contractility. The end-systolic pressure–volume line is displaced to the left in a pressure-loaded ventricle ($E–S_1$), reflecting preserved systolic function. *A*, $A_1$, end diastole; *B*, $B_1$, onset isovolumetric contraction; *C*, $C_1$ onset ventricular ejection; *D*, $D_1$, end systole; *E–S*, $E–S_1$, end-systolic pressure–volume lines.

It is important to appreciate that such clinical scenarios can be present after surgery in patients who have significant residual intracardiac shunts that cause an increase in *Q*p : *Q*s. It may be manifest during the early postoperative course as a low *CO* state (see below) or become apparent some days after surgery with an inability to wean from mechanical ventilation or persistent requirement for vasoactive support.

### Decreased pulmonary blood flow

Pulmonary blood flow may be reduced either from pulmonary outflow obstruction or a right-to-left intracardiac shunt. While elevated *PVR* is the primary cause of an intracardiac right-to-left shunt at the atrial level via a patent foramen ovale (PFO) in neonates with non-cardiac diseases, such as persistent pulmonary hypertension of the newborn or congenital diaphragmatic hernia, the shunt in newborns with congenital heart defects usually results from right ventricle (RV) outflow obstruction, such as in TOF and pulmonary

**Table 27.2** Factors to consider in a post-cardiac surgery patient who has an arterial oxygen saturation lower than the anticipated range.

| Etiology | Considerations |
|---|---|
| Low $FIO_2$ | Inappropriately low dialed oxygen concentration<br>Failure of oxygen delivery device |
| Pulmonary vein desaturation | Impaired diffusion:<br>Alveolar process: Edema<br>Infectious<br>Restrictive process: Effusion<br>Atelectasis<br>Intrapulmonary shunt:<br>RDS<br>Pulmonary AVM<br>PA-to-PV collateral vessel(s) |
| Reduced pulmonary blood flow | Anatomic RV outflow obstruction<br>Anatomic pulmonary artery stenosis<br>Increased *PVR*<br>Atrial level right-to-left shunt:<br>RV hypertension<br>Restrictive RV physiology (low compliance)<br>Severe tricuspid regurgitation<br>Large fenestration (modified Fontan operation)<br>Intra-atrial baffle leak<br>Ventricular level right-to-left shunt:<br>RV hypertension and residual VSD |
| Low dissolved $O_2$ content | Low mixed venous oxygen level:<br>Increased $O_2$ extraction: Hypermetabolic state<br>Decreased $O_2$ delivery: Low cardiac output state<br>Anemia |

AVM, arteriovenous malformation; $FIO_2$, fractional inspired concentration of oxygen; PA, pulmonary artery; PV, pulmonary vein; *PVR*, pulmonary vascular resistance; RDS, respiratory distress syndrome; RV, right ventricle; VSD, ventricular septal defect.

atresia. Pulmonary blood flow is reduced and *PVR* is usually low in these patients. The decreased flow during fetal development can lead to diminished arborization of the pulmonary vessels and a decrease in total surface area of the pulmonary vascular bed, resulting in a relatively increased and fixed *PVR*.

Pulmonary mechanics and lung volumes are generally normal in patients with reduced pulmonary blood flow. Dead space ventilation is increased although minute ventilation is only slightly increased to maintain normocapnia. The lung fields appear oligemic on chest radiograph.

It is very important to know what the target $SaO_2$ should be in the immediate postoperative period. If the $SaO_2$ is lower than anticipated, there are a number of important causes which must be evaluated (Table 27.2). These include:

1 A reduction in pulmonary venous oxygen saturation indicating an intrapulmonary shunt such as from pulmonary edema, lung collapse or pleural effusion.
2 A reduction in effective pulmonary blood flow, such as from pulmonary ventricle outflow tract obstruction or increased pulmonary artery resistance, an intracardiac right-to-left shunt across an ASD or VSD, or a decompressing vessel from the pulmonary artery to pulmonary vein.
3 A reduction in mixed venous oxygen saturation, such as from reduced oxygen delivery secondary to a low *CO* state or low hematocrit, or increased oxygen extraction in a febrile or hyper-metabolic state following surgery.

## Outflow obstruction

Severe left or right ventricular outflow obstruction in the newborn may be associated with ventricular hypertrophy and vessel hypoplasia distal to the level of obstruction. The increased pressure load may cause ventricular failure, mixing or shunting at the atrial and/or ventricular level occurs to maintain *CO*.

A typical pressure–volume loop from a chronic pressure load on the ventricle is shown in Fig. 27.2. The end-diastolic pressure is elevated, and the end-systolic pressure–volume line displaced to the left reflecting increased contractility. Maintenance of preload, afterload, and normal sinus rhythm is important to prevent a fall in *CO* or coronary hypoperfu-

sion. As the time course to develop significant ventricular dysfunction is longer in patients with a chronic pressure load compared to a chronic volume load, symptoms of congestive heart failure are uncommon unless the obstruction is severe and prolonged.

In the immediate postoperative period it is important to evaluate both systolic and diastolic ventricular function in a previously obstructed but still hypertrophied ventricle.

1. A hyperdynamic state may be present particularly following left ventricle (LV) outflow reconstruction. This will be manifest as systemic hypertension and should be treated promptly with β-blockers to reduce myocardial work and protect surgical suture lines.
2. Systolic dysfunction of a hypertrophied ventricle may be apparent early after cardiac surgery secondary to myocardial ischemia and ventricular dysrhythmias. Ischemia may occur particularly if there has been a long aortic cross-clamp time, or if there has been inadequate protection of the subendocardium with cardioplegia solution or by hypothermia. In the case of the RV, dysfunction may also be present after surgery if an extended ventriculotomy has been performed (e.g. TOF or truncus arteriosus repair) or there has been direct injury to a coronary artery across the right ventricular outflow tract.
3. Diastolic dysfunction is usually manifest as a poorly compliant or stiff ventricle that often contracts well but is unable to relax and fill effectively during diastole. On the left side of the heart, this is usually manifest as left atrial hypertension with either pulmonary edema, atrial dysrhythmias or pulmonary hypertension. On the right side of the heart, an increase in RV end-diastolic pressure is demonstrated by right atrial hypertension along with clinical signs such as a lower $Sa{O_2}$ from a right-to-left atrial shunt (in the presence of a PFO or residual ASD), hepatomegaly, ascites and pleural effusions.

In all the above examples of mixing, shunting and outflow obstruction, the mode and method of mechanical ventilation may have a substantial impact on hemodynamics and systemic perfusion. Particularly for neonates and infants, cardiorespiratory interactions are essential to recognize during postoperative management. In addition to evaluating the adequacy of mechanical ventilation settings by arterial blood gases and chest radiography, it is very important that ventilator settings be continually evaluated and adjusted according to hemodynamic response. This is completely different from the general concepts of mechanical ventilation used in general pediatric and neonatal ICUs. The application of standard or accepted practices for mechanical ventilation as applied to pediatric patients with respiratory disease, or as applied to the premature newborn or newborn with hyaline membrane disease, will often result in an ineffective matching of ventilation with perfusion in patients with congenital cardiac disease, and contribute to delayed postoperative recovery and possible adverse outcomes.

## Airway and ventilation management

Altered respiratory mechanics and positive pressure ventilation may have a significant influence on hemodynamics following congenital heart surgery. While changes in alveolar oxygen ($Pa{O_2}$), $Pa{CO_2}$ and pH significantly affect *PVR*, the mean airway pressure and changes in lung volume during positive pressure ventilation will also affect *PVR*, preload and ventricular afterload. Therefore, the approach to mechanical ventilation should not only be directed at achieving a desired gas exchange, but is also influenced by the potential cardiorespiratory interactions of positive pressure ventilation and method of weaning.

### Airway management

Intubation of the trachea in an awake neonate or young infant with CHD may illicit major undesirable hemodynamic and metabolic responses, and therefore appropriate anesthetic and muscle relaxant techniques are necessary to secure the airway under most circumstances.

The narrowest part of the airway before puberty is below the vocal cords at the level of the cricoid cartilage, and the use of uncuffed endotracheal tubes has been generally recommended. While a leak around the endotracheal tube at an inflation pressure of approximately 20 $cmH_2O$ is desirable, a significant air leak may have a detrimental effect on mechanical ventilation and delivery of a consistent ventilation pattern. Examples include patients with extensive chest and abdominal wall edema following CPB and patients with labile *PVR* and increased *Q*p : *Q*s. If a significant air leak exists around the endotracheal tube, lung volume, and in particular functional residual capacity (*FRC*), will not be maintained and fluctuations in gas exchange can occur. During the weaning process, a significant leak will also increase the work of breathing for some neonates and infants. In these situations, it is therefore preferable to change the endotracheal tube to a larger size or to use a cuffed endotracheal tube.

In certain circumstances, a smaller than expected endotracheal tube may be necessary. This is particularly the case in patients with other congenital defects such as Down's syndrome (trisomy 21). Small airway compression is common among patients with TOF with absent pulmonary valve. Tracheal stenosis may also occur in association with some congenital cardiac defects such as a pulmonary artery sling. Extrinsic compression of the bronchi may occur secondary to pulmonary artery and left atrial dilation. This may be suspected by persistent hyperinflation or lobar atelectasis.

### Mechanical ventilation

Altered lung mechanics and ventilation/perfusion abnormalities are common problems in the immediate postoperative

period.[11,12] Patients who have an increased $Q$p : $Q$s greater than 2 : 1 may have cardiomegaly and congested lung fields on radiograph. Patients who have an elevated left atrial pressure from some form of outflow tract obstruction to the LV may demonstrate signs of pulmonary venous hypertension and pulmonary edema. Additional considerations include the surgical incision and lung retraction, increased lung water following CPB, possible pulmonary reperfusion injury, surfactant depletion in neonates, and restrictive defects from atelectasis and pleural effusions.

In general, patients with known limited physiologic reserve should not be weaned from mechanical ventilation until hemodynamically stable, and problems contributing to an increase in intrapulmonary shunt and altered respiratory mechanics have improved.

## Cardiorespiratory interactions

Cardiorespiratory interactions vary significantly between patients, and it is not possible to provide specific ventilation strategies or protocols that are appropriate for all patients. Rather, the mode of ventilation must be matched to the hemodynamic status of each patient to achieve adequate *CO* and gas exchange. The influence of positive pressure ventilation on preload and afterload are shown in Table 27.3. Frequent modifications to the mode and pattern of ventilation may be necessary during recovery after surgery, with attention to changes in lung volume and airway pressure.

### Influence of lung volume

Changes in lung volume have a major effect on *PVR*, which is lowest at *FRC*, while both hypo- or hyperinflation may result in a significant increase in *PVR*.[13] At low tidal volumes, alveolar collapse occurs because of reduced interstitial traction on alveolar septae. In addition, radial traction on extra-alveolar vessels such as the branch pulmonary arteries is reduced, therefore reducing the cross-sectional diameter. Conversely, hyperinflation of the lung may cause stretching of the alveolar septae and compression of extra-alveolar vessels.

An increase in *PVR* increases the afterload or wall stress on the RV, compromising RV function and contributing to decreased LV compliance secondary to interventricular septal shift. In addition to low *CO*, signs of RV dysfunction including tricuspid regurgitation, hepatomegaly, ascites, and pleural effusions may be observed.

**Table 27.3** The effect of a positive pressure mechanical breath on afterload and preload to the pulmonary and systemic ventricles.

| | Afterload | Preload |
|---|---|---|
| Pulmonary ventricle | **Elevated**<br>Effect: ↑ *RVEDP*<br>↑ *RVP*<br>↓ Antegrade *PBF*<br>↑ PR and/or TR | **Reduced**<br>Effect: ↓ *RVEDV*<br>↓ *RAP* |
| Systemic ventricle | **Reduced**<br>Effect: ↓ *LVEDP*<br>↓ *LAP*<br>↓ Pulmonary edema | **Reduced**<br>Effect: ↓ *LVEDV*<br>↓ *LAP*<br>Hypotension |

*LAP*, left atrial pressure; *LVEDP*, left ventricle end-diastolic pressure; *LVEDV*, left ventricle end-diastolic volume; *PBF*, pulmonary blood flow; PR, pulmonary regurgitation; *RAP*, right atrial pressure; *RVEDP*, right ventricle end-diastolic pressure; *RVEDV*, right ventricle end-diastolic volume; *RVP*, right ventricle pressure; TR, tricuspid regurgitation.

### Influence of intrathoracic pressure

An increase in mean intrathoracic pressure during positive pressure ventilation decreases preload to both pulmonary and systemic ventricles, but has opposite effects on afterload to each ventricle.[14,15]

### Right ventricle

The increase in pressure in the right atrium and reduction in RV preload that occurs with positive pressure ventilation may reduce *CO*. Normally the RV diastolic compliance is extremely high and the pulmonary circulation is able to accommodate changes in flow without a large change in pressure. An increase in mean intrathoracic pressure increases the afterload on the RV from direct compression of extra-alveolar and alveolar pulmonary vessels. This has a number of clinical consequences (Table 27.3). An increase in afterload causes an increase in RV end-diastolic pressure and myocardial work, which may lead to ischemia in a patient with limited coronary perfusion. An example of the increase in RV pressure during a positive pressure breath is demonstrated in Fig. 27.3. The increase in afterload on the RV will also reduce antegrade pulmonary blood flow and therefore preload to the systemic ventricle. If there is pulmonary or tricuspid valve incompetence, the amount of regurgitant flow across these valves will also increase during positive pressure ventilation from the increase in RV afterload.

Patients with normal RV compliance and without residual volume load or pressure load on the ventricle following surgery usually show little change in RV function from the alteration in preload and afterload that occurs with positive pressure ventilation. However, these effects can be magnified in patients with RV hypertrophy and those with restrictive RV physiology following congenital heart surgery, in particular neonates who have required a right ventriculotomy for repair of TOF, pulmonary atresia or truncus arteriosus, and patients with concentric RV hypertrophy. While systolic RV function may be preserved, the ventricles have diastolic

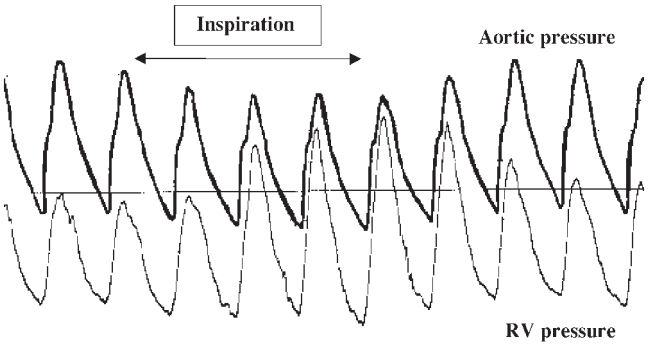


**Fig. 27.3** Simultaneous tracings of aortic and right ventricle (RV) pressure waveforms during positive pressure ventilation in a child with pulmonary artery stenosis. Note the increase in RV pressure to approximately systemic (aortic) level during inspiration when the afterload on the RV is increased.

dysfunction with increased RV end-diastolic pressure and impaired RV filling.

The potential deleterious effects of mechanical ventilation on RV function are important to emphasize. The aim should be to ventilate with a mode that enables the lowest possible mean airway pressure, yet maintaining a tidal volume of 12–15 $cm^3$/kg. While ventilating with a low peak inspiratory pressure, short inspiratory time, increased intermittent mandatory ventilation (*IMV*) rate, and low levels of positive end-expiratory pressure (*PEEP*) has been recommended as one ventilation strategy in patients with restrictive RV physiology, the smaller tidal volumes, e.g. 6–8 $cm^3$/kg, with this pattern of ventilation may reduce lung volume and *FRC*, thereby increasing *PVR* and afterload on the RV.

An alternative strategy in a pressure-limited mode of ventilation is to use larger tidal volumes of 12–15 $cm^3$/kg, with a longer inspiratory time of 0.9–1.0 seconds, increased peak inspiratory pressure of around 30 $cmH_2O$ and low *PEEP* (i.e. wide *P*), and slow *IMV* rate of 12–15 breaths/minute. For the same mean airway pressure, RV filling is maintained and RV output augmented by maintaining lung volume and reduced RV afterload.

### Left ventricle

Left ventricular preload is also affected by changes in lung volume. Pulmonary blood flow, and therefore preload to the systemic ventricle, may be reduced by an increase or decrease in lung volume secondary to alteration in radial traction on alveoli and extra-alveolar vessels.

The systemic arteries are under higher pressure and not exposed to radial traction effects during inflation or deflation of the lungs. Therefore, changes in lung volume will affect LV preload, but the effect on afterload is dependent upon changes in intrathoracic pressure alone rather than changes in lung volume.

In contrast to the RV, a major effect of positive pressure ventilation on the LV is a reduction in afterload. Using Laplace's law, wall stress is directly proportional to the transmural LV pressure and the radius of curvature of the LV. The transmural pressure across the LV is the difference between the intracavity LV pressure and surrounding intrathoracic pressure. Assuming a constant arterial pressure and ventricular dimension, an increase in intrathoracic pressure, as occurs during positive pressure ventilation, will reduce the transmural gradient and therefore wall stress on the LV. Therefore, positive pressure ventilation and *PEEP* can have significant beneficial effects in patients with left ventricular failure (see Table 27.3).

Patients with LV dysfunction and increased end-diastolic volume and pressure can have impaired pulmonary mechanics secondary to increased lung water, decreased lung compliance and increased airway resistance. The work of breathing is increased and neonates can fatigue early because of limited respiratory reserve. A significant proportion of total body oxygen consumption is directed at the increased work of breathing in neonates and infants with LV dysfunction, contributing to poor feeding and failure to thrive. Therefore, positive pressure ventilation has an additional benefit in patients with significant volume overload and systemic ventricular dysfunction by reducing the work of breathing and oxygen demand.

Weaning from positive pressure ventilation may be difficult in patients with persistent systemic ventricular dysfunction. As spontaneous ventilation increases during the weaning process, swings in mean intrathoracic pressure may substantially alter afterload on the systemic ventricle. Once extubated, the subatmospheric intrapleural pressure means that the transmural pressure across the systemic ventricle is increased. This sudden increase in wall stress may contribute to an increase in end-diastolic pressure and volume, leading to pulmonary edema and a low output state. It may be difficult to determine which patients are likely to fail extubation because of ventricular failure; even a small amount of positive pressure as used during continuous positive airway pressure (CPAP) or pressure support modes of ventilation may be sufficient to reduce afterload and myocardial work. Inotropic agents, vasodilators, and diuretics should be continued throughout the weaning process and following extubation to maintain stable ventricular function in these patients.

### Positive end-expiratory pressure

The use of *PEEP* in patients with CHD has been controversial. It was initially perceived not to have a significant positive impact on gas exchange, and there was concern that the increased airway pressure could have a detrimental effect on hemodynamics and contribute to lung injury and air leak.

Nevertheless, *PEEP* increases *FRC* enabling lung recruitment and redistributes lung water from alveolar septal regions

to the more compliant perihilar regions. Both of these actions will improve gas exchange and reduce *PVR*. Positive end-expiratory pressure should, therefore, be used in all mechanically ventilated patients following congenital heart surgery. However, excessive levels of *PEEP* can be detrimental by increasing afterload on the RV. Usually 3–5 $cmH_2O$ of *PEEP* will help maintain *FRC* and redistribute lung water without causing hemodynamic compromise.

The use of *PEEP* in patients who have undergone a Fontan procedure or cavopulmonary anastomosis has also been debated. In this group of patients, pulmonary blood flow is non-pulsatile and depends on the pressure gradient between the superior vena cava (SVC) and pulmonary venous atrium. During positive pressure ventilation, pulmonary blood flow can be diminished, and during a Valsava maneuver and at high levels of *PEEP*, retrograde pulmonary blood flow may be demonstrated by Doppler. Nevertheless, the beneficial effects of *PEEP* to 5 $cmH_2O$ as outlined above, can be demonstrated following the Fontan procedure and rarely contribute to a significant clinical decrease in effective pulmonary blood flow.

## Weaning from mechanical ventilation

Weaning from mechanical ventilation is a dynamic process that requires continued re-evaluation. While most patients following congenital cardiac surgery who have had no complications with repair or CPB will wean without difficulty, some patients with borderline cardiac function and residual defects may require prolonged mechanical ventilation and a slow weaning process.

The method of weaning varies between patients. Most patients can be weaned using either a volume- or pressure-limited mode by simply decreasing the *IMV* rate. Guided by physical examination, hemodynamic criteria, respiratory pattern, and arterial blood gas measurements, the mechanical ventilator rate is gradually reduced. Patients with limited hemodynamic and respiratory reserve may demonstrate tachypnea, diaphoresis and shallow tidal volumes as they struggle to breathe spontaneously against the resistance of the endotracheal tube. The addition of pressure- or flow-triggered pressure support 10–15 $cmH_2O$ above *PEEP* is often beneficial in reducing the work of breathing.

A flow-triggered mode of pressure or volume support, with a back-up ventilator rate if the patient becomes apneic, such as synchronized intermittent mandatory ventilation with pressure or volume support, is particularly useful for neonates and infants who have either required prolonged ventilation following surgery or who have a residual volume or pressure load after surgery compromising ventricular function. Patients are often more comfortable weaning in this mode and have reduced work of breathing, and the level of pressure support is adjusted according to their gas exchange, respiratory rate and tidal volume.

**Table 27.4** Factors contributing to the inability to wean from mechanical ventilation after congenital heart surgery.

| |
|---|
| *Residual cardiac defects:* |
| Volume and/or pressure overload |
| Myocardial dysfunction |
| Arrhythmias |
| *Restrictive pulmonary defects:* |
| Pulmonary edema |
| Pleural effusion |
| Atelectasis |
| Chest wall edema |
| Phrenic nerve injury |
| Ascites |
| Hepatomegaly |
| *Airway:* |
| Subglottic edema and/or stenosis |
| Retained secretions |
| Vocal cord injury |
| Extrinsic bronchial compression |
| Tracheobronchomalacia |
| *Metabolic:* |
| Inadequate nutrition |
| Diuretic therapy |
| Sepsis |
| Stress response |

Numerous factors contribute to the inability to wean from mechanical ventilation following congenital heart surgery (Table 27.4). As a general rule, however, residual defects following surgery causing either a volume or pressure load must be excluded first by echocardiography or cardiac catheterization.

### Restrictive defects

Pulmonary edema, pleural effusions and persistent atelectasis may delay weaning from mechanical ventilation. Residual chest and abdominal wall edema, ascites, and hepatomegaly limit chest wall compliance and diaphragmatic excursion. Chest tubes and peritoneal catheters may be necessary to drain pleural effusions and ascites, respectively.

If atelectasis persists, bronchoscopy is often useful to remove secretions and to diagnose extrinsic compression from enlarged and hypersensitive pulmonary arteries, a dilated left atrium, or conduits. Upper airway obstruction from vocal cord injury (e.g. recurrent laryngeal nerve damage during aortic arch reconstruction), edema or bronchomalacia can also be evaluated.

Phrenic nerve injury can occur during cardiac surgery, either secondary to traction, thermal injury from electrocautery or direct transection as a complication of extensive

aortic arch and pulmonary hilar disection, particularly for repeat operations. Diaphragmatic paresis (no motion) or paralysis (paradoxical motion), should be investigated in any patient who fails to wean.[16] Increased work of breathing on low ventilator settings, increased $PaCO_2$ and an elevated hemidiaphragm on chest radiograph are suggestive of diaphragmatic dysfunction. Ultrasonography or fluoroscopy is useful for identifying abnormal diaphragmatic movement. Surgical plication of the diaphragm may be necessary as a last resort when the patient fails to wean repeatedly from mechanical ventilation.

## Fluid and nutrition

Fluid restriction and aggressive diuretic therapy can result in metabolic disturbances and limit nutritional intake. A hypochloremic, hypokalemic metabolic alkalosis with secondary respiratory acidosis is a common complication from high-dose diuretic use and can delay the ventilator weaning process. Diuretic therapy should be continually re-evaluated based on fluid balance, daily weight (if possible), clinical examination and measurement of electrolyte levels and blood, urea, nitrogen (BUN). Chloride and potassium supplementation is essential to correct the metabolic acidosis.

It is essential to maintain adequate nutrition, particularly as patients will be catabolic early following cardiac surgery and may have a limited reserve secondary to preoperative failure to thrive. Fluid restriction may limit parenteral nutrition, and enteral nutrition may be poorly tolerated from splanchnic hypoperfusion secondary to low *CO* or diastolic pressure.

## Sedation

Sedation is often necessary to improve synchronization with the ventilator and maintain hemodynamic stability. However, excessive sedation and/or withdrawal symptoms from opioids and benzodiazepines will impair the weaning process.

## Sepsis

Sepsis is a frequent cause for failure to wean from mechanical ventilation in the ICU. Invasive monitoring catheters are a common source for blood infections. Beside blood culture surveillance and antibiotics, removing or replacing central venous and arterial catheters should be considered as soon as possible during an episode of suspected or culture-proven sepsis.

The signs of sepsis may be subtle and non-specific, and often broad spectrum intravenous antibiotic coverage is started before culture results are known. Signs to note in neonates and infants include temperature instability (hyper- or hypothermia), hypoglycemia, unexplained metabolic acidosis, hypotension and tachycardia with poor extremity perfusion and oliguria, increased respiratory effort and ventilation requirements, altered conscious state, and leukocytosis with left shift on blood count.

Colonization of the airway occurs frequently in patients mechanically ventilated for an extended period, but may not require intravenous antibiotic therapy unless there is evidence of either increased secretions with fever, leukocytosis, new chest radiograph abnormalities or detection of an organism on Gram stain together with abundant neutrophils. Urinary tract infection and both superficial and deep surgical site infections must also be excluded in patients with clinical suspicion of sepsis (i.e. sternotomy or thoracotomy wounds).

## Airway

Bronchospasm can complicate mechanical ventilation and the weaning process. While this may reflect intrinsic airway disease, bronchospasm can also result from increased airway secretions and extrinsic airway compression. Treatment with inhaled or systemic bronchodilators may be beneficial, although they should be used with caution because of their chronotropic and tachyarrhythmic potential. Levoalbuterol has less chronotropic potential and is the preferred bronchodilator among children who may be harmed by tachycardia.

The sudden onset of bronchospasm with increased peak inspiratory pressure and difficult hand ventilation should raise immediate concern for acute endotracheal tube obstruction or pneumothorax. Bronchospasm in patients with labile *PVR* may reflect acute pulmonary hypertension, and treatment is directed at maneuvers to lower pulmonary artery pressure and improve *CO*.

Post-extubation stridor may be due to mucosal swelling of the large airway, and treatment with dexamethasone before extubation can be beneficial to reduce edema in patients who have required prolonged ventilation. Stridor following extubation is initially treated with nebulized racemic epinephrine, which promotes vasoconstriction and decreases airway hyperemia and edema. If reintubation is necessary, a smaller endotracheal tube should be used. Vocal cord dysfunction should also be considered, particularly as surgery around the ductus arteriosus and left pulmonary artery may injure the recurrent laryngeal nerve.

The ability to clear secretions and potential for nosocomial infection are additional concerns in patients who have been ventilated for an extended period of time. Inability to clear secretions because of sedation, bulbar and vocal cord dysfunction, ineffective cough following prolonged intubation and poor nutritional state with muscle fatigue will

result in atelectasis and respiratory failure. Frequent chest physiotherapy, mask CPAP and nasopharyngeal suction are beneficial, provided patients are hemodynamically stable with adequate gas exchange. In tachypneic patients, the use of nasopharyngeal CPAP can be beneficial by reducing the work of breathing; however, these patients have limited reserve and frequent reassessment is essential.

## Myocardial dysfunction and monitoring

### Assessment of cardiac output

The accurate assessment of the postoperative patient's *CO* should be a focus of management in the ICU. Establishing an adequate *CO* is important, because low *CO* is associated with longer duration of mechanical ventilatory support, ICU stay, and hospital stay, all of which can increase the risk of morbidity and/or mortality. Data from physical examination, routine laboratory testing, bedside hemodynamic monitoring, echocardiography, and occasionally bedside *CO* determination typically are sufficient to manage patients optimally. If patients are not progressing as expected and low *CO* persists, a cardiac catheterization should be performed to investigate and exclude the possibility of residual or undiagnosed structural defects.

The systemic *CO* is defined as the product of ventricular stroke volume (in liters/beat) multiplied by heart rate (in beats/minute).[17] The ventricular stroke volume is determined chiefly by three factors: afterload (the resistance to ventricular emptying), preload (the atrial filling pressure), and myocardial contractility. Cardiac output is usually indexed to body surface area (*BSA*, in meters squared) because it is a function of body mass. Thus, *CO*/*BSA* is the designated cardiac index (*CI*) (in L/minute/$m^2$). The *CI* varies inversely with age, so that normal values in children at rest are 4.0–5.0 L/minute/$m^2$, whereas the normal resting *CI* at age 70 is 2.5 L/minute/$m^2$.[18]

Postoperative patients with low *CO* can present with a variety of abnormalities on physical exam or in bedside monitoring and laboratory values. These manifestations of low *CO* are listed in Table 27.5. Clinical signs on examination include cool extremities and diminished peripheral perfusion, tachycardia, hypotension, oliguria, and hepatomegaly. An increase in the arterial to mixed venous oxygen saturation difference (a–$vO_2$) of greater than 30% and a metabolic acidosis provide biochemical evidence for a low *CO* state. The atrial pressure is a useful measure to follow, and both an increase and decrease could be observed in a low *CO* state. Factors that should be considered when evaluating the atrial pressure following surgery are shown in Table 27.6.

The mechanism(s) underlying low *CO* in a specific patient can be related to one or a combination of factors following surgery.

### Surgical factors

#### Residual or unrecognized defects

A thorough understanding of the underlying cardiac anatomy, surgical findings and surgical procedures is essential because this will direct the initial postoperative evaluation and examination. Residual lesions may be evident by auscultation, intracardiac pressures and waveforms, and oxygen saturation data. For example, a large v-wave on the left atrial waveform may indicate significant residual mitral valve regurgitation. A step-up of the right atrial to pulmonary artery oxygen saturation of more than 10% may indicate a significant intracardiac shunt across a residual VSD.

However, if there are significant concerns for important residual lesions that are compromising *CO* and ventricular function, further evaluation with echocardiography and/or cardiac catheterization should be considered. Imaging of the heart may be difficult immediately after surgery because of limited transthoracic access and acoustic windows. During transthoracic echocardiography, it is important that hemodynamics be closely observed, because inadvertent pressure applied with the transducer may adversely affect filling pressures and mechanical ventilation. Similarly, vigorous antegrade flexion of a transesophageal echocardiography probe may alter left atrial filling or compromise ventilation by partial obstruction of a main stem bronchus.

#### Surgical procedure and technique

While surgery may be routine for many uncomplicated defects, such as ASD closure, the approach for more complex intracardiac repairs may cause specific postoperative problems. For example, if a ventriculotomy is performed to close the VSD in a patient with TOF, RV dyskinesia and poor contraction may be apparent. On the other hand, if a transatrial approach had been used to close the VSD in the same patient, the risk for atrioventricular valve injury or dysrhythmias such as junctional ectopic tachycardia and heart block is increased. Often unexpected findings or technical difficulties at the time of surgery means that modifications to the approach or procedure are necessary. A difficult procedure may lead to a longer time on CPB or additional traction on cardiac structures.

### Complications related to surgery

Failure to secure adequate hemostasis may expose the patient to significant volumes of tranfused blood products, and if there is inadequate drainage via chest drains placed at the time of surgery, the risk for cardiac tamponade is significant. This may be an acute event, but more commonly it is evident by progressive hypotension with a narrow pulse width, tachycardia, an increase in filling pressures and reduced peripheral

**Table 27.5** Manifestations of low cardiac output.

| | |
|---|---|
| *Physical examination* | |
| Mental status: | Lethargy or irritability |
| Vital signs: | Core hyperthermia (often associated with peripheral vasoconstriction)<br>Tachycardia or bradycardia<br>Tachypnea<br>Hypotension (for age and weight)<br>Narrow pulse pressure |
| Peripheral perfusion: | Pale or mottled skin color and cool skin temperature<br>Prolonged (> 3 s) distal extremity capillary refill<br>Poorly palpable pulses |
| Signs of congestive heart failure: | Failure to thrive, poor feeding and diaphoresis<br>Increased respiratory work, chest wall retraction<br>Tachypnea, grunting<br>Gallop rhythm<br>Hepatomegaly |
| *Bedside monitoring data* | |
| ECG tracing: | Rhythm other than normal sinus |
| Arterial waveform: | Blunted upstroke and narrow pulse pressure |
| Atrial pressure change: | See Table 27.6 |
| Urine output: | < 1.0 mL/kg/h in neonates, infants and children<br>< 25 mL/h in older patients |
| *Laboratory and radiographic data* | |
| $Svo_2$: | Decreased (< 65–70%) with an increased (> 25–30%) AV $O_2$ difference |
| Acid-base balance: | Metabolic acidosis with increased anion gap<br>Increased arterial lactate (> 2.2 mM/L) |
| Electrolytes: | Hyperkalemia<br>Elevated BUN and Cr<br>Increased liver transaminases |
| Chest radiography: | Cardiac enlargement<br>Abnormal (increased or decreased) pulmonary blood flow<br>Pulmonary edema |

AV, arteriovenous; BUN, blood, urea, nitrogen; Cr, creatinine; ECG, electrocardiogram; $Svo_2$, systemic venous oxygen saturation.

perfusion with possible evolving metabolic acidosis. This is primarily a clinical diagnosis and treatment (i.e. opening of the sternum) should not be delayed while waiting for possible echocardiographic confirmation.

Myocardial ischemia from inadequate coronary perfusion is often an under-appreciated event in the postoperative pediatric patient. Nevertheless, there are a number of circumstances in which ischemia may occur, compromising ventricular function and *CO*. Myocardial ischemia may occur intraoperatively because of problems with cardioplegia delivery or insufficient hypothermic myocardial protection, and from intracoronary air embolism. In the ICU setting, mechanical obstruction of the coronary circulation is usually the cause of myocardial ischemia rather than coronary vasospasm. Examples include extrinsic compression of a coronary artery by an outflow tract conduit or annulus of a prosthetic valve, and kinking or distortion of a transferred coronary artery button. While ECG changes may indicate ischemia (ST segment abnormalities), a sudden increase in left atrial pressure or sudden onset of a dysrhythmia such as ventricular fibrillation or complete heart block may be an earlier warning sign.

## Cardiopulmonary bypass and the systemic inflammatory response

The effects of prolonged CPB relate in part to the interactions of blood components with the extracorporeal circuit. This is

**Table 27.6** Factors that should be considered when there is a change in the measured atrial pressure outside of the anticipated range for a particular postoperative patient.

| |
|---|
| *Increased* |
| Increased ventricular end-diastolic pressure: |
| Decreased ventricular systolic or diastolic function |
| Myocardial ischemia |
| Ventricular hypertrophy |
| Ventricular outflow obstruction |
| Semilunar valve disease |
| Mitral or tricuspid valve disease |
| Large left-to-right anatomic shunt: |
| Residual ventricular septal defect |
| Systemic-to-pulmonary artery connection |
| Chamber hypoplasia |
| Intravascular or ventricular volume overload |
| Cardiac tamponade |
| Dysrhythmia: |
| Tachyarrhythmia |
| Complete heart block |
| Artifactual: |
| Catheter tip not in the atrium (e.g. in a ventricle or wedged in a pulmonary vein) |
| Pressure transducer below level of heart or improperly calibrated or zeroed |
| Concomitant drug infusions through the atrial line |
| *Decreased* |
| Inadequate preload |
| Artifactual: |
| Catheter malfunction (e.g. cracked or clotted) |
| Pressure transducer above level of heart, or improperly calibrated or zeroed |

magnified in children due to the large bypass circuit surface area and priming volume relative to patient blood volume. Humoral responses include activation of complement, kallikrein, eicosinoid, and fibrinolytic cascades; cellular responses include platelet activation and an inflammatory response with an adhesion molecule cascade stimulating neutrophil activation and release of proteolytic and vasoactive substances.[19,20]

The clinical consequences include increased interstitial fluid and generalized capillary leak, and potential multiorgan dysfunction. Total lung water is increased with an associated decrease in lung compliance and increase in $A–aO_2$ gradient. Myocardial edema results in impaired ventricular systolic and diastolic function. A secondary fall in *CO* by 20–30% is common in neonates in the first 6–12 hours following surgery, contributing to decreased renal function and oliguria.[21] Sternal closure may need to be delayed due to mediastinal edema and associated cardiorespiratory compromise when closure is attempted. Ascites, hepatic ingestion and bowel edema may affect mechanical ventilation, causing a prolonged ileus and delay in enteral feeding. A coagulopathy post-CPB may contribute to delayed hemostasis.

## Dysrhythmias

The ECG is an essential component of the initial postoperative evaluation because the ICU team must identify whether the patient is in sinus rhythm early in the recovery period. If the rhythm cannot be determined with certainty from a surface 12- or 15-lead ECG, temporary epicardial atrial pacing wires, if present, can be used with the limb leads to generate an atrial ECG.[22] Also right and left atrial waveforms are useful in diagnosing atrioventicular synchrony (see Chapter 7). Temporary epicardial atrial and/or ventricular pacing wires are routinely placed in most patients to allow mechanical pacing should sinus node dysfunction or heart block occur in the early postoperative period. Because atrial wires are applied directly to the atrial epicardium, the electrical signal generated by atrial depolarization is significantly larger and thus easy to distinguish compared to the P wave on a surface ECG. Sinus tachycardia, which is common and often secondary to medications (e.g. sympathomimetics), pain and anxiety, or diminished ventricular function, must be distinguished from a supraventricular, ventricular, or junctional tachycardia. Any of these tachyarrhythmias can lower *CO* by either compromising diastolic filling of the ventricles or depressing their systolic function.[23,24] High-grade second-degree heart block and third-degree (or complete) heart block can diminish *CO* by producing either bradycardia or loss of atrioventricular synchrony or both. Third-degree block is transient in approximately one third of cases. If it persists beyond postoperative day 9–10, it is unlikely to resolve, and a permanent pacemaker is indicated.[25]

## Low preload

The diagnosis of insufficient preload is usually made by monitoring the mean atrial pressure or central venous pressure (CVP). The most common cause in the ICU is hypovolemia secondary to blood loss from postoperative bleeding. Initially after surgery and CPB, the filling pressures may be in the normal range or slightly elevated, but this often reflects a centralized blood volume secondary to peripheral vaso- and venoconstriction following hypothermic CPB. As the patient continues to rewarm and vasodilate in the ICU, considerable intravenous volume may be necessary to maintain the circulating blood volume. There may also be considerable third-space fluid loss in neonates and small infants who manifest the most significant systemic inflammatory response following CPB. The "leaking" of fluid into serous cavities (e.g.

ascites) and the extracellular space (progressive anasarca) requires that these patients receive close monitoring and volume replacement to maintain the circulating blood volume. Patients with a hypertrophied or poorly compliant ventricle, and those with lesions dependent on complete mixing at the atrial level, also often require additional preload in the early postoperative period.

## High afterload

Elevated afterload in both the pulmonary and systemic circulations frequently follows surgery with CPB.[26] Excessive afterload in the systemic circulation is caused by elevated systemic vascular resistance (*SVR*) and typically produces both diminished peripheral perfusion and low urine output. Treatment of elevated *SVR* includes recognizing and improving conditions that exacerbate vasoconstriction (e.g. pain and hypothermia) and administering a vasodilating agent. A vasodilator, which can be either a phosphodiesterase inhibitor (e.g. milrinone) or a nitric oxide donor (e.g. nitroprusside), is frequently added to an inotropic agent such as dopamine to augment *CO*.[27–30] Neonates are intolerant of increased afterload, and appear to derive particular benefit from afterload reduction therapy.

## Decreased myocardial contractility

Because decreased myocardial contractility occurs frequently after reparative or palliative surgery with CPB, pharmacologic enhancement of contractility is used routinely in the ICU. Before initiating treatment with an inotrope, however, the patient's intravascular volume status, serum ionized $Ca^{2+}$ level, and cardiac rhythm and acid-base status should be considered. Inotropic agents enhance *CO* more effectively if preload is adequate, so intravenous colloid or crystalloid administration should be given if preload is low. If hypocalcemia (normal serum ionized $Ca^{2+}$ levels are 1.14–1.30 mmol/L)[31] is detected, supplementation with intravenous calcium gluconate or calcium chloride is appropriate, because $Ca^{2+}$ is a potent positive inotrope itself, particularly in neonates and infants.[32]

Dopamine is usually the first-line agent to treat of either mild (10–20% decrease in normal mean arterial blood pressure for age) or moderate (20–30% decrease in normal mean arterial blood pressure for age) hypotension. This sympathomimetic agent promotes myocardial contractility by elevating intracellular $Ca^{2+}$, both via direct binding to myocyte $\beta_1$-adrenoceptors and by increasing norepinephrine levels. Dopamine is administered by a constant infusion because of its short half-life, and usual starting doses for inotropy are 5–10 μg/kg/minute. Dopamine should be infused through a central venous catheter to avoid superficial tissue damage should extravasation occur. The dose is titrated to achieve the desired systemic blood pressure, although some patients, especially older children and adults, may develop an undesirable dose-dependent tachycardia.

If a patient does not respond adequately to dopamine at 10–15 μg/kg/minute or has severe hypotension (more than 30% decrease in mean arterial blood pressure for age), treatment with epinephrine should be considered. Epinephrine should be given exclusively via a central venous catheter and can be added to dopamine at a starting dose of 0.05–0.10 μg/kg/minute, with subsequent titration of the infusion to achieve the target systemic blood pressure. At high doses (i.e. 0.5 μg/kg/minute), epinephrine can produce significant renal and peripheral vasoconstriction, tachycardia, and increased myocardial oxygen demand. Patients with severe ventricular dysfunction who require persistent or escalating doses of epinephrine greater than 0.3–0.5 μg/kg/minute may benefit from opening of the sternum and/or should be evaluated for the possibility of mechanical circulatory support with a ventricular assist device (VAD) or extracorporeal membrane oxygenation (ECMO) (see below).

A combination of epinephrine at low doses (e.g. < 0.1 μg/kg/minute) or dopamine with an intravenous afterload reducing agent such as nitroprusside or milrinone is frequently beneficial to support patients with significant ventricular dysfunction accompanied by elevated afterload. Epinephrine is preferred to the equally potent inotrope norepinephrine because it generally is well tolerated in pediatric patients and causes less dramatic vasoconstriction. Norepinephrine is a direct-acting α-agonist, primarily causing intense arteriolar vasoconstriction, but it also has positive inotropic actions. At doses of 0.01–0.2 μg/kg/minute, it can be considered in patients with severe hypotension and low *SVR* (e.g. "warm" or "distributive" shock), inadequate coronary artery perfusion or inadequate pulmonary blood flow with a systemic-to-pulmonary artery shunt.

## Delayed sternal closure

Pericardial and sternal closure following cardiac surgery causes a restriction to cardiac function and can interfere with efficient mechanical ventilation. This is particularly important for neonates and infants in whom considerable capillary leak and edema develops following CPB, and in whom cardiopulmonary interactions impair *CO*. In the operating room, mediastinal edema, unstable hemodynamic conditions and bleeding are indications for delayed sternal closure. Patients who commonly develop hemodynamic or respiratory instability in the immediate postoperative period (e.g. following a Norwood procedure for HLHS) should also be considered for delayed sternal closure. Urgent reopening of the sternum in the ICU following surgery is associated with higher mortality compared to leaving the sternum open in the operating room, and successful sternal closure can usually be achieved by postoperative day 4 with a low risk for surgical site infection.[33,34]

## Mechanical support of the circulation

Mechanical assist devices have an important role providing short-term circulatory support to enable myocardial recovery after cardiac surgery or myocarditis, and can also provide longer-term support while awaiting cardiac transplantation. Although a variety of assist devices are available for adult-sized patients, other than ECMO, the development of alternate pediatric VADs has lagged behind adult devices. A problem for pediatric patients is determining which method of support is optimal. While venoarterial ECMO provides biventricular support with oxygenation, a number of patients may benefit from univentricular support with a left or right VAD.

### Extracorporeal membrane oxygenation

Extracorporeal membrane oxygenation has become the most widely used mode of mechanical cardiopulmonary support for children with CHD. Venoarterial ECMO (venous cannula in the right atrium or SVC and arterial cannula in the aorta or innominate artery) is the mode of support necessary for patients with cardiac failure. Extracorporeal membrane oxygenation fully supports the heart and lungs, similar to conventional bypass, and requires significant systemic anticoagulation. Figure 27.4 depicts a standard ECMO circuit. Over 300 children per year receive ECMO for cardiac support according to the Extracorporeal Life Support (ELSO) Registry, with the majority of patients placed on ECMO following cardiotomy.[35] The percentage of patients who are successfully decannulated from ECMO (approximately 40–45%), and the percentage of patients subsequently discharged home after cardiac ECMO (approximately 37%), has remained largely unchanged over the last 5 years.[36–38] Therefore, critical appraisal of indications and techniques is required if the success rate for cardiac ECMO is to increase to levels currently achieved in neonates with respiratory distress syndrome (approximately 90%).

Centers with an efficient and well-established ECMO service are more likely to utilize this form of support, and indications for the use of ECMO vary among centers. Therefore, comparisons of the use and outcomes from ECMO between institutions are difficult to interpret. Nevertheless, this form of mechanical support clearly is life-saving and must be available for selected patients following congenital heart surgery. Extracorporeal membrane oxygenation may be used to stabilize critically ill patients prior to cardiac surgery, thereby limiting end-organ dysfunction prior to surgery. Indications include severe low output state, pulmonary hypertension and severe hypoxemia.

The best outcomes from ECMO are in postoperative patients who have a period of relative stability after reparative surgery, but then develop progressive myocardial or respiratory failure, or have a sudden cardiac arrest. Hospital survival in this group of patients has been reported to be as high as 70%.[39] The outcome of patients who require ECMO because of inability to wean from CPB in the operating room is generally poor, with a reported survival between 10% and 33%.[36–39] Other than factors such as primary myocardial dysfunction, pulmonary hypertension, severe hypoxemia, and cardiac dysrhythmia after surgical repair, lack of a significant residual defect(s) is the major factor determining successful outcome.

Patients with a systemic-to-pulmonary artery shunt also have worse outcomes from ECMO. In a shunt-dependent pulmonary circulation, runoff through the shunt will limit

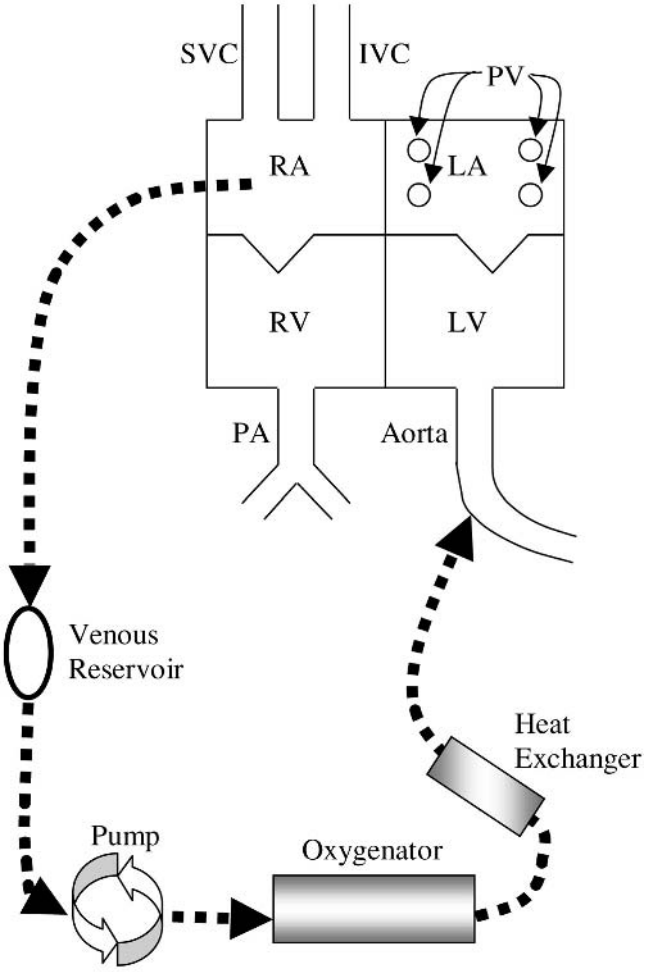


**Fig. 27.4** Extracorporeal membrane oxygenation (ECMO) circuit. The dashed lines represent flow through a venoarterial ECMO circuit. Blood is drained from the right atrium by direct atrial cannulation, or from a superior vena cava catheter advanced into the right atrium. When using a roller pump, the blood is first drained to a small venous reservoir, with a centrifugal pump, and a reservoir is not used. Blood then passes through a membrane oxygenator and heat exchanger before returning to the ascending aorta, which is cannulated directly or via the right carotid artery. IVC, inferior vena cava; LA, left atrium; LV, left ventricle; PA, pulmonary artery; PV, pulmonary vein; RA, right atrium; RV, right ventricle; SVC, superior vena cava.

systemic flow and contribute to both pulmonary overcirculation and ventricular volume overload. Therefore, temporary occlusion of the shunt is necessary while on ECMO. When attempting to discontinue ECMO, shunt flow is re-established, potentially causing a reperfusion injury in the pulmonary vasculature and severe pulmonary hypertension. Reducing the shunt size to allow a limited amount of pulmonary flow while on ECMO will reduce the incidence of this complication.

The survival of pediatric patients who require in-hospital resuscitation following a cardiorespiratory arrest is extremely poor.[40] Nevertheless, intact survival following pediatric cardiac surgery has been reported after prolonged cardiac arrest unresponsive to conventional closed or open chest cardiac massage with the use of ECMO.[38,41] Prolonged resuscitation, particularly when combined with the obligatory time necessary to set up the ECMO circuit, increases the likelihood of significant neurologic and other end-organ injury. To address this issue, we now have a mobile ECMO circuit set up and primed for immediate use in the ICU at all times.[41] Patients who do not demonstrate recovery of cardiac function within 10–15 minutes of the initiation of advanced life support are cannulated either through the chest, neck or groin and ECMO is initiated.

Extracorporeal membrane oxygenation may also be used as a bridge to cardiac transplantation. However, prolonged support from ECMO is associated with increasing potential complications such as bleeding, renal failure, and sepsis. In our experience, if there is no significant recovery of myocardial function after 48–72 hours on ECMO support, the transplant evaluation is completed.[42]

A brief review of ECMO management principles follows. In the emergency situation an asanguinous prime is used, with blood added later after initiation of ECMO. Initially the patient is supported with ECMO flows approaching full bypass flow, i.e. 100–150 mL/kg/minute for patients less than 10 kg. This provides opportunity for a completely unloaded myocardium to recover from ischemic insult, and fully supports other organ systems. Inotropic agents are discontinued or minimized, in order to prevent downregulation of adrenergic receptors in the myocardium and peripheral vasculature. Vasodilating agents such as milrinone, nitroprusside, or phentolamine are often required to maintain mean arterial pressure within desired limits. The left atrium may need to be decompressed with a small cannula in patients who have blood return to the left heart, i.e. those with systemic to pulmonary collaterals. Left atrial pressure may also be elevated if ECMO flow is inadequate. The lungs are ventilated with "lung rest" settings to prevent atelectasis, but also to avoid oxygen toxicity and barotrauma, e.g. a slow rate of 10–20 breaths/minute, $F_{IO_2}$ less than 0.50, and *PEEP* of 5 cm or less with long inspiratory times and low peak inflating pressures. Anticoagulation is maintained with a heparin infusion, usually 10–20 U/kg/hour, titrated to keep activated clotting time (ACT) within 200–250 seconds. Ongoing bleeding and coagulopathy is common, and ample blood products must be available for infusion into the circuit. The need for surgical exploration is common in these patients due to accumulation of blood or clot in the mediastinum or under a patch covering an open sternum. The platelet count is maintained above 100 000, the hematocrit above 30, and the prothrombin time within normal ranges. Aminocaproic acid has been shown to be effective at reducing blood loss and transfusion in cardiac ECMO.[43] Central nervous system bleeding is a catastrophic complication and should be suspected when there is sudden volume loss without other explanation. Cranial ultrasound in infants is adequate for screening or diagnostic purposes. Infectious complications are prevented by meticulous sterile technique, and in many cases, broad spectrum antibiotics are required. Inadequate ECMO circuit volume is indicated by excessive negative pressure readings on the venous side of the circuit, and an inability to maintain target flows and mean arterial pressures. Renal insufficiency can be managed by placing a hemofilter in the circuit for continuous dialysis and removal of inflammatory mediators. Sedation, analgesia, and paralysis are required for these patients, and tolerance develops rapidly. Extracorporeal membrane oxygenation support is weaned when the compromised myocardium has recovered, which may vary from as little as 24–48 hours to 3–4 weeks. Transthoracic echocardiography may give an estimate of contractility if volume is added to the heart. Before weaning inotropic agents must be restarted or increased, hematocrit and electrolytes optimized, and ventilation increased. The ECMO flow is gradually reduced, additional cardiovascular support with intravascular volume and intropic support may be required, and *CO* is assessed at lower levels of flow. After repeated unsuccessful attempts to wean, the caregivers and parents or guardians must decide if support should be withdrawn or the patient listed for transplantation.

## Ventricular assist devices

The experience with VAD in children remains relatively small primarily due to technical considerations and concerns regarding suitability of children with CHD for univentricular support.[44] A major limitation of the application of adult systems for pediatric patients is the risk of thromboembolism when lower flows are used.

The majority of pediatric patients reported have received left ventricular support, which has been particularly beneficial in patients with an ischemic myocardium secondary to an anomalous left coronary artery from the pulmonary artery, and in patients who require retraining of an "unprepared" LV in D-TGA and intact ventricular septum or a small VSD after an arterial switch procedure.[39] Survival results reported to date are similar to those achieved with cardiac ECMO. A typical left ventricular assist device (LVAD) circuit used for failure to wean from bypass is shown in Fig. 27.5.

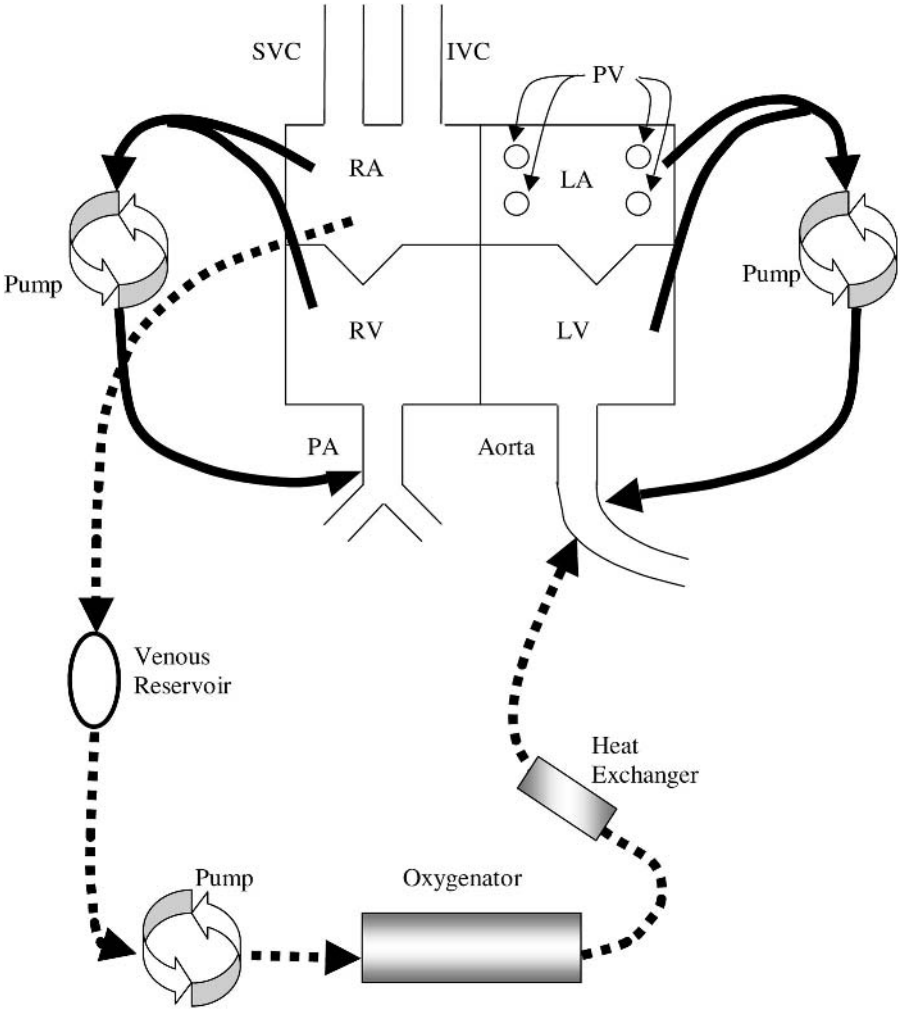


**Fig. 27.5** Ventricular assist device (VAD) circuit. The VAD flow is shown in the solid lines. With a left ventricular assist device (LVAD), blood is drained from the left atrium or left ventricle and pumped to the aorta. With a right ventricular assist device (RVAD), blood is drained from the right atrium or right ventricle and pumped to the pulmonary artery. With a biventricular assist device (BIVAD), both LVAD and RVAD circuits are utilized. An ECMO circuit (dashed lines) is shown for comparison. IVC, inferior vena cava; LA, left atrium; LV, left ventricle; PA, pulmonary artery; PV, pulmonary vein; RA, right atrium; RV, right ventricle; SVC, superior vena cava.

A VAD has a number of advantages. The circuit is simple in design, takes less time to prime, and requires little technical assistance once established. It may more effectively decompress the LV, and pulsatile flow is possible with some devices. Bleeding complications and platelet consumption are often less problematic in patients on VAD compared to ECMO. Because of the lower complications associated with VAD, patients may be supported for a longer period as a bridge to transplantation.[45]

Management of the patient on VAD support is similar to ECMO in some respects, but the following important differences exist. An oxygenator is not used, requiring full ventilatory support. Decreased intravascular volume causes a reduction in flow; therefore, left and right atrial pressures are monitored to establish a Starling curve for each patient. The circuit volume is smaller, and because there is no oxygenator in the circuit, a lower level of anticoagulation is required (ACT of 180–200 seconds). Consequently, bleeding complications are fewer with VAD. A patient receiving LVAD support must have a RV capable of pumping blood into the lungs. Inotropic support and RV afterload reduction to reduce *PVR* (i.e. milrinone, nitric oxide) may be necessary. If the RV fails, either biventricular assist device or ECMO needs to be instituted. Since the patient's lungs provide oxygenation, ventilation and pulmonary toilet must be optimized. Patients with intracardiac shunts (i.e. a PFO) may not be suitable candidates for VAD because arterial desaturation may develop from right-to-left shunting, and there is increased risk of paradoxical emboli. The principles for weaning attempts are similar to those discussed above for ECMO.

Application of adult VAD technology to larger pediatric patients and the miniaturization of existing technology have increased the availability of VAD in children and the potential to provide longer periods of mechanical support of the circulation with fewer complications. The patients can potentially be extubated, and ambulate. Two such devices are the Thoratec,[46] available for patients down to 20 kg, and the Berlin Heart,[47] which has been miniaturized for patients even down to infant sizes. Survival rate for infants and children with application of these technologies is 50–70%.

### Intra-aortic balloon pump

Intra-aortic balloon pumps have been used with success in infants and children, although experience is limited.[48] Problems in pediatric patients include size constraints of the device and balloon, difficulty synchronizing the balloon inflation–deflation cycle with faster heart rates, and the increased elasticity of the aorta, which makes effective counterpulsation ineffective.

## Fluid management and renal function

Because the inflammatory response to CPB often leads to an increase in total body water, fluid management in the immediate postoperative period is critical. Capillary leak and interstitial fluid accumulation continue for the first 24–48 hours following surgery, necessitating ongoing volume replacement with colloid or blood products. A fall in *CO* and increased antidiuretic hormone secretion contribute to delayed water clearance and potential pre-renal dysfunction, which could progress to acute tubular necrosis and renal failure if a low *CO* state persists.

During bypass, optimizing the circuit prime hematocrit and oncotic pressure, attenuating the inflammatory response with steroids and protease inhibitors such as aprotinin, and the use of modified ultrafiltration techniques have all been recommended to limit interstitial fluid accumulation.[49,50] During the first 24 hours following surgery, maintenance fluids should be restricted to 50% of full maintenance, and volume replacement titrated to appropriate filling pressures and hemodynamic response.

Oliguria in the first 24 hours after complex surgery and CPB is common in neonates and infants until *CO* recovers. While diuretics are commonly prescribed in the immediate postoperative period, *CO* must also be enhanced with volume replacement and vasoactive drug infusions for these to be most effective. In addition to supporting *CO*, low dose dopamine (3 μg/kg/minute) has the advantage of increasing renal blood flow and promoting diuresis. Fenoldopam mesylate, a selective dopamine ($DA_1$) receptor agonist, leads to both renal and splanchnic vasodilation, and has been used to provide renal protection during periods of ischemia and hypoxia such as during hypothermic CPB.[51] At a dose of 0.1–0.5 μg/kg/minute it may also have a role in postoperative ICU management to enhance renal perfusion by decreasing renal vascular resistance.

Furosemide 1 mg/kg i.v. every 8–12 hours is a commonly prescribed loop diuretic that must be excreted into the renal tubular system before producing diuresis. Low *CO* therefore reduces its efficacy. Bolus dosing may result in a significant diuresis over a short period, thereby causing changes in intravascular volume and possibly hypotension. Rapid boluses may also damage the hair cells of the inner ear in premature and full term newborns, causing hearing loss. A continuous infusion of 0.2 to 0.3 mg/kg/hour after initial bolus of 1 mg/kg i.v. often provides a consistent and sustained diuresis without sudden fluid shifts. Chlorothiazide 10 mg/kg i.v. or p.o. every 12 hours is also an effective diuretic, particularly when used in conjunction with loop diuretics.

Peritoneal dialysis, hemodialysis and continuous venovenous hemofiltration (CVVH) provide alternate renal replacement therapy in patients with persistent oliguria and renal failure.[52,53] In addition to enabling water and solute clearance, fluids with increased nutritional content can be increased in volume to ensure adequate nutrition. The indications for renal support vary, but include BUN greater than 100 mg/dL, life-threatening electrolyte imbalance such as severe hyperkalemia, ongoing metabolic acidosis, fluid restrictions limiting adequate nutrition, and increased mechanical ventilation requirements secondary to persistent pulmonary edema, reduced chest wall compliance, or ascites.

A peritoneal dialysis catheter can be placed into the peritoneal cavity at the completion of surgery or later in the ICU. Indications in the ICU include the need for renal support or to reduce intra-abdominal pressure from ascites that may be compromising mechanical ventilation. Drainage may be significant in the immediate postoperative period as third space fluid losses continue, and replacement with albumin and/or fresh frozen plasma may be necessary to treat hypovolemia and hypoproteinemia.

To enhance fluid excretion if oliguria persists, "mini-volume dialysis" may be effective using 10 $cm^3$/kg of 1.5% or 2.25% dialysate over a 30–40 minute cycle. A persistent communication between the peritoneum, mediastinum and/or pleural cavities following surgery will limit the effectiveness of peritoneal dialysis and is a relative contraindication.

Arteriovenous hemofiltration or hemodialysis through double lumen femoral or subclavian vein catheters can be used effectively in neonates. Complications related to venous access, catheter-related thrombosis and hemodynamic instability are potential complications that require close monitoring.

## Hemostasis

Hemostasis after surgery may be difficult to obtain, particularly if CPB has been prolonged, if there are extensive suture lines, and following repeat cardiac surgery. Prompt management and meticulous control of surgical bleeding is essential to prevent the complications associated with a massive transfusion. Generally, if postoperative bleeding greater than 10 $cm^3$/kg/hour persists in the immediate postoperative period with a normal coagulation profile and platelet count, surgical bleeding should be suspected, and re-exploration considered.

Factors contributing to a coagulopathy after CPB include

hemodilution of coagulation factors and platelets from the bypass circuit prime, stimulation of the intrinsic coagulation pathway, and both platelet activation and aggregation. In addition, several preoperative factors may contribute to postoperative coagulopathy: chronic cyanosis, low *CO* with tissue hypoperfusion and disseminated intravascular coagulopathy, hepatic immaturity, and the use of platelet inhibitors such as prostaglandin $E_1$ ($PGE_1$) infusion and aspirin.

Transfusion of platelets and fresh frozen plasma or cryoprecipitate is often necessary. Fresh whole blood less than 24 hours old has been demonstrated to be beneficial in neonates after bypass, but not older patients. Antifibrinolytic drugs such as ε-aminocaproic acid, tranexamic acid and aprotinin are used intraoperatively to reduce postoperative bleeding, but may also be effective in the ICU if coagulopathy and fibrinolysis persists.

Hypothermia and hypocalcemia following bypass will also contribute to delayed hemostasis and should be corrected in conjunction with the above-mentioned maneuvers.

## Neurologic injury

While patients with CHD may have coexisting abnormalities of the central nervous system, they are also at risk for acquired neurologic injury throughout the perioperative period, which include paradoxical air and thrombotic emboli, cerebral abscess, and venous or arterial thrombosis from erythrocytosis caused by chronic cyanosis.[54] Premature newborns are at risk for intraventricular hemorrhage (IVH); cerebral ultrasonography is recommended before and after CPB. Although there are no data to support an increased incidence of IVH related to CPB, this should be viewed with caution based on the ECMO experience with IVH.

Patients with CHD may develop circulatory collapse and/or severe hypoxemia which may contribute to global hypoxic–ischemic neurologic damage. Encephalopathy and seizures are manifestations of neurologic injury; however, preoperative assessment is often difficult because of the need for mechanical ventilation, sedation and paralysis. An electroencephalogram (EEG) and a computed tomography (CT) scan may help localize specific sites of neurologic injury, but there is poor correlation with longer-term neurologic outcome. The potential for neurologic recovery of the immature brain is greater compared to older children and adults.[55] Because of the risk (transport to radiology) and lack of proven benefit, these patients often proceed to surgery with an uncertain neurologic status.

The application of deep hypothermia provides protection of the central nervous system during periods of ischemia. However, prolonged periods (> 45 minutes) of hypothermic arrest may cause an ischemic reperfusion injury to the brain. In addition, there are other variables that increase the risk for brain injury during CPB. These include problems related to aortic and venous cannula placement, the duration of bypass, the rate of cooling, perfusion pressure and flow rate, air embolism, pH and $P_{CO_2}$ management during deep hypothermia, degree of hypothermia, type of oxygenator, circuit hematocrit, and duration of circulatory arrest.[56,57] For a more detailed discussion see Chapters 5 and 8.

Seizures are the most frequently observed neurologic complication following cardiac surgery using deep hypothermic circulatory arrest (DHCA) with a reported incidence of 4–25%.[58,59] Both focal and generalized seizures have been described, usually occurring on the first or second postoperative day, and can usually be controlled with anticonvulsants; status epilepticus is uncommon. A brain CT scan is usually non-diagnostic, although indicated in patients with persistent focal seizures, because a larger area of damage, or a focal lesion such as an intracerebral hemorrhage, may be seen. Postoperative seizures do not increase the risk of seizures later in life, and in the past were thought to be benign.[60] However, an ongoing, prospective, randomized trial of DHCA versus low-flow bypass during the arterial switch operation for D-TGA has demonstrated that seizures are a marker of neurologic damage and a prognostic indicator of worse neurodevelopmental outcome.[61–63]

Detection of seizures in the postoperative period is a diagnostic challenge in the ICU. Clonic, tonic, or myoclonic manifestations of seizures may be difficult to detect because of sedation or paralysis. Autonomic manifestations such as the sudden onset of tachycardia, hypertension, and pupillary dilation are suggestive of seizure activity, although the cause of these signs is difficult to distinguish from other hemodynamic causes. Nevertheless, the early detection and management of seizures post-deep hypothermic low-flow CPB (DHCPB) is important, and they should not be considered a benign event, rather both a marker for and manifestation of ongoing neurologic injury. In a prospective study following the arterial switch procedure (the Boston Circulatory Arrest Study),[64] clinical seizures were detected in 11% of infants, but continuous EEG monitoring detected seizure activity in 25% of these infants. Over recent years, postoperative clinical seizures have become a rare event, with an incidence less than 4%,[65] which is most likely secondary to improved techniques for neurological protection. Deep hypothermic circulatory arrest is now performed less frequently, and when used, the duration of cooling on CPB is longer, pH-stat blood gas management strategy is used, and circulatory arrest time kept to less than 40 minutes, when possible.

Follow up of neonates and infants enrolled in the Boston Circulatory Arrest Study at 1, 4, and 8 years of age indicates that seizure activity following DHCA is associated with longer-term neurodevelopmental abnormalities. At 1 year of age, scores on the Psychomotor Development Index of the Bayley Scales (a measure of fine and gross motor ability) were significantly lower in children randomized to circulatory arrest versus low-flow CPB and in those who developed

seizures in the early postoperative period. At 4 years of age lower verbal and performance intelligence quotient was also detected in this group of patients.

Postoperative factors contributing to neurologic injury include cerebral embolism, persistent low output state with low cerebral perfusion pressure, and hyperventilation with low $PaCO_2$ reducing cerebral blood flow. Post-bypass hyperthermia may develop from low *CO* and peripheral vasoconstriction, or from aggressive rewarming practices, and may contribute to neurologic injury. Post-ischemia brain temperature has been shown to be important in influencing delayed neuronal death and subsequent neurologic recovery following traumatic brain injury. Recent data from a neonatal porcine model of circulatory arrest also demonstrated the detrimental effect of hyperthermia on neurologic outcome following DHCA.[66] Mild hypothermia may help attenuate neurologic injury following DHCA, and hyperthermia in the immediate postoperative period should be aggressively treated. A recent study of children after CPB documented that cerebral hyperthermia (measured with jugular venous bulb thermistors) develops in a majority of patients. The mean cerebral temperature was 39.6°C (one patient with 41.4°C) and was underestimated by the use of rectal temperature monitoring (mean 37.7°C).[67]

Choreoathetosis is a rare, yet sometimes devastating, complication following cardiac surgery in children with or without the use of DHCA. It is reported in the neonate, but is more common in older infants. Factors that contribute to the development of choreoathetosis include inadequate brain cooling, particularly to deeper structures such as the basal ganglia and midbrain, a rapid rate of cooling, an alkaline (i.e. α-stat) blood gas strategy during cooling, and the presence of systemic-to-pulmonary artery collateral vessels that may result in a "cerebral steal."[68,69]

## Gastrointestinal problems

Splanchnic hypoperfusion may be secondary to low *CO* from ventricular dysfunction, or from low diastolic pressure in patients with systemic-to-pulmonary artery runoff. It often manifests as a persistent ileus or feeding intolerance; gut ischemia or necrotizing enterocolitis may also develop.

Besides splanchnic hypoperfusion, other causes of feeding intolerance include bowel edema following CPB, delayed gastric emptying secondary to opioids, gastroesophageal reflux, and small bowel obstruction secondary to malrotation, which occurs in some patients with heterotaxy syndrome. Patients with decreased ventricular function may be unable to increase their *CO* sufficiently to meet the metabolic demand associated with oral feeding. Coexisting problems such as tachypnea also restrict oral intake. To ensure adequate nutrition in these situations, placement of a transpyloric feeding tube should be considered.

As in adult ICUs, stress ulceration and gastritis occur in pediatric patients. Prophylaxis with $H_2$ receptor blocking drugs and/or antacids should be used in any patient requiring protracted hemodynamic and respiratory support. Early resumption of enteral nutrition is encouraged to reduce the risk of nosocomial pulmonary and blood infections by preventing bacterial overgrowth.

The onset of abdominal distension, ileus, blood within stool, and pneumatosis intestinalis on abdominal radiograph suggests necrotizing enterocolitis. Severe cases manifest additional signs of abdominal wall cellulitis, sepsis, hemodynamic instability, and gut perforation. Initial treatment includes stopping enteral feeds, and initiating intravenous maintenance fluids and broad-spectrum intravenous antibiotics. Hemodynamic support may be necessary, and occasionally laparotomy if perforation occurs or hemodynamic instability persists.

Factors contributing to postoperative liver dysfunction include complications during CPB secondary to low perfusion pressure or inadequate venous drainage, and persistent low *CO* causing ischemic hepatitis. Following a Fontan procedure, patients may be at particular risk because of hepatic venous congestion from elevated central venous pressure. Marked elevations in liver transaminases may begin within hours of surgery and remain elevated for 2–3 days before gradually returning to normal. These patients also typically have significantly elevated prothrombin and partial thromboplastin times, and thus are at increased risk of bleeding complications. Fulminant hepatic failure is uncommon.

## Chylothorax

Chylothorax may occur from injury to the thoracic duct anywhere along its course from the lower mediastinum to its drainage into the systemic venous system near the left innominate vein. Inadvertent surgical trauma is the most common cause of thoracic duct injury, particularly in repeat operations where identification of anatomic structures is difficult. Chylotorax is heralded by pleural effusions, often left sided, that do not clear with diuresis, and worsen with enteral feeding. First line treatment involves eliminating or restricting enteral intake to non-fat-containing feedings, such as portagen. Persistent chylothorax can be treated with ocreotide, tube drainage, or in severe cases, pleurodesis, or ligation of the thoracic duct. Superior vena cava thrombosis may also cause chylothorax. Most cases can be managed conservatively without surgery.

## Sedation and analgesia

Maintenance of adequate analgesia and sedation is an essential component of patient management following congenital heart surgery. Besides relieving pain and anxiety after surgery

and during procedures, attenuation of the stress response and promoting synchrony with mechanical ventilation are important considerations.

A number of patients, particularly newborns, require resuscitation and stabilization prior to surgery. Sedation and analgesia, with or without neuromuscular blockade, is often necessary to minimize cardiorespiratory work, assist with coordinated mechanical ventilation, and limit patient movement during painful procedures such as catheter placement and balloon septostomy. Drug doses should be titrated to the desired effect; however, children will develop tolerance after a few days of exposure to opioids and have increased dose requirements following surgery.

## Early extubation

Recovery following cardiac surgery and duration of mechanical ventilation depend upon numerous factors, including the patient's preoperative clinical condition, type and duration of surgical procedure, hemodynamic stability, and complications such as postoperative bleeding and dysrhythmias. For the majority of patients with stable preoperative hemodynamics undergoing uncomplicated prolonged surgical repair, postoperative ventilation is not necessary. Once hemodynamically stable, normothermic, and no longer bleeding, patients can be rapidly weaned and extubated. Examples include infants and older children undergoing uncomplicated ASD and VSD repair, RV outflow tract reconstruction and conduit replacement, and following LV outflow tract reconstruction such as aortic valve replacement. Low-dose opioid techniques are used to maintain anesthesia, and following repairs such as an ASD, extubation in the operating room or soon after transfer to the ICU is usually possible.[70] A similar approach for early extubation is applicable to patients following a cavopulmonary anastomosis when early resumption of spontaneous ventilation is preferable because of the potential deleterious effects of positive pressure ventilation on preload and pulmonary blood flow.

Patients undergoing early extubation can be managed with intermittent doses of opioids to ensure adequate analgesia without respiratory depression, and may also benefit from sedation with benzodiazepines to treat restlessness or agitation to prevent dislodgment of transthoracic catheters and chest drains.

Several problems should be anticipated following extubation in the operating room or soon after transfer to the ICU. A mild respiratory acidosis is common and usually resolves within the first 6 hours following surgery.[70] Hypertension and tachycardia may develop during emergence from anesthesia and sedation, increasing the risk for bleeding from operative suture lines; therefore antihypertensive agents may be necessary. Warming blankets should be used to prevent hypothermia and shivering, and the patient closely observed for possible airway obstruction.

## Stress response

Newborns and infants can generate a significant stress response following cardiac surgery and CPB.[71,72] High-dose opioid anesthesia continuing into the initial postoperative recovery has been demonstrated to significantly attenuate this stress response, leading to a reduction in morbidity and possibly mortality. The patients who would most benefit from this approach include those with limited myocardial reserve, labile pulmonary hypertension, myocardial ischemia, and those undergoing complex repairs that have required prolonged CPB and aortic cross-clamp times.

Improvements in preoperative assessment, earlier interventions, and modifications to surgical techniques and CPB have all contributed to improved patient outcome and reduced total ICU stay. Therefore, the notion of extending anesthesia into the ICU is not necessary for all patients, but rather should be considered on a case-by-case basis according to hemodynamic stability after surgery.

Prolonged ventilation may be necessary for some patients because of residual hemodynamic or respiratory complications. Examples include persistent cardiac failure, pulmonary disease, recurrent pleural effusions, sepsis, phrenic nerve injury with diaphragm paresis, and muscle weakness from inadequate nutrition and prolonged paralysis. A slow wean from mechanical ventilation is necessary and appropriate analgesia and sedation is important. Commonly, a combination of benzodiazepines and opioids are effective, although this should be frequently re-evaluated to avoid the complications of tolerance and dependence.

## Assessment

The assessment of adequate analgesia in children can be difficult, particularly when paralyzed and ventilated. Primarily, autonomic signs such as hypertension, tachycardia, pupillary size and diaphoresis are used. If unparalyzed, children will grimace and withdraw from a painful stimulus, and if breathing spontaneously, changes in respiratory pattern such as tachypnea, grunting and splinting of the chest wall may be evident.

However, changes in autonomic signs do not only reflect pain. Other causes include awareness, fever, hypoxemia, hypercapnea, changes in vasoactive drug infusions, and seizures. If not diagnosed correctly, patients may receive additional opioid or benzodiazepine doses when hypertensive and tachycardic, which will only contribute to tolerance and possible withdrawal symptoms later.

## Sedatives

Chloral hydrate is commonly used to sedate children prior to medical procedures and imaging studies.[73] It can be administered orally or rectally in a dose ranging from 50 to 100

mg/kg (maximum dose 1 g). Onset of action is within 15–30 minutes with a duration of action between 2 and 4 hours. Between 10% and 20% of children may have a dysphoric reaction following chloral hydrate, causing them to become excitable and uncooperative. On the other hand, some children may become excessively sedated with associated respiratory depression and inability to protect their airway.

The regular administration of chloral hydrate to provide sedation in the ICU is controversial. Administered intermittently, it can be used to supplement benzodiazepines and opioids, may assist sedation during drug withdrawal, and is useful as a nocturnal hypnotic when trying to establish normal sleep cycles. Repetitive dosing to maintain prolonged sedation is not recommended by the American Academy of Pediatrics and should be avoided in the ICU.[74]

Benzodiazepines are the most commonly used sedatives in the ICU because of their anxiolytic, anticonvulsant, hypnotic, and amnestic properties. While providing excellent conscious sedation, they may cause dose-dependent respiratory depression and result in significant hypotension in patients with limited hemodynamic reserve. Following chronic administration, tolerance and withdrawal symptoms are common.

Midazolam, when administered as a continuous infusion at 0.05–0.10 mg/kg/hour is useful in children following congenital heart surgery.[75] It is short-acting and water soluble, although if *CO* and splanchnic perfusion are diminished, hepatic metabolism is reduced and drug accumulation can occur. Tachyphylaxis can occur within days of commencing a continuous infusion, and withdrawal symptoms of restlessness, agitation and visual hallucinations can occur following prolonged administration. A reversible encephalopathy has been reported following the abrupt discontinuation of midazolam and fentanyl infusions, characterized by movement disorders, dystonic posturing and poor social interaction.[76]

Both diazepam and lorazepam can be effectively used within the ICU, and they possess the advantage of longer duration of action. Prescribed on a regular basis, lorazepam can provide useful longer-term sedation, supplementing an existing sedation regimen and assisting with withdrawal from opioids.

## Opioid analgesics

Opioid analgesics are the mainstay of pain management in the ICU, and in high doses can provide anesthesia. They also provide sedation for patients while mechanically ventilated and blunt hemodynamic responses to procedures such as endotracheal tube suctioning. Hypercyanotic episodes associated with TOF and air hunger associated with congestive heart failure are also effectively treated with opioids.

Intermittent dosing of opioids can provide effective analgesia and sedation following surgery, although periods of over-sedation and under-medication can occur because of peaks and troughs in drug levels. A continuous infusion is therefore advantageous.

Intermittent morphine doses of 0.05–0.1 mg/kg i.v. or as a continuous infusion at 50–100 μg/kg/hour provides excellent postoperative analgesia for most patients. The sedative property of morphine is an advantage over the synthetic opioids; however, histamine release can cause systemic vasodilation and an increase in pulmonary artery pressure. It should therefore be used with caution in patients with limited myocardial reserve and labile pulmonary hypertension.

The synthetic opioids, fentanyl, sufentanil, and alfentanil, have a shorter duration of action than morphine and do not cause histamine release, therefore producing less vasodilation and hypotension. Fentanyl is commonly prescribed following cardiac surgery. It blocks the stress response in a dose-related fashion while maintaining both systemic and pulmonary hemodynamic stability.[77,78] A bolus dose of 10–15 μg/kg i.v. effectively ameliorates the hemodynamic response to intubation in neonates.[79] Patients with high endogenous catecholamine levels, e.g. severe cardiac failure or critical aortic stenosis in the neonate, can become hypotensive after a bolus induction dose, and fentanyl must be used with caution in these conditions. Chest wall rigidity is an idiosyncratic and dose-related reaction that can occur with a rapid bolus in newborns as well as older children.

A continuous infusion of fentanyl 3–10 μg/kg/hour provides analgesia following surgery, although it often needs to be combined with a benzodiazepine to maintain sedation. Large variability between children in fentanyl clearance exists, making titration of an infusion difficult. The experience with ECMO indicates tolerance and dependence to a fentanyl infusion develops rapidly and significant increases in infusion rate may be required.

Sufentanil is more potent than fentanyl, although it has similar effects and offers no specific advantage. A continuous infusion of the ultra-short acting synthetic opioid, remifentanil, may be useful in the ICU for patients with limited hemodynamic reserve undergoing short procedures.

The development of tolerance is dose- and time-related, and is a particular problem following cardiac surgery in patients who received a high-dose opioid technique to maintain anesthesia. Physical dependence with withdrawal symptoms such as dysphoria, fussiness, crying, agitation, piloerection, tachypnea, tachycardia, and diaphoresis may be seen in children and can be managed by gradually tapering the opioid dose or administering a longer-acting opioid such as methadone. Methadone has a similar potency to morphine with the advantage of a prolonged elimination half-life between 18 and 24 hours. It can be administered intravenously and is absorbed well orally. It is particularly useful, therefore, to treat patients with opioid withdrawal.

Alternate methods of opioid delivery which are often effective following cardiac surgery include patient-controlled analgesia and epidural opioids, either as a bolus or continuous infusion. Patients receiving epidural opioids must be closely monitored for potential respiratory depression, and

side effects include pruritis, nausea, vomiting, and urinary retention.

## Non-steroidal analgesics

Non-steroidal anti-inflammatory drugs (NSAIDs) can provide effective analgesia following cardiac surgery, either as a sole analgesic agent or in combination with opioids or local anesthetics. Ketorolac 0.5 mg/kg i.v. every 8 hours is particularly useful as an adjunct to opioids for patients who are weaned and extubated in the early postoperative period. However, there are significant concerns regarding nephrotoxicity and inhibition of platelet aggregation. The incidence of acute renal failure is increased if ketorolac administration is continued for more than 3 days postoperatively, and in general it should be avoided in patients potentially predisposed to renal failure, such as those with hypovolemia, pre-existing renal disease, and low *CO*, and those receiving medications such as angiotensin-converting enzyme (ACE) inhibitors. Acute renal failure is more commonly seen after initiation of treatment, or after an increase in dose, and is reversible in most cases.[80]

Inhibition of platelet aggregation and increased bleeding time may occur following a single intravenous dose of ketorolac, although it has not been demonstrated to increase the risk of surgical site bleeding following cardiac surgery.

Actetaminophen can be given rectally, in an initial dose of 30–40 mg/kg, followed by 15–20 mg/kg every 6 hours for 24–48 hours following surgery. This regimen is desirable because of its adjunctive ability to treat pain and lower temperature without platelet inhibition effects or narcotic side effects.

## Anesthetic agents

### Barbiturates

Thiopental and methohexital are rarely used in the ICU because of direct myocardial depression and venodilation that may cause severe hypotension in patients with limited cardiac reserve.

### Propofol

Propofol is an anesthesia induction agent that can be suitable for use in the ICU for short procedures such as transesophageal echocardiography, pericardiocentesis and cardioversion. Its use, however, is limited because of the potential for hypotension from a decrease in *SVR* and direct myocardial depression. Although it has short duration of action and rapid clearance, propofol is currently not approved for longer-term continuous infusion for sedation in pediatric patients. Nevertheless, it has a useful role in facilitating early extubation. Rather than relying on frequent intermittent doses of opioids and benzodiazepines in small children, a short-term (i.e. 4–6 hours) continuous infusion of propofol at 50–100 μg/kg/minute will keep the patient comfortable, allow for initial recovery after surgery (i.e. to achieve hemostasis and normothermia), and permit rapid weaning and extubation after the infusion is discontinued.

### Ketamine

Ketamine is a "dissociative" anesthetic agent with a rapid onset and short duration of action. It can be effectively administered intravenously or intramuscularly and provides adequate anesthesia for most ICU procedures including intubation, draining of pleural and pericardial effusions, and sternal wound exploration and closure. It produces a type of catalepsy whereby the eyes remain open, usually with nystagmus and intact corneal reflexes. Occasionally nonpurposeful myoclonic movements occur. It causes cerebral vasodilation and should be avoided in patients with intracranial hypertension.

Because hemodynamic stability is generally maintained, it is commonly used in ICUs. Heart rate and blood pressure are usually increased through sympathomimetic actions secondary to central stimulation and reduced post-ganglionic catecholamine uptake. However, it is important to remember that this drug does have direct myocardial depressant effects and should be used with caution in patients with limited myocardial reserve, e.g. neonates with critical aortic stenosis and poor LV function.

Dose-related respiratory depression may occur; however, most patients continue to breathe spontaneously after an induction dose of 2–3 mg/kg i.v. Airway secretions are increased, and even though airway reflexes seem intact, aspiration may occur. It is essential that patients be fasted prior to administration of ketamine and complete airway management equipment must be available. An increase in airway secretions may cause laryngospasm during airway manipulation, and an antisialagogue such as atropine or glycopyrrolate should be administered concurrently. Side effects of emergence delirium and hallucinations may be ameliorated with the concurrent use of benzodiazepines.

There are conflicting reports about the effect of ketamine on *PVR*. One small study in children undergoing cardiac catheterization concluded that *PVR* was increased following ketamine in patients predisposed to pulmonary hypertension.[81] However, another demonstrated minimal effects in young children either breathing spontaneously or during controlled ventilation.[82] On balance, ketamine has minimal effects on *PVR* and can be used safely in patients with pulmonary hypertension, provided secondary events such as airway obstruction and hypoventilation are avoided.

### Etomidate

Etomidate is an anesthetic induction agent with the advantage

of minimal cardiovascular and respiratory depression.[83] An intravenous dose of 0.3 mg/kg induces a rapid loss of consciousness with a duration of 3–5 minutes. It can cause pain on injection and is associated with spontaneous movements, hiccoughing and myoclonus. Etomidate may be used as an alternative to the synthetic opioids for induction of patients with limited myocardial reserve. It is not approved for continuous infusion because adrenal steroidogenesis can be inhibited.

### Muscle relaxants

Muscle relaxants are more commonly used in pediatric ICUs compared to adult units. In addition to their ability to facilitate intubation and controlled mechanical ventilation, patients with limited cardiorespiratory reserve also benefit from paralysis because of reduced myocardial work and oxygen demand. However, prolonged paralysis carries the concomitant risks of prolonged ventilatory support and delayed establishment of entral nutrition, and can result in tolerance and prolonged muscle weakness after discontinuance.

Succinylcholine is a depolarizing muscle relaxant with rapid onset and short duration of action. While frequently used in the pediatric ICU to facilitate intubation, the potential for bradycardia and hyperkalemia side effects following cardiac surgery may be disastrous. Its use should therefore be restricted to patients requiring a rapid sequence induction because of the risk for aspiration of gastric contents. The usual intravenous dose of 1 mg/kg should be increased in newborns and infants to 2 mg/kg because of the greater surface area-to-weight ratio in these patients. It can also be administered intramuscularly in an urgent situation where no vascular access is available, at a dose usually double the intravenous dose (i.e. 3–4 mg/kg). The risk for bradycardia is exaggerated in children, especially after multiple doses, and atropine 20 μg/kg i.v. should be administered concurrently.

Rocuronium is an aminosteroid, non-depolarizing muscle relaxant with fast onset and intermediate duration of action. Time to complete neuromuscular blockade for an intubating dose of 0.6 mg/kg i.v. ranges from 30 to 180 seconds, although adequate intubating conditions are usually achieved within 60 seconds. It is therefore a suitable alternative to succinylcholine during rapid sequence induction. The duration of action averages 25 minutes, although recovery is slower in infants. It is a safe drug to administer to patients with limited hemodynamic reserve and does not cause histamine release.

Vecuronium and *cis*-atracurium are non-depolarizing muscle relaxants with intermediate durations of actions. They can be administered as an intravenous bolus or continuous infusion within the ICU. Both of these agents have minimal effect on the circulation and can be administered safely to patients with limited hemodynamic reserve.

Pancuronium is a commonly used, longer-acting, non-depolarizing relaxant that can be administered intermittently at a dose of 0.1 mg/kg i.v. It can cause a mild tachycardia and increase in blood pressure, but is also safe to administer to patients with limited hemodynamic reserve.

## Criteria for intensive care unit discharge

As patients improve after surgery and require less intensive monitoring and therapy, the timing of discharge from the ICU becomes an important management decision. For the majority of patients who have stable hemodynamics without significant residual defects, and who have been weaned and extubated uneventfully after surgery, the decision to transfer out of the ICU is not difficult. The function of all organ systems should be assessed and considered in this decision, although the focus will be on cardiovascular and respiratory function. The cost of intensive care medicine is high, and early rather than delayed discharge is recommended. Indeed, as the mortality and morbidity associated with congenital cardiac surgery have declined, length of ICU stay, total hospital stay, and cost effectiveness have become important outcome variables.

In addition to poor *CO* and residual anatomic lesions, there are a variety of non-cardiac problems that can complicate recovery and prolong ICU stay. Many of these problems affect respiratory function and cause inability to wean from mechanical ventilation (see the Mechanical ventilation section above). Table 27.7 provides a list of cardiovascular and

**Table 27.7** Criteria for intensive care unit discharge.

*Cardiovascular*
- Stable and desired blood pressure without requiring intravenous vasoactive support
- Invasive intravascular monitoring no longer required for monitoring or blood sampling
- No requirement for mechanical pacing using temporary wires and an external pacemaker
- Stable cardiac rhythm (preferably sinus) with a stable blood pressure and cardiac output

*Respiratory*
- Not dependent on mechanical ventilatory support
- Stable and adequate ventilation rate and pattern, and no signs of airway obstruction
- Stable and adequate oxygenation ($Po_2$ depends on lesion and physiology after repair or palliation) ± supplemental $O_2$ via nasal cannula, mask, or blow-by
- Neurologic status adequate to protect airway from aspiration
- Appropriate nursing intensity:
  - Chest physical therapy or bronchodilator treatments at least 3 h apart in frequency
  - Established nutrition plan (enteral or parenteral)
  - Controlled analgesic or sedation requirements

respiratory criteria for consideration prior to patient discharge from the ICU. It is important to emphasize that this decision should be multidisciplinary, with particular attention paid to nursing availability and experience, and availability of adequate monitoring.

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## Appendix: Texas Children's Hospital Pediatric Cardiovascular Anesthesia Drug Sheet

November 2003

**Vasoactive infusions** – standard concentrations denoted.

| | |
|---|---|
| Dopamine 3.2 mg/ml | 3–20 mcg/kg/min |
| Dobutamine 4 mg/ml | 3–20 mcg/kg/min |
| Milrinone 0.2 mg/ml | 0.125–0.75 mcg/kg/min<br>Loading: 25–50 mcg/kg/over 30″ |
| Epinephrine 0.1 mg/ml | 0.03–1 mcg/kg/min |
| Norepinephrine 0.1 mg/ml | 0.05–1 mcg/kg/min |
| Isoproterenol 0.1 mg/ml | 0.03–1 mcg/kg/min |
| Phenylephrine 20 mcg/ml | 0.05–0.5 mcg/kg/min |
| Sodium nitroprusside 0.4 mg/ml | 0.05–5 mcg/kg/min |
| Nitroglycerine 0.4 mg/ml | 0.5–5 mcg/kg/min |
| Prostaglandin E1 20 mcg/ml | 0.03–0.1 mcg/kg/min |
| Lidocaine 5 mg/ml | 20–50 mcg/kg/min<br>Loading: 1–2 mg/kg |
| Procainamide 10 mg/ml | 20–80 mcg/kg/min<br>Loading: 10–15 mg/kg over 60″ |
| Esmolol 10 mg/ml | 50–100 mcg/kg/min<br>Loading: 250–500 mcg/kg over 1″ |
| Vasopressin 0.2 units/ml | 0.0003–0.002 units/kg/min |
| Fenoldepam 40 mcg/ml | 0.025–0.3 mcg/kg/min initially, titrate to max 1.6 mcg/kg/min |

**Vasoactive bolus drugs**

| | |
|---|---|
| Epinephrine | 0.5–10 mcg/kg |
| Atropine | 10–20 mcg/kg IV; 20–40 mcg/kg IM; max 1 mg |
| Phenylephrine | 0.5–3 mcg/kg |
| $CaCl_2$ | 10 mg/kg |
| Ca gluconate | 30 mg/kg |
| Adenosine | 25–50 mcg/kg – double if ineffective |
| Labetalol | 0.25–0.5 mg/kg |
| Amiodarone | 5 mg/kg over 10–15″, may repeat × 2 to max 15 mg/kg |
| Verapamil | 0.1–0.3 mg/kg |
| Propranolol | 0.01–0.1 mg/kg |
| Bretylium | 5 mg/kg; increase to 10 mg/kg if ineffective |
| Phenoxybenzamine | 0.25–1 mg/kg |
| Hydralazine | 0.1–0.2 mg/kg |
| Phentolamine | 0.1–0.2 mg/kg on CPB |
| Ephedrine | 0.1 mg/kg, max 5 mg |

**Miscellaneous drugs for cardiac anesthesia**

| | |
|---|---|
| Heparin (100 units = 1 mg) | 300–400 U/kg for CPB; 100 U/kg for heparinization for closed cases |
| Protamine | 1–1.3 times the heparin dose in mg |
| Furosemide | 0.5–1 mg/kg, max 20 mg |
| Sodium Bicardonate | 1–3 meq/kg; dilute 1:1 sterile $H_2O$ for newborns |
| THAM | 3–6 ml/kg |
| Cefazolin | 25–30 mg/kg |
| Nafcillin | 50 mg/kg, max 2 g |
| Gentamycin | 2 mg/kg, max 120 mg |
| Ampicillin | 50 mg/kg, max 2 g |
| Clindamycin | 20 mg/kg max 600 mg |
| Cefuroxime | 20–30 mg/kg |
| Vancomycin | 20 mg/kg, max 1 g |
| Methylprednisolone | 30 mg/kg in CPB circuit |
| Dexamethasone | 0.25 mg/kg for airway edema |
| Hydrocortisone | 1–2 mg/kg for adrenal suppression |
| Digoxin | 8–10 mcg/kg 1st loading dose |
| Naloxone | 1–10 mcg/kg, repeat as necessary |
| Flumazenil | 1–5 mcg/kg, repeat as necessary |
| Dextrose 50% | 0.5–1 ml/kg; dilute 1:1 sterile $H_2O$ |
| Mannitol | 0.25–0.5 g/kg |
| Amicar | 75 mg/kg load into patient over 5–10″, then 75 mg/kg/hr infusion; and 75 mg/kg into CPB circuit; 75 mg/kg/hr after bypass |
| Aprotinin | 60,000 KIU/kg load over 30″, 60,000 KIU/kg into CPB circuit, then 7000 KIU/kg/hr infusion; max 200 ml load and 50 ml/hr |
| KCI | 0.5–1 meg/kg over 1 hour |
| MgSO4 | 25–50 mg/kg/over 1 hour |
| Ranitindine | 1 mg/kg |
| Diphenhydramine | 1–2 mg/kg |
| Albuterol | 8–16 puffs MDI per ETT |
| Metaclopromide | 0.15–0.3 mg/kg; max 10 mg |
| Ondansetron | 0.1–0.15 mg/kg; max 4 mg |
| Inhaled nitric oxide | 10–40 PPM |

**Anesthetic agents and muscle relaxants**

| | |
|---|---|
| Isoflurane | 0.2–2% inspired concentration |
| Halothane | 0.2–3% inspired concentration; for induction only |
| Sevoflurane | 0.5–6% inspired concentration |
| $MSO_4$ | 0.05–0.2 mg/kg |
| Fentanyl | 1–10 mcg/kg bolus; 50–200 mcg/kg total dose; 5–20 mcg/kg/hr infusion |
| Remifentanil | (50 mcg/cc) 0.05–2 mcg/kg/min IV infusion |
| Midazolam | 0.03–0.1 mg/kg per dose; 0.5–1 mg/kg total dose |
| Lorazepam | 0.05–0.1 mg/kg |
| Pancuronium | 0.1–0.2 mg/kg |
| Vecuronium | 0.1–0.4 mg/kg |
| Rocuronium | 0.6–1.2 mg/kg IV; 2 mg/kg IM |
| Atracurium | 0.4–0.5 mg/kg |
| Succinylcholine | 1–2 mg/kg IV; 4 mg/kg IM |
| Neostigmine | 70 mcg/kg |
| Glycopyrrolate | 14 mcg/kg |
| Thiopental | 1–4 mg/kg |
| Ketamine | 1–2 mg/kg IV; 5–10 mg/kg IM |
| Etomidate | 0.1–0.3 mg/kg |
| Propofol | 1–3 mg/kg industion; 50–200 mcg/kg/min maintenance |
| Bupivacaine 0.25% (caudal) | 0.5–1 ml/kg |
| Ropivacaine 0.2% (caudal) | 0.5–1 ml/kg |
| Clonidine (caudal) | 1–2 mcg/kg |
| $MSO_4$ (caudal, preservative-free) | 25–75 mcg/kg |

**Blood products and volume expanders**

| | |
|---|---|
| 5% albumin | 10–20 ml/kg |
| 25% albumin | 2–4 ml/kg; 0.5–1 g/kg |
| Platelets | 1 unit per 5 kg will increase plt count by approximately 50,000 |
| FFP | 10–20 ml/kg |
| PRBC's | 10–15 ml/kg |
| Cryoprecipitate | 1 unit per 5 kg; max 4 units |
| Whole blood | 10–15 ml/kg |
| Hetastarch | 5–10 ml/kg; max 15 ml/kg per 24 hours |

**DC defibrillation / sychronized cardioversion**

Internal defibrillation: 5 J; increase to 10
External defibrillation: 2–5 J/kg; increase if ineffective
External synchronized cardioversion: 0.5 J/kg

# Index

Note: Page numbers in **bold** refer to tables; those in *italics* refer to figures.

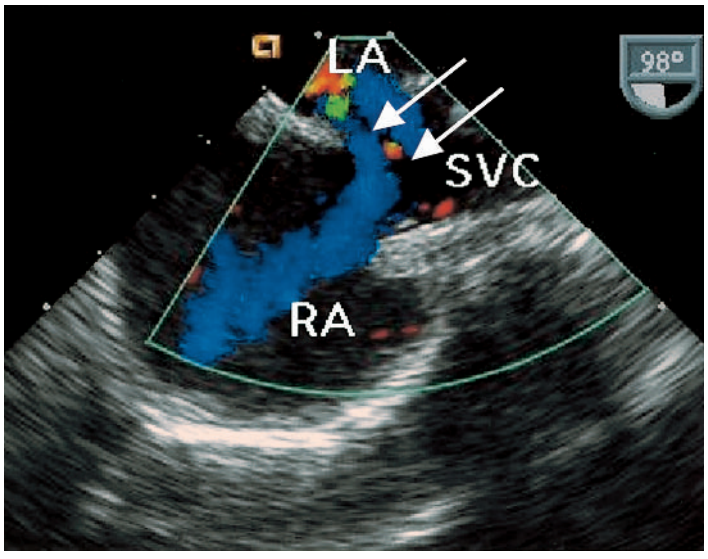


**Fig. 9.7** (b) Sinus venosus atrial septal defect. Color Doppler exam a of superior vena cava-type sinus venosus atrial septal defect in the bicaval view. Left-to-right shunting across the defect is noted in the superior aspect of the interatrial septum (arrows).

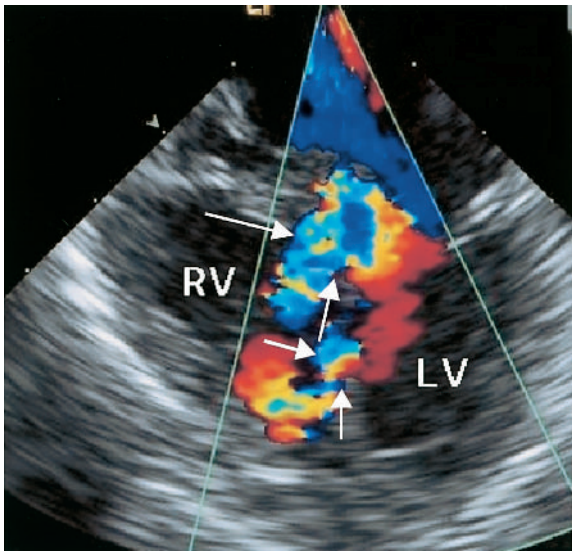


**Fig. 9.7** (e) Muscular ventricular septal defects. Color Doppler interrogation of the muscular septum in the four-chamber view documents multiple levels of ventricular shunting.

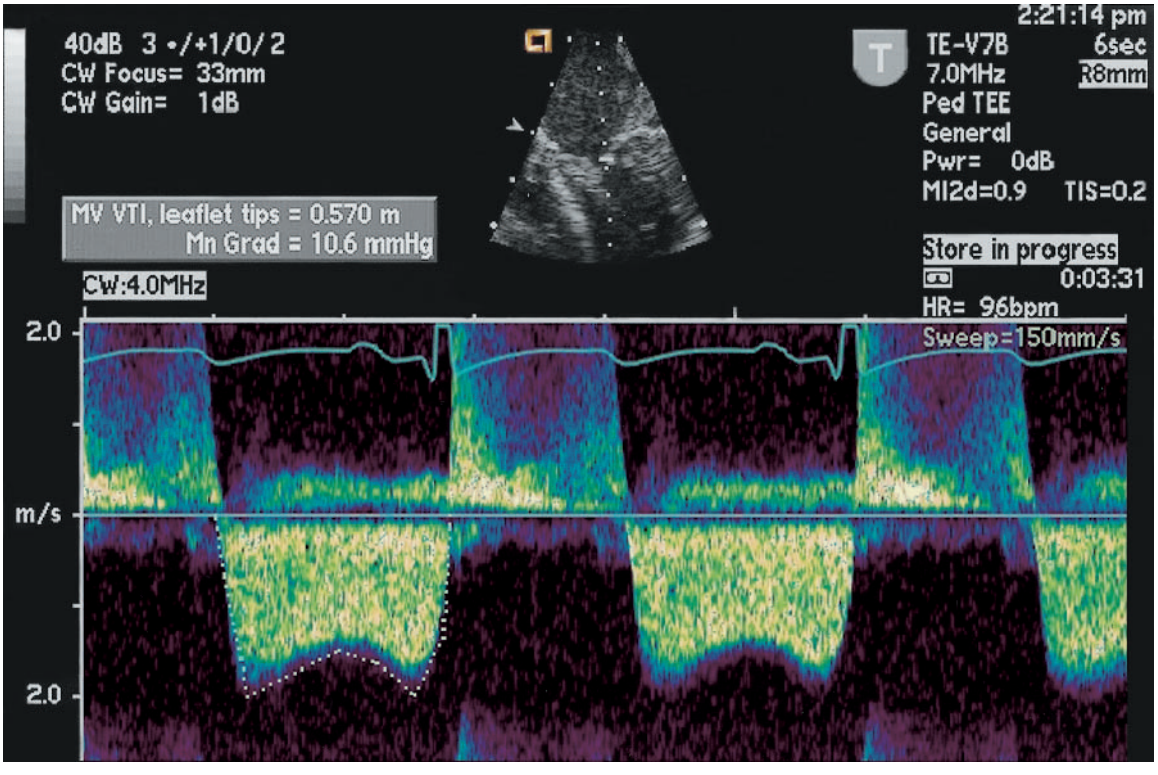


**Fig. 9.8** (f) Mitral stenosis. Spectral Doppler interrogation in a patient with moderate to severe mitral valve obstruction demonstrating an estimated mean transmitral gradient of 10.8 mmHg by continuous wave Doppler.

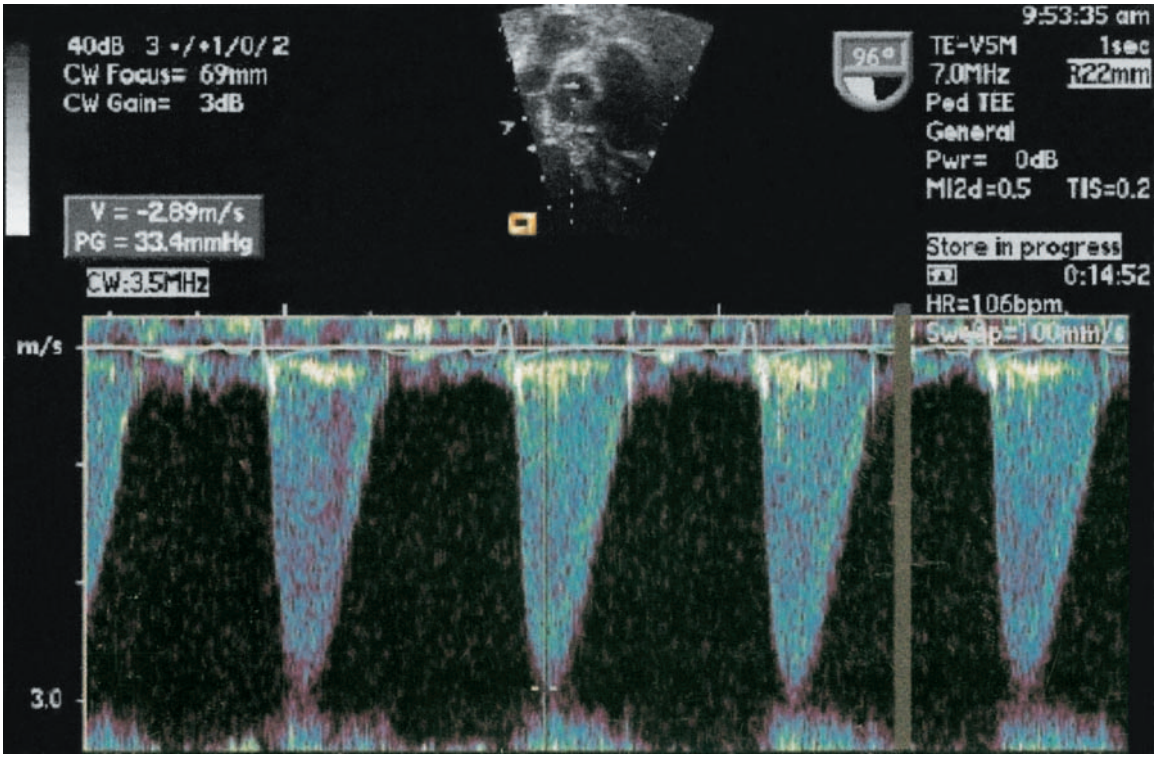


**Fig. 9.10** Continuous wave Doppler interrogation of left ventricular outflow tract in patient with subaortic obstruction demonstrating gradient estimation peak velocity across outflow measures 2.89 m/second, predicting a peak gradient of 33.4 mmHg (obtained by application of the modified Bernoulli equation or $4(V)^2$).

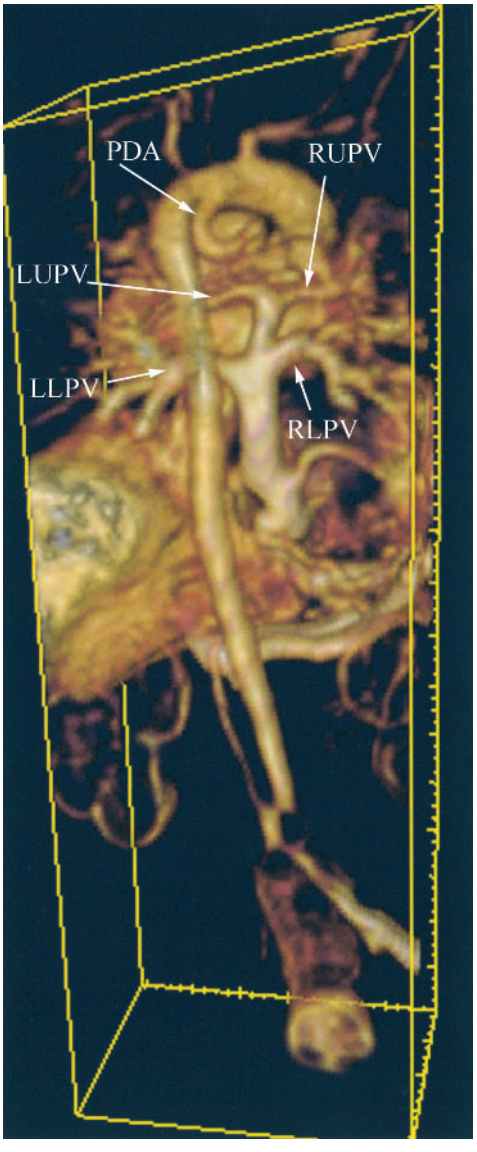


**Fig. 26.1** A neonate with infradiaphragmatic total anomalous pulmonary venous return. LLPV, left lower pulmonary vein; PDA, patent ductus arteriosus; RLPV, right lower pulomonary vein; RUPV, right upper pulmonary vein.