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## KEY POINTS

- Organ system maturation, from birth through adolescence, affects physiologic function and therefore anesthetic and surgical management and outcome.
- The understanding of congenital heart disease (CHD) and consequent anesthetic management is based on the pathophysiologic determinants of four categories of defects: shunts, mixing lesions, stenotic lesions, and regurgitant lesions.
- The chronic sequelae of CHD (repaired, palliated, or unrepaired) affect anesthetic management: ventricular failure, residual hemodynamic effects (e.g., valve stenosis), arrhythmias, and pulmonary blood flow changes (e.g., pulmonary artery hypertension).
- Preoperative assessment of cardiac status and planning are the keys to a successful anesthesia outcome.
- Intraoperative transesophageal echocardiography and central nervous system (CNS) monitoring enhance surgical outcome and reduce morbidity.
- The induction technique needs to consider degree of cardiac dysfunction, cardiac defects, level of sedation achieved with premedication, and the presence of an indwelling venous catheter. Other factors to be considered include pulmonary hypertension, electrical rhythm disorders, and other comorbidities.
- The maintenance of anesthesia depends on the age and condition of the patient, the nature of the surgical procedure, the duration of cardiopulmonary bypass (CPB), and the need for postoperative ventilation. It is usually desirable to return the patient to an arousable, sedated state with spontaneous ventilation at the end of the procedure.
- The physiologic effects of CPB on neonates, infants, and children are significantly different from the effects on adults. During CPB, pediatric patients are exposed to biologic extremes not seen in adults, including deep hypothermia (18°C), increased hemodilution, low perfusion pressures, and wide variation in pump flow rates.
- After repair of complex congenital heart defects, separating patients from CPB may be difficult. The causes may be an inadequate surgical result, pulmonary artery hypertension, low systemic vascular resistance, low hemoglobin, and right or left ventricular dysfunction.
- The use of modified ultrafiltration (MUF) reverses the deleterious effects of hemodilution and the inflammatory response associated with CPB in children. Furthermore, with MUF perioperative blood loss and blood use are significantly reduced, left ventricular function and systolic blood pressure are improved, oxygen delivery is increased, and pulmonary compliance and brain function are also better.
- Neonates, infants, and children undergoing cardiac surgery with CPB have a more frequent rate of postoperative bleeding than that seen in older patients. This is due to an inflammatory response that a disproportionate exposure to the nonendothelialized extracorporeal circuit produces, the type of surgery performed in neonates and infants that involves more extensive reconstruction and suture lines, the frequent utilization of deep hypothermia or circulatory arrest, a more immature coagulation system in neonates, and an increased bleeding tendency in patients with cyanotic heart disease.
- The management of the postoperative patient warrants an understanding of both normal and abnormal convalescence after anesthesia and cardiac surgery, as it is characterized by continuous physiologic change.
- The care of adults with CHD is a new and expanding field of medicine that requires the skilled management of an experienced multidisciplinary team.
- Additional anesthetic considerations exist in patients with CHD who undergo transplantation, closed heart operations without CPB, cardiac interventional procedures, and noncardiac surgery.

Cardiac surgery is an established and effective treatment for children with congenital heart defects. Early successes in surgical treatment led to a new therapeutic era in the management of congenital heart disease (CHD) and fostered the development of the subspecialties for pediatric cardiology and cardiac surgery and their collaboration. Through this cooperative effort, tremendous progress in medical diagnosis and surgical treatment has been achieved. In turn, these accomplishments gave rise to the development of pediatric cardiac anesthesiologists, individuals who understand the pathophysiology of congenital heart malformations, the diagnostic and surgical procedures used to treat heart disease, and the principles of pediatric and cardiac anesthesia and intensive care medicine. Pediatric cardiac anesthesia continues to evolve as an exciting and technically demanding subspecialty in which anesthetic management is based on physiologic principles.

Cardiovascular surgery and anesthesia in CHD are often performed under unusual physiologic conditions. Rarely in clinical medicine are patients exposed to such biologic extremes as during surgery for CHD. Commonly, patients are cooled to 18°C, are acutely hemodiluted by more than 50% of their extracellular fluid volume, and undergo periods of total circulatory arrest lasting up to 1 hour. Management of patients under these physiologic extremes is a vital function of the pediatric cardiovascular anesthesiologist. As with other areas of medicine, the application and management of technology preceded a comprehensive understanding of its physiologic effects.

Clearly, the perioperative management of these complex cases requires a group of physicians (surgeon, anesthesiologist, cardiologist, critical care specialist), nurses, and perfusionists to work as a team. Although the quality of the surgical repair, the effects of cardiopulmonary bypass (CPB), and postoperative care are the major determinants of outcome, meticulous anesthetic management is also imperative. Ideally, despite the complexity of the cases and the marked physiologic changes attributed to CPB and the surgical procedures, anesthetic care should never contribute substantially to morbidity or mortality.<sup>1</sup> The challenge is to understand the principles underlying the management of patients with CHD and apply them to clinical anesthesia.

## Unique Features of Pediatric Cardiac Anesthesia

Pediatric cardiovascular management is unique, with important differences from adult cardiac surgery (Box 78.1). These differences are attributable to normal organ system maturation in the neonate and young infant, differing pathophysiologic conditions in CHD, the diversity of surgical repairs, and the use of specialized CPB techniques such as deep hypothermia, total circulatory arrest, cerebral regional perfusion, and three-region perfusion techniques.

## PHYSIOLOGIC CONSIDERATIONS AND MATURATIONAL FEATURES OF THE PEDIATRIC PATIENT

The cardiovascular system changes markedly at birth because of a dramatic alteration in blood flow patterns

### BOX 78.1 Unique Characteristics of Pediatric Cardiac Anesthesia

#### Patient

Normal organ system development and maturational changes of infancy

*Cardiovascular:* Blood flow patterns of circulation at birth, myocardial compliance, systemic and pulmonary vasculature, and  $\beta$ -adrenergic receptors

*Pulmonary:* Respiratory quotient, closing capacity, chest compliance

*Central nervous system:* Brain growth, cerebral blood flow, autonomic regulation

*Renal:* Glomerular filtration rate, creatinine clearance

*Hepatic:* Liver blood flow, microsomal enzyme activity

Disease and growth interrelationship

Effects of systemic disease alter somatic and organ growth

Compensatory ability of developing organs to recover from injury

Immunologic immaturity of the infant

Obligatory miniaturization (i.e., small patient size and body surface area)

#### Congenital Heart Disease

Diverse anatomic defects and physiologic changes

Altered ventricular remodeling owing to myocardial hypertrophy and ischemia

Chronic sequelae of congenital cardiac disease

#### Surgical Procedures

Diversity of operations

Frequent intracardiac and right ventricular procedures

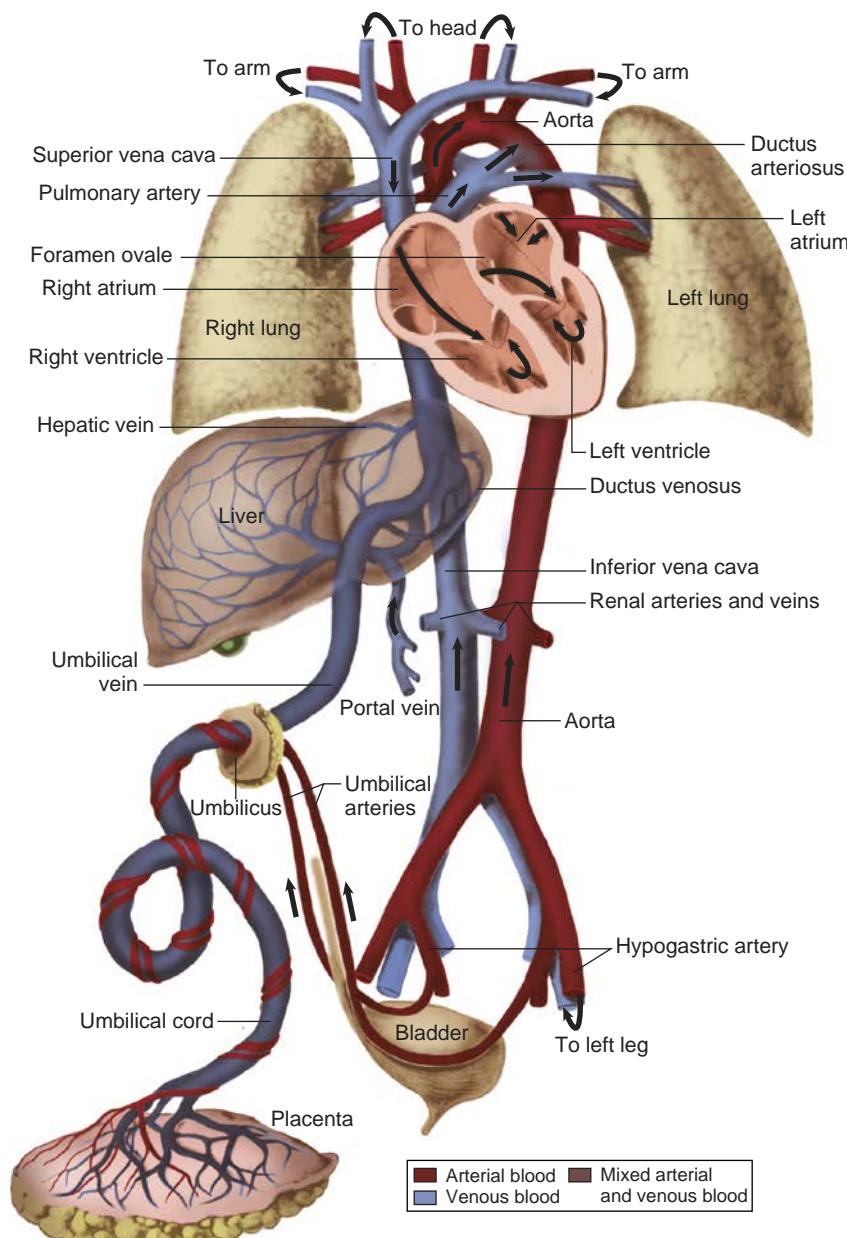
Use of deep hypothermia and circulatory arrest during repair

Trend toward repair in early infancy

Evolution of surgical techniques to avoid residua and sequelae

Trend toward wider application of certain operations

(Fig. 78.1). During fetal life, blood flow returning to the right atrium (RA) bypasses the unventilated fluid-filled lungs. Blood is then preferentially shunted across the patent foramen ovale into the left atrium (LA) or passes from the right ventricle (RV) across the patent ductus arteriosus (PDA) to the systemic circulation. At birth, physiologic closure of the PDA and of the foramen ovale brings about the normal adult circulatory pattern. The presence of certain congenital heart defects or pulmonary disease can disrupt this normal adaptive process, creating a transitional circulation in which right-to-left shunting persists across the foramen ovale or the PDA. Under such circumstances, the continued presence of a transitional circulation can lead to severe hypoxemia, acidosis, and hemodynamic instability, which are poorly tolerated in the neonate. In contrast, when initially treating some forms of CHD, the prolongation of this transitional circulation is actually beneficial, promoting systemic blood flow or pulmonary blood flow (PBF) and postnatal viability. An example of the latter is pulmonary atresia, in which PBF is supplied via the PDA. In the absence of collateral vessels, closure of the PDA eliminates the principal source of PBF, resulting in hypoxemia and death. In such patients, ductal patency can be maintained with the administration of prostaglandin E1. Importantly, the transitional circulation can be manipulated by pharmacologic and ventilatory strategies, thereby promoting hemodynamic stability.



**Fig. 78.1 Course of the fetal circulation in late gestation.** Note the selective blood flow patterns across the foramen ovale and the ductus arteriosus.

Another unique feature of the normal neonatal and infant cardiovascular system is the reduced myocardial reserve in contrast to that in the healthy adult. The newborn left ventricular function is restricted by a reduced number of  $\alpha$ -adrenergic receptors, high resting levels of circulating catecholamines, limited recruitable stroke work, an immature calcium transport system, and decreased ventricular compliance.<sup>2</sup> These factors limit contractile reserve with the result of a left ventricle (LV) with a high level of resting tone. Although the resting performance of the neonatal myocardium may be greater than in adults and older children, sensitivity to  $\beta$ -blockade is greater and only modest increases occur in cardiac performance after administration of the  $\beta$ -agonist drugs dobutamine and isoproterenol.<sup>3</sup> Furthermore, the contractile mass of the heart is effectively reduced, resulting in a ventricle with

low compliance. Preload augmentation is effective at low filling pressures (1-7 mm Hg). However, when left-sided filling pressures exceed 7 to 10 mm Hg, further increases in left ventricular stroke volume are minimal.<sup>2</sup> As a consequence, neonates are more dependent on heart rate and, to a lesser extent, on preload, to maintain cardiac output at filling pressures of 7 to 10 mm Hg or greater.<sup>4</sup> Additionally, the calcium transport system in the neonatal myocardium is underdeveloped. The neonatal heart therefore depends more on extracellular calcium levels than the adult myocardium,<sup>5,6</sup> and normal or even elevated plasma levels of ionized calcium may be necessary to augment or maintain an effective stroke volume. This is in contrast to adult cardiac patients, in whom calcium use during cardiac surgery has fallen into some disfavor, owing to direct concerns over myocardial ischemia and reperfusion injury.

Another unique feature relates to the pulmonary circulation. The pulmonary circulation undergoes significant changes during the first months of life. In the immediate newborn period, the large decrease in pulmonary vascular resistance (PVR) is due to lung expansion and the vasodilatory effects of a higher  $\text{PaO}_2$  than existed in utero. Further decline in PVR throughout the next 2 months of life is attributable to regression of the smooth muscle layer in the pulmonary arterioles. A corresponding decrease in pulmonary artery pressure occurs as PVR declines. Acute physiologic stress in the newborn period, such as hypoxemia or acidosis, may increase pulmonary artery pressure and thus PVR. If the resulting right ventricular hypertension causes reduced right ventricular compliance, right-to-left shunting can occur at the foramen ovale. Once PVR exceeds systemic vascular resistance (SVR), right-to-left shunting develops at the PDA. Either phenomenon will worsen the hypoxemia and eventually limit tissue oxygen ( $\text{O}_2$ ) delivery. In contrast, left-to-right shunts, such as those present with a ventricular septal defect (VSD), increase PBF which over time produces intimal changes in the pulmonary vasculature, delaying regression of medial muscle hypertrophy and producing persistent elevation of PVR.

Size differences between adult and pediatric cardiac patients require different anesthetic techniques and miniaturization. Anatomically, pediatric patients have smaller upper and lower airways, smaller veins and arteries, and decreased body surface area compared to adult patients; these differences have anesthetic implications. Availability of ultrasound has made placement of arterial catheters more expedient, even in the smallest patients, reducing the need for arterial cutdown. Pulmonary artery catheters are used infrequently because of technical difficulties in positioning the tip in the pulmonary artery and because of the fundamental fact that pulmonary flow bears no obligatory relationship to systemic output in children with either intracardiac or extracardiac communications. Transthoracic catheters for pressure monitoring and delivery of vasoactive substances may be placed from the surgical field instead of percutaneous approach via the neck. Adequacy of surgical repair and function is assessed by transesophageal echocardiography (TEE) with Doppler color flow imaging with miniaturized probes.<sup>7,8</sup>

Patient size also influences CPB management. The ratio of pump priming volume to patient blood volume is considerably higher in small children than in adults, resulting in a greater degree of hemodilution. Several studies demonstrated a heightened inflammatory response to CPB in children in contrast to in adults<sup>9</sup> related to the disproportionate exposure of the child's blood elements to the nonendothelialized surfaces of the pump circuit per body surface area.

In pediatric patients with CHD, the cardiovascular system often represents the sole cause of the medical problem. A special disease and growth interrelationship, unique to growing infants and children, permits developing organs to compensate for and modify existing disease processes. Reparative and recuperative processes in children are greater as a result of this compensatory ability of developing organ systems. Despite adaptation to their cardiovascular pathologic processes CHD pediatric patients do experience

detrimental and sometimes permanent effects on somatic growth and on the growth and development of the brain, myocardium, and lung.

The premature infant with CHD deserves special consideration. Premature infants are classified as low birth weight (31-34 weeks, 1-1.5 kg), very low birth weight (26-30 weeks, 600 g-1 kg), and extremely low birth weight (<26 weeks, 400-600 g). Respiratory failure is common and multifactorial. The small airways are prone to obstruction, which results in increased airway resistance and work of breathing with easy fatigability. Lung compliance is reduced because of a deficiency of surfactant, resulting in intrapulmonary shunting and ventilation-perfusion mismatch. Mechanical ventilation prevents alveolar collapse, maintains patency of the airway, and maintains lung volume, preventing hypoxia, but must be used cautiously as premature lungs are susceptible to barotrauma and oxidant injury. Ventilatory strategies for lung protection include reduced peak inspiratory pressures and the lowest inspired oxygen concentration that produces reasonable levels of oxygenation.

Premature infants are also prone to perioperative periods of apnea that may be central in origin or obstructive, either of which can be aggravated by anesthetic drugs. Apnea may also be precipitated by abrupt changes in oxygenation or pulmonary mechanics, brain hemorrhage, and hypothermia. After emergence from anesthesia, sustained apnea may occur and persist for up to 48 hours. Continuous apnea and saturation monitoring with correction of anemia (hematocrit > 30) and intravenous administration of caffeine are therapeutic options. The incidence of postoperative apnea is related to postconceptional and gestational age, the presence of anemia, and the type of surgical procedure.

Cardiac pathophysiology can compound respiratory concerns. The premature heart is a poorly contractile organ with poor diastolic function, and is sensitive to changes in intracellular calcium. Cardiac output depends chiefly on heart rate, with marginal reserve. The premature infant also has a relatively low absolute blood volume and tolerates blood loss poorly. Autoregulation is not well developed, and blood loss compromises cerebral and coronary flow before other manifestations of hypovolemia. However, fluid overload is also not well tolerated. Patency of the ductus arteriosus results in left-to-right shunting and pulmonary overcirculation with heart failure (HF). If uncorrected, this would result in pulmonary hypertension secondary to the development of pulmonary vascular intimal hypertrophy.

Thermoregulation by nonshivering thermogenesis is also poor owing to inadequate stores of brown fat in prematurity. It is critical to maintain normothermia by increasing the operating room temperature, using incubators for transport, warming and humidifying respiratory gases, and warming all intravenous fluids. Glycemic control is difficult, with a tendency to both hypoglycemia and hyperglycemia. Frequent glucose checks are important. Parenteral glucose solutions should be continued in the perioperative period. Premature infants are also prone to retinopathy of prematurity with high inspired  $\text{O}_2$  concentrations and intraventricular hemorrhage. Every

attempt should be made to avoid hemodynamic perturbances and fluctuation in  $O_2$  saturations. In general, immaturity of organ systems results in both increased drug effect and duration of action, warranting careful titration of drugs.

Premature infants have a twofold increase in cardiovascular malformations compared with term infants.<sup>10</sup> One in six infants with CHD, not including those with PDA or atrial septal defect (ASD), is born prematurely. Some malformations such as tetralogy of Fallot (TOF), pulmonary stenosis, pulmonary atresia with VSD, complete atrioventricular (AV) septal defect, large VSDs in isolation or associated with coarctation, and aortic stenosis are more prevalent in this population.<sup>11</sup> A significant increase in the likelihood of being small for gestational age is seen among infants with TOF, complete AV septal defect, hypoplastic left heart, pulmonary stenosis, or large VSD.<sup>12</sup>

While cardiac catheterization, intervention, and complete surgical repair in the newborn of very low birth weight ( $<1.5$  kg) can be successfully undertaken with low risk, it is notable that given the complexity of premature organ systems and superimposed cardiorespiratory pathophysiology, morbidity and mortality are increased.<sup>13,14</sup> Low-birth-weight neonates with complex single ventricle disease undergoing surgical palliation have a significant mortality risk.<sup>15,16</sup> Interventional catheterization in premature infants is associated with a higher risk for complications related to vascular access, arrhythmias, and respiratory compromise.<sup>13</sup> Maintenance of euglycemia and normothermia and attention to fluid and electrolyte balance are important.  $O_2$  delivery is optimized by maintaining age-appropriate blood pressures, adequate intravascular volume, and hematocrit. Any acidosis must be sought and aggressively corrected. Whenever possible, such infants should recover in a specialized pediatric cardiac intensive care unit (ICU).

## CONGENITAL HEART DISEASE

The marked array of anatomic and physiologic conditions seen with CHD distinguishes these processes from acquired adult cardiac disease. The spectrum of intracardiac shunts, valve pathologies, disrupted great artery connections, and the absence of one or more chambers of the heart preclude a uniform anesthetic approach to patients with CHD. Moreover, myocardial changes result from the hemodynamic impact and increased cardiac work incurred by these defects. Functionally, these myocardial changes place the ventricles at great risk for the development of intraoperative ischemia and failure. Therefore, an understanding of the isolated defect, associated myocardial changes, and hemodynamic consequences is fundamental to planning an appropriate anesthetic regimen. Distilling CHD into a finite number of physiologic categories enables the anesthesiologist to construct a strategy that employs the qualitatively predictable impact of drugs, ventilatory management, and fluid administration to optimize cardiovascular performance. Although an isolated heart malformation may be identified, the entire cardiopulmonary system is usually affected.

**TABLE 78.1** Classification of Congenital Heart Defects

Physiologic Classification	Pulmonary Blood Flow	Comments
Left-to-right shunts		
VSD	↑	Volume-overloaded ventricle
ASD		
PDA		Development of CHF
AV canal		
Right-to-left shunts		
Tetralogy of Fallot (TOF)	↓	Pressure-overloaded ventricle
Pulmonary atresia/VSD		Cyanotic
Eisenmenger complex		Hypoxemia
Mixing lesions		
Transposition/VSD	Generally↑ but variable Qp/Qs	Variable pressure versus volume loaded
Tricuspid atresia		Usually cyanotic
Anomalous venous return		
Univentricular heart		
Obstructive lesions		
Interrupted aortic arch		Ventricular dysfunction
Critical aortic stenosis		Pressure-overloaded ventricle
Critical pulmonic stenosis		Ductal dependence
Hypoplastic left heart syndrome		
Coarctation of the aorta		
Mitral stenosis		
Regurgitant lesions		
Ebstein anomaly		Volume-overloaded ventricle
Other secondary causes		
		Development of CHF

ASD, Atrial septal defect; AV, atrioventricular; CHF, congestive heart failure; PDA, patent ductus arteriosus; Qp, pulmonary blood flow; Qs, systemic blood flow; VSD, ventricular septal defect.

## Physiologic Approach to Congenital Heart Disease

Although the structural variations seen in CHD constitute an encyclopedic list of malformations, anesthetic management is more logically designed to achieve physiologic goals. A general physiologic classification is listed in Table 78.1. Fortunately, although structurally complex, these defects can be understood within a more limited physiologic spectrum. Identification and classification on the basis of physiology provide an organized framework for the intraoperative anesthetic management and postoperative care of children with complex congenital cardiac defects. In general, congenital heart lesions fit into one of four categories: shunts, mixing lesions, flow obstruction, and regurgitant valves (see Table 78.1). Each category imposes at least one of three pathophysiologic states: ventricular volume overload, ventricular pressure overload, or hypoxemia. Ultimately, these pathophysiologic conditions can result in myocardial failure or pulmonary vascular disease. Medical and surgical perioperative

management strategies focus on minimizing the pathophysiological consequences of these lesions.

**Shunt Lesions.** Shunts are intracardiac connections between chambers (e.g., ASD or VSD) or extracardiac connections between a systemic and pulmonary artery (e.g., PDA). The direction of blood flow through the shunt depends on the relative resistances on either side of the shunt and on the size of the shunt orifice. The direction and magnitude of shunt at the atrial level are additionally governed by the relative differences in ventricular compliance and respective AV valve function. With a nonrestrictive VSD or PDA that does not impede blood in either direction, the main determinant of the direction of blood flow is relative resistance between the pulmonary and systemic vascular beds. The effect that a shunt lesion has on the cardiovascular system depends on both the size of the shunt and its direction.

Left-to-right shunts occur when the PVR is lower than the SVR, so that blood flow is preferentially directed toward the lungs, resulting in increased PBF. In patients with large left-to-right shunts and low PVR, this increase in PBF can be substantial and result in three pathophysiologic problems: (1) congestion of the pulmonary circulation; (2) intravascular volume overload with resulting increased cardiac work for the LV; and (3) excessive PBF, resulting in progressive elevation in PVR. Volume overload causes ventricular dilation that places the heart at a mechanical and physiologic disadvantage, resulting in reduced diastolic compliance. Diastolic changes lead to engorgement of the respective venous beds, which produces the signs and symptoms of clinical congestive heart failure (CHF) early in the natural history of volume-overload condition. The demand for increased cardiac output placed on the LV is limited in the infant by virtue of its immature structure, so that large left-to-right shunts may outstrip the capacity of the left side of the heart to maintain adequate systemic perfusion.

Surgical closure of a hemodynamically significant VSD usually provides immediate benefit by dramatically lowering left ventricular volume output demands. Occasionally, the sudden increase in wall stress imposed on a dilated ventricle that must now pump solely against SVR can produce worsening ventricular failure during the early postoperative period after eliminating the low-resistance “pop off” into the pulmonary circulation. If the left-to-right shunt is not repaired, prolonged exposure to increased PBF results in progressive elevations in PVR. Fixed changes in pulmonary arterioles may occur, leading to pulmonary vascular obstructive disease, which may become irreversible. Table 78.1 lists common left-to-right shunt lesions.

Right-to-left shunts occur when pulmonary vascular or right ventricular outflow tract resistance exceeds SVR, thereby reducing PBF. The systemic circulation receives an admixture of deoxygenated blood via the shunt. This manifests clinically as cyanosis and hypoxemia. Pure right-to-left shunting resulting from increased PVR is seen in the Eisenmenger complex and persistent pulmonary hypertension of the newborn with shunt at both the atrial and ductal levels. More commonly, PVR is low, and the right-to-left shunt is produced by a more complex lesion with obstruction of pulmonary outflow proximal to the pulmonary vasculature. A classic example of right-to-left shunt is TOF, where

**TABLE 78.2** Ductal-Dependent Lesions

PDA Provides Systemic Flow	PDA Provides Pulmonary Flow
Coarctation of the aorta	Pulmonary atresia
Interrupted aortic arch	Critical pulmonary stenosis
Hypoplastic left heart syndrome	Severe subpulmonic stenosis with VSD
Critical aortic stenosis	Tricuspid atresia with pulmonic stenosis

PDA, Patent ductus arteriosus; VSD, ventricular septal defect.

shunting occurs through the VSD because of pulmonary outflow obstruction. Systemic perfusion is generally normal with right-to-left shunting lesions unless hypoxemia becomes severe enough to impair O<sub>2</sub> delivery to tissues. Right-to-left shunting produces two pathophysiologic problems: (1) reduced PBF resulting in systemic hypoxemia and cyanosis, and (2) increased impedance to right ventricular ejection, which may ultimately lead to ventricular dysfunction and RV failure. However, the physiologic mechanisms designed to compensate for pressure overload rarely create abnormalities in systolic or diastolic function early in the natural history of the disease process. In contrast to lesions that produce excessive ventricular volume, lesions that produce isolated pressure overload typically require years to cause ventricular dysfunction and failure.

**Mixing Lesions.** Mixing lesions constitute the largest group of cyanotic congenital heart defects (see Table 78.1). In these defects, the mixing between the pulmonary and the systemic circulation is so large that the systemic and pulmonary artery O<sub>2</sub> saturations approach each other. The pulmonary-to-systemic flow ratio Qp/Qs is independent of shunt size, and is completely dependent on vascular resistance or outflow obstruction. The pulmonary and systemic circulations tend to be in parallel with one another rather than in series (see Table 78.1). In patients with no outflow obstruction, flow to the systemic or pulmonary circulation depends on the relative vascular resistances of both circuits, such as with univentricular hearts or double-outlet RV. If SVR exceeds PVR, as in the typical circumstance, the tendency is toward excessive PBF, and the predominant pathophysiologic process is left-to-right shunting. These patients have increased PBF, ventricular volume overload, and a gradual elevation of PVR over time. If PVR exceeds SVR, as may occur episodically in ductal-dependent lesions such as hypoplastic left heart syndrome (HLHS), systemic blood flow predominates and PBF dramatically decreases, causing hypoxemia (Table 78.2).

In patients with a mixing lesion and left ventricular outflow obstruction, PBF may be sufficiently excessive to impair systemic perfusion. In patients with mixing lesions and a right ventricular outflow obstruction, such as a single ventricle with subpulmonic stenosis, systemic-to-pulmonary flow can vary from balanced flow to significantly decreased PBF in which the severity of hypoxemia depends on the degree of obstruction. Typical mixing lesions include truncus arteriosus, univentricular heart, total anomalous pulmonary venous return, pulmonary atresia with large VSD, and single atrium.

**Obstructive Lesions.** Obstructive lesions range from mild to severe. Severe lesions manifest in the newborn period with a pressure-overloaded, diminutive, or profoundly dysfunctional ventricle proximal to the obstruction. Such lesions include critical aortic stenosis, critical pulmonic stenosis, coarctation of the aorta, and interrupted aortic arch. Although aortic and pulmonary atresia represent the most extreme variants of outflow tract obstruction, they are associated with such significant hypoplasia of the ventricle (HLHS and pulmonary atresia with intact ventricular septum, respectively) that the ventricle's function does not contribute to the circulatory physiology. As with other critical obstructive lesions, these extreme variants have ductal-dependent circulations, but beyond that similarity they are perhaps better understood as univentricular hearts for which the management characteristics of a mixing lesion dominate in importance.

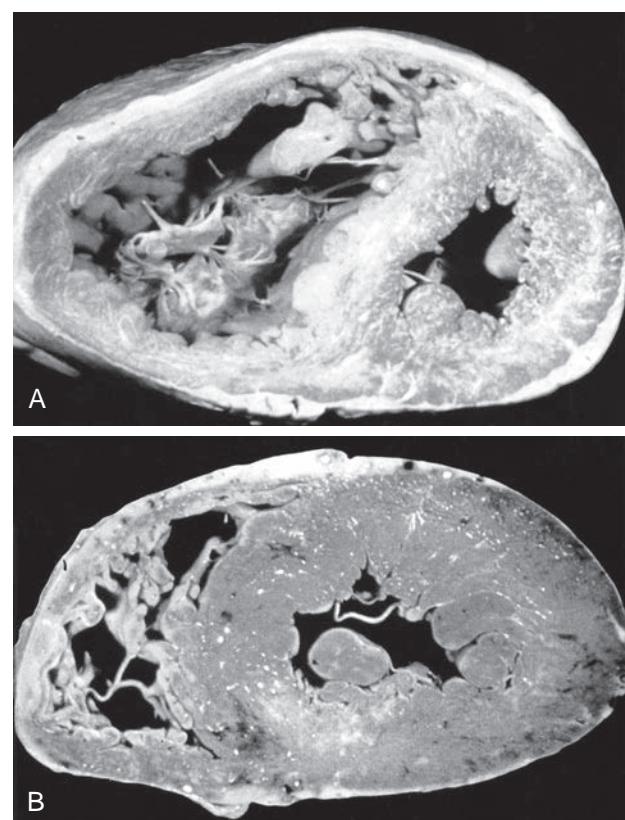
In critical neonatal left-sided obstructive defects, systemic perfusion depends on desaturated blood flow from the RV via the PDA; the coronary perfusion is supplied by retrograde flow from the descending aorta (see Table 78.2). In right-sided lesions, PBF is supplied from the aorta via the PDA and right ventricular function is impaired.

Pathophysiologic problems in critical neonatal left-sided heart obstructive lesions include (1) profound left ventricular failure, (2) impaired coronary perfusion with an increased incidence of ventricular ectopy, (3) systemic hypotension, (4) PDA-dependent systemic circulation, and (5) systemic hypoxemia. The pathophysiologic problems in critical neonatal right-sided heart obstructive lesions include (1) right ventricular dysfunction, (2) decreased PBF, (3) systemic hypoxemia, and (4) PDA-dependent PBF. Apart from the most extreme variants that become evident in the neonatal period, infants and children with outflow obstruction (e.g., mild-to-moderate aortic or pulmonary stenosis, coarctation of the aorta) manifest compensatory mechanisms for pressure overload, and often remain clinically asymptomatic for many years.

**Regurgitant Valves.** Regurgitant valves are uncommon as primary congenital defects. Ebstein malformation of the tricuspid valve is the only pure regurgitant defect manifesting in the newborn period. However, regurgitant lesions are frequently associated with an abnormality of valve structure, such as incomplete or partial AV canal defect, truncus arteriosus, and TOF with an absent pulmonary valve. The pathophysiology of regurgitant lesions includes (1) volume-overloaded circulation and therefore (2) progression toward ventricular dilation and failure.

When considering the incidence of all the congenital heart defects, three uncomplicated left-to-right shunts (VSD, ASD, PDA) and two obstructive lesions (pulmonic stenosis, aortic coarctation) constitute 60% of all congenital cardiac defects. Mixing lesions, complicated obstructive defects, and right-to-left shunting lesions account for the vast majority of the remaining 40%. The latter group of defects, which are more difficult to manage, have a significantly higher morbidity and mortality rate.

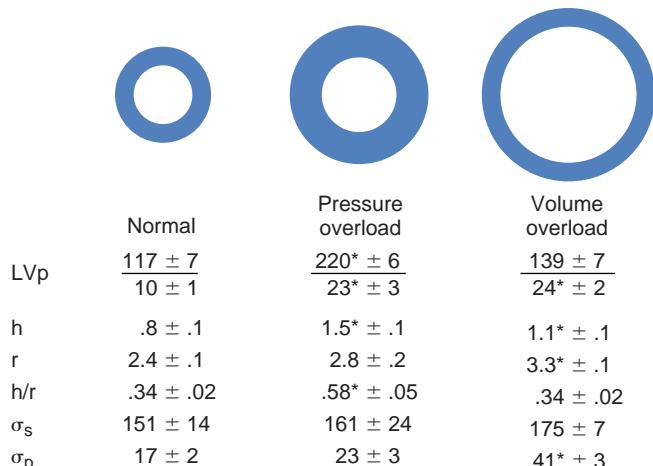
**Chronic Consequences of Congenital Heart Disease.** The chronic effects of CHD are a consequence of the



**Fig. 78.2 Comparison of ventricular hypertrophy patterns demonstrating altered ventricular remodeling in two different congenital heart defects.** (A) Note the right ventricular hypertrophy and the diminutive left ventricle in tetralogy of Fallot. (B) Note the severe left ventricular hypertrophy and septal bulging into the right ventricle in aortic stenosis.

imposed hemodynamic stress of the defect or the residua and sequelae after cardiac surgery. These effects continue to alter normal growth and development of the cardiovascular system and other organ systems throughout life. Complete surgical cures are rarely achieved, and some repairs are palliative rather than corrective; therefore, abnormalities before and after repair produce long-term effects in patients with CHD.<sup>17</sup> Many of the abnormalities are trivial and have no major import. Others affect major organ system processes, such as ventricular function, the conduction system of the heart, central nervous system (CNS) growth, or PBF. Whether anesthetizing these patients for their primary or subsequent cardiac repair or for noncardiac surgery, these chronic changes should be ascertained and reflected in the anesthetic plan.

The myocardium is continually remodeled by specific hemodynamic stresses in utero and throughout life. Abnormal hemodynamic loading conditions associated with CHD interrupt the normal ventricular modeling process (Fig. 78.2).<sup>18</sup> Abnormal ventricular remodeling typically begins in utero and stimulates an increase in ventricular mass. Increased ventricular mass is due to both hyperplasia and hypertrophy of myocytes in response to altered wall stress on the developing ventricle. The resultant biomechanical deformation of the ventricle alters its geometry, affecting normal systolic and diastolic function.



**Fig. 78.3 Changes in ventricular physiology that accompany abnormal pressure and volume loading in human adolescents and adults.** Schematic diagram represents the changes in cross-sectional ventricular geometry that accompany abnormal pressure and volume loads. Data are measured and derived from catheterization and echocardiography of 30 adolescent and adult human subjects. Pressure overload triggers significant increases in wall thickness and wall thickness-to-radius ratio (h/r), but these compensatory mechanisms preserve  $\sigma$  within normal limits. Whereas volume overload causes dilation and enough hypertrophy to preserve normal  $\sigma_s$ , diastolic function deteriorates significantly.  $^*P = .01$ .  $\sigma_d$ , End-diastolic wall stress;  $\sigma_s$ , peak systolic wall stress; h, wall thickness (mm); LVp, left ventricular pressure; r, radius of the left ventricular chamber. (From Grossman W, Jones D, McLaurin LP. Wall stress and patterns of hypertrophy in the human left ventricle. *J Clin Invest*. 1975;56[1]:56–64.)

Abnormalities of ventricular performance at rest and with exercise can be detected in patients with chronic hemodynamic overload and complex cyanotic lesions. These abnormalities in ventricular function are the consequences of chronic ventricular overload, repeated episodes of myocardial ischemia, and residua or sequelae of surgical treatment (ventriculotomy, altered coronary artery supply, inadequate myocardial protection). Although chronic volume or pressure overload of the LV results in CHF, the compensatory mechanisms for pressure overload create less physiologic disturbance than volume overload, particularly in diastolic function. Consequently, CHF occurs later in the natural history of isolated obstructive lesions that do not require treatment in the neonatal period. Similarly, chronic right ventricular volume overload as seen in pulmonic insufficiency after TOF repair is more likely to be associated with chronic ventricular dysfunction and failure than a pressure-loaded RV that manifests with residual pulmonic stenosis. In fact, the most potent combination for inducing ventricular dysfunction and failure occurs when a pressure overload is superimposed on a dilated, volume-overloaded ventricle (e.g., postoperative TOF with pulmonic insufficiency and branch pulmonary artery stenosis).

Initial manifestations of CHF reflect alterations in ventricular compliance that result from a variety of biophysical responses to abnormal loading conditions. The ventricular dilation and compensatory hypertrophy that accompany excessive intravascular volume provide effective compensation to preserve normal systolic wall stress, but alterations in diastolic wall stress become evident (Fig. 78.3). Ultimately, chronic or severe pressure overload causes similar changes as the resultant myocardial hypertrophy outgrows

vascular supply and results in ischemia and fibroblast proliferation. Permanent changes in myocardial structure and function are the end result.

In patients with cyanotic heart defects, the long-term compensation for chronic hypoxemia is major redistribution of organ perfusion with selected blood flow to the heart, brain, and kidney and decreased flow to the splanchnic circulation, skin, muscle, and bone. Chronic hypoxemia is associated with increased work of breathing in an attempt to increase  $O_2$  uptake and delivery. The most dramatic complications are decreased rate of somatic growth, increased metabolic rate, and an increase in hemoglobin concentrations.

Congenital syndromes may have associated CHD that will influence long-term outcome (Table 78.3).

**Surgical Procedures and Special Techniques.** The ultimate objectives for congenital heart surgery are (1) physiologic separation of the circulation, (2) relief of outflow obstruction, (3) preservation or restoration of ventricular mass and function, (4) normalization of life expectancy, and (5) maintenance of quality of life. The available surgical procedures to accomplish these objectives are diverse and complex (Table 78.4). In general, operations performed for congenital heart defects can be divided into corrective and palliative procedures. The type and timing of repair depend on the age of the patient, the specific anatomic defect, and the experience of the surgeon and the team (see Table 78.4).

Palliation in infancy is usually performed when anatomic parts are missing, as in pulmonary atresia (absent RV and pulmonary artery), tricuspid atresia (absent RV and tricuspid valve), HLHS (aortic atresia and hypoplastic LV), univentricular heart (absent RV or LV), and mitral atresia (absent LV). These palliative procedures can be further subdivided into those that increase PBF, those that decrease PBF, and those that increase mixing (see Table 78.4). Palliative procedures that increase PBF include shunts (Blalock-Taussig, central, and Glenn), outflow patch, and enlargement of the VSD. Those that decrease PBF include pulmonary artery banding and ligation of a PDA. Those that improve intracardiac mixing include atrial septostomy (balloon, blade, and Blalock-Hanlon).

The improvements in surgical technique, coupled with advancements in anesthetic and technologic support, make repair in early infancy not only feasible but in many cases preferable.<sup>19,20</sup> Currently, repair in infancy can be offered for a number of congenital heart defects, as shown in Table 78.4. The timing of surgical intervention reflects medical necessity, physiologic and technical feasibility, and optimal outcome. Cardiac defects that require a PDA to sustain sufficient systemic blood flow or PBF (e.g., pulmonary atresia, HLHS, interrupted aortic arch, critical aortic stenosis, and critical pulmonic stenosis) require an intervention in the neonatal period. A variety of defects are optimally repaired in early infancy. Lesions such as transposition of the great arteries (TGA) may exhibit better left ventricular function if the arterial switch operation is performed in the first few weeks of life when the PVR has recently been high enough to increase left ventricular systolic pressure, whereas other repairs may manifest less volatile postoperative physiology if deferred a few weeks or months until PVR has consistently fallen (e.g., TOF, AV

**TABLE 78.3** Syndromes Associated with Congenital Heart Disease

Syndrome	Lesion	Cardiac Lesion	Comments
<b>SYNDROMES WITH AIRWAY ISSUES AND CHD</b>			
CHARGE syndrome (association)		VSD, ASD, PDA, TOF	Micrognathia, possible difficult airway
Edwards syndrome	Trisomy 18	VSD, ASD, PDA	Micrognathia, small mouth, difficult intubation
Di George sequence	Microdeletion 22q11.2	Aortic arch and conotruncal lesions	Short trachea—tendency to endobronchial intubation
Goldenhar syndrome		VSD, PDA, TOF, CoA	Maxillary and mandibular hypoplasia, C-spine anomalies—difficult intubation
Hurler syndrome	MPS 1, storage disorder	Multivalvular disease, CAD, cardiomyopathy	Macroglossia, short neck—extremely difficult intubation
Noonan syndrome		PS, ASD, cardiomyopathy	Short webbed neck, macrognathia—difficult intubation
Turner syndrome	Monosomy X	LVOT O, AS, HLHS, CoA	Micrognathia, webbed neck—difficult intubation
VATER association		VSD, TOF, ASD, PDA	Potential for difficult intubation
<b>SYNDROMES WITH RISK FOR ARRHYTHMIAS</b>			
Long QT syndrome (LQTS)		Torsade de pointes, SCD	
Brugada syndrome		VT/VF/SCD	
Arrhythmogenic right ventricular dysplasia (ARVD)		VT/SCD	
Catecholaminergic polymorphic ventricular tachycardia		Polymorphic VT/SCD	
Wolff-Parkinson-White syndrome		SVT	
Maternal lupus		CCHB in the newborn	
<b>CHROMOSOMAL DISORDERS ASSOCIATED WITH CHD</b>			
Down syndrome	Trisomy 21	VSD, ASD, CAVC	
Edwards syndrome	Trisomy 18	VSD, ASD, PDA	
Patau syndrome	Trisomy 13	VSD, PDA, ASD	
Turner syndrome	Monosomy X	LVOT O, AS, HLHS, CoA	
3p-syndrome	Deletion 3p	CAVC	
Cri du chat syndrome	Deletion 4p	Variable	
8p-syndrome	Deletion 8p	CAVC	
9p-syndrome	Deletion 9p	VSD, PDA, PS	
Williams syndrome	Microdeletion 7q11	SVAS, SVPS, branch PS	
Smith-Magenis syndrome	Microdeletion 17p11.2	ASD, VSD, PS, AV valve malformations	
Miller-Dieker syndrome	Microdeletion 17p13.3	TOF, VSD, PS	
CHARGE association		VSD, ASD, PDA, TOF	Coloboma, heart, choanal atresia, retardation, genital and ear anomalies

AS, Atrial stenosis; ASD, atrial septal defect; AV, atrioventricular; CAD, coronary artery disease; CAVC, complete atrioventricular canal; CCHB, congenital complete heart block; CHARGE, coloboma of the eye, heart defects, atresia of the nasal choanae, restriction of growth and/or development, genital and/or urinary abnormalities, and ear abnormalities and deafness; CHD, congenital heart disease; CoA, coarctation of the aorta; HLHS, hypoplastic left heart syndrome; LVOT O, left ventricular outlet obstruction; MPS 1, mucopolysaccharidosis type 1; PDA, patent ductus arteriosus; PS, pulmonary stenosis; SCD, sudden cardiac death; SVAS, supravalvular aortic stenosis; SVPS, supravalvular pulmonic stenosis; SVT, supraventricular stenosis; TOF, tetralogy of Fallot; VATER, vertebral defects, imperforate anus, tracheoesophageal fistula, and radial and renal dysplasia; VSD, ventricular septal defect; VT/VF, ventricular tachycardia/ventricular fibrillation.

canal defect). Each defect may have mitigating factors for which deferred definitive repair will enable an optimal surgical result (e.g., TOF with aberrant coronary branching pattern or multiple VSDs; TGA with VSD and severe left ventricular outflow tract obstruction).

Pediatric cardiovascular surgery aims to preferentially repair defects in infancy rather than palliate.<sup>21</sup> This trend reflects improved technical capabilities coupled with a desire to limit the morbidity and mortality associated with long-term medical management and the sequelae

**TABLE 78.4** Congenital Cardiac Defects and Their Repair

Anatomic Defects	Palliation	Complete Repair
Tetralogy of Fallot (TOF)		VSD closure and RVOT patch
With PA atresia	Shunt	
With anomalous right coronary artery	Rastelli	
HLHS	Norwood I/transplant	
Transposition of the great arteries		Arterial switch
Unfavorable coronary anatomy	Atrial switch (Senning)	
Tricuspid atresia	Shunt followed by Fontan	
Pulmonary atresia with VSD	Shunt followed by Fontan	
With intact septum	Shunt followed by Fontan	
Critical aortic stenosis		Aortic valvotomy
Interrupted aortic arch		End-to-end anastomosis/reverse subclavian flap/tube graft
Total anomalous pulmonary		Anastomosis of pulmonary veins to left atrium venous return and ASD closure
Single ventricle/normal PAs	Band followed by Fontan	
With small PAs	Shunt followed by Fontan	
Truncus arteriosus		RV-PA conduit and VSD closure
Atrioventricular canal		Repair valve clefts/patch closure of ASD/attach valves to patch

ASD, Atrial septal defect; HLHS, hypoplastic left heart syndrome; PA, pulmonary artery; RV, right ventricle; RVOT, right ventricular outflow tract; VSD, ventricular septal defect.

of multiple palliative operations. Early correction should decrease the incidence of the chronic complications of CHD, such as the problems associated with ventricular overload, cyanosis, and pulmonary vascular obstructive disease.<sup>22</sup> Early repair also may have the selective advantage of enhancing organ system protection during repair because of poorly understood factors promoting resistance to injury and enhanced recovery potential (i.e., enhanced plasticity). With the continued improvement in surgical techniques and the early treatment of CHD, specific organ systems such as the brain, heart, and lungs will be spared the detrimental effects of chronic derangements of hemodynamics and O<sub>2</sub> delivery.

Procedures for the treatment of CHD continue to evolve to decrease long-term morbidity and enhance survival. For example, the long-term problems with right ventricular dysfunction and failure associated with the Mustard procedure for repair of TGA encouraged many surgical groups to develop the neonatal arterial switch operation,

which probably provides an anatomic correction with better long-term results. A second example of the continuing evolution of technique is surgery for TOF. Long-standing pulmonary insufficiency after right ventricular outflow repair for TOF is associated with right ventricular dysfunction and failure. Preservation of the pulmonary valve at initial repair using a combined transatrial and transpulmonary approach during correction and the early insertion of a pulmonary homograft in the setting of pulmonary insufficiency are techniques employed to avoid the long-term problems of right ventricular dysfunction and failure.<sup>23</sup>

Surgery for HLHS, once considered a fatal disease, has achieved significant long-term survival after a series of staged reconstructive procedures.<sup>24,25</sup> The use of RV-PA conduits as an alternative to traditional systemic-to-pulmonary shunts confers some advantage in survival after stage 1 palliation owing to elimination of diastolic runoff into the pulmonary circulation with concurrent unloading of the systemic RV. Myocardial perfusion improves with higher diastolic pressures, no run off to the pulmonary circulation, and decreased myocardial work. The long-term impact of a right ventriculotomy in a univentricular heart is unknown.<sup>26-28</sup> In 2008, the Pediatric Heart Network, an organization sponsored by the National Institutes of Health, completed enrollment in a randomized control trial comparing the effects of modified Blalock-Taussig shunt (mBTS) to RV-PA conduits as part of the stage 1 Norwood procedure.<sup>29</sup> Recent results revealed infants treated with an RV-PA shunt had improved survival over those with mBTS, although the long-term outcomes were not different.<sup>29,30</sup>

Neurologic outcome after surgical repair is an ongoing concern. Preoperative cerebral blood flow (CBF) was shown to be diminished in patients with a variety of congenital heart defects, and low CBF values were associated with periventricular leukomalacia.<sup>31</sup> Some centers routinely advocate regional low-flow cerebral perfusion and measurement of regional cerebral O<sub>2</sub> saturation index and CBF velocity using transcranial Doppler imaging during arch reconstruction in this population. Reductions in the regional cerebral O<sub>2</sub> saturation index or CBF greater than 20% of baseline are treated aggressively in an attempt to increase cerebral O<sub>2</sub> delivery by increasing the mean perfusion pressure, red blood cell (RBC) transfusion, and maintenance of high normal levels of PaCO<sub>2</sub> to achieve cerebral vasodilation.

Techniques have evolved to a “three-region” perfusion strategy for aortic arch reconstruction in the Norwood procedure. This technique involves direct perfusion of the coronaries and distal thoracic aorta as well as continuous cerebral perfusion via innominate cannulation. The arch repair occurs from distal to proximal at warmer patient temperatures, theoretically allowing decreased coronary and splanchnic ischemic times, decreasing the risk of cardiac dysfunction and abdominal organ damage, and mitigating the negative hypothermic effects on the hematologic system.<sup>32,33</sup>

Surgical management has evolved in a broader application of certain surgical procedures initially designed for a specific defect. For example, modifications of the Fontan operation, which was originally devised for patients with

tricuspid atresia, are now being used to repair a variety of univentricular hearts, including HLHS.<sup>34,35</sup> Initially, the wider application of the Fontan operation to include complex defects once considered inoperable was associated with a rise in morbidity and mortality. However, this trend has been reversed in recent years by several groups who have demonstrated improved outcome with the staging of the operation (superior cavopulmonary anastomosis, subsequent completion of the Fontan operation), the creation of a fenestration between the RA and LA at the time of the Fontan operation, and the use of modified ultrafiltration (MUF) at least in the early years.<sup>36</sup>

However, as patients who undergo the Fontan procedure grow older, they present with the unique pathophysiologic challenges of refractory arrhythmias, a failing single ventricle, protein-losing enteropathy, and plastic bronchitis. Most of these adults are cared for in a combined pediatric and adult cardiac program and require intensive multidisciplinary care to optimize cardiorespiratory status. Ingenuity and innovation such as demonstrated with the Fontan procedure have permitted continued improvements in survival for all patients with CHD. As incisions in the myocardium become smaller and sutures more precisely placed, and as improvements in surgical techniques continue to evolve, the complications of ventricular dysfunction, arrhythmias, and residual obstruction should decline, contributing to improved patient quality of life.

One final difference unique to congenital heart surgery that has a major impact on anesthetic management relates to the type of cardiopulmonary support. Because of the complexity of repair in small patients, surgery often requires significant alterations in the bypass techniques, such as the use of deep hypothermic CPB at temperatures of 18°C and total circulatory arrest. Despite widespread use of these techniques during CPB, their physiologic effects on major organ system function are just beginning to be understood. These effects are discussed in subsequent sections.

## Anesthetic Management

### PREOPERATIVE MANAGEMENT

#### Anesthetic Evaluation

Caring for children with CHD presents the anesthesiologist with a wide spectrum of anatomic and physiologic abnormalities. Patients range from young, healthy, asymptomatic children who are having closure of a small ASD to the neonate with HLHS requiring aggressive perioperative hemodynamic and ventilatory support. Intertwined with the medical diversity of these patients are the psychological factors affecting both the patient and their parents. Preparation of the patient and the family is time-consuming, but omitting or compromising this aspect of patient care is a major deterrent to a successful outcome and patient and parental satisfaction. This team-oriented approach also serves as a safeguard to prevent errors and omissions in the exacting perioperative care necessitated by the complexity of cardiac surgery for CHD. The preoperative visit offers the family the opportunity to meet the surgeon and anesthesiologist.

Parents should be questioned about the general health and activity of their child. Fundamentally, a child's general health and activity will reflect cardiorespiratory reserve. Deficiencies may point toward cardiovascular or other systems that may influence anesthetic or surgical risk. Does the child have impaired exercise tolerance? Is the child gaining weight appropriately, or exhibiting signs of failure to thrive on the basis of cardiac cachexia? Does the child exhibit signs of CHF (diaphoresis, tachypnea, poor feeding, recurrent respiratory infections)? Is there progressive cyanosis or new onset of cyanotic spells? Any intercurrent illness such as a recent upper respiratory tract infection or pneumonia must be ascertained. Lower respiratory tract infections may require a delay in proposed surgery, based on the negative impact that airway reactivity and elevations in PVR may have on surgical outcome. Recurrent pneumonia is frequently associated with pulmonary overcirculation and altered lung compliance in patients with increased PBF.

A good history will delineate previous surgical and cardiologic interventions, which may impact both surgical and anesthetic plans for the current procedure. Patients who have had their subclavian artery sacrificed for a subclavian flap angioplasty to correct coarctation or a Blalock-Taussig shunt will not accurately display systemic arterial pressure or perhaps even pulse oximetry readings when the monitoring is applied to the affected side. Likewise, children who have femoral venous occlusion after catheterization are not candidates for femoral venous access, particularly for femoral CPB should sternotomy prove impossible. It is equally important to obtain current medications, previous anesthetic problems, and family history of anesthetic difficulties.

In the modern era of echocardiography and cardiac catheterization, physical examination rarely contributes additional anatomic information about the underlying cardiac lesion. However, it is extremely useful in assessing the overall clinical condition of the child. For example, an ill-appearing, cachectic child in respiratory distress has limited cardiorespiratory reserve and the use of excessive premedication or a prolonged inhaled induction of anesthesia could result in significant hemodynamic instability.

#### Concurrent Medications and Drug Interactions

Drug interactions are common both among the co-therapeutic cardiovascular agents and between hemodynamic drugs and anesthetic drugs. An understanding of the mechanisms and interactions is useful to the pediatric cardiovascular anesthesiologist. Some common cardiovascular medications and anesthesia considerations are shown in **Table 78.5**.

Pediatric oncology patients presenting for cardiac or noncardiac procedures may manifest higher cardiovascular risk because of cardiotoxic chemotherapy.<sup>37</sup> Common cardiotoxic agents include the antimetabolite 5-fluorouracil, the anthracycline antibiotics doxorubicin and daunorubicin, and the alkylating agent cyclophosphamide. The acute form of toxicity is characterized by acute ST segment/T wave changes on the electrocardiogram (ECG), serious dysrhythmias, and CHF associated with pericardial effusion. Chronic cardiotoxic HF is cumulative, dose related, and unresponsive to digoxin therapy. Serious cardiomyopathy can occur and is related to dose, irradiation, and use of an anthracycline. The mortality rate can

**TABLE 78.5** Common Perioperative Medications and Considerations

Cardiac Drug Class	Interactions	Considerations
Angiotensin-converting enzyme inhibitors	Hypotension with induction of general anesthesia	Consider withholding morning dose, or reducing dosage, in hypotensive patients; avoid fixed dose induction regimens with drugs having a profound vagomimetic effect
β-Blockers	Acute withdrawal can precipitate tachycardia and arrhythmias; can potentiate hypotension with volatile anesthesia; can decrease response to inotropic agents	Continue in the perioperative period
Calcium channel blockers	May augment the negative inotropic and chronotropic effects of volatile anesthesia	Continue in the perioperative period
Diuretics	Hypovolemia/hypokalemia; may augment effect of neuromuscular blocking agents	Discontinue preoperatively
Antiarrhythmics	Can be proarrhythmic with inotropes, electrolyte disturbances; high catecholaminergic states; can interact with other antiarrhythmics and precipitate bradycardia	Avoid electrolyte imbalance Avoid drugs that are proarrhythmic Monitor carefully
α <sub>2</sub> -Agonists	Reduces perioperative shivering, ischemia, anesthetic and analgesic requirements	Continue into the perioperative period with appropriate monitoring

exceed 50%. These patients should undergo thorough preoperative evaluation, including a full blood cell count, assessment of renal and hepatic function and coagulation parameters, and an echocardiogram. An isoflurane/nitrous oxide (N<sub>2</sub>O)-based anesthetic might confer better hemodynamic stability than opioid-based anesthesia in such patients.<sup>38</sup>

Anesthetics can induce torsade de pointes, a malignant arrhythmia. Risk factors include female gender, electrolyte imbalances such as hypokalemia and hypomagnesemia, genetic ion channel polymorphisms of congenital long QT syndrome (LQTS), subclinical LQTS, baseline QT prolongation, and use of QT-prolonging drugs especially in high concentrations or as rapid intravenous infusions. Conditions with reduced repolarization reserve such as CHF or digoxin toxicity can also precipitate torsade de pointes. Drugs that may cause torsade de pointes in patients with congenital LQTS are shown in Table 78.6. The website <https://crediblemed.org> provides an updated list of drugs that prolong the QT interval.

Traditionally, patients undergoing cardiac surgery have blood drawn for laboratory evaluation as standard of care (hemoglobin, electrolytes, type, and screen). Recently the utility of this practice has been questioned especially in the patient coming from home. These tests are expensive, utilize significant hospital resources, cause pain and anxiety to the patient, and rarely lead to a change in care.<sup>39</sup> A more thoughtful, directed, and individualized strategy can limit costs and discomfort without sacrificing patient safety. On the other hand, special populations such as patients with trisomy 21, cyanotic heart disease, and those on antiplatelet therapy may require additional specific testing.

An increased hematocrit in a normovolemic child gives an indication of the magnitude and chronicity of hypoxemia. A hematocrit more than 60% may predispose to capillary sludging and secondary end organ damage, including stroke. Despite these risks, liberalized guidelines for nothing by mouth that permit children to consume

**TABLE 78.6** Drugs That May Cause Torsade De Pointes in Patients With Congenital Long QT Syndrome

Drug Category	Drug Name
Antiarrhythmics	Amiodarone Procainamide Disopyramide Ibutilide Quinidine Sotalol
Antipsychotics	Chlorpromazine Haloperidol Thioridazine Mesoridazine
Antimicrobials	Erythromycin Clarithromycin
Miscellaneous	Cisapride Arsenic Methadone Droperidol Domperidone Dolasetron Ondansetron Glycopyrrolate

clear liquids up to 2 hours before anesthetic induction have virtually eliminated the need to admit these patients to the hospital early for preoperative intravenous hydration.<sup>40,41</sup>

Echocardiography with Doppler color flow imaging (echo-Doppler) is an invaluable tool that provides a non-invasive means of assessing intracardiac anatomy, blood flow patterns, and estimates of physiologic data.<sup>42</sup> For many cardiac defects, more invasive studies are generally not required if a good echocardiographic assessment is made. Echo-Doppler imaging is especially helpful for defining intracardiac abnormalities. Extracardiac abnormalities, such as pulmonary artery or vein stenosis, are more difficult to define by echo-Doppler and may require

computed tomography (CT) or cardiac catheterization. The ability to interpret anatomy and physiology accurately requires a skilled echocardiographer, reaffirming the need for a well-integrated interactive team. Although the complexities posed by extreme anatomic variation and changing loading conditions render intraoperative echo-Doppler challenging even for experienced echocardiographers, the pediatric cardiac anesthesiologist should develop some familiarity with its capabilities and limitations so as to participate in critical intraoperative management decisions.

Magnetic resonance imaging (MRI) of the heart and major vessels has become a very useful noninvasive imaging tool in children with heart disease. Typically, MRI is used for segmental description of cardiac anomalies; evaluation of thoracic aortic anomalies; noninvasive detection and quantification of shunts, stenoses, and regurgitations; evaluation of conotruncal malformations and complex anomalies; identification of pulmonary and systemic venous anomalies; and postoperative studies and evaluation of CHD in adult patients.<sup>43,44</sup> MRI is particularly useful in quantifying ventricular function, regional wall motion, valvular competence, and velocity flow mapping. It is especially useful for imaging the aortic arch, pulmonary arteries, and the mediastinal vessels in children with complex CHD. Lesions for which MRI provides accurate and useful information include coarctation of the aorta, anomalies of the pulmonary arteries, anomalous pulmonary venous connections and persistent left superior vena cava, and intracardiac baffles, conduits, and shunts.<sup>43,44</sup> MRI is also useful in older patients with poor acoustic windows and patients with chest wall deformities. It may be an alternative to cardiac catheterization in select patients and may provide noninvasive assessment of coronary anomalies, myocardial perfusion defects, and the detection of conditions associated with myocardial scarring (e.g., arrhythmogenic RV dysplasia). Even more novel, MRI images are now being used to reconstruct complex lesions using 3D printers to build a model of the heart to help plan the surgical procedure.<sup>45,46</sup> Adenosine stress cardiac MRI is used to delineate areas of inducible ischemia. However, physiologic data such as O<sub>2</sub> saturations cannot be obtained with MRI.

Anesthetic considerations remain the same as for all cardiac lesions, with the additional concerns for MRI safety and restricted access to an anesthetized patient with suboptimal monitors. MRI scans are prolonged and traditionally require absolute patient immobility, with control of ventilator parameters to obtain optimal images. However, with advances in technology such as respiratory gating and use of free-breathing protocols, images can be acquired with the patient spontaneously breathing. This eliminates the need for general anesthesia with an endotracheal tube and breath-holds, thus allowing for intravenous sedation with spontaneous breathing instead.

Cardiac catheterization remains the gold standard for assessing anatomy and physiologic function in CHD. Although many anatomic questions can now be reliably answered noninvasively, catheterization remains a vital tool for cases that present complex anatomic questions or require knowledge of physiologic data. Important

catheterization data for the anesthesiologist include the following:

1. Child's response to sedative medications
2. Pressure and O<sub>2</sub> saturation in all chambers and great vessels
3. Location and magnitude of intracardiac and extracardiac shunt Qp/Qs
4. PVR and SVR
5. Chamber size and function
6. Valvular anatomy and function
7. Distortion of systemic or pulmonary arteries related to prior surgery
8. Coronary artery anatomy
9. Anatomy, location, and function of previously created shunts
10. Acquired or congenital anatomic variants that might have an impact on planned vascular access or surgery

Careful review of the cardiac catheterization data and an understanding of their potential impact on the operative and anesthetic plan are essential. Not all medical problems can be evaluated and corrected preoperatively; the surgeon, cardiologist, and anesthesiologist must discuss the potential management problems and need for further evaluation or intervention before arrival in the operating room. Appropriate communication and cooperation will optimize patient care and facilitate perioperative clinical management.

## INTRAOPERATIVE MANAGEMENT

### Operating Room Preparation

Advance, careful preparation of the operating room and anesthesia equipment is essential. The anesthesia machine must have the capacity to provide air, O<sub>2</sub>, and N<sub>2</sub>O to help balance pulmonary and systemic blood flow. Some anesthetic machines may be equipped with carbon dioxide (CO<sub>2</sub>) as an additional gas that can be added to help balance the circulations. NO is invaluable to help lower the PVR and is usually added into the inspiratory limb of the circuit via a separate machine, which then also allows continuous NO administration, also while transporting the patient. Intravenous tubing must be free from air bubbles to prevent paradoxical air embolism, and air filters should be added to all infusion lines. Resuscitative drugs, labeled and ready for administration, should include succinylcholine, calcium gluconate or calcium chloride, sodium bicarbonate, atropine, lidocaine, phenylephrine, and epinephrine. An inotropic infusion, usually epinephrine or dopamine, should be premixed and ready for administration in high-risk cases, but additional infusions are prepared if their need is strongly suspected (e.g., milrinone, vasopressin). For all pediatric cases, certain anesthetic drugs should be available (etomidate, propofol, ketamine). No single drug can be recommended; how a particular drug is used is more important. In pediatric cardiac anesthesia, many patients have limited reserve and high endogenous catecholamine levels released in an adaptive response to their underlying cardiac disease. The resuscitative drugs should therefore be prepared and immediately available before anesthetic induction.

**BOX 78.2 Monitoring of Organ Systems****Cardiopulmonary System**

- Esophageal stethoscope
- Electrocardiogram
  - Standard five-lead system, ST-T wave analysis, esophageal electrocardiographic lead
- Pulse oximetry
- Automated oscillatory blood pressure
- Capnograph
- Ventilator parameters
- Indwelling arterial catheter
- Central venous pressure catheter
- Pulmonary artery catheter
- Transthoracic pressure catheter
  - Left or right atrium, pulmonary artery
- Echocardiography with Doppler color flow imaging
- Epicardial or transesophageal

**Central Nervous System**

- Peripheral nerve stimulator
- Processed electroencephalography
- Specialized
  - Cerebral blood flow: Xenon clearance methodology
  - Cerebral metabolism: Near-infrared spectroscopy, oxygen consumption measurements
  - Transcranial Doppler
  - Jugular venous bulb saturations

**Temperature**

- Nasopharyngeal, rectal, esophageal, tympanic

**Renal Function**

- Foley catheter

For congenital heart surgery, the ability to alter body temperature rapidly for cooling and rewarming is essential. During deep hypothermic CPB, patients are cooled to 18°C. Surface cooling with a heating and cooling water mattress, ice in watertight bags, and an efficient room and ambient temperature control system are important in the operative management of these patients.

**Physiologic Monitoring**

The specific monitoring used should depend on the child's condition and the magnitude and nature of the planned surgical procedure. The perioperative monitoring techniques available are listed in **Box 78.2**. Noninvasive monitoring equipment is ideally placed before induction of anesthesia, although the anesthesiologist may elect to defer application of monitoring devices in the crying child until immediately after the induction. Standard monitoring includes electrocardiography, pulse oximetry, capnography, and an appropriate-sized blood pressure cuff (either oscillometric or Doppler). Additional monitoring includes an indwelling arterial catheter and temperature probes. Foley catheters are generally employed when surgical intervention entails CPB or might produce renal ischemia, or when the anesthetic management includes a regional technique associated with urinary retention. Most centers routinely employ percutaneously placed central venous pressure (CVP) monitoring or alternatively, directly placed transthoracic atrial lines by the surgeons to help with separation from CPB and the hemodynamic management in the postoperative period.

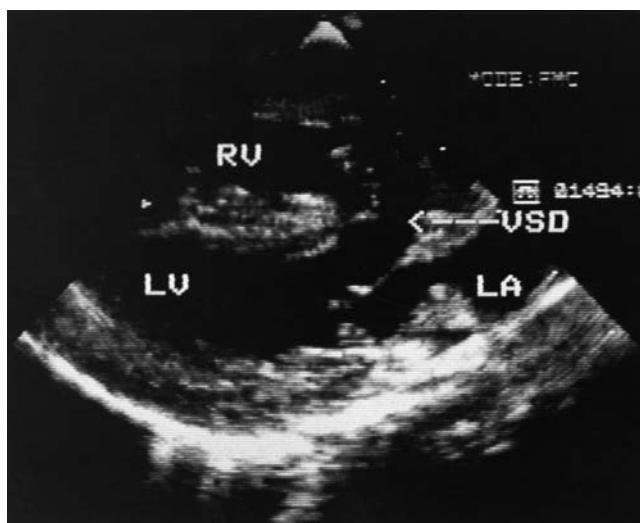
Continuous monitoring of arterial pressure is possible only through an indwelling intraarterial catheter. In young children, cannulation of the radial artery with a 22- or 24-gauge catheter is preferred. In older children and adolescents, a 20-gauge catheter may be substituted. Careful inspection, palpation, four-extremity noninvasive blood pressure determinations, and ultrasound use help ensure that previous or currently planned operative procedures (e.g., a previous radial artery cutdown, subclavian flap for coarctation repair, or Blalock-Taussig shunt) do not interfere with the selected site of arterial pressure monitoring. Other sites available for cannulation include the ulnar, femoral, axillary, and umbilical (in neonates) arteries. Cannulation of the posterior tibial or dorsalis pedis arteries is not usually sufficient for complex operative procedures. Peripheral arterial catheters, principally of the distal lower extremities, function poorly after CPB and do not reflect central aortic pressure when distal extremity temperature remains low.<sup>47</sup>

Myocardial and cerebral preservation is maintained principally through hypothermia; therefore, the accurate and continuous monitoring of body temperature is crucial. Rectal and nasopharyngeal temperatures are monitored because they reflect core temperature and brain temperature, respectively. Monitoring of esophageal temperature is a good reflection of cardiac and thoracic temperature. Tympanic probes, although a useful reflection of cerebral temperature, can cause tympanic membrane rupture.

Pulse oximetry and capnography provide instantaneous feedback concerning adequacy of ventilation and oxygenation. They are useful guides in ventilatory and hemodynamic adjustments to optimize  $\dot{Q}_p/\dot{Q}_s$  before and after surgically created shunts and pulmonary artery bands. Peripheral vasoconstriction in patients undergoing deep hypothermia and circulatory arrest renders digital O<sub>2</sub> saturation probes less reliable. In the newborn, the use of a tongue sensor has been advocated to provide a more central measure of O<sub>2</sub> saturation, with less temperature-related variability.<sup>48</sup>

The use of transthoracic or transvenous pulmonary artery catheters is determined on an individual basis based on the disease process, physiologic state, and surgical intervention. For example, in children undergoing a Fontan procedure for tricuspid atresia or a univentricular heart, catheters in the Fontan pathway and the pulmonary venous atrium are especially useful. After a Fontan operation, PBF must occur without benefit of a ventricular pumping chamber. Subtle changes in preload, PVR, and pulmonary venous pressure will influence PBF and thus systemic cardiac output. Data derived from the difference between the CVP and left atrial pressure ([LAP]; also known as the transpulmonary gradient) help identify the relative importance of intravascular volume (CVP), PVR (CVP-LAP gradient), or ventricular compliance (LAP), each of which requires a different therapeutic approach.

As a general guideline, a transvenous pulmonary artery catheter may be placed using the internal jugular approach in children weighing more than 7 kg. A 5.0-Fr catheter is used for children weighing between 7 and 25 kg, and a 7.0-Fr one is used for children weighing more than 25 kg. For infants weighing less than 7 kg, percutaneous placement of a pulmonary artery catheter can be performed from the femoral vein. Occasionally, the latter technique will require



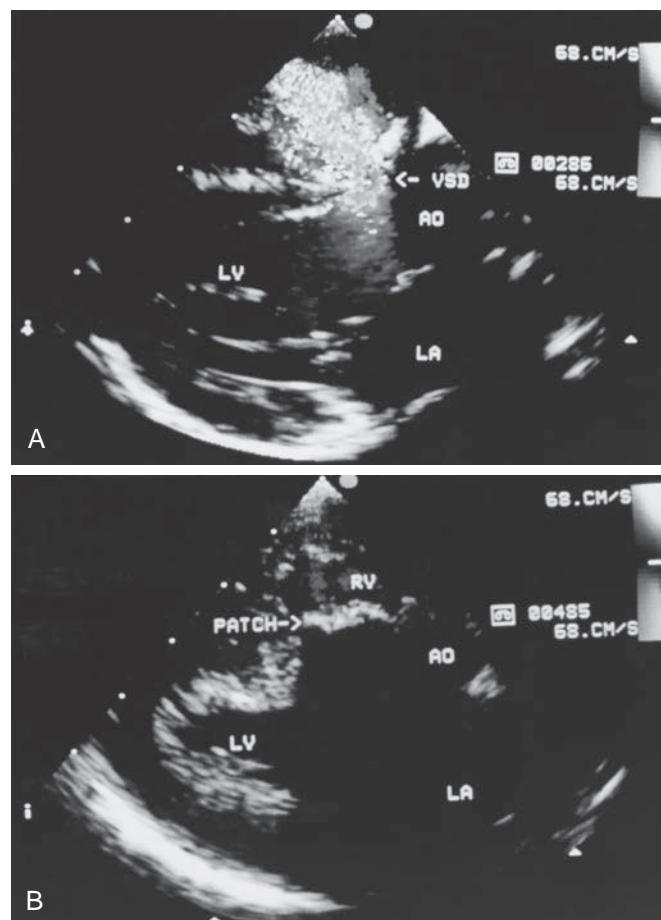
**Fig. 78.4** Intraoperative pre-cardiopulmonary bypass epicardial echocardiogram in the long-axis view. Note the insertion of the papillary muscle of the tricuspid valve on the interventricular septum. On the basis of this view, the surgeon decided that ventricular septal defect (VSD) closure was possible in a child thought preoperatively to be a candidate for only palliation. LA, Left atrium; LV, left ventricle; RV, right ventricle.

fluoroscopy. The use of intraoperative transthoracic monitoring lines and echo-Doppler imaging limits the need for transvenous pulmonary artery catheters in most cases.

### Special Monitoring

**Intraoperative Echocardiography.** The use of echo-Doppler imaging is now regarded as standard of care for almost all pediatric cardiac surgeries.<sup>49,50</sup> Two-dimensional echocardiography combined with pulsed-wave Doppler ultrasonography and color flow mapping provide detailed morphologic and physiologic information in the majority of operative cases. Using echo-Doppler in the operating room, anatomic and physiologic data can be obtained before CPB, thus refining the operative plans. Prebypass echo-Doppler precisely defines anesthetic and surgical management.<sup>49</sup> Because of the unrestricted epicardial and TEE approaches in anesthetized patients, new findings are frequently discovered and management plans changed accordingly (Fig. 78.4).

Postbypass echo-Doppler evaluation is able to immediately assess the quality of the surgical repair and cardiac function by examining ventricular wall motion and systolic thickening.<sup>49</sup> This technique can show residual structural defects after bypass, which can be immediately repaired, thus avoiding the patient leaving the operating room with significant residual structural defects that will require reoperation at a later time (Fig. 78.5). By identifying patients with right or left ventricular contraction abnormalities after bypass, as determined by a change in wall motion or systolic thickening, echo-Doppler provides guidance for immediate pharmacologic interventions. Importantly, postbypass ventricular dysfunction and residual structural defects identified by echo-Doppler imaging are associated with an increased incidence of reoperation and higher morbidity and mortality rates. Thus, this monitoring tool is helpful in assessing surgical repair and identifying operative risk factors, which will hopefully improve outcomes.



**Fig. 78.5** (A) Echocardiogram with a Doppler flow map in the long-axis view illustrating a residual ventricular septal defect (VSD) resulting from patch dehiscence after initial repair. Turbulent flow through the VSD appears as a mosaic of white particles (arrow). This finding necessitated immediate reinstatement of cardiopulmonary bypass and repeat repair. (B) Repeat Doppler flow map in the long-axis view illustrates patch closure (arrow) of the VSD after repeat repair. Note the absence of turbulent flow with the loss of the mosaic of white particles. AO, Aorta; LA, left atrium; LV, left ventricle; RV, right ventricle.

Two techniques for intraoperative echo-Doppler imaging have been described: epicardial and TEE. Using TEE, the probe is placed after induction of anesthesia and intubation and is then available for monitoring of the patient. The advantage of this technique is its utility as a continuous monitor of cardiac structure and function, without interrupting surgery.<sup>49,51</sup> Because of its ideal imaging location, TEE has been especially helpful in evaluating pulmonary venous return and the integrity of the left AV valve after mitral valvuloplasty, complete AV valve repair, and correction of complex CHD. Early limitation in views has been virtually eliminated as a result of clinical experience and improved biplane images. Pediatric biplane TEE probes have now extended the patient weight limits to neonates between 2.5 and 3 kg.<sup>52</sup> Potential hazards of TEE that merit particular vigilance include descending aorta and airway compression because of probe size or during probe flexion. There have been reports of esophageal damage during hypothermia and low or no flow states because of the heat energy the probe produces while connected to the TEE machine, leading most institutions to pause the imaging ability of the probe, disconnect the probe from the

machine, or even remove it during the CPB period of the procedure.

A second technique for intraoperative echocardiographic analysis in children is the epicardial approach.<sup>52</sup> This approach requires passing a clean, short-focused 5.0- or 7.0-MHz transducer over the anesthesia screen into a sterile sheath, where it then can be placed on the epicardial surface of the heart. This technique best facilitates the probe manipulations necessary for thorough interrogation of the major structures and dynamic function of the heart. The advantage of this approach is that all views can be obtained in patients of any size. Among the disadvantages are the need for sufficient operator skill and experience to perform the manipulations, the need to interrupt surgery to manipulate the probe, and the possible deleterious impact of direct myocardial mechanical manipulation. Given current TEE capabilities, epicardial imaging is rarely employed.

**Specialized Central Nervous System Monitoring.** The primary goal of brain monitoring is to improve our understanding of cerebral function during cardiac surgery so that effective brain protection strategies can be developed. Because many of the determinants of normal brain perfusion become externally controlled by the cardiac team during CPB, such as flow rate (cardiac output), perfusion pressure, temperature, hematocrit, and  $\text{PaCO}_2$ , a knowledge of the effect of these factors on the brain in neonates, infants, and children is essential. Numerous intraoperative techniques have been used for monitoring the brain to prevent secondary brain injury from hypoxia, ischemia, emboli, and electrophysiologic derangements. These have primarily included the following three modalities in isolation or combination: (1) electroencephalography (EEG) to assess perfusion-related changes in cortical activity; (2) transcranial Doppler imaging to measure arterial flow and resistance; and (3) near-infrared spectroscopy (NIRS) to provide a measure of venous-weighted, tissue oxyhemoglobin saturation. Additionally, the measurement of CBF and metabolism with specialized clinical research tools has been very important in furthering our understanding of brain function during and after surgery. Multimodal neurologic monitoring is also used to guide CPB, deep hypothermic circulatory arrest (DHCA), and regional low-flow cerebral perfusion techniques in neonatal arch reconstruction.<sup>53-55</sup>

Electroencephalographic monitoring allows detection of ischemia or recognition of an adequate decrease in cerebral metabolic activity during hypothermia before DHCA. EEG is helpful in monitoring physiologic functions of the CNS during deep hypothermic bypass and total circulatory arrest. For example, during deep hypothermia and before total circulatory arrest, the processed EEG can identify residual cerebral electrical activity. Isoelectric silence can then be induced by further cooling and any further brain activity detected by EEG. Because this residual electrical activity during arrest is associated with ongoing cerebral metabolism, an isoelectric state may prevent ischemic injury to the brain during circulatory arrest. EEG also may be useful in detecting the level and depth of anesthesia. Postoperative electroencephalographic analysis has demonstrated subclinical seizure activity in a number of high-risk patients, potentially linking these abnormalities to poorer

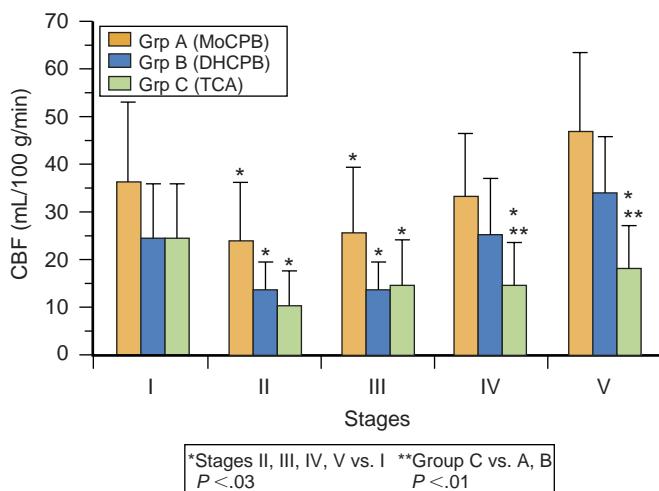
neuropsychologic outcome. The value of intraoperative electroencephalographic monitoring after CPB and the significance of the findings remain to be determined.

Transcranial Doppler imaging has been used primarily for research purposes in infants and allows detection of venous or arterial flow abnormalities and the detection of microemboli.<sup>56</sup> This technology uses the Doppler principle to detect shifts in the frequency of reflected signals from blood in the middle cerebral artery to calculate blood flow velocity.<sup>57</sup> Because the diameter of this large cerebral artery is relatively constant, flow velocity can be used to approximate CBF. Transcranial Doppler imaging has several advantages: (1) it is noninvasive, (2) it does not require radiation exposure, (3) it is a continuous monitor, and (4) it captures rapid alterations in blood flow velocity caused by temperature or perfusion changes. The limitations of transcranial Doppler monitoring include (1) reproducibility, especially at low flow rates, when small movements of the patient's head can dramatically alter the signal, and (2) the lack of validating studies during hypothermic CPB, when hypothermia, reduced flow rates, and the laminar flow characteristics of non-pulsatile perfusion may limit the accuracy of CBF velocity measurements.

Transcranial Doppler imaging has been used to investigate the effect of CPB and DHCA on cerebral hemodynamics in children, as well as to assess the incidence of cerebral emboli. Recent studies examining the brain using transcranial Doppler have enabled several investigative groups to provide important information regarding questions of normal and abnormal brain perfusion during cardiac surgery in children. Questions regarding cerebral perfusion pressure, autoregulation, effect of  $\text{PaCO}_2$ , and temperature have been addressed using transcranial Doppler imaging in children.<sup>58-60</sup> This technique also has provided qualitative information regarding the presence of gaseous emboli in the middle cerebral artery during cardiac surgery.<sup>61</sup>

NIRS is a noninvasive monitor of cerebral tissue oxygenation, reflecting the balance of  $\text{O}_2$  delivery and consumption. Cerebral NIRS reflects  $\text{O}_2$  saturation of the venous compartment, and values correlate with jugular venous bulb saturations.<sup>62</sup> There is significant interest in studying the ability of NIRS to predict outcomes, particularly on the neurodevelopmental spectrum. A study of infants undergoing the stage 1 Norwood procedure for HLHS demonstrated an association between low NIRS (particularly when less than 50%-60%) and poor neurodevelopmental outcomes.<sup>63</sup> Although there was not a linear association, it provides evidence that NIRS can be used to detect clinically consequential hypoxia. Somatic and cerebral saturations are further clinically relevant in the immediate postoperative period by predicting overall morbidity and mortality in patients with HLHS stage 1 palliation.<sup>64</sup> The number of minutes of cerebral desaturation below 50% predicts morbidity and serves as an early warning sign for hypoxia, bleeding, and/or low cardiac output state.<sup>65</sup> A decrease of greater than 20% from baseline in renal saturation as detected by NIRS for a period of 20 minutes has been associated with a longer duration of mechanical ventilation and ICU convalescence.<sup>66</sup>

A 2016 review of NIRS use in pediatric cardiac surgery identified several prospective trials, mostly observational, that found inconsistent results overall regarding improved



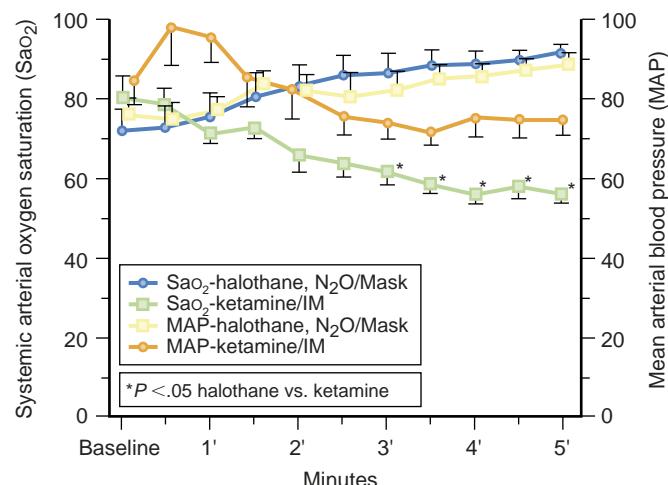
**Fig. 78.6 Bar chart of the changes in cerebral blood flow (CBF) before, during, and after cardiopulmonary bypass (CPB) in 67 infants and children (mean  $\pm$  SD).** Group A underwent repair with moderate hypothermic bypass (MoCPB) at 28°C to 32°C; group B, with deep hypothermic bypass at 18°C to 22°C; and group C, with total circulatory arrest (TCA) at 18°C. Note the impaired cerebral reperfusion after total circulatory arrest (group C). Stage I, prebypass; stages II and III, during hypothermic bypass; stage IV, rewarmed on bypass; stage V, after bypass. (From Greeley WJ, Brusino FG, Ungerleider RM, et al. The effects of cardiopulmonary bypass on cerebral blood flow in neonates, infants, and children. *Circulation*. 1989;80:I209.)

clinical outcomes with NIRS use.<sup>67</sup> Importantly, the current evidence does not provide clear thresholds for cerebral or somatic NIRS, below which the chance of morbidity would increase. Differences in longer-term cardiac, renal, or neurodevelopmental outcomes have not been demonstrated based on differences in NIRS values. Despite these reservations, NIRS remains an important clinical tool to interpret alongside other monitoring technologies.

CBF studies using xenon clearance technology have improved the understanding of cerebrovascular dynamics in young children during CPB and especially during deep hypothermia and after periods of circulatory arrest.<sup>68-71</sup> In general, this investigational tool has described the effects of CPB, temperature, and various perfusion techniques on CBF and, indirectly, on brain metabolism (Fig. 78.6). Studies using this methodology have shown that some of the mechanisms of CBF autoregulation, such as pressure-flow regulation, are lost with deep hypothermia and that cerebral reperfusion is impaired after a period of total circulatory arrest.

## Induction and Maintenance of Anesthesia

The principles of intraoperative management of cardiothoracic surgical procedures are based on an understanding of the pathophysiology of each disease process and a working knowledge of the effects of the various anesthetic and other pharmacologic interventions on a particular patient's condition. Selecting a technique for induction of anesthesia needs to consider the degree of cardiac dysfunction, the cardiac defect, the degree of sedation provided by the pre-medication, and the presence of an indwelling catheter. In children with good cardiac reserve, induction techniques can be quite varied in well-monitored patients. The titration of anesthetics for induction of anesthesia is more important



**Fig. 78.7 Comparative changes in arterial oxygen saturation ( $Sao_2$ ) and mean arterial pressure (MAP) during mask halothane nitrous oxide ( $n = 7$ ) and intramuscular ketamine ( $n = 7$ ) inductions in children with tetralogy of Fallot at risk for right-to-left shunting.** Note the maintenance of  $Sao_2$  in the halothane group despite the significant drop in MAP.  $N_2O$ , Nitrous oxide. (From Greeley WJ, Bushman GA, Davis DP, et al. Comparative effects of halothane and ketamine on systemic arterial oxygen saturation in children with cyanotic heart disease. *Anesthesiology*. 1986;65:666–668.)

than the specific anesthetic technique in patients with reasonable cardiac reserve. A wide spectrum of anesthetic induction techniques have been used safely and successfully, including sevoflurane, isoflurane,  $\text{N}_2\text{O}$ , intravenous and intramuscular ketamine, and intravenous propofol, fentanyl, and midazolam.<sup>72</sup> Ketamine is often used in anesthetic induction in patients with cyanotic conditions because it increases SVR and cardiac output, thereby diminishing the magnitude of right-to-left shunting. Administration of ketamine can be intravenous or intramuscular, with the caveat that an intramuscular injection may result in pain, agitation, and subsequent arterial desaturation.

Inhaled inductions are generally well received and tolerated by most children. An inhaled induction of anesthesia with sevoflurane can easily and safely be performed even in cyanotic patients, such as those with TOF (Fig. 78.7). In these patients, who are at risk for right-to-left shunting and systemic desaturation, oxygenation is well maintained with a good airway and ventilation despite reduction in systemic arterial pressure.<sup>73</sup> Skilled airway management and efficiency of ventilation are equally essential components of anesthetic induction. Recognizing the complexities of shunts and vascular resistance changes, as well as airway and ventilation effects on the cardiovascular system, is of primary importance during the induction of anesthesia.

After anesthetic induction, intravenous access is established or augmented as appropriate. A nondepolarizing muscle relaxant is usually administered and an intravenous opioid and/or inhaled anesthetic chosen for maintenance of anesthesia. The child is preoxygenated with 100%  $\text{FiO}_2$ , and an endotracheal tube is carefully positioned. Some degree of alveolar preoxygenation is recommended, even in the infant whose systemic perfusion might be jeopardized by lowering PVR with resulting increase in PBF, as this maneuver delays desaturation during intubation. A nasal

route is usually selected in neonates and other patients who will remain intubated postoperatively, as it may provide greater stability and patient comfort than an oral endotracheal tube. However, with the trend of earlier and even intraoperative extubation, as well as new data showing an association between nasal intubation and increased infections in children older than 6 months of age, the prevalence of nasal intubation has decreased. If the child arrives in the operating room with an endotracheal tube in place, it is prudent to assess the depth and the overall state of the endotracheal tube. Inspissated secretions in a tube with a small internal diameter can cause significant obstruction to gas flow and may be made worse during periods of bypass when humidified ventilation is discontinued. This may be minimized by placing a new endotracheal tube at the beginning of the procedure.

Because of the diverse array of congenital heart defects and surgical procedures, an individualized anesthetic management plan is essential. The maintenance of anesthesia in these patients depends on the age and condition of the patient, the nature of the surgical procedure, the duration of the CPB, and the need for postoperative ventilation. An assessment of the hemodynamic objectives designed to lessen the pathophysiologic loading conditions should be developed for each patient, taking advantage of the known qualitative effects of specific anesthetic drugs and ventilatory strategies. These individualized plans must also be integrated with the overall perioperative goals to configure the optimal anesthetic. In patients with complex defects requiring preoperative inotropic and mechanical ventilatory support, a carefully controlled induction and maintenance anesthetic with a potent opioid is generally chosen. In patients with a simple ASD or VSD, a balanced anesthetic with inhaled anesthetics, opioid titration, and the use of dexmedetomidine is preferred. This allows for intraoperative tracheal extubation and a less prolonged period of intensive care monitoring. More important than the specific anesthetic techniques and drugs is the skilled execution of the anesthetic plan, taking into account patient response to drugs, the changes associated with surgical manipulation, and early recognition of intraoperative complications.

The reported changes in arterial blood pressure and heart rate from the inhaled anesthetic in normal children are observed in pediatric cardiac surgical patients as well. We use potent inhaled anesthetics in almost all cases, including while on CPB, as part of a balanced anesthetic technique and for their direct protective effects against ischemia/reperfusion myocardial injury.<sup>74,75</sup> Although isoflurane decreases blood pressure in neonates, infants, and children, the vasodilatory properties of isoflurane may improve overall myocardial contractility in contrast to the effects of halothane.<sup>76</sup> Despite improved cardiac reserve with isoflurane, the incidence of laryngospasm, coughing, and desaturation during induction of anesthesia limits its use as an induction agent in children with congenital heart defects.<sup>77</sup>

Desflurane has cardiorespiratory properties similar to those of isoflurane.<sup>78</sup> Its main advantage is low blood gas and tissue solubility, allowing for rapid equilibration between the inspired and alveolar concentrations and rapid decrease of alveolar concentrations during elimination.<sup>79</sup> This provides greater precision in drug dosing during the operative period and may make desflurane a more titratable

adjunctive drug for pediatric cardiac anesthesia. The three main disadvantages of desflurane are potency, pungency, and negative inotropic effect.<sup>80,81</sup> Studies in normal infants and children suggest that 1 minimum alveolar concentration of desflurane requires concentrations of 8% to 10%.<sup>82,83</sup> Desflurane is also quite pungent, and, although its uptake is rapid, early experience with this drug for inhalation induction in children has reported a fairly high incidence of airway reactivity and laryngospasm.<sup>83-85</sup> Although its negative inotropic effect is significantly less potent than that of halothane, desflurane should not be used as the sole anesthetic in patients with significant cardiac dysfunction.<sup>85</sup>

Sevoflurane, our volatile anesthetic of choice, offers a more tolerable aroma without the magnitude of myocardial depression that accompanies halothane.<sup>86</sup> In addition, its blood gas solubility is nearly as low as that of desflurane. Hemodynamically, sevoflurane tends to produce some tachycardia, particularly in older children, and preserve systemic arterial pressure.<sup>87</sup> Reductions in heart rate and systemic arterial pressure are more modest in infants anesthetized with sevoflurane than in control subjects anesthetized with halothane, and the former exhibit echocardiographic evidence of normal contractility and cardiac index. This effect is particularly seen in children with trisomy 21.<sup>88,89</sup>

Children with complex CHD and limited cardiac reserve demand an anesthetic technique that provides hemodynamic stability. Inhalation anesthetics are less well tolerated as a sole primary anesthetic in patients who have limited cardiac reserve, especially after CPB. Fentanyl is an excellent induction and maintenance anesthetic for this group of patients. Low-to-moderate doses of this opioid can be supplemented with inhalation anesthetics. Adding low concentrations of inhalation anesthetics to smaller doses of opioids shortens or eliminates the need for postoperative mechanical ventilation while maintaining the advantage of intraoperative hemodynamic stability. Postoperative mechanical ventilation will be required when a high-dose (e.g., fentanyl > 20 µg/kg) opioid technique is used. The hemodynamic effects of fentanyl at a dose of 25 µg/kg with pancuronium given to infants in the postoperative period after operative repair of a congenital heart defect include no change in LAP, pulmonary artery pressure, PVR, and cardiac index and a small decrease in SVR and mean arterial pressure.<sup>90</sup> Because of its cardiovascular effects, pancuronium was an ideal neuromuscular blocking drug for pediatric heart surgery, but it is no longer available for clinical use. Therefore, either vecuronium or rocuronium are most often used. Larger doses of fentanyl at 50 to 75 µg/kg with rocuronium or vecuronium compared to doses of fentanyl at 50 to 75 µg/kg with pancuronium result in a slightly larger decrease in arterial blood pressure and heart rate in infants undergoing repair for complex congenital heart defects.<sup>91</sup> Despite the wide safety margin exhibited by this opioid, a selected population of infants and children with marginally compensated hemodynamic function sustained by endogenous catecholamines may manifest more extreme cardiovascular changes with these doses. Fentanyl also has been shown to block stimulus-induced pulmonary vasoconstriction and contributes to the stability of the pulmonary circulation in neonates after congenital diaphragmatic hernia repair.<sup>92</sup> Thus, the use of fentanyl may be

extrapolated to the operating room, where stabilizing pulmonary vascular responsiveness in newborns and young infants with reactive pulmonary vascular beds is crucial to weaning from CPB and stabilizing shunt flow. Fentanyl in the 8 to 12  $\mu\text{g}/\text{kg}$  dose range should provide sufficient analgesia, but still allow adequate ventilation efforts to allow for intraoperative extubation with stable hemodynamics during the procedure.

Children receiving sufentanil for induction of anesthesia as a single dose of 5 to 20  $\mu\text{g}/\text{kg}$  have a stable preintubation period.<sup>93,94</sup> Intubation and other stimuli such as sternotomy do not produce clinically significant alterations in hemodynamics, although changes are more than with equipotent doses of fentanyl. The use of fentanyl as an infusion (1-2  $\mu\text{g}/\text{kg}/\text{h}$ ) produces fewer alterations in heart rate and blood pressure. This is particularly important in infants, in whom significant hemodynamic changes are poorly tolerated. For neonates with critical CHD, sufentanil anesthetic and postoperative infusion reduce morbidity after cardiac surgery when compared with a halothane anesthetic and routine morphine postoperatively.<sup>95</sup> The blunting of the stress response observed in this study probably accounted for the differences in morbidity; no comparison group representing a more typical dose of a phenylpiperidine opioid (e.g., fentanyl, 0-75  $\mu\text{g}/\text{kg}$ ) was included to permit conclusions as to whether such large opioid doses are optimal.

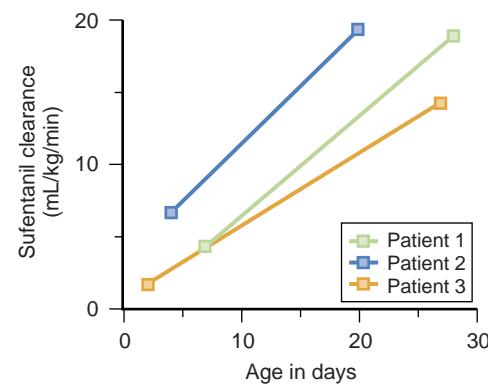
In contrast to other opioids, remifentanil, an ultra-short-acting opioid, offers the unique advantage of metabolism by nonspecific and tissue esterases, thereby limiting the potential for accumulation related to protracted elimination.<sup>96</sup> Remifentanil may provide advantages in the selected group of patients for whom the blunting of endogenous responses is desirable intraoperatively but potentially deleterious at the end of the procedure. A randomized controlled trial comparing equipotent doses of alfentanil and remifentanil for outpatient pediatric surgery revealed delayed emergence, requiring naloxone only in the alfentanil group.<sup>97</sup> In both adults and children, remifentanil is associated with qualitative hemodynamic changes similar to those with other opioids, a variable tendency to bradycardia, and a small decrease in arterial blood pressure.<sup>98-101</sup>

Because of the widespread use of the opioids for pediatric cardiac surgery and the availability of invasive monitoring, the pharmacokinetics and pharmacodynamics of these drugs have been well studied.<sup>93,99</sup> In general, the clinical pharmacology of fentanyl and sufentanil share the same age-related pharmacokinetic and pharmacodynamic features. For example, sufentanil has an increased clearance in patients 1 month to 12 years of age, comparable to adult clearance in adolescents (12-16 years of age), and a decreased clearance during the neonatal period (newborn to 1 month of age) (Table 78.7).<sup>84,88</sup> Furthermore, sequential sufentanil anesthetics in neonates with CHD show marked increases in clearance and elimination between the first week and the third or fourth week of life (Fig. 78.8).<sup>101</sup> The latter observation is most likely attributable to maturational changes in hepatic microsomal activity and improved hepatic blood flow from closure of the ductus venosus. The variability in clearance and elimination, coupled with limited cardiovascular reserve in the neonate during the first month of life, makes opioid dosing difficult in this age group.

**TABLE 78.7** Sufentanil Pharmacokinetics in Pediatric Cardiovascular Patients

Age Group	$t_{1/2} \alpha$ (min)	$t_{1/2} \beta$ (min)	Clearance (mL/kg/min)	$V_{dss}$ (L/kg)
1-30 days	23 $\pm$ 17	737 $\pm$ 346	6.7 $\pm$ 6.1	4.2 $\pm$ 1.0
1-24 months	16 $\pm$ 5	214 $\pm$ 41	18.1 $\pm$ 2.7	3.1 $\pm$ 1.0
2-12 years	20 $\pm$ 6	140 $\pm$ 30	16.9 $\pm$ 2.2	2.7 $\pm$ 0.5
12-18 years	20 $\pm$ 6	209 $\pm$ 23	13.1 $\pm$ 0.4	2.7 $\pm$ 0.5

All values are mean  $\pm$  standard deviations (see Forbess et al.<sup>386</sup>).  
 $t_{1/2} \alpha$ , Slow distribution half-life;  $t_{1/2} \beta$ , elimination half-life;  $V_{dss}$ , volume of distribution at steady state.



**Fig. 78.8** Sequential sufentanil clearance during the first month of life in three neonates with congenital heart disease. Clearance of sufentanil increases above adult rates within the neonatal period. (Data from Greeley WJ, de Brujin NP. Changes in sufentanil pharmacokinetics within the neonatal period. *Anesth Analg*. 1988;67:86-90.)

Careful titration of fentanyl 5 to 10  $\mu\text{g}/\text{kg}$  or sufentanil 1 to 2  $\mu\text{g}/\text{kg}$  or a continuous infusion technique provides the most reliable method of achieving hemodynamic stability and an accurate dose response. CPB, different institutional anesthetic practices, and individual patient differences influence pharmacokinetic and pharmacodynamic disposition of the opioids in ways that are not predictable. Even certain disease states such as TOF or pathophysiologic conditions such as increased intraabdominal pressure alter pharmacokinetic processes.<sup>90,91</sup>

Intraoperative use of methadone is an alternative pain control strategy introduced as an answer to counter acute tolerance to fentanyl infusions in the postoperative period. Adult data suggest that intraoperative use of methadone as the primary opioid in CPB cases significantly reduced the use of other opioids in the postoperative period, improved pain scores, and enhanced patient-perceived quality of pain management.<sup>102</sup> There is no pharmacokinetic data in children having CPB surgery, but available data show that the pharmacokinetic parameters in children and neonates are similar to those reported in adults, and that there is no clearance maturation with age.<sup>103</sup> For non-CPB cases, a dose of 0.2 mg/kg is suggested; we have used total doses of 0.3 to 0.4 mg/kg in CPB cases and extubated intraoperatively. Other strategies to address opioid tolerance include alternating opioid drugs, instituting opioid holidays, the addition of benzodiazepines on an as-needed basis, and the use of dexmedetomidine infusions.

Dexmedetomidine is an  $\alpha_2$ -agonist approved by the U.S. Food and Drug Administration for sedation in adults. It has been used in pediatric anesthesia as part of a balanced technique preoperatively and intraoperatively for sedation, anxiolysis, and analgesia, and postoperatively for prevention of emergence delirium and sedation.<sup>104</sup> Dexmedetomidine has significant analgesic and antiinflammatory effects, attenuates the neuroendocrine response to surgery, and has no neurotoxic effects; it is a crucial adjunct to a balanced anesthetic as it reduces the need for other analgesics and hypnotics.<sup>105-107</sup>

The pharmacodynamic effects of dexmedetomidine when used as an infusion are generally well tolerated.<sup>108</sup> The clinical effects are predictable and usually insignificant with slight lowering of both heart rate and arterial blood pressure compared to baseline.<sup>109</sup> However, when administered as a rapid bolus, the first physiologic effect noted is hypertension along with heart rate slowing, lasting approximately 2 to 5 minutes before arterial blood pressure decreases.<sup>110</sup>

Dexmedetomidine demonstrates cardiac conduction effects, via both direct depression of the sinus and AV nodes in the heart, and decreased sympathetic tone in the locus coeruleus.<sup>111</sup> Clinically, this translates into a significant reduction of the incidence of junctional ectopic tachycardia post-CPB.<sup>112</sup> However, some studies and case reports, mostly in the adult literature, have documented clinically significant bradycardia, hypotension, and even asystole with its use. It is necessary to remain vigilant and titrate dexmedetomidine carefully. Dexmedetomidine should be used with particular caution in children at risk for bradycardia or sinus or AV node dysfunction, and possibly in patients who have had a heart transplant.<sup>113</sup> At our institution, dexmedetomidine is used in almost every case, with an infusion of 0.2  $\mu$ g/kg/h in neonates and 0.5  $\mu$ g/kg/h in all other cases initiated postinduction. The infusion is continued throughout the surgery and into the postoperative period. This practice is particularly helpful in patients that are extubated intraoperatively and we will often increase the dose to 1 to 2  $\mu$ g/kg/h after extubation to keep the child calm for transport to the ICU.

## Cardiopulmonary Bypass

### DIFFERENCES BETWEEN ADULT AND PEDIATRIC CARDIOPULMONARY BYPASS

The physiologic effects of CPB on neonates, infants, and children are significantly different from the effects on adults (Table 78.8). During CPB, pediatric patients are exposed to biologic extremes not seen in adults, including deep hypothermia (18°C), hemodilution (threefold to fivefold greater dilution of circulating blood volume), low perfusion pressures (20-30 mm Hg), wide variation in pump flow rates (ranging from total circulatory arrest to 200 mL/kg/min), and differing blood pH management techniques ( $\alpha$ -stat, pH-stat, or both sequentially). These parameters deviate far from normal physiology and affect preservation of normal organ function during and after CPB. In addition to these prominent changes, subtle variations in glucose

**TABLE 78.8** Differences Between Adult and Pediatric Cardiopulmonary Bypass

Parameter	Adult	Pediatric
Hypothermic temperature	Rarely below 25°C -30°C	Commonly 15°C-20°C
Use of total circulatory arrest	Rare	Common
Pump prime		
Dilution effects on blood volume	25%-33%	150%-300%
Additional additives in pediatric primes		Blood, albumin
Perfusion pressures	50-80 mm Hg	20-50 mm Hg
Influence of $\alpha$ -stat versus pH-stat management strategy	Minimal at moderate hypothermia	Marked at deep hypothermia
Measured $\text{Paco}_2$ differences	30-45 mm Hg	20-80 mm Hg
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

supplementation, cannula placement, presence of aortopulmonary collaterals, and patient age affect organ function during CPB.

Adult patients are infrequently exposed to such biologic extremes; temperature is rarely lowered below 25°C, hemodilution is more moderate, perfusion pressure is generally maintained at 50 to 80 mm Hg, flow rates are maintained at 50 to 65 mL/kg/min, and pH management strategy is less consequential because of moderate hypothermic temperatures and rare use of circulatory arrest. Variables such as glucose supplementation rarely pose a problem in adult patients owing to large hepatic glycogen stores. Venous and arterial cannulas are less deforming of the atria and aorta, and their placement is more predictable. Although superficially similar, the conduct of CPB in children is considerably different from that in adults. Marked physiologic differences in the response to CPB in children can occur. Additionally, several modifiable intraoperative factors can influence neuropsychologic morbidity (Box 78.3).

### Volume of Priming Solutions

The priming solutions used in pediatric CPB take on great importance because of the disproportionately large priming volume-to-blood volume ratio in children. In adults, the priming volume is equivalent to 25% to 33% of the patient's blood volume, whereas in neonates and infants the priming volume may exceed the patient's blood volume by 200%. With contemporary low-volume bypass circuits (e.g., small volume oxygenators, smaller tubing), priming volume is not more than one blood volume in a small neonate. Care must be taken, therefore, to achieve a physiologically balanced priming solution and limit the volume as much as

### BOX 78.3 Central Nervous System Injury and Potential Modifiable Intraoperative Factors

- Air or particulate embolus
- Rate and depth of core cooling (if used)
- Deep hypothermic circulatory arrest (if used)
- Reperfusion injury and inflammation
- Rate of core rewarming/hyperthermia
- Hyperglycemia
- Hyperoxia
- pH management during cardiopulmonary bypass
- Hematocrit management during cardiopulmonary bypass

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 solution 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 priming 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, colloid, and, if necessary, banked blood to maintain a temperature-appropriate hematocrit. Other potential supplements are fresh frozen plasma, mannitol, a buffer (sodium bicarbonate or trishydroxymethylaminomethane [THAM]), and steroids. Low concentrations of plasma proteins have been shown experimentally to impair lymphatic flow and alter pulmonary function by increasing capillary leak.<sup>114</sup> Although adding albumin to the pump prime has not been shown to alter outcome in adults during CPB, one study suggested that maintaining normal colloid osmotic pressure may improve survival in infants undergoing CPB.<sup>115,116</sup>

Whole blood, if available, is an alternative to adding both packed RBCs and fresh frozen plasma. Blood cells are added to the prime solution to maintain a postdilutional hematocrit of at least 20% to 25% (usually higher in patients with cyanotic CHD), and plasma restores levels of procoagulants. Low-volume bypass circuits enable perfusionists and anesthesiologists to share a single unit of whole blood, thereby limiting the donor.

The addition of any blood products will cause a much higher glucose load in the priming solution. Hyperglycemia may increase the risk for neurologic injury if brain ischemia occurs. Mannitol is added to promote an osmotic diuresis and scavenge O<sub>2</sub> free radicals from the circulation. Steroids are added to stabilize membranes and produce the theoretic advantage of reducing ion shifts during periods of ischemia, attenuating inflammation caused by CPB, decreasing low cardiac output states, and improving fluid balance in the postoperative period. Steroids, however, may raise glucose levels, which can be detrimental if there is a period of cerebral ischemia, and may suppress immune function. Steroids remain a controversial additive in priming solutions. Recent retrospective data suggest negative effects with its use and an association with decreased survival in neonates having the Norwood procedure.<sup>117</sup> A number of prospective studies are ongoing to address the role of steroids in pediatric cardiac surgery.

### Temperature

Hypothermic CPB is used to preserve organ function during cardiac surgery. Three distinct methods of CPB are used: moderate hypothermia (25°–32°C), deep hypothermia (18°C), and DHCA. The choice of method of bypass is based on the required surgical conditions, patient size, type of operation, and 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 cannulas are less obtrusive and the heart can easily accommodate superior and inferior vena cava 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, such as an ASD or uncomplicated VSD. Most surgeons are willing to cannulate the inferior and superior venae cavae in neonates and infants. In these patients, however, this approach is technically more difficult and likely to induce brief periods of hemodynamic instability. Additionally, the pliability of the venae cavae and the rigidity of the cannulas 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 (50 mL/kg/min) improve the operating conditions for the surgeon by providing a nearly bloodless field. DHCA allows the surgeon to remove the atrial or aortic cannula. If this technique is used, 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. Three-region perfusion techniques may be an option to deep hypothermic CPB, but further studies are needed to assess feasibility and outcomes of this newer strategy.

### Hemodilution

Hemodilution is used during CPB to decrease homologous blood use and improve microcirculatory flow by reducing blood viscosity during periods of hypothermia. Although hemoconcentrated blood has an improved O<sub>2</sub>-carrying capacity, its viscosity reduces efficient flow through the microcirculation. With hypothermic temperatures, blood viscosity increases significantly and flow decreases. Hypothermia, coupled with the nonpulsatile 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. Further, hemodilution reduces perfusion pressure; increases CBF, thereby potentially increasing the microembolic load to the brain; and reduces the O<sub>2</sub>-carrying capacity of blood.<sup>118</sup> Using an animal model, one group of investigators found

that extreme hemodilution to a hematocrit less than 10% resulted in inadequate O<sub>2</sub> delivery, but with higher hematocrit levels of 30%, there was improved cerebral recovery after DHCA.<sup>119</sup> Jonas and colleagues<sup>120</sup> confirmed these findings in a randomized trial using two hemodilution protocols (20% vs. 30% hematocrit) in infants younger than 9 months of age. In the short term, the group with lower hematocrit values had lower nadirs of cardiac index, higher serum lactate levels 1 hour after CPB, and a greater increase in total body water on the first postoperative day. At 1 year of age, mental development index scores were similar but psychomotor development index scores were significantly lower in the group with lower hematocrit values. Also, infants in this group had psychomotor development scores that were 2 standard deviations below the mean. Because RBCs serve as the major reservoir of O<sub>2</sub> during circulatory arrest, especially during rewarming, hematocrit values closer to 30% are generally preferred for deep hypothermia when this technique is contemplated. Currently, most centers maintain hematocrit levels approximately 25% to 30% during CPB, enhancing O<sub>2</sub> delivery to vital organs such as the brain. Cerebral O<sub>2</sub> delivery is an especially important consideration because cerebral autoregulation is impaired at deep hypothermic temperatures and after DHCA.

To achieve a hematocrit level of 25% to 30% in neonates and infants, banked blood should be added to the priming solution. The mixed hematocrit level on CPB (the hematocrit level of the total priming volume plus the patient's blood volume) can be calculated by the following formula:

$$\text{Hct}_{\text{CPB}} = \text{BV}_{\text{pt}} \times \text{HCT}_{\text{pt}} / \text{BV}_{\text{pt}} + \text{TPV}$$

where Hct<sub>CPB</sub> is the mixed hematocrit (TPV + BV<sub>pt</sub>), BV<sub>pt</sub> is the patient's blood volume (weight in kilograms × estimated blood volume in milliliters per kilogram), TPV is the total priming volume, and Hct<sub>pt</sub> is the starting hematocrit level of the patient. This calculation allows an estimate of the hematocrit level of the patient using an asanguinous priming solution and is therefore useful for older children and adolescents. In neonates and infants, the perfusionist must add blood to the pump prime to achieve a desired hematocrit level during hypothermic CPB. The following formula estimates the amount of packed RBCs in milliliters that must be added to the prime volume to achieve this hematocrit level:

$$\begin{aligned} \text{Added RBCs (mL)} &= (\text{BV}_{\text{pt}} + \text{TPV}) (\text{Hct}_{\text{desired}}) \\ &\quad - (\text{BV}_{\text{pt}}) (\text{Hct}_{\text{pt}}) \end{aligned}$$

where BV<sub>pt</sub> is the patient's blood volume, TPV is the total priming volume, Hct<sub>desired</sub> is the desired hematocrit level on CPB, and Hct<sub>pt</sub> is the starting hematocrit level of the patient.

Like in adults, the optimal hematocrit level after weaning from CPB is not clear for pediatric patients. Decisions concerning post-CPB hematocrit levels are made based on the patient's post-repair function and anatomy. Neonates, patients with residual hypoxemia, and those with moderate-to-severe myocardial dysfunction benefit from the improved O<sub>2</sub>-carrying capacity of hematocrit levels of 40% or higher. Patients with a physiologic correction and excellent myocardial function may tolerate hematocrit levels of 25% to 30%.<sup>121</sup> In children with mild-to-moderate myocardial dysfunction, accepting hematocrit values

between these levels 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 postbypass period.

## BLOOD GAS MANAGEMENT

The theoretic benefit of α-stat versus pH-stat blood gas management during hypothermic CPB has been a topic of great debate. Although the pH-stat strategy may not be optimal for adults in whom the principal risk for brain injury is microembolism, this risk is thought to be lower in infants because of the lack of atherosclerotic disease. With pH-stat management, the addition of CO<sub>2</sub> to the inspired gas mixture during cooling on CPB increases CBF and may improve cerebral tissue oxygenation and outcomes.

The controversial issue of pH management during CPB has been addressed in a large study from Boston Children's Hospital. In this study, infants younger than 9 months of age were randomized to α-stat versus pH-stat during deep hypothermic CPB with excellent long-term follow-up.<sup>122,123</sup> Neurodevelopmental outcomes were evaluated in infants undergoing biventricular repair for a variety of cardiac defects when younger than 9 months of age. The short-term benefits identified with the pH-stat strategy included a trend toward less postoperative morbidity and shorter recovery time to first electroencephalographic activity. In patients with TGA, there was a shorter duration of intubation and ICU stay in patients.<sup>122</sup> However, the use of either the α-stat or pH-stat strategies was not consistently related to either improved or impaired neurodevelopmental outcomes at 2- and 4-year follow-up.<sup>123</sup>

## INITIATION OF CARDIOPULMONARY BYPASS

Arterial and venous cannula placed in the heart before initiating CPB may result in significant problems in the peri-bypass period. A malpositioned venous cannula has the potential for vena cava obstruction. The problems of venous obstruction are magnified during CPB in the neonate because arterial pressures are normally low (20-40 mm Hg), and large, relatively stiff cannulas easily distort these very pliable venous vessels.<sup>114,116</sup> A cannula in the inferior vena cava may obstruct venous return from the splanchnic bed, resulting in ascites from increased hydrostatic pressure 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 superior vena cava obstruction. This condition may be more ominous during bypass. Under these circumstances, three problems may ensue: (1) cerebral edema, (2) a reduction in regional or global CBF, and (3) reduced proportion of pump flow reaching the cerebral circulation, causing inefficient brain cooling.

In the operating room, superior vena cava pressures via an internal jugular catheter should be monitored by examining the patient's head for signs of suffusion after initiating bypass. Discussions with the perfusionist regarding

adequacy of venous return and large cooling gradients between the upper and lower body should alert the anesthesiologist and the surgeon to potential venous cannulae problems. Patients with anomalies of the large systemic veins (persistent left superior vena cava or azygous continuation of an interrupted inferior vena cava) are at particular risk for problems with venous cannulation and drainage.

Problems with aortic cannula placement can occur. The aortic cannula may slip beyond the takeoff of the innominate artery, with blood therefore selectively flowing 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 hemispheres after initiating CPB. The presence of large aortic-to-pulmonary collaterals, such as a large PDA, also may divert blood to the pulmonary circulation from the systemic circulation, thereby reducing CBF and the efficiency of brain cooling during CPB. The surgeon should gain control of the ductus either before or immediately after instituting CPB to eliminate this problem and, if possible, large aortopulmonary collaterals should be embolized in the cardiac catheterization laboratory before 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. Such adaptations require careful vigilance to ensure effective, thorough perfusion and cooling of vital organs.

Once the aortic and venous cannulas 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 ensured, 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 caused by 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 increased by using vacuum-assisted drainage under certain circumstances.

In neonates and infants, deep hypothermia is commonly used. For this reason, 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. 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.

CPB 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 RA 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-priming volume ratio, and intravascular volume falls precipitously if the venous drainage precedes aortic inflow. Once the aortic cannula position is verified, pump flow rates are rapidly increased to maintain effective systemic perfusion. Because coronary artery disease is rarely a consideration, the myocardium should cool evenly unless distortion caused by the cannulas compromises the coronary arteries. When a cold prime is used, caution must be exercised in using the pump to infuse volume before initiating CPB. Infusion of cold perfusate may result in bradycardia and impaired cardiac contractility before the surgeon is prepared to initiate CPB.

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

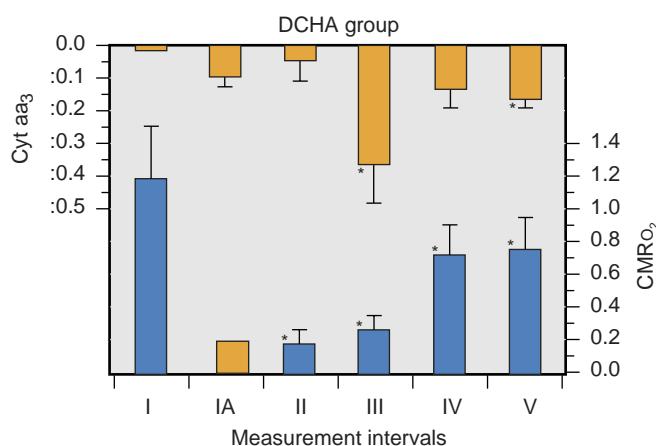
## PUMP FLOW RATES

Recommendations for optimal pump flow rates for children have historically been based both on the patient's body mass and on evidence of efficient organ perfusion as determined by arterial blood gases, acid-base balance, and whole-body O<sub>2</sub> consumption during CPB.<sup>124</sup> At hypothermic temperatures, metabolism is reduced, and CPB flow rates can therefore be reduced and still meet or exceed the tissue's metabolic needs (see the discussion of low-flow CPB in the following section).

## SPECIAL TECHNIQUES

### Deep Hypothermic Circulatory Arrest

A certain subset of neonates, infants, and children with CHD require extensive repair of complex congenital heart defects using DHCA. This technique facilitates precise surgical repair under optimal conditions, with no blood or cannulae in the operative field and providing maximal organ protection and often resulting in shortened total CPB time. The scientific rationale for the use of deep hypothermic temperatures rests primarily on a temperature-mediated reduction of metabolism. Whole-body and cerebral O<sub>2</sub> consumption during induced hypothermia decreases the metabolic rate for O<sub>2</sub> by a factor of 2 to 2.5 for every 10°C reduction in temperature.<sup>125</sup> These results are consistent with in-vitro models, which relate temperature reduction to a decrease in the rate constant of chemical reactions, as originally described by Arrhenius using the equation  $k = Ae^{-RT}$ . The reduction in O<sub>2</sub> supply during deep hypothermic low-flow CPB is associated with preferential increases in vital organ perfusion (e.g., to the brain) and increased extraction of O<sub>2</sub>.<sup>126</sup> Therefore, to some extent, deep hypothermic low-flow CPB



**Fig. 78.9 Bar graph of variations in cytochrome oxidase (cyt aa<sub>3</sub>) near-infrared spectroscopic signals and cerebral metabolic rate for oxygen (CMRO<sub>2</sub>) in subjects with deep hypothermic circulatory arrest (DCHA).** Each point of cyt aa<sub>3</sub> represents mean  $\pm$  SE in six subjects; CMRO<sub>2</sub> values are mean  $\pm$  SD. Negative values in cyt aa<sub>3</sub> represent relative decreases in quantity of oxidized enzyme. \*CMRO<sub>2</sub> and cyt aa<sub>3</sub> are significantly different from control,  $P < .05$ .

exerts a protective effect by reducing the metabolic rate for O<sub>2</sub>, promoting preferential organ perfusion, and increasing tissue O<sub>2</sub> extraction.

The duration of the safe period for DHCA has not clearly been delineated.<sup>127</sup> 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 to and the least tolerant of these effects. Brainstem and cortical evoked potentials as well as processed electroencephalograms are altered after DHCA.<sup>127-129</sup> The abnormalities in 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 (Fig. 78.9; also see Fig. 78.6).<sup>70</sup> Importantly, during the use of these extremes of temperature, autoregulation is lost and cerebral perfusion becomes highly dependent on the extracorporeal perfusion and presumably postbypass hemodynamic performance.

The potentially deleterious effects of prolonged DHCA in infants and neonates are well described. In general, it is agreed that very prolonged periods of uninterrupted DHCA may have adverse neurologic outcomes. However, considerable disagreement exists if a “safe” period of DHCA exists and whether patient-specific, procedure-specific, or postoperative management strategies may attenuate or promote CNS damage from DHCA. Cases have been reported of detrimental effects of DHCA on a variety of outcomes regarding the CNS, while others have described an inconsistent effect or no effect.<sup>122,130,131</sup> Three issues have become clear over time: (1) the effects of short durations of DHCA are inconsistently related to adverse outcomes, (2) the effect of DHCA is not a linear phenomenon, and (3) the effects are most likely modified by other patient-related, preoperative, and postoperative factors.<sup>131-133</sup> A large-scale study of 549 subjects undergoing the Norwood stage 1 procedure with DHCA found duration of greater than 45 minutes to be a risk factor for 30-day mortality.<sup>134</sup>

## Regional Cerebral Perfusion

Some surgeons have developed innovative and challenging strategies to provide continuous cerebral perfusion during complex reconstruction of the aortic arch or intracardiac repair to avoid or minimize the use of DHCA. However, avoiding DHCA, the duration of CPB is necessarily lengthened, and longer durations of CPB have been shown to adversely affect both short- and long-term outcomes.<sup>51,52</sup> The relative risks and benefits of longer CPB versus less (or no) DHCA remain a subject of continued controversy. In efforts to study this newer strategy, two recent studies have evaluated the technique of regional cerebral perfusion. In one non-randomized study, Wypij and colleagues<sup>135</sup> followed 29 infants who underwent a stage 1 palliation, 9 of whom received regional cerebral perfusion at 30 to 40 mL/kg/min. The authors reported no difference in mental or psychomotor developmental indices at 1 year of age between the regional cerebral perfusion group and those who received DHCA as a primary strategy. A larger randomized trial of DHCA with or without regional cerebral perfusion at 20 mL/kg/min in patients with a functional single ventricle included 77 patients with similar survival to hospital discharge (88%) and at 1-year follow-up (75%).<sup>136</sup> No significant difference was seen in either the psychomotor development index or the mental development index scores between the two groups at any time points, although the scores tended to be lower in the regional cerebral perfusion group.

A further innovation to the previously described technique is a three-region perfusion strategy for aortic arch reconstruction in the Norwood procedure. This strategy involves direct perfusion of the coronaries via a proximal aortic cannula, splanchnic beds via a distal thoracic aorta cannula, and cerebral perfusion via an innominate cannula. The arch repair occurs from distal to proximal at warmer patient temperatures and with a beating heart. This theoretically provides the potential for decreased coronary and splanchnic ischemic times, decreasing the risk of cardiac dysfunction and abdominal organ damage, and mitigating the negative hypothermic effects on the hematological system.<sup>2,3</sup> Larger, long-term studies are needed to assess the efficacy of this technique in improving cardiovascular, renal, and other outcomes.

## Glucose Regulation

The detrimental effects of hyperglycemia during complete, incomplete, and focal cerebral ischemia are well demonstrated.<sup>137,138</sup> The role of glucose in potentiating cerebral injury appears to rest on two factors: adenosine triphosphate (ATP) usage and lactic acidosis.<sup>139,140</sup> 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, though its role 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.<sup>141</sup>

Although the detrimental effects of hyperglycemia during ischemia are clear, very little evidence supports a relationship between a worsening neurologic outcome and

hyperglycemia during CPB or DHCA in children. A review of acquired neurologic lesions in patients undergoing the Norwood stage 1 procedure for HLHS suggested hyperglycemia as a significant associated finding in patients with extensive cerebral necrosis or intraventricular hemorrhage. A host of other potentially damaging factors (e.g., periods of hypoxia, low diastolic and systolic pressure, thrombocytopenia) were statistically associated with the observed neuropathology.<sup>142</sup> Whether glucose directly contributes to neurologic injury or merely serves as a marker for a high-risk population that ultimately suffers neurologic insult as a result of other factors is not clear.

Hypoglycemia is also a frequent concern in neonates during the perioperative period. Reduced hepatic gluconeogenesis coupled with decreased glycogen stores places the newborn at increased risk for hypoglycemic events. In newborns with CHD, reduced systemic perfusion (e.g., critical coarctation, HLHS, 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% to 30% dextrose infusions to maintain euglycemia in the prebypass period. Older children are not immune to hypoglycemic events and are therefore susceptible to hypoglycemia-induced neurologic injury. Patients with low cardiac output states (cardiomyopathies, pre-transplant patients, critically ill postoperative patients) requiring reoperation and when on substantial inotropic support are at high risk for reduced glycogen stores and intraoperative hypoglycemia.<sup>143</sup>

The impact of hypoglycemia during CPB is further complicated by the consequences of hypothermia, CO<sub>2</sub> 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 electroencephalographic findings. However, after 10 minutes of hypocapnic hypoglycemia, the electroencephalogram became flat.<sup>144</sup> The loss of electroencephalographic activity from hypoglycemia alone does not normally occur above glucose levels of 8 mg/dL.<sup>145</sup>

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.<sup>142</sup> The common practice of using hyperventilation to reduce PVR in neonates and infants during weaning from CPB and in the early postbypass period can further exacerbate hypoglycemic injury. Glucose monitoring and rigid maintenance of euglycemia are an important part of CPB management in the patient with CHD.

### Renal Effects

After CPB, the combined effects of hypothermia, nonpulsatile perfusion, and reduced mean arterial pressure cause release of angiotensin, renin, catecholamines, and antidiuretic hormones.<sup>146-148</sup> These circulating hormones promote renal vasoconstriction and reduce renal blood flow. However, despite the negative impact of CPB on renal function, low-flow, low-pressure, nonpulsatile perfusion has not been linked with postoperative renal dysfunction (Table 78.9).<sup>147</sup> The factors that best correlate with

**TABLE 78.9** Sequelae of Pediatric Cardiopulmonary Bypass

End-Organ Injury	Cause and Signs
Renal injury	Organ immaturity, preexisting renal disease Post-cardiopulmonary bypass low cardiac output, use of DHCA Renal dysfunction characterized by reduced GFR and ATN
Pulmonary injury	Endothelial injury, increased capillary leak, complement activation, and leukocyte degranulation Pulmonary dysfunction characterized by reduced compliance, reduced FRC, and increased A-a gradient
Cerebral injury after DHCA	Loss of autoregulation, suppressed metabolism and cerebral blood flow, cellular acidosis, and cerebral vasoparesis CNS dysfunction characterized by seizures, reduced developmental quotients, choreoathetosis, learning disabilities, behavioral abnormalities

A-a, Alveolar-arterial; ATN, acute tubular necrosis; CNS, central nervous system; DHCA, deep hypothermic circulatory arrest; FRC, functional residual capacity; GFR, glomerular filtration rate.

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.<sup>148</sup>

Acute kidney injury after pediatric cardiac surgery has an incidence between 20% to 60% depending on criteria used.<sup>149</sup> Multiple causative factors are involved, and the final common result is oliguria and an increased serum creatinine. Diuretics have been the mainstay of promoting urine flow after pediatric CPB. Furosemide in a dose of 1 to 2 mg/kg or ethacrynic acid 1 mg/kg every 4 to 6 hours, or both, induces diuresis and may reverse renal cortical ischemia associated with CPB. After DHCA, a 24-hour period of oliguria or anuria can occur that resolves over the next 12- to 24-hour period. The use of diuretics is effective only after spontaneous urine output has been initiated in these patients.

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 results in 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.<sup>150,151</sup>

### Pulmonary Effects

Cardioplegia protects the heart, but no parallel protection is afforded to the lungs during bypass. Pulmonary dysfunction is common after CPB, and its pathogenesis is poorly understood (see Table 78.9). In the broadest terms, lung injury is mediated in one of two ways: first, by an inflammatory

response resulting from leukocyte and complement activation and, second, by a mechanical effect culminating in surfactant loss, atelectasis with resultant ventilation-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.<sup>152,153</sup> Atelectasis and increased capillary leak due to hemodilution and hypothermic CPB are the most likely causes. 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.<sup>154</sup> Leukocytes and complement are important in causing capillary-alveolar membrane injury and microvascular dysfunction through platelet plugging and release of mediators, which increase PVR. The technique of MUF is highly effective in reducing lung water and pulmonary morbidity during the postoperative period.

## 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, endorphins, and other substances, characterizes the stress response during hypothermic CPB.<sup>9,155</sup> The likely causes of the elaboration of these substances include contact of blood with the nonendothelialized surface of the pump tubing and oxygenator, nonpulsatile flow, low perfusion pressure, hemodilution, hypothermia, and light anesthesia depth. Other factors that may contribute to elevations of stress hormones include delayed renal and hepatic clearance 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. Strong evidence indicates that the stress response can be blunted by increasing the depth of anesthesia.<sup>9,155</sup>

The stress response in return can 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 have been demonstrated.<sup>95,156</sup> Although blunting the stress response seems warranted, additional evidence suggests that the newborn stress response, especially the endogenous release of catecholamines, may be an adaptive metabolic response necessary for survival at birth.<sup>157</sup> Thus, the complete elimination of an adaptive stress response may not be desirable. To what extent acutely ill neonates with CHD depend on the stress response for maintaining hemodynamic stability is currently unknown.

A depth of anesthesia adequate to attenuate the stress response should be used, but to attempt to block the response altogether is likely not necessary. Acceptable anesthesia

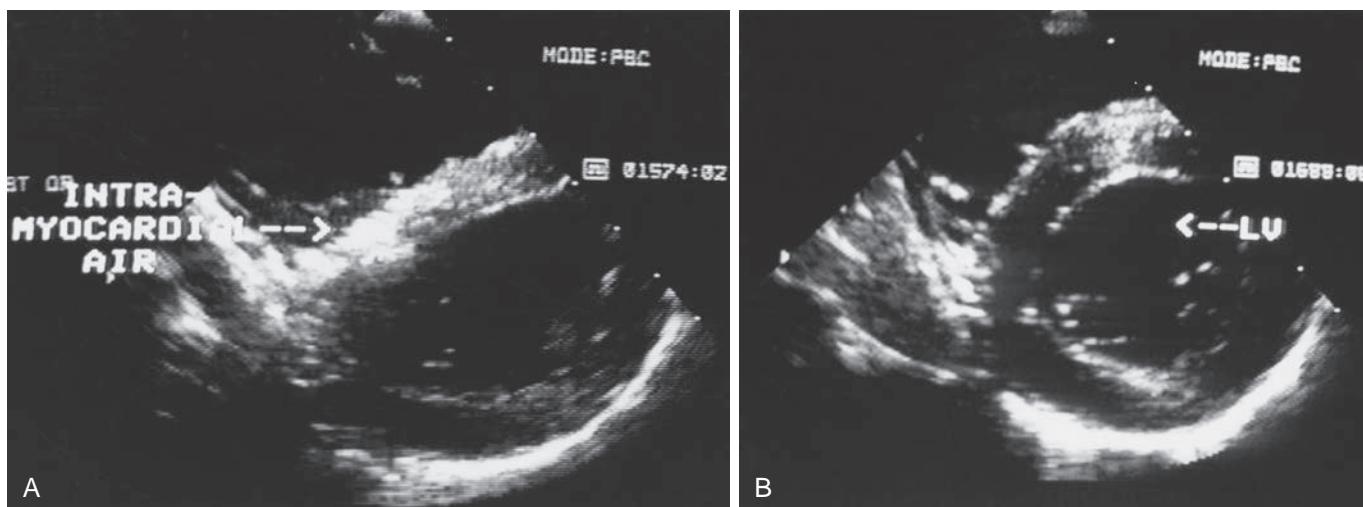
during CPB may be best accomplished by the continuous administration of an inhaled anesthetic via a vaporizer connected to the pump oxygenator, dexmedetomidine infusion, careful titration of incremental doses of opioids, or the precise administration of an opioid or opioid and benzodiazepine by a continuous infusion technique. Primary opioid anesthetic techniques result in reduced stress hormone release and decreased postoperative metabolic acidosis and lactate production compared with halothane anesthesia and may therefore be a preferred technique in complex CHD.<sup>95</sup> If an adequate depth of anesthesia is accomplished by the administration of excessively large doses of opioids (e.g., fentanyl or sufentanil), postoperative mechanical ventilation will be necessary. By contrast, residual levels of inhaled anesthetics (e.g., halothane or isoflurane) can produce transient myocardial depression at the termination of CPB, complicating separation from CPB. Because of the improved surgical techniques coupled with the reduced morbidity of CPB, the use of high doses of an opioid anesthetic is infrequent in current practice.

## DISCONTINUATION OF CARDIOPULMONARY BYPASS

In separating the patient 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 is fully warmed, acid-base status is normalized, heart rate is adequate, and sinus rhythm has been achieved, the venous drainage is stopped 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 a transthoracic left or right atrial catheter, by a percutaneous internal jugular catheter, or by the use of intraoperative echocardiography. Pulse oximetry also can be used to assess the adequacy of cardiac output.<sup>158</sup> Low 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.<sup>159</sup>

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 (1) an inadequate surgical result with a residual defect requiring repair, (2) pulmonary artery hypertension, and (3) right or left ventricular dysfunction.

Two general approaches are customarily used, either independently or in conjunction. 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 O<sub>2</sub> saturation data to examine for residual shunts).<sup>160</sup> Alternatively, echo-Doppler imaging may be used to provide an intraoperative image of structural or functional abnormalities to assist in the evaluation of the postoperative cardiac repair.<sup>7,161</sup> If structural abnormalities are found, the patient can be placed back on CPB and residual defects can be repaired before the patient leaves



**Fig. 78.10** (A) Two-dimensional echocardiogram in the short-axis view across the ventricles demonstrating the presence of intramyocardial air (arrow) in the ventricular septum and right ventricular wall. The intramyocardial air appears as a dense, "snowy" echogenic area. Note the associated wall motion abnormality appearing as flattening of the ventricular septum. (B) The patient was treated with phenylephrine, increasing systemic and coronary perfusion pressure, resulting in clearance of the air, normalization of the echogenic density, and restoration of normal left ventricular (LV) wall motion and configuration.

the operating room. Leaving the operating room with a significant residual structural defect adversely affects survival and increases patient morbidity (see Fig. 78.5).<sup>7,161</sup> Echo-Doppler imaging can rapidly identify right and left ventricular dysfunction and suggest the presence of pulmonary artery hypertension. In addition, echo-Doppler imaging can identify regional wall motion abnormalities caused by ischemia or intramyocardial air that will direct specific pharmacologic therapy and provide a means of assessing the results of these interventions (Fig. 78.10).<sup>162</sup>

## ULTRAFILTRATION

Institution of CPB in neonates, infants, and young children results in a profound proinflammatory response and significant hemodilution. This may contribute to post-CPB morbidity and mortality resulting from poor organ function. The organ systems most affected by this are the heart, lungs, and brain. Although contact between the patient's blood and the foreign surface of the bypass circuit is a potent stimulus to trigger the inflammatory cascade, other factors including ischemia, profound hypothermia, rewarming, and surgical trauma are also important in its genesis. These inflammatory mediators include complement anaphylatoxins, vasoactive amines, and cytokines (e.g., tumor necrosis factor- $\alpha$  [TNF- $\alpha$ ]) that lead to an increase in vascular permeability.<sup>163</sup> Hemodilution occurs at the onset of CPB despite the use of physiologically balanced priming solutions that include blood, crystalloid, albumin, and buffer and smaller volume circuits. Hemodilution may, however, be advantageous in patients in whom the surgery is performed under hypothermic conditions ranging from mild hypothermia to DHCA. Initiation of CPB will change the viscoelastic properties of blood, and these changes have been shown to continue into the post-CPB period.<sup>164</sup> Although the mode of perfusion, cardiotomy suction, arterial roller pump type, and shear forces of the CPB circuit are important, it is the temperature and hematocrit of the

blood that play the most important role in changing viscoelasticity. It has been shown that low temperature with a high hematocrit leads to a higher viscosity.<sup>165</sup> This elevated viscosity may lead to altered organ perfusion, particularly in the brain. Because of these alterations in blood viscosity, hemodilution is tolerated in the cooling phases of CPB. Although advantageous early, this hemodilution combined with the inflammatory response will lead to transudation of fluid into the extravascular space, which in turn leads to the potential for organ dysfunction as eluded to earlier. Prevention of organ dysfunction and improved oxygenation by the removal of excess fluid and inflammatory mediators are the rationale, therefore, in the use of ultrafiltration. The end result is removal of plasma water and low-molecular-weight solutes across a semipermeable membrane.

Essentially, five forms of ultrafiltration are used in modern perfusion practice, three of which are while the patient is on CPB. Prime ultrafiltration is used when packed RBCs are added to the prime solution and is performed in the prebypass phase; prime ultrafiltration aims to replace crystalloid prime with blood prime, adjust pH, alter electrolyte concentration to safer levels, and remove inflammatory mediators potentially present in the donor blood.<sup>166</sup> Conventional ultrafiltration (CUF) involves the removal of fluid at any time while the patient is being supported by CPB. A common use for this method is removal of the volume of clear fluid equal to the volume of cardioplegia used. CUF can be performed during all phases of CPB. It involves the placement of an ultrafilter within the circuit and connected either to the venous line or the venous reservoir. The removal of an excess of ultrafiltrate will result in low reservoir volumes. In zero balance ultrafiltration, once fluid has been removed it is replaced with crystalloid to avoid inadequate reservoir volume, and thus there is no net removal of volume.

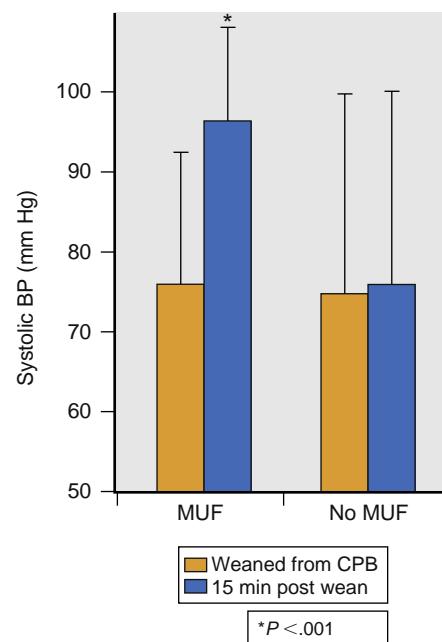
The third method of on-bypass ultrafiltration is dilutional ultrafiltration, which is employed when the concentration of a given electrolyte (e.g., potassium) is deemed elevated.

The method involves removal of ultrafiltrate with its replacement by half with normal saline, thus diluting the concentration of the given electrolyte to safer levels. All on-bypass ultrafiltration have similar end points—that is, attempted removal of excess clear fluid resulting in hemoconcentration, removal of inflammatory mediators, and manipulation of electrolyte concentrations to safe levels.

MUF, first described by Naik and associates<sup>150</sup> in 1991, involves filtration of blood once the patient has been weaned from bypass. This can be achieved either by a venovenous technique in which blood is removed and returned to the atrium once concentrated or by an arteriovenous technique in which blood is removed via the aortic cannula and returned via the venous line.<sup>150,167,168</sup> In more detail, in this technique blood is removed in a retrograde fashion by the aortic cannula and passes through the ultrafilter along with remaining circuit volume from the venous reservoir and oxygenator. Flow through the ultrafilter is maintained by a roller pump at flows of between 10 and 30 mL/kg, with the slower rates resulting in a more gradual change in the intravascular fluid compartment and thus potentially better tolerated. A constant atrial pressure is maintained throughout the procedure by adding crystalloid into the venous reservoir as needed. Suction is applied to the filtrate port to achieve a maximal transmembrane pressure, thus allowing for ultrafiltration rates of between 100 and 150 mL/min. End points for the process of MUF are time (15–20 minutes) and reaching of a target hematocrit (usually 40%) once the circuit volume has been replaced by crystalloid or should the patient's hemodynamics not tolerate the procedure.

Cardiac surgeries in the very young may be complex with potentially protracted CPB and cross-clamp times. Therefore, myocardial performance is more commonly depressed after weaning from CPB. Although ultrafiltration is used during CPB in an attempt to remove excess body water, it appears from studies that it is the use of MUF that significantly improves myocardial performance (Fig. 78.11).<sup>169,170</sup> Using echocardiographic measurements in a study of infants undergoing corrective surgery under non-hypothermic arrested conditions, Davies and associates<sup>171</sup> found improvements in both systolic and diastolic function in the children studied. They found that the preload recruitable stroke work, which is load independent, improved after MUF and was thus a good indicator of improved systolic function. The same study showed that after MUF a decrease in the myocardial wall thickness and cross-sectional area occurred that was not present in the control group of patients who received no ultrafiltration. These reductions result in an increase in end-diastolic length and a fall in end-diastolic pressure, both of which are indicators of improved diastolic function. Although presumably it was the decrease in myocardial edema that was the cause for these improvements, increased hematocrit also was observed. Because these positive effects were not seen past 24 hours, the absolute benefit of MUF is not clear.<sup>171</sup>

Pulmonary dysfunction is one of the most common negative effects of CPB<sup>172</sup>; MUF is utilized to improve oxygenation, decrease the effects of inflammatory mediators on the alveolar capillary membrane, and decrease pulmonary vascular reactivity. Studies have demonstrated that in patients in whom ultrafiltration and MUF were used, improvements in pulmonary compliance, decreased airway resistance,

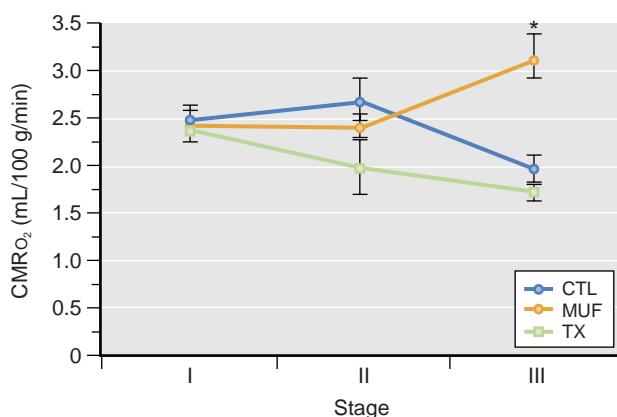


**Fig. 78.11 Systolic blood pressure (BP) after separating from cardiopulmonary bypass (CPB) and 15 minutes after separating with and without modified ultrafiltration (MUF).** Note the significant improvement in systolic BP with the use of MUF. (From Ungerleider RM. Effects of cardiopulmonary bypass and use of modified ultrafiltration. *Ann Thorac Surg*. 1998;65:S35; reprinted with permission from the Society of Thoracic Surgeons.)

pulmonary arterial reactivity, and improved oxygenation were demonstrated.<sup>172–175</sup> It is therefore obvious why these methods have found such wide acceptance in pediatric cardiac surgery, particularly in patients in whom normal compliance with low PVR is vital (i.e., those with single-ventricle physiology). Although these studies commonly find improvement in pulmonary function immediately after weaning from CPB and the completion of MUF, disagreement exists as to whether these effects result in improved function much beyond 6 hours, with some showing little if any benefit at 24 hours. A conclusion, however, from these studies is that combination of on-bypass ultrafiltration coupled with MUF has the best results in the early postbypass period.

In a study performed on a piglet model of DHCA, the use of MUF after CPB improved hematocrit, cerebral O<sub>2</sub> delivery, and cerebral O<sub>2</sub> consumption, thus representing a potential reduction in cerebral injury. Further studies have made similar conclusions, demonstrating that four variables are of importance in improving cerebral oxygenation: PCO<sub>2</sub>, mean arterial pressure, hematocrit, and MUF flow rate.<sup>176,177</sup> Increasing all except MUF flow rate improved O<sub>2</sub> delivery. Increasing the flow rate appeared to cause a steal-like phenomenon in which apparent diastolic runoff occurred into the MUF circuit from the aortic cannula. Thus, although the process of MUF is important for recovery of normal cerebral function, care must be used not to negate the benefits by decreasing the time on MUF by increasing the flow rates (Fig. 78.12).

Common to the improvement in cardiac and pulmonary function are the associated decrease in inflammatory mediators seen after ultrafiltration. Studies have shown



**Fig. 78.12 Cerebral metabolic rate for oxygen measurements (CMRO<sub>2</sub>) before and after deep hypothermic circulatory arrest.** Note the significant increase in CMRO<sub>2</sub> in the MUF animals compared with the control and transfusion groups at stage 3. CTL, Control; MUF, modified ultrafiltration; TX, transfusion. (From Skaryak LA, Kirshbom PM, DiBernardo LR, et al. Modified ultrafiltration improves cerebral metabolic recovery after circulatory arrest. *J Thorac Cardiovasc Surg*. 1995;109:744–751.)

that the ultrafiltrate contains a wide variety of low-molecular-weight inflammatory mediators, including C3a, C5a, interleukin (IL)-6, IL-8, TNF, myocardial depressant factor, and endothelin.<sup>173,178,179</sup> It is the removal of endothelin-1 after MUF that results in the improvement of pulmonary vascular reactivity, which is of great importance, particularly in infants younger than 4 to 6 months of age, when pulmonary vascular reactivity is high, and in patients who are having staged cavopulmonary reconstructions. TNF, a potent inflammatory mediator implicated in the development of capillary leak syndrome seen after CPB, has been shown to be removed best by MUF. Despite these positive effects of MUF, the literature does not give a clear advantage of one form of ultrafiltration over the other, and it may be the combination of these methods that once again shows the best potential results.

Another important post-CPB issue is ongoing blood loss. The use of MUF will result in an elevation of the patient's hematocrit secondary to the removal of the excess body water, as already discussed. This further results in decreased blood use and the observation that there is less postoperative bleeding.<sup>180</sup> Indeed, in older children attempts can thus be made to avoid the use of donor blood altogether.

Disadvantages to these techniques are noted. The addition of an ultrafilter to the CPB circuit adds a level of complexity to the circuitry and thus another potential area in which circuit-related complications may occur. Opponents of MUF note also the following potential problems: the potential for air entrainment into the arterial cannula, additional time in which the patient is anticoagulated, potential for hypovolemia as volume is drawn off from the patient, hypothermia because the filtered volume does not pass through the heater/oxygenator, and the potential for the increase in the plasma concentration of drugs (e.g., fentanyl).<sup>181</sup> Another interesting complication potentially associated with ultrafiltration was the reduction in thyroid hormone. This acute hypothyroidism may lead to depressed function, manifesting as decreased contractility, heart rate, cardiac output, and elevated SVR, all of which will

clearly affect the immediate post-CPB period.<sup>182</sup> As with other techniques in medicine the benefit versus risk must be seriously considered, but from the presented evidence the use of ultrafiltration both on and off CPB is extremely beneficial and these methods are thus commonly used in modern pediatric cardiac surgery with good result and little complication.<sup>143,145,183,184</sup>

In the preceding paragraphs the discussion concluded that no clear advantage has been determined of one method of ultrafiltration over the other. Unfortunately, comparing a wide range of patients having different surgeries under different conditions is difficult, and thus it appears that from the articles referenced the best strategy would include both the use of on-CPB ultrafiltration and the use of MUF once the patient has been separated from bypass to achieve the goals of decreasing total-body water; removal of inflammatory mediators; improved hematocrit, and thus O<sub>2</sub>-carrying capacity; and preservation of vital organ function. With the miniaturization of CPB circuits and resultant reduced hemodilution, some institutions have stopped using MUF because it simplifies and decreases the volume of the CPB circuit. They believe there is an advantage to preventing hemodilution rather than reversing hemodilution with MUF. Significantly miniaturizing circuits is also not without safety concerns as it may limit the ability to increase CPB flow rates. At our institution we continue to use MUF for the many reasons previously described.

### SPECIFIC PROBLEMS ENCOUNTERED IN DISCONTINUING CARDIOPULMONARY BYPASS

#### Left Ventricular Dysfunction

The contractile state of the LV may be reduced after pediatric cardiac surgery, due to surgically induced ischemia during the repair, the preoperative condition of the myocardium, the effects of DHCA on myocardial compliance, and new, altered loading conditions on the LV caused by the repair.<sup>185,186</sup> Left ventricular dysfunction can be treated by optimizing preload, increasing heart rate, increasing coronary perfusion pressure, correcting ionized calcium levels, and adding inotropic support. The neonate's heart rate-dependent cardiac output, reduced myocardial compliance, and diminished response to calcium and catecholamines are factors influencing the need for inotropic support. Inotropic support usually begins with epinephrine 0.03 to 0.05 µg/kg/min or dopamine 3 to 10 µg/kg/min. Several studies suggest that the effect of dopamine in children is age dependent. After cardiac surgery in young children, dopamine increases cardiac output, which correlates more with elevations in heart rate than augmentation of stroke volume, whereas, in young adults, dopamine clearly increases stroke volume. Nonetheless, infants and neonates respond favorably to epinephrine and dopamine infusions with increased systemic arterial blood pressure and cardiac output and improved systemic perfusion.

Calcium supplementation is important in augmenting cardiac contractility. Although calcium supplementation has fallen into some disfavor because of concerns over reperfusion injury, it remains an important therapy after pediatric cardiac surgery. Fluctuations in ionized calcium levels occur commonly in the immediate post-CPB period in children. This is most often due to the relatively large

transfusions of citrate-rich and albumin-rich blood products, such as whole blood, fresh frozen plasma, platelets, and cryoprecipitate necessary for hemostasis, all of which bind calcium.<sup>187</sup> Routine calcium supplementation during the early post-CPB period is especially helpful in patients with diminished left ventricular function. In patients with a slow sinus or junctional rate, calcium must be administered cautiously because marked slowing of AV conduction may occur.

Epinephrine 0.02 to 0.2  $\mu\text{g}/\text{kg}/\text{min}$  is useful in patients with significant left ventricular dysfunction who remain hypotensive with high left atrial filling pressures or echodoppler imaging evidence of reduced contractility or regional ischemia.<sup>188</sup>

Milrinone, a potent phosphodiesterase-3 inhibitor, is also an effective inotrope-vasodilator in infants and children. Studies in neonates after open-heart surgery reveal significant reductions in SVR and PVR and increases in cardiac index, primarily as a result of larger stroke volume.<sup>189</sup> Infants and children demonstrate a larger volume of distribution and clearance of milrinone than that in adults; thus, the initial loading dose necessary to achieve therapeutic levels may be as large as 100  $\mu\text{g}/\text{kg}$ .<sup>190</sup> In neonates, the initial dose of milrinone on CPB is 25 to 100  $\mu\text{g}/\text{kg}$ , followed by a continuous infusion to be started within 90 minutes of the initial dose at a rate of 0.2  $\mu\text{g}/\text{kg}/\text{min}$  to maintain a therapeutic level. In older infants and children, the rate of continuous infusion is larger, usually 0.5 to 1  $\mu\text{g}/\text{kg}/\text{min}$ .

Dobutamine is an effective, albeit weaker, inotropic agent in children. Although it is reported to have a lesser chronotropic effect than dopamine in neonates, significant tachyarrhythmias may occur. This may be related to structural similarities between dobutamine and isoproterenol.<sup>188</sup> In children after cardiac surgery, dobutamine increases cardiac output primarily through increased heart rate. This is consistent with reduction in  $\alpha$ -receptors and a higher level of circulating catecholamines in newborns.

### Right Ventricular Dysfunction

Primary right ventricular dysfunction is a common finding after CPB in neonates, infants, and children. For example, after repair of TOF, preexisting right ventricular hypertrophy, a right ventriculotomy, and the placement of a transannular patch across the right ventricular outflow tract, resulting in acute pulmonary regurgitation and right ventricular volume overload, are common causes of postoperative right ventricular dysfunction.<sup>17</sup> The treatment of right ventricular dysfunction consists of measures directed at lowering PVR and preserving coronary perfusion without distending the RV. In cases of ventricular dysfunction, low-dose epinephrine (0.01–0.03  $\mu\text{g}/\text{kg}/\text{min}$ ) may provide inotropy without vasoconstriction.<sup>186</sup> Mechanical ventilation should be adjusted to assist right ventricular function and minimize PVR.

In contrast to the LV, the low intracavitory pressure of the normal RV receives two thirds of its coronary filling during ventricular systole. In patients with right ventricular dysfunction, maintaining a normal or slightly elevated systolic arterial pressure maximizes coronary perfusion to the RV and augments contractility. A vasopressin infusion can prove advantageous in such circumstances. If the need for inotropic support persists after the early post-CPB

period, a critical evaluation for other structural and functional abnormalities should be aggressively pursued. Preload should be maintained at a normal to slightly elevated level. Because right ventricular contractility is reduced, it is important to maximize preload to the highest portion of the Starling curve. Overdistention of the RV, however, is not well tolerated, owing to diminished ventricular compliance and diastolic dysfunction. Excessive volume loading may result in significant diastolic dysfunction, tricuspid regurgitation, and worsening forward flow. Generally, CVP much above 12 to 14 mm Hg is poorly tolerated in neonates and infants with right ventricular dysfunction.<sup>191</sup> If right ventricular dysfunction is severe, the sternum should be left open.<sup>192</sup> This eliminates the impedance imposed by the chest wall and mechanical ventilation, allowing the RV to maximize its end-diastolic volume. An additional strategy in neonates, infants, and children with significant post-CPB right ventricular dysfunction is to allow right-to-left shunting at the atrial level. Typical patients who would benefit from this strategy include neonates undergoing repairs for TOF and truncus arteriosus. Allowing an atrial communication to remain open, with blood shunting in a right-to-left direction, preserves cardiac output and  $\text{O}_2$  delivery to the systemic circulation. Although these patients have somewhat diminished systemic  $\text{O}_2$  saturation, their effective cardiac output and tissue  $\text{O}_2$  delivery are enhanced, systemic perfusion pressure improves and coronary perfusion of the RV is maintained. As right ventricular function improves, right atrial pressure falls, right-to-left shunting decreases, and systemic arterial saturation rises.

If right ventricular dysfunction persists to the extent that systemic cardiac output is compromised, consideration should be given to extracorporeal life support (extracorporeal membrane oxygenation [ECMO]). When ECMO is used for circulatory support, venoarterial cannulation is preferred. Venous and arterial access may be achieved through a large central artery and vein, usually the carotid artery and internal jugular vein, or by direct chest cannulation. Recovery from severe ventricular dysfunction is predicated on the concept that the myocardium has sustained a transient injury (i.e., “stunned myocardium”) and is capable of recovery with time.<sup>193,194</sup> ECMO is used to decrease ventricular wall tension, increase coronary perfusion pressure, and maintain systemic perfusion with oxygenated blood. ECMO also may be used for left ventricular failure, although success with this condition is less common than that seen with right ventricular dysfunction or pulmonary artery hypertension. Patients placed on ECMO because they fail to separate from CPB demonstrate significantly greater mortality than do those for whom ECMO was instituted later in the postoperative course.<sup>195</sup> The children who consistently have the lowest survival rate are those who require ECMO after a Fontan operation.<sup>196</sup> The role of ECMO in patients with myocardial injury or pulmonary hypertension is to provide adequate systemic  $\text{O}_2$  transport and systemic perfusion while allowing the ventricles to rest and recover. ECMO may even provide an effective means of resuscitation for postoperative cardiac patients, particularly if instituted promptly.<sup>197</sup> In larger infants and children with predominantly right ventricular dysfunction and satisfactory pulmonary function, a selective right ventricular assist device (VAD) may be preferable to ECMO.<sup>198</sup>

## Pulmonary Artery Hypertension

Primary pulmonary hypertension is a devastating disease. The progressive and sustained elevation in PVR eventually leads to right-sided HF and death.<sup>199,200</sup> Pulmonary arterial hypertension (PAH) is defined by the presence of mean pulmonary arterial pressure greater than 25 mm Hg at rest or 30 mm Hg during exercise.<sup>201</sup> In two studies, the presence of PAH was shown to be a significant predictor of major perioperative cardiovascular complications, including pulmonary hypertensive crises, cardiac arrest, and death in patients undergoing cardiac catheterization or noncardiac surgery under anesthesia.<sup>202,203</sup> Suprasystemic pulmonary artery pressure was predictive of major complications. Complications, however, were not associated with age, cause, type of anesthetic, or airway management. Preanesthesia evaluation should gauge disease severity. A history significant for chest pain, syncope, and dizziness, with signs of dyspnea at rest, low cardiac output state, metabolic acidosis, hypoxemia, and signs of right-sided HF warrants caution. Acute increases in PVR resulting in pulmonary hypertensive crises cause an increase in right ventricular afterload, right ventricular dysfunction, and hemodynamic decompensation. Suprasystemic pulmonary artery pressure results in inadequate PBF, inadequate left ventricular preload, low cardiac output, and biventricular failure. The associated hypotension results in coronary ischemia, which worsens this cycle. Perioperative factors thought to precipitate a pulmonary hypertensive crisis include hypoxia, hypercarbia, acidosis, hypothermia, pain, and airway manipulations in patients with pulmonary hypertension. Such patients present for hemodynamic catheterization, drug study, and noncardiac and cardiac surgical procedures. Although each anesthetic has to be tailored to the patient's pathophysiologic condition and surgical procedure, certain common principles remain. Pulmonary vasodilator therapy and inotropes must be continued in the perioperative period. Investigations include a comprehensive echocardiogram with occasional chest computed tomography angiography to exclude pulmonary thromboembolic disease. After premedication, the patient should be monitored with pulse oximetry to ensure the patient does not hypoventilate or become hypoxic. An intravenous induction with carefully titrated doses of ketamine may be the safest; if no intravenous is present, an inhalational induction with sevoflurane can be performed safely with 100% O<sub>2</sub>, keeping the end-tidal sevoflurane concentration as low as possible and quickly obtaining intravenous access. Procedures with potential for blood loss, hemodynamic instability, and changes in ventilatory status mandate invasive arterial monitoring. Care should be taken to avoid systemic hypotension while achieving general anesthesia. Ventilation and oxygenation are controlled, and acidosis is treated aggressively. Hypotension in the presence of euvoolemia may need to be treated with inotropes and, if necessary,  $\alpha_1$ -agonists.<sup>204,205</sup>

Therapy for elevated pulmonary artery pressures is directed at lowering PVR and unloading the RV. Reduction of PVR is accomplished by altering ventilation pattern, inspired O<sub>2</sub> concentration, and blood pH. Specifically, manipulating the pulmonary vascular bed in newborns and infants is a matter of regulating partial pressure of CO<sub>2</sub> in arterial blood (PaCO<sub>2</sub>), pH, PaO<sub>2</sub>, partial pressure of alveolar oxygen, and ventilatory mechanics.<sup>206,207</sup> PaCO<sub>2</sub>

is a potent mediator of PVR, especially in the newborn and young infant. Reducing PaCO<sub>2</sub> to 20 mm Hg and increasing pH to 7.6 produces a consistent and reproducible reduction in PVR in infants with pulmonary artery hypertension. Manipulating serum bicarbonate levels to achieve a pH of 7.5 to 7.6 while maintaining a PaCO<sub>2</sub> of 40 mm Hg has equal salutary effects on PVR.<sup>208</sup> An increase in the FiO<sub>2</sub> and the PaO<sub>2</sub> decreases PVR as well. In the circumstance of intracardiac shunts, changes in FiO<sub>2</sub> have little effect on PaO<sub>2</sub>. Thus, by inference, a reduction in PVR induced by increasing the inspired O<sub>2</sub> concentration is probably a direct pulmonary vasodilatory effect of PaO<sub>2</sub> rather than FiO<sub>2</sub>.

Ventilatory mechanics also play a major role in reducing PVR. Neonates and infants have a closing volume above functional residual capacity. Thus, at the end of a normal breath, some airway closure occurs. This process results in areas of lung that are perfused and yet underventilated. As these lung segments become increasingly hypoxic, secondary hypoxic vasoconstriction occurs. The net effect is an increase in PVR. Therefore, careful inflation of the lungs to maintain functional residual capacity will selectively reduce PVR. In practice, this is accomplished with relatively large tidal volumes and low respiratory rates, which produce an exaggerated chest excursion. Respiratory rates of 15 to 25 breaths/min are used for neonates and infants.

Because PBF occurs predominantly during the expiratory phase of the respiratory cycle, the ventilatory pattern should be adjusted to allow an adequate distribution of gas throughout the lung during inspiration and a more prolonged expiratory phase to promote blood flow through the lungs. End-expiratory pressure must be applied cautiously during the post-CPB period. Low positive end-expiratory pressure (PEEP) (3-5 mm Hg) prevents narrowing of the capillary and precapillary blood vessels, thereby reducing PVR. Higher PEEP or excessive mean airway pressure results in alveolar overdistention and compression of the capillary network in the alveolar wall and interstitium. This condition elevates PVR and reduces PBF.<sup>153</sup>

The final and perhaps the least well-recognized use of the mechanical ventilator is to assist in unloading the RV. During positive pressure inspiration, intrathoracic pressure increases and creates an increased pressure gradient from the lung to the LA, promoting cardiac output. This ventilatory assist is commonly seen in patients with PAH or right ventricular dysfunction. An augmentation of the arterial pressure trace during inspiration is seen. The use of the ventilator to augment systemic blood flow is very similar to the thoracic pump concept used to explain blood flow during CPR.<sup>209</sup> The inspiratory assist must be balanced by the potential negative effects of increased mean airway pressure on PVR and right ventricular afterload. To maximize these cardiopulmonary interactions, high tidal volume with low respiratory rates should be employed.

Attempts to manipulate PVR through pharmacologic interventions are also possible. Drugs that have shown promise in decreasing PVR both clinically and experimentally have been the phosphodiesterase inhibitors such as amrinone and milrinone. Both reduce PVR and SVR and increase RV contractility.<sup>210</sup> Isoproterenol has mild pulmonary artery-vasodilating properties in the normal pulmonary circulation.<sup>211</sup> It reduces PVR in adults after cardiac

transplantation, but very few data support PVR reduction in infants and young children after cardiac surgery. In immature animals, the myocardium is less responsive to isoproterenol and causes tachycardia and increased myocardial O<sub>2</sub> consumption. These latter effects may reduce coronary perfusion and result in relative myocardial ischemia. Both prostaglandin E1 and prostacyclin have a pulmonary vasodilating effect; however, both drugs produce systemic hypotension, which severely limits their use.<sup>212,213</sup>

There are now ultra-short-acting intravenous vasodilators and inhaled vasodilating agents such as NO. Ultra-short-acting intravenous vasodilators are nonspecific potent vasodilators, with a half-life of seconds. Infusion of these drugs into the right side of the circulation produces a potent short-lived relaxation of the pulmonary artery smooth muscle.<sup>214</sup> Once the drug reaches the systemic circulation it is no longer functional. Adenosine and ATP-like compounds have these properties and may have clinical applicability in pulmonary artery hypertension in the future.<sup>215</sup>

Beginning in the past decade, several potent therapies for pulmonary hypertension have evolved.<sup>206,207</sup> A continuous intravenous infusion of prostacyclin improves pulmonary vascular hemodynamics, exercise tolerance, and survival in pulmonary hypertension.<sup>216</sup> Sildenafil is a selective phosphodiesterase type 5 inhibitor. Phosphodiesterase type 5 breaks down cyclic guanosine monophosphate. Sildenafil produces acute and relatively selective pulmonary vasodilatation and acts synergistically with NO.<sup>217-219</sup> Bosentan is a dual endothelin receptor blocker. Preliminary reports indicate that bosentan improves symptoms, exercise tolerance, and hemodynamics in patients with pulmonary hypertension. The drug is well tolerated and free of side effects apart from a dose-dependent increase in liver enzymes.<sup>220</sup> Lung transplantation is the only available surgical therapy for primary pulmonary hypertension; however, the 5-year survival remains less than 50%, and bronchiolitis obliterans remains the single most common cause of death.<sup>221,222</sup> Before listing for transplantation, all patients undergo a hemodynamic cardiac catheterization and drug study in which reversibility of pulmonary hypertension with increased inspired O<sub>2</sub> concentrations and NO is determined.<sup>223</sup> Prostacyclin analogues including inhaled iloprost or intravenous epoprostenol, although used in adult centers, have not become routine in pediatric practice.

CPB with associated endothelial injury predisposes to the development of postoperative pulmonary hypertension in patients with CHD. Anatomic factors that impose either obstruction to PBF or residual left-to-right shunting need to be surgically addressed. Elevated LAP resulting from mitral valve disease or left ventricular dysfunction, pulmonary venous obstruction, branch pulmonary artery stenosis, or surgically induced loss of the pulmonary vascular cross-sectional area all raise right ventricular pressure and impose a burden on the right side of the heart.

NO, an endothelium-derived vasodilator that is administered as an inhaled gas, represents the most promising development in the therapy for elevated PVR in patients with CHD. Although nonselective, it is rapidly inactivated by hemoglobin and, when inhaled, produces no systemic vasodilation.<sup>224</sup> NO reduces pulmonary artery pressure in adult patients with mitral valve stenosis and in selected

pediatric cardiac patients with PAH.<sup>225-227</sup> The congenital cardiac patient population in whom NO appears to be effective is patients with acute PVR elevation after open-heart surgery, as well as preoperative pulmonary hypertension accompanying specific anatomic conditions (e.g., total anomalous pulmonary venous return, congenital mitral stenosis).<sup>225,227</sup> Because it acts directly on vascular smooth muscle, NO remains effective despite the post-CPB endothelial injury frequently encountered in children.<sup>228</sup> Some centers routinely employ low-dose NO (1-5 ppm) after a Fontan operation when the CVP-LAP gradient exceeds 10 mm Hg.<sup>229</sup> At our institution, a dose of 20 ppm is the standard dose in both the ICU and the cardiac operating room. Finally, NO can provide diagnostic information that helps distinguish reactive pulmonary vasoconstriction from fixed anatomic obstructive disease either in the postoperative surgical patient or in the patient undergoing pre-transplant evaluation.<sup>230,231</sup> In the latter, the distinction between pulmonary vasoconstriction and advanced pulmonary vascular occlusive disease will influence the prediction as to whether a child with pulmonary hypertension in association with either CHD or cardiomyopathy will survive a heart transplant or requires replacement of both heart and lungs.

Management strategies for postoperative pulmonary hypertension and treatment of pulmonary hypertensive crises include sedation, moderate hyperventilation (maintaining CO<sub>2</sub> partial pressure [PCO<sub>2</sub>] between 30 and 35 mm Hg), moderate alkalosis (pH > 7.5), increased inspired O<sub>2</sub>, optimization of PEEP (to maximize functional residual capacity), pulmonary vasodilators (e.g., NO), and the creation or maintenance of an intracardiac right-to-left shunt in an attempt to maintain cardiac output.<sup>232,233</sup> NO is also useful in the manipulation of PVR after Fontan-type procedures.<sup>234</sup> Care should be exercised in weaning NO in patients, because abrupt withdrawal can precipitate rebound pulmonary hypertension and pulmonary hypertensive crises.<sup>234,235</sup>

## Anticoagulation, Hemostasis, and Blood Conservation

Pediatric anesthesiologists must manage coagulation, hemostasis, and blood conservation in the perioperative period of cardiac surgery. Coagulopathy after CPB remains a significant problem in pediatric cardiac surgery.<sup>223</sup> Continuing blood loss after CPB requiring blood component replacement is associated with hemodynamic compromise as well as morbidity. In pediatric patients, restoration of hemostasis has proved difficult; diagnosis of the problem and treatment are marginally effective.

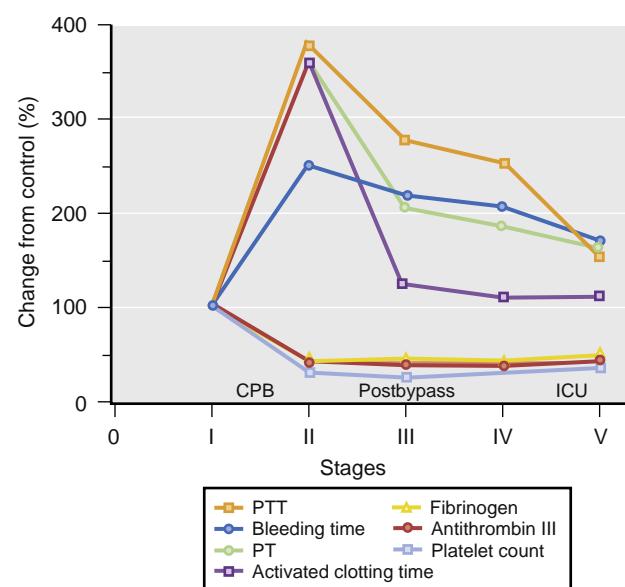
Neonates, infants, and children undergoing cardiac surgery with CPB have a higher rate of postoperative bleeding than that seen in older patients.<sup>236</sup> First, the ratio of patient body surface area to the nonendothelialized extracorporeal circuit volume is disproportionate; the relatively large inflammatory-type response provoked in response to CPB is inversely related to patient age—the younger the patient, the more pronounced is the response.<sup>9</sup> Because complement and platelet activation are linked to the activation of other protein systems in the blood (i.e., fibrinolytic proteins), it is probable that this hemostatic activation, which

results in impaired hemostasis and increased bleeding tendency, plays a major role during pediatric cardiac surgery. Second, the type of operation performed in neonates and infants usually involves more extensive reconstruction and suture lines, creating more opportunities for surgical bleeding than in adult cardiac patients. Operations are also frequently performed using DHCA, which may further impair hemostasis.<sup>237</sup> Third, the immature coagulation system in neonates is also likely to contribute to impaired hemostasis.<sup>238</sup> Although procoagulant and factor levels may be reduced in young patients with CHD resulting from immature or impaired hepatosynthesis,<sup>239</sup> functional bleeding tendencies are usually not present before surgery. Furthermore, compounding the problem of immature coagulation proteins is the massive hemodilution that occurs when initiating CPB in infants and small children. Despite advances in circuit miniaturization, initiation of CPB induces a dilutional thrombocytopenia and reduces levels of factors II, V, VII, VIII, IX, X, ATIII, and fibrinogen.<sup>240</sup> Patients with cyanotic heart disease demonstrate an increased bleeding tendency before and after CPB because of a range of factors including thrombocytopenia, low numbers of von Willebrand factor multimers, clotting factor deficiencies, and poor fibrinogen function.<sup>241</sup>

CPB is a significant stimulant of the coagulant and inflammatory systems, requiring anticoagulation with heparin before its initiation. Heparin is traditionally administered based on patient weight, at an empiric dose of 400 units/kg. Adequacy of heparinization is monitored by the activated clotting time (ACT), a measure of inhibition of the contact activation pathway, with a goal ACT of greater than 480 seconds prior to initiation of CPB. An accurate ACT requires normothermia, normal platelet count and function, and normal levels of other coagulation proteins including antithrombin III. As these derangements are common in children having cardiac surgery, the ACT may not be the ideal monitor of anticoagulation in this population. In neonates, infants, and young children, the ACT does not correlate with plasma heparin concentration,<sup>242</sup> and children exhibit evidence of ongoing thrombin generation and coagulation activity despite very high ACT values.<sup>243</sup>

An alternative to weight-based heparin dosing is use of a blood heparin concentration-based system, which utilizes protamine titration to indicate whole blood heparin concentration at the bedside. Such a setup allows for individual variability in heparin efficacy and metabolism. Although blood heparin concentration devices have shown disappointing results in adults, results in children suggest greater suppression of thrombin generation and hemostatic activity,<sup>244</sup> reduced number of blood transfusions, and improvement in clinical outcomes of ventilator hours and ICU stay.<sup>245</sup> Blood heparin concentration systems also account for bypass circuit characteristics when deciding heparin dose in the bypass prime. In the absence of such a system, empiric dosing is recommended at 1 to 3 units/mL of priming solution.

An important caveat to anticoagulation management in infants is the role of antithrombin III, the body's most abundant natural anticoagulant and target for heparin efficacy. Neonates have low levels of antithrombin III activity,<sup>246,247</sup> and those with CHD have a functional antithrombin III level of approximately 50%.<sup>248</sup> Heparin exerts its anticoagulant



**Fig. 78.13 Plot of blood coagulation profile changes before, during, and after cardiopulmonary bypass (CPB) in 25 children.** Clotting times and coagulant factors are shown as percent change from control. Stage I, baseline, before CPB; stage II, post-CPB, before protamine reversal of heparin; stage III, after protamine; stage IV, just before leaving the operating room; stage V, after 3 hours in the intensive care unit (ICU). PT, Prothrombin time; PTT, partial thromboplastin time.

effect by accelerating the reaction between thrombin and antithrombin. Low antithrombin activity is one reason for low heparin sensitivity in the pediatric cardiac population; however, large clinical trials examining antithrombin III replacement have not been conducted. In addition, other heparin cofactors, including  $\alpha_2$ -macroglobulin, may play an important, though poorly understood, role in anticoagulation in young children.<sup>249</sup>

Heparin is neutralized with protamine according to the quantity of heparin administered or based on body weight, usually 2 to 4 mg/kg, accounting for heparin administered to the patient only (excluding heparin added to the pump prime). Blood heparin concentration devices may be used to dose protamine according to the amount of circulating heparin in the patient, accounting for metabolism or recent dosing. Delayed hepatic clearance of heparin resulting from organ immaturity and the predominant use of hypothermic circulatory arrest in the young decrease metabolism and excretion of heparin. Younger children require relatively more protamine compared to older children and adults, as reflected by higher circulating heparin levels after CPB.<sup>250</sup> Prolonged ACT after adequate protamine dosing may indicate platelet dysfunction, hypofibrinogenemia, or other coagulation abnormalities. This should be assessed before administering additional protamine, which in excess may contribute to postoperative bleeding.<sup>251</sup>

Bleeding after CPB is not an unusual occurrence. The surgeon should first attempt to identify any obvious source of surgical bleeding at the sites of repair. In general, standard coagulation tests show a prolongation of the partial thromboplastin time, prothrombin time, hypofibrinogenemia, dilution of other procoagulants, and prolonged bleeding time in many pediatric patients, with and without bleeding (Fig. 78.13). The most common reason for persistent

bleeding is platelet dysfunction,<sup>252-254</sup> and empiric platelet administration can be warranted. Routine administration of blood products to correct laboratory coagulation abnormalities in the absence of bleeding is never clinically indicated. Under most circumstances, meticulous surgical technique, appropriate administration of protamine, adequate patient temperature, and platelet infusion will correct excessive bleeding.

Risk factors for bleeding after bypass include lower body weight,<sup>255,256</sup> lower temperatures on bypass,<sup>257</sup> resternotomy,<sup>257</sup> preoperative congestive HF,<sup>257</sup> and presence of cyanotic CHD.<sup>256</sup> In these populations, a more aggressive approach is warranted. Although use of transfusion algorithms demonstrate reduced transfusion and even decreased mortality in adults having cardiac surgery,<sup>258,259</sup> no large or multicenter trials have been conducted examining transfusion algorithms in children. Complicating the development of algorithms in children is the heterogeneity in congenital defects, the surgical operation performed, and the complexity across congenital heart centers.<sup>260</sup>

However, several single-center studies show that use of viscoelastic testing (particularly rotational thromboelastography) to guide transfusion after bypass surgery may reduce transfusion requirement<sup>256,261,262</sup> and ICU days.<sup>262</sup> These studies provide reasonable thresholds for initiating transfusion after bypass as guided by rotational thromboelastometry (ROTEM) parameters, but no large prospective studies have been conducted to validate the targets. Importantly, use of either thromboelastography or ROTEM in children having cardiac surgery must be interpreted against age-appropriate reference values.<sup>263,264</sup>

Pharmacologic interventions are increasingly used to reduce bleeding after CPB. Antifibrinolytics exert their effects by reversibly binding to lysine analogue sites on plasminogen, a molecule primarily responsible for the breakdown of fibrin. By inhibiting plasminogen, and therefore plasmin, the procoagulant effects of fibrin remain. Lysine analogues epsilon amino-caproic acid and tranexamic acid are efficacious in reducing bleeding and transfusion requirement in pediatric cardiac surgery.<sup>265</sup> A large-scale observational study of 22,258 patients found that the serine protease inhibitor aprotinin had effects similar to those of both aminocaproic acid and tranexamic acid in terms of reducing bleeding requiring surgical intervention and mortality.<sup>266</sup> Unfortunately, aprotinin was removed from the United States market because of concerns of life-threatening anaphylactic reactions.<sup>237,267-271</sup> Dosing schemes for anti-fibrinolytic therapy are variable, though neonates require reduced loading and infusion doses compared to older children and adults because of decreased clearance.<sup>272</sup> After bypass surgery, desmopressin acetate has been administered to improve platelet function with variable success in reducing postoperative blood loss.<sup>273,274</sup>

Factor concentrates are increasingly used off-label in pediatric cardiac populations to provide needed coagulation factors in small children who may not tolerate the volume of fresh frozen plasma or cryoprecipitate required to satisfactorily raise factor levels.<sup>275</sup> Observational evidence suggests that recombinant activated factor VII is efficacious as a rescue agent for protracted after-bypass bleeding, after the transfusion of platelets, fibrinogen, and coagulation factors to provide adequate scaffolding for its

action.<sup>275</sup> Fibrinogen concentrate has also been used to replace fibrinogen in pediatric cardiac patients and may be used in place of cryoprecipitate.<sup>276</sup> Prothrombin complex concentrates (PCCs) are purified plasma-derived products containing vitamin-K-dependent clotting factors (II, VII, IX, X) in either 3- (3F) or 4- (4F) factor preparations. PCCs are included in many transfusion algorithms in adult cardiac surgical populations but the safety and efficacy in pediatrics remains understudied.<sup>277</sup> Both 3- and 4-factor PCC improve thrombin generation in ex vivo studies of neonatal plasma,<sup>278,279</sup> but most evidence for clinical use is limited to case reports or small case series. At our institution, we administer 3-factor PCC as part of a transfusion algorithm in severe hemorrhage, after replacement of platelets, fibrinogen, and other coagulation factors.

Blood transfusion during the perioperative period must be thoughtful and intentional. Injudicious use of blood products to correct individual coagulation abnormalities separately further exacerbates dilution of existing procoagulants, and carries the risk of multiple donor exposures. Transfusion should be undertaken as specifically indicated by an impairment in tissue oxygenation or documented coagulopathies with clinically significant bleeding. Interestingly, while transfusion algorithms may reduce transfusion, in pediatric populations they may be more likely to alter the pattern of transfusion,<sup>262</sup> for example decreasing RBC transfusion while increasing platelet and cryoprecipitate use. Algorithms may improve hemodynamic stability<sup>262</sup>; research is needed to confirm improved outcomes.

Determining the optimal hematocrit is necessary to guide transfusion and is best decided in conjunction with the surgeon based on an individual patient's lesion, complexities, and planned procedure. RBCs should be administered to maintain a postdilutional hematocrit of at least 20% on CPB<sup>280</sup>; children with cyanotic CHD require a higher hematocrit. A recent study demonstrated an association between the indication for blood transfusion and postoperative morbidity in a cohort of children having cardiac surgery. Study results indicated that patients who required transfusion to maintain a target postdilutional hematocrit on pump had no increase in morbidity, while those requiring a therapeutic transfusion experienced severe morbidity and mortality.<sup>281</sup>

An increasingly recognized problem in pediatric cardiac surgical populations is thrombosis. Approximately 11% of children having cardiac surgical procedures experience a thrombotic complication<sup>282</sup>; risk factors include younger age,<sup>282,283</sup> cyanotic disease,<sup>282,283</sup> use of DHCA,<sup>282</sup> longer duration of in situ central lines,<sup>282</sup> and administration of blood products in the absence of intraoperative coagulation testing.<sup>284</sup> Alterations in levels of pro- and anti-coagulants in the immature pediatric patient combined with the inflammatory effects of bypass create a hypercoagulable state in many patients postoperatively.<sup>285</sup> Decreased anti-thrombin III levels after cardiac surgery are associated with thrombotic events in adults<sup>286</sup> but this has not been evaluated in children. Further, the ability of the infant's immature antifibrinolytic system to lyse clots composed of adult fibrinogen may be impaired.<sup>287</sup>

The techniques of thoughtful transfusion and blood conservation must be continued as the patient is transferred

to the ICU. Isolated coagulation abnormalities are often present in the postoperative patient with uncomplicated cardiac issues (see Fig. 78.13), but are not associated with excessive bleeding and self-correct during the first postoperative day. Routine correction of these abnormalities with infusion of blood products is not warranted. Administration of blood products should not occur in the absence of clinical evidence of bleeding and the identification of a specific defect requiring targeted component therapy. Routine use of blood products for volume replacement is also to be avoided; lactated Ringer or saline solution can be satisfactorily administered at a reduced cost without the hazards associated with transfusion.

## Postoperative Management

Immediate postoperative care of the pediatric patient who has undergone cardiothoracic surgery is an important period in the overall sequence of anesthetic and surgical management. Although the primary influence on outcome is determined by the conduct of the operation, postoperative care is an important factor. As a member of the operative team, it is necessary that the anesthesiologist understand and become involved during the immediate postoperative period. Detailed principles of postoperative management of pediatric cardiac surgical patients are beyond the scope of this chapter. However, a few general guiding principles and approaches are given to provide fundamental knowledge for the anesthesiologist.

The postoperative period can be characterized by a series of physiologic and pharmacologic changes as the body convalesces from the abnormal biologic conditions of CPB and cardiac surgery. During this period, the effects of the cardiac operation, any underlying disorders, the effects of hypothermic CPB, and special techniques such as DHCA may create special problems. In the immediate postoperative setting, abnormal convalescence and specialized problems must be recognized and managed appropriately. Fortunately, most patients are able to balance the cost imposed by the physiologic trespass created by the surgical repair and the effects of CPB against the benefit of reduced pathophysiologic loading conditions, resulting in low morbidity and mortality.

Therefore, the guiding principle in the management of the postoperative patient is an understanding of both normal and abnormal convalescence after anesthesia and cardiac surgery. The immediate postoperative period, even that of normal convalescence, is one of continuous physiologic change because of the pharmacologic effects of residual anesthetic agents and the ongoing physiologic changes secondary to abrupt alteration in hemodynamic loading conditions, surgical trauma, and extracorporeal circulation. Anesthesia and surgery affect not only the patient's conscious state but also cardiovascular, respiratory, renal, and hepatic function; fluid and electrolyte balance; and immunologic defense mechanisms. Despite these changes, postoperative care should be predictable and standardized for most patients undergoing cardiac procedures.

In general, the four temporal phases of postoperative management in the cardiac patient are (1) transport to the

ICU, (2) stabilization in the ICU, (3) weaning from inotropic and ventilatory support, and (4) mobilization of fluids. Patients proceed through these phases at variable rates based on such factors as the underlying disease process, preoperative medical condition, sequelae of the surgical procedure, duration of CPB, and presence or absence of intraoperative complications. One of the most important functions of the ICU team is to identify postoperative complications in the patient who convalesces abnormally and to provide interventional therapy. Because physiologic change after cardiac surgery is dramatic but self-limiting during normal convalescence, recognition of abnormal processes can be difficult. Under such circumstances a uniform, multidisciplinary approach with experienced clinicians and nurses facilitates the identification of any abnormalities in convalescence. These abnormalities often are indications for closer observation, more invasive monitoring, pharmacologic intervention, and increased cardiopulmonary technical support. Complications include hypovolemia, residual structural heart defect, right and left ventricular failure, hyperdynamic circulation, pulmonary artery hypertension, cardiac tamponade, arrhythmias, cardiac arrest, pulmonary insufficiency, oliguria, seizures, hypercoagulable state, thrombosis, and brain dysfunction. It is critical to detect these departures from the normal convalescent course and to treat them aggressively.

One important area in which the anesthesiologist can aid the recovery of the cardiac patient is pain control. Pain and sedation are among the most common problems requiring ICU intervention. Many factors influence the onset, incidence, and severity of postoperative pain. The attenuation of the stress response in the immediate postoperative period using infusions of potent opioids in the critically ill infant reduces morbidity.<sup>95</sup> Attenuation of postoperative pain can be attempted with a preoperative medication and an intraoperative anesthetic management technique that includes the use of potent opioids. Patients who receive no opioids preoperatively or during the operative procedure will require analgesics in the immediate postoperative period once the inhalation anesthetic is eliminated. Most cases of postoperative pain can be managed by the administration of small intravenous doses of opioids, usually morphine or hydromorphone. This is important in a patient being weaned from the ventilator during the early postoperative period. Patients who are intubated and ventilated overnight should receive adequate sedation and pain control until ventilatory weaning is begun. This is usually accomplished by a continuous infusion of a benzodiazepine and an opioid. Continuous infusion of sedatives and analgesics results in a more consistent and reliable control of postoperative pain. When separated from mechanical ventilation, the patient is concurrently weaned from the sedatives and analgesics. In patients with reactive pulmonary artery hypertension, opioids have been shown to prevent hypertensive crisis.<sup>92</sup>

Regional anesthesia may be used for postoperative pain control in infants and children after thoracotomy. This method avoids opioid-induced respiratory depression from intravenous doses of these drugs. The administration of opioids in the epidural space is a very effective approach to pain management. This technique is used in children for postoperative pain control via the caudal route as a "single

shot" or by a small caudal catheter. Morphine or hydro-morphone provides effective analgesia with a duration of 6 to 12 hours, with no significant respiratory depression. Caudal morphine 0.05 to 0.075 mg/kg delivered in a total volume of 1.25 mL/kg of sterile saline has been used with good success in our practice. The use of regional anesthesia for postoperative pain appears to be best suited for the child extubated in the early postoperative period. Relative contraindications of this technique include hemodynamic instability and patients with abnormal clotting profiles and/or continued active bleeding. Using regional analgesia can result in better arterial oxygenation, a more rapid ventilator weaning, and decreased postoperative respiratory complications. However, urinary retention occurs frequently in patients without a bladder catheter.

Children requiring large thoracotomies or a bilateral thoracosternotomy (i.e., "clamshell") incision merit consideration for thoracic epidural analgesia. This technique significantly reduces the respiratory depression and pulmonary mechanics abnormalities that accompany the quantity of systemic opioids that would be necessary to provide adequate analgesia for these excruciatingly painful incisions. If the procedure requires systemic heparinization, we will typically defer placement of these catheters until the heparin effect is neutralized. For the patient undergoing coarctation repair via a left thoracotomy there is some concern for paraplegia following the operation. However, as the incidence of paraplegia in children is exceedingly low, we usually choose to place the caudal or epidural catheter before surgical incision to maximize the benefit intraoperatively; however some centers choose to place it at the end of surgery after it is clear there is no neurologic impairment. For patients undergoing heart, lung, or dual transplants, a thoracic epidural catheter is placed at a time in the postoperative period when the patient can be weaned from intravenous medications that would adversely affect the patient's ability to breathe in close proximity to the planned extubation. It is helpful for these patients to have a functioning thoracic epidural catheter for several days.

## POSTOPERATIVE NEUROPSYCHOLOGIC MORBIDITY

Neurologic morbidity has been identified to be increasingly problematic in neonates and infants with CHD as surgical mortality rates have improved. Although early postoperative CNS sequelae such as stroke and seizures occur in a small percentage of neonates with CHD, the importance of more subtle neurologic abnormalities at long-term follow-up is being increasingly recognized.<sup>222,231,288</sup>

These findings may include fine and gross motor impairments, speech and language delays, disturbances in visual-motor and visual-spatial abilities, attention-deficit disorders, learning disorders, and impaired executive functioning. The presence of congenital brain disease in patients with CHD represents a challenge in improving long-term neurologic outcomes. Many neonates with CHD have congenital structural brain abnormalities, chromosomal abnormalities, or both, as well as physiologic abnormalities that may impair brain development. Brain abnormalities on head ultrasonography have been noted in one fifth

of full-term infants undergoing heart surgery, with half of them being present preoperatively.<sup>288</sup>

Postoperatively, secondary neurologic injury may be related to post-CPB alterations in cerebral autoregulation and additional hypoxic-ischemic insult, seizures, or other issues associated with prolonged ICU stay. In addition to prenatal and modifiable perioperative factors, genetic and environmental factors are known to be important. Unfortunately, modifiable perioperative factors may explain less of the variability in long-term outcomes than do patient-specific factors.

New, postoperative neurologic injury may be detected clinically in over 10% of infants,<sup>288a</sup> increasing to over 50% using more sensitive brain imaging techniques such as MRI.<sup>289,290</sup> Given that new neurologic injury can occur at various time points during the neonate's hospitalization, perioperative attention to reducing known risk factors is critical. Mechanisms of CNS injury in infants undergoing cardiac surgery include hypoxia-ischemia, emboli, reactive O<sub>2</sub> species, and inflammatory microvasculopathy. Preoperatively, the primary focus is on preventing hypoxic-ischemic injury and thromboembolic insults. Modifiable intraoperative factors associated with CNS injury include, but are not limited to, pH management, hematocrit during CPB, regional cerebral perfusion, and the use of DHCA. The adverse effects of CPB may be greater in infants than larger children or adults given the immaturity of their organ function and tissues, and the size of the CPB circuit relative to their body size.<sup>291</sup> However, a significant amount of research has been conducted in the area of intraoperative prevention of neurologic injury. With ongoing changes in technology and new therapies, the conduct of CPB and other support techniques have been actively under investigation.

The developmental consequences of exposure to general anesthetics are not well understood and are difficult to elaborate on in the absence of prospective randomized controlled trials, because of multiple factors that affect neurologic outcome in this population. Current literature suggests that multiple exposures, cumulative doses of exposure, and exposure in infancy might increase the risk for neurodevelopmental delay.<sup>292-298</sup> Thus, pediatric cardiac anesthesia is associated with all three risk factors, so attempting to minimize time of exposure, bundling of necessary procedures only if it will shorten the overall exposure to anesthesia, and delaying nonessential procedures to an age associated with less neurologic risk might be appropriate. Careful choice of anesthetic agents that do not act on different neuroreceptors at key time points in development might be critical.

Our current practice has evolved to minimize neurotoxicity with time under anesthesia minimized by getting help early if there is difficulty with intravenous access and having the surgeon in the room and ready to start immediately postinduction. NIRS monitors are used in all cases to optimize cardiac output and help define the need for blood transfusions. Multiple anesthetics are combined and administered in lower individual doses with the thinking that this is less toxic than a single anesthetic at a higher concentration. In all cases, a dexmedetomidine infusion is administered to decrease the dose of the other hypnotics and, when possible, regional techniques are used to reduce the total anesthesia dose.

## MECHANICAL ASSIST DEVICES

Survival in children with congenital cardiac as well as pulmonary defects has improved over recent decades as a result of improved preoperative management, surgical techniques, anesthesia management, drug therapies, and postoperative management. Despite these advances, patients may still require therapies for both acute and chronic HF that are refractory to medical therapy. Mechanical support in the form of ECMO or VADs may then need to be instituted. Examples of conditions that may require support include failure to wean from CPB, acute cardiac arrest, malignant arrhythmia, and worsening myocardial function secondary to the underlying congenital defect or related to acquired cardiomyopathy. Fortunately, however, the incidence is small, with less than 2% of post-CPB patients requiring this intervention.<sup>299</sup> Mechanical support can thus be used as a treatment option to allow for recovery of ventricular function, as a bridge to transplant, or to support the heart in those with marginal functional reserve requiring invasive diagnostics or treatments (e.g., Williams syndrome with severe supravalvular pulmonary or aortic stenosis). As with any therapy, contraindications must be excluded before embarking on the use of a mechanical assist device. These may include extreme prematurity, severe and irreversible multiorgan failure, incurable malignancy, and preexisting neurologic devastation.<sup>299</sup> Anesthetic management in the use of ECMO is supportive, with management limited to assistance in the resuscitative efforts and hemorrhage associated with the cardiac surgery that was ongoing at the time of conversion to ECMO. Once the patient is on full ECMO support, ventilation is continued but at a slower rate of ventilation on the order of 10 breaths/min, with a peak pressure of 20 cm H<sub>2</sub>O, PEEP set at 5 to 10 cm H<sub>2</sub>O, and FiO<sub>2</sub> decreased to about 40%. These settings aid in the prevention of atelectasis with management of CO<sub>2</sub> and O<sub>2</sub> related to flow across the circuit membrane.

This is very different from the patient into whom a VAD is placed. Here the anesthesiologist continues to manage the patient as for routine CPB weaning. If a systemic VAD is placed, careful attention must be given to the ventricle pumping blood into the pulmonary bed because failure of this ventricle will have disastrous consequences. Thus, management tailored to unload this pulmonary ventricle is vitally important and will include inodilators in the form of phosphodiesterase inhibitors, inotropic support, and possibly even inhaled NO to decrease PVR and promote forward flow. In association with the perfusionist, intravascular volume loading is assessed and maintained for effective functioning of the VAD and thus adequate offloading of the assisted ventricle. Careful attention to pulmonary function is also vital. Adequate pulmonary toilet, recruitment maneuvers, and appropriate ventilatory parameters must be used. Bleeding is a potential complication in the implantation of the VAD and thus a clear strategy must be planned for in the form of antifibrinolytics, adequate volumes of blood and blood products, and even possibly the use of activated clotting factors (e.g., factor VII, PCCs).<sup>300</sup>

As can be seen in Table 78.10 differences can be appreciated between assist devices. The potential for bleeding exists at the time of insertion of both of these modalities; however, it would seem from clinical experience that because of the

**TABLE 78.10** Comparison of Extracorporeal Membrane Oxygenation Versus Ventricular Assist Device

Comparison Factors	ECMO	VAD
Bleeding at insertion	++	++
Sternotomy	Not required	Required
Left atrial venting	±	—
Blood product use	+++	+
Number of cannulae for biventricular support	2	4
Pulmonary support	+	—
Intravenous anticoagulation	+	±
Duration of support	Weeks	Months
Emergent support	Yes	No
Patient mobility	—	+

ECMO, Extracorporeal membrane oxygenation; VAD, ventricular assist device.

extensive dissection and need for sizeable ventriculotomy, implantation of a VAD (and especially bi-VAD) is more problematic. The requirements of anticoagulation to keep the ACT in the range of 180 to 200 for ECMO also may lead to ongoing and significant bleeding, especially if placed into a patient who requires support in the immediate perioperative phase. The use of an ECMO circuit with a membrane oxygenator requires ongoing intravenous anticoagulation with maintenance of the ACT in the aforementioned range. Apart from the immediate postoperative phase, patients with VAD systems can be transitioned to oral agents. A two-part therapy is recommended. Antiplatelet therapy includes aspirin or clopidogrel. The second part of the therapy will entail the use of anticoagulation with either warfarin (Coumadin) or subcutaneous low-molecular-weight heparin.<sup>299</sup>

Three potential disadvantages exist in the use of the VAD system. The lack of pulmonary support when using the VAD limits its use to patients whose lung function is adequate. Second, Table 78.10 illustrates that biventricular support requires two separate VAD devices, necessitating the placement of four cannulas, which may be technically difficult in a very young child. The third disadvantage is that VAD placement cannot be performed in a code situation or at the bedside as with ECMO.

Important advantages of the VAD system are the ability of patients to ambulate while on support and that VAD support can be maintained for months in contrast to the weeks only of ECMO support. Another important advantage over ECMO is that these patients will not require further venting of the LA. In patients on ECMO this is achieved by the placement of a left atrial vent at the time of sternotomy or a balloon atrial septostomy, which may require transfer to the catheterization laboratory with the possible complications associated with transport of a patient on an ECMO circuit.

Despite successful resuscitation and placement onto mechanical assist devices, morbidity and mortality remain high, with ECMO appearing to have worse outcomes. The mortality rate for ECMO in the 1990s was on the order of 47%, with survival in series published in the early 2000s not showing much improvement.<sup>301-304</sup> In contrast, the survival for those into whom a VAD is placed appears to

be superior within the quoted series, with up to 80% of patients surviving to transplantation or being successfully weaned from support.<sup>303,305</sup> In the study by Blume and co-workers,<sup>302</sup> however, it was noted that associated CHD, and patients who are younger and smaller, have a higher mortality than those with fulminant myocarditis and cardiomyopathy.<sup>302</sup> Alongside survival data, the next most important marker is neurologic outcome, and it appears that this is also better in the VAD group.<sup>306,307</sup> Risk factors for poor neurologic outcome were once again of low weight and duration of DHCA, both of which place patients on ECMO at a survival disadvantage because patients on ECMO will be smaller and some of those who undergo DHCA for repair of congenital anomalies will require emergent ECMO support to wean from CPB or in the immediate postoperative phase.<sup>308</sup>

Survival predictors are important in our management of these patients. One common variable that can predict survival is the return of ventricular function between 3 and 5 days after the initiation of support.<sup>304,308</sup> Both of these modalities have been used successfully as a bridge to transplantation, with patients with a VAD having a greater than 80% survival to transplantation and patients on ECMO showing a less than 60% survival. Yet ECMO is used often in the infant population and in those with complex CHD, both of which are factors known to increase mortality among VAD patients.<sup>308</sup> The important causes of morbidity and mortality in patients on both of these modalities include cerebrovascular events secondary to either hemorrhagic or embolic phenomena, circuit-related issues (e.g., circuit thrombosis), renal failure requiring hemofiltration, sepsis, ongoing hemorrhage, and multiple-organ failure.

Although these modalities are often compared to each other, they both have unique places in the care of children with cardiac disability. ECMO has a great advantage in that it can be employed rapidly in a code situation for a patient of any age or size. In the past, size has been the limiting factor for implantation of VAD systems into pediatric patients. The Berlin Heart VAD (Berlin Heart AG, Berlin, Germany) is a pulsatile-flow device and available for use even in neonates. The system has been employed in Europe for over 20 years and has pump sizes from 10 to 80 mL.

Although this is currently the only FDA-approved VAD for children, a high incidence of adverse events such as embolic stroke, bleeding, and infections are noted.<sup>309</sup> This has led to the increased use of adult continuous-flow devices including the HeartMate II (Thoratec Corp., Pleasanton, CA) and HeartWare HVAD (HeartWare Inc., Framingham, MA) in children who may need it for longer periods of time, or who will potentially discharge home on the device. The Infant Jarvik VAD, a pediatric-specific continuous-flow device is currently undergoing pre-clinical testing. There are a number of other short-term VAD options that can provide additional organ support including oxygenation, hemodialysis, and plasma exchange if needed. The CentriMag/PediMag (Thoratec Corp., Pleasanton, CA) and the Jostra Rotaflo (MAQUET Cardiovascular, Wayne, NJ) are both rotary or centrifugal pumps used for short-term VAD support in multiorgan failure patients. Finally, there are percutaneous VADs now small enough to place in children. The Impella 2.5 (Abiomed Inc., Danvers, MA) is an axial VAD catheter that has been used in children as small

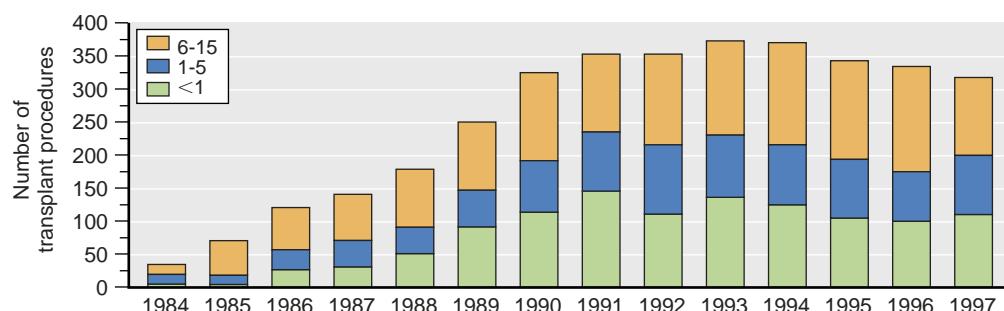
as 22 kg. One can appreciate how these modalities complement each other, with ECMO being used acutely, and then once the patient is physiologically stable, but still requiring support, a VAD can be implanted for intermediate or long-term support. Recent data from the Organ Procurement and Transplant Network supports a survival to transplant advantage for patients with VAD (in particular, CentriMag) compared to ECMO.<sup>310</sup>

A newer mechanical assist device for use in children is the temporary Total Artificial Heart (TAH) system. The TAH system is indicated for use as a bridge to transplant for patients at imminent risk for death from biventricular failure. The implantation and use of this device is unique in that it requires the complete removal of the native myocardium, such that recovery without transplantation is not possible. Once the myocardium is removed, inflow and outflow pumping chambers are sown into the right and left heart vessels. Sizing requirements include patient body surface area of 1.7 m<sup>2</sup> or greater, echocardiographic left ventricular end-diastolic diameter of 70 mm or greater, a CT scan with an anterior-to-posterior dimension at the 10th thoracic vertebrae of 10 cm or greater, and a chest radiograph with a cardiothoracic ratio of 0.5 or greater. Smaller TAH devices may be available soon, which would allow implantation in smaller patients. This device has been used successfully as a bridge to transplant in a patient with failing Fontan physiology who later went on to receive a heart transplant.

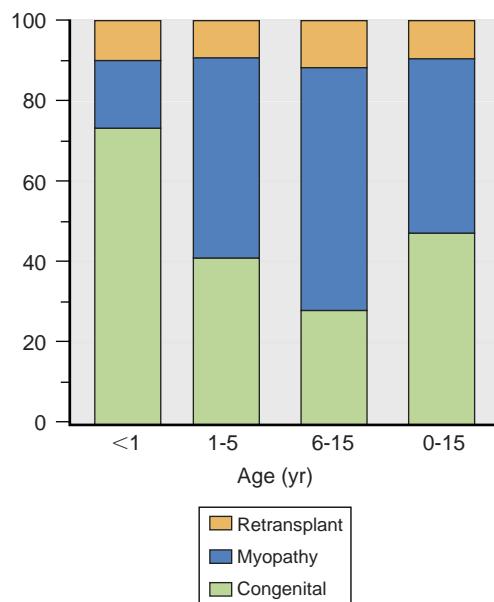
## Anesthesia for Heart and Lung Transplantation

Although perioperative management for thoracic organ transplantation is considered elsewhere in this text, the application of these procedures to children requires some specific modification. Differences include the characteristics of the candidates, preparation of these children, anesthetic management, surgical considerations, post-CPB management, and outcome. Even though some of the earliest heart transplant procedures were performed for congenital heart malformations, this indication became rare by the early 1980s. In 1984, over 60% of the few pediatric heart transplant procedures were performed in patients with cardiomyopathy, usually adolescents. In the next decade, a dramatic rise in the number of infants and young children with congenital heart malformations treated with heart transplantation resulted in a marked shift in the demographics (Fig. 78.14).<sup>311</sup> By 1995, over 70% of the children receiving heart transplants were younger than 5 years of age, with half of those younger than 1 year. The overwhelming majority of these infants received transplants for congenital heart malformations for which reconstructive options either had failed or were not believed to exist (Fig. 78.15).<sup>311</sup> The implications of this shift reach into every element of perioperative management.

Children considered for heart transplantation are more likely to have pulmonary hypertension than adults. Most adult transplant programs will not offer heart transplant therapy to patients with PVR over 6 Wood units/m<sup>2</sup>.<sup>312</sup> The exclusion threshold in infants and children remains controversial. Some programs accept patients with PVR as high



**Fig. 78.14 Demographic data for pediatric heart transplantation by age.** Stacked bar graph illustrates the total number and age distribution for heart transplantation in patients younger than 16 years of age. Note the rapid rise in transplant procedures performed during the late 1980s, with particular growth in the population of children 5 years of age and younger. Having peaked in the mid-1990s, the total number of transplant procedures (both adult and pediatric) has declined slightly, but the relative age proportions within the pediatric population remain relatively constant. (Data from the Registry of the International Society for Heart and Lung Transplantation, Addison, TX.)



**Fig. 78.15 Indication for heart transplantation in children.** Over the past 2 decades, the major indications for pediatric heart transplantation were nearly equally divided between congenital malformation and cardiomyopathy. In later years, pediatric recipients with congenital malformations assumed a slight plurality as a result of shifting age demographics. As illustrated, younger children are more likely to undergo heart transplantation because of congenital malformation. (Data from the Registry of the International Society for Heart and Lung Transplantation, Addison, TX.)

as 12 Wood units/m<sup>2</sup>, particularly if the pulmonary vasculature responds to vasodilators such as O<sub>2</sub>, NO, calcium channel blockers, or prostacyclin.<sup>313</sup> Neonates are generally assumed to have elevated PVR, but outcome data from some programs suggest that the importance of this factor for postoperative outcome is substantially less in the first year of life, perhaps because the infant donor hearts, having recently undergone transitional circulation, are better prepared to cope with the right ventricular pressure load that elevated PVR imposes.<sup>314</sup>

The anesthetic plan for pediatric heart transplantation must accommodate a wide spectrum of pathophysiology. Recipients with congenital heart malformations benefit from the analysis of loading conditions and optimizing hemodynamics discussed previously. Although a few

of these patients undergo heart transplantation because the natural history of reconstructive heart surgery poses greater risk despite reasonable ventricular function, most candidates exhibit some manifestations of impaired ventricular performance. Accordingly, they require careful titration of anesthetic agents with minimal myocardial depressant characteristics to avoid cardiovascular collapse. In this fragile population, even modest doses of opioids can be associated with marked deterioration in systemic hemodynamics, presumably by reducing endogenous catecholamine release. As with most congenital heart patients, skilled management of the airway and ventilation represents crucial elements in a satisfactory induction, particularly in the presence of elevated PVR. No matter how elegant the anesthetic plan in conception and implementation, a certain proportion of these children will decompensate on induction, necessitating resuscitative therapy. A particularly critical time is that of central line placement, when transplant patients may not tolerate the Trendelenburg position; a level table and the use of ultrasound is sufficient to place a central line.

Although orthotopic heart transplantation poses technical challenges in neonates and young infants, the replacement of an anatomically normal heart is less complex than several reconstructive heart procedures commonly performed in patients at this age. However, the need to adapt this procedure to incorporate repair of major concurrent cardiovascular malformations requires the consummate skill and creativity that remain the province of a few exemplary heart surgeons in congenital disease.<sup>315,316</sup>

Having withstood extended ischemic periods, heart grafts are extraordinarily intolerant of superimposed residual hemodynamic loads that may accompany imperfect vascular reconstruction. The extensive vascular repair and, particularly in older children with long-standing hypoxemia, the propensity to coagulopathy together elevate hemorrhage to a major cause of morbidity and even mortality in pediatric heart transplantation. Nevertheless, once successfully implanted, these grafts will respond to physiologic factors that stimulate growth and adaptation in the developing infant and child.<sup>317</sup>

Management considerations during separation from CPB and the early postoperative period are primarily focused on three pathophysiologic conditions: myocardial preservation, denervation, and PVR. Even expeditious transplant

procedures usually force the heart to endure ischemic periods that exceed those encountered during reconstructive surgery. Although some researchers believe the infant heart is more tolerant of extended ischemia, these hearts will demonstrate a period of reperfusion injury, and virtually all require pharmacologic and, in some cases, mechanical support.<sup>314</sup> In addition, endogenous adaptive responses and exogenous pharmacologic agents that act by myocardial sympathetic activation are ineffective in the denervated graft. Because the majority of children presenting for heart transplantation exhibit some element of elevated PVR, even with isolated end-stage cardiomyopathy, the RV of a newly implanted heart is particularly vulnerable to failure.

Ventilatory and pharmacologic interventions are usually configured to exert a favorable impact on PVR and provide inotropic and chronotropic support. Once the lungs are fully expanded, we ventilate to  $\text{PaCO}_2$  values in the low 30 mm Hg range using an  $\text{FiO}_2$  of 1. Virtually all recipients receive low-dose inotropic support such as epinephrine, milrinone, dopamine, and/or isoproterenol to promote inotropy, chronotropy, and lower PVR. As mentioned previously, a major concern is RV dysfunction, hence we will generally start iNO for the immediate post-CPB period.

Most transplant centers have a specific regimen for immunosuppression to be initiated in the perioperative period. As with adults, pediatric transplant programs typically employ triple-drug immunosuppression with a calcineurin inhibitor (e.g., cyclosporine, tacrolimus), antimetabolite (e.g., azathioprine), and steroid. After an interval without rejection, some pediatric programs will taper and discontinue one or even two of these agents, particularly in neonates, in whom some element of tolerance develops.<sup>318,319</sup>

Survival after pediatric heart transplant is improving. The principal risk factors are age younger than 1 year and congenital heart defects. Because these factors are closely related (i.e., the vast majority of infants younger than 1 year of age undergo transplantation for a congenital heart defect), it is difficult to determine the independent effect of age. Concurrent repair of structural cardiovascular anomalies substantially increases perioperative risks for hemorrhage, residual hemodynamic loading conditions, and right-sided HF from elevated PVR. The greatest risk of mortality is found in the first year after transplant; however, infants who survive the first postoperative year have better long-term survival than other age groups.<sup>320</sup> Average survival for infants is 18 years of age, which is the time at which 50% of patients are alive after transplant.<sup>321</sup> Average survival is 15 years for those transplanted at ages 1 to 10 years of age, and 11 years survival for those transplanted as teenagers. The sequelae of rejection and the consequences of the immunosuppression result in significant ongoing morbidity and mortality; despite advances in pharmacologic therapy, rates of acute rejection in the first year have not changed appreciably.<sup>321</sup>

A unique quality of neonates is that their immune system remains immature, unable to produce antibodies effectively against foreign blood cells, until approximately 12 to 24 months of age. Infants also have a poorly developed complement system. These developmental characteristics allow for transplantation of an ABO-mismatched organ into an infant, which has expanded the pool of available organs for that population. Anesthetic implications for infants who are candidates for ABO-incompatible transplant surround

transfusion management—these patients should receive only ABO compatible blood products before transplant, and should not receive whole blood.<sup>321</sup>

Lung and heart-lung transplantation have achieved respectable operative survival rates in children.<sup>322</sup> They remain the only viable surgical therapy for infants and children with severe pulmonary vascular disease and selected progressive pulmonary diseases. These remain uncommon procedures in pediatrics. Lung transplantation carries the additional morbidity of obliterative bronchiolitis, a debilitating small airway disease that results in gradual deterioration in flow-related pulmonary functions over time. Despite a low operative mortality rate, 5-year survival is only 53%.<sup>322</sup>

Patients with transplanted hearts also present for surveillance cardiac catheterizations, biopsies, and other procedures.<sup>299,323-325</sup> The anesthesia plan in these patients should take into account the physiologic and pharmacologic problems of allograft denervation, the side effects of immunosuppression, the risk for infection, and the potential for rejection.<sup>323-325</sup> Cardiac allograft vasculopathy is the leading cause of morbidity and mortality after transplantation, leading to progressive graft dysfunction with HF, an increased risk for dysrhythmia, and the possibility of arrhythmogenic sudden death. Conventional revascularization procedures are ineffective because cardiac allograft vasculopathy is caused by intimal proliferation leaving retransplantation as the only therapeutic option.

Hyperlipidemia after heart transplantation is a common occurrence in both adults and children and is aggravated by chronic steroid therapy and other immunosuppressive agents. Statins are used with good results in controlling hyperlipidemia after transplantation and are likely to manifest inherent immunosuppressive effects. Risk factors for posttransplant renal dysfunction are the use of calcineurin inhibitors, mechanical circulatory support, prolonged inotropic support, and preexisting renal dysfunction. Newer, more potent immunosuppressive agents (e.g., tacrolimus) have led to steroid-sparing regimens late after transplantation, eliminating the detrimental effects of long-term steroid administration. Agents such as sirolimus may now be used in combination with lower levels of calcineurin inhibitors, thus minimizing long-term nephrotoxicity.

Posttransplant lymphoproliferative disorders represent a pathologic spectrum of abnormal lymphoid proliferation ranging from localized early lesions to polymorphic disease or, in some cases, monomorphic lymphomatous disease. From a clinical perspective, the most common sites of disease and presenting symptoms included the gastrointestinal tract and pulmonary systems. Patients with polymorphic disease are treated primarily by a reduction or temporary cessation of immunosuppression, along with adjunctive surgical therapy for tissue diagnosis or obstructive lesions. Most centers reserve traditional chemotherapeutic regimens for patients with nonresponsive polymorphic disease and monomorphic disease. As a result of cardiac denervation, autonomic regulatory mechanisms are not available to prevent the wide swings in a patient's hemodynamic state and the stress response is slower than usual. Cardiac parameters are significantly altered, and patients may experience a decrease in systemic blood pressure and cardiac filling pressures. Compensatory mechanisms are delayed, and reductions in cardiac output lead to decreased coronary

and cerebral perfusion, especially on the background of hypertension. Drugs with direct myocardial and vascular effects are the mainstay of therapy. Most immunosuppressive agents affect hepatic and renal functions and interact with anesthetic drugs.

## Anesthesia for Closed-Heart Operations

Early corrective repair in infancy has significantly reduced the number of non-corrective, palliative closed-heart operations. Corrective closed-heart procedures include PDA ligation and repair of coarctation of the aorta. Non-corrective closed-heart operations include pulmonary artery banding and extracardiac shunts such as the Blalock-Taussig shunt. These procedures are performed without CPB. Therefore, venous access and intraarterial monitoring are important in evaluating and supporting these patients. A pulse oximeter and NIRS monitors (cerebral and somatic) are invaluable devices during intraoperative management.

Ligation of a PDA is typically performed through a left thoracotomy, although video-assisted thoracoscopic techniques are increasingly common.<sup>326,327</sup> Physiologic management is that of a left-to-right shunt producing volume overload. Patients with a large PDA and low PVR generally present with excessive PBF and CHF. Neonates and premature infants also run the risk for having substantial diastolic runoff to the pulmonary artery, potentially impairing coronary perfusion. Thus, patients range from an asymptomatic healthy young child to the sick ventilator-dependent premature infant on inotropic support. The health of the former patient allows a wide variety of anesthetic techniques culminating in extubation in the operating room. The latter patient requires a carefully controlled anesthetic and fluid management plan. Generally, a trial of medical management with indomethacin and fluid restriction is attempted in the premature infant before surgical correction. Transport of the premature infant to the operating room can be especially difficult and potentially hazardous, requiring great vigilance to avoid extubation, excessive patient cooling, and venous access disruption. For these reasons, many centers are now performing ligation in the neonatal ICU.

A subset of premature infants with PDAs is located at institutions without cardiac surgical teams. Ligation of the PDA in these patients requires either transfer of these high-risk neonates to a center that has a team who routinely perform the procedure or the availability of a team capable of performing the procedure who is willing to travel to perform the procedure in the neonate's home neonatal ICU (NICU). Gould and associates<sup>328</sup> reviewed the experience with onsite and off-site ligations of a team composed of a pediatric cardiac attending anesthesiologist, a certified registered nurse anesthetist, an attending pediatric cardiothoracic surgeon and fellow, and cardiac operating room nurses. There were no anesthetic-related complications in their group. No differences were found in the incidence of perioperative complications in the procedures in the two sites. This study showed PDA ligations can be performed safely in the NICUs of hospitals lacking onsite pediatric cardiac surgical units, without incurring the risk inherent in transport of critically ill infants. In addition, patient care is

continued by the neonatology team most familiar with the child's medical and social history and the patient's family is minimally inconvenienced.

Complications of PDA ligation include inadvertent ligation of the left pulmonary artery or descending aorta, recurrent laryngeal nerve damage, and excessive bleeding as a result of inadvertent PDA disruption. Placement of a pulse oximeter on the lower extremity should alert the anesthesiologist and surgeon in the case of inadvertent aortic ligation. After ductal ligation in premature infants, worsening pulmonary compliance can precipitate a need for increased ventilatory support, and manifestations of an acute increase in left ventricular afterload should be anticipated, especially if left ventricular dysfunction has developed preoperatively. PDA ligation has been performed in infants and children using thoracoscopic surgical techniques. This approach has the advantage of limited incisions at thoracoscopic sites, promoting less postoperative pain and discharge from the hospital the same day of surgery.

Coarctation of the aorta is a narrowing of the descending aorta near the insertion of the ductus arteriosus. Obstruction to aortic flow results and may range from severe obstruction with compromised distal systemic perfusion to mild upper extremity hypertension as the only manifestation. Associated anomalies of both the mitral and aortic valves can occur. In the neonate with severe coarctation, systemic perfusion depends on right-to-left shunting across the PDA. In these circumstances, left ventricular dysfunction is very common and prostaglandin E1 is necessary to preserve sufficient systemic perfusion. Generally, a peripheral intravenous line and an indwelling arterial catheter, in the right upper extremity, are recommended for intraoperative and postoperative management. In patients with left ventricular dysfunction, a central venous catheter may be desirable for pressure monitoring and inotropic support.

The surgical approach is through a left thoracotomy, whereby the aorta is cross-clamped and the coarctation repaired with an end-to-end anastomosis, patch aortoplasty, or subclavian patch. During cross-clamping, we usually allow significant proximal hypertension (20%–25% increase over baseline), based on evidence that vasodilator therapy may jeopardize distal perfusion and promote spinal cord ischemia. Intravascular crystalloid administration of 10 to 20 mL/kg is given just before removal of the clamp. The anesthetic concentration is decreased, and additional blood volume support is given until the blood pressure rises. Postrepair rebound hypertension as a result of heightened baroreceptor reactivity is common and often requires medical therapy. After cross-clamping, aortic wall stress resulting from systemic hypertension is most effectively lowered by institution of  $\beta$ -blockade with esmolol or  $\alpha/\beta$ -blockade with labetalol.<sup>329</sup> Recent work indicates that patients younger than 6 years of age should receive an initial dose of esmolol 250 to 500  $\mu$ g/kg, followed by an infusion of 250 to 750  $\mu$ g/kg/min, depending on the blood pressure. Despite an esmolol infusion, 25% to 50% of patients have a blood pressure that is above the targeted range, requiring a second drug. Sodium nitroprusside or nicardipine is usually chosen as the second drug. Propranolol is useful in older patients but can cause severe bradycardia in infants and young children. Although it actually increases calculated aortic wall stress in the absence of  $\beta$ -blockade by accelerating dP/

$\Delta T$  (contractile force), the addition of sodium nitroprusside may be necessary to control refractory hypertension. Captopril or an alternative antihypertensive regimen is begun in the convalescent stage of recovery in patients with persistent hypertension.

The management of infants undergoing placement of extracardiac shunts without CPB centers on goals similar to those of other shunt lesions—balancing pulmonary and systemic blood flow by altering  $\text{PaCO}_2$ ,  $\text{PaO}_2$ , and ventilatory dynamics. Central shunts are usually performed through a median sternotomy, whereas Blalock-Taussig shunts may be performed through a thoracotomy or sternotomy. In patients in whom PBF is critically low, partial cross-clamping of the pulmonary artery required for the distal anastomosis causes further reduction of PBF and desaturation, necessitating meticulous monitoring of pulse oximetry. Careful application of the cross-clamp to avoid pulmonary artery distortion will help maintain PBF. Under circumstances in which severe desaturation and bradycardia occur with cross-clamping, CPB will be required for the procedure.

Intraoperative complications include bleeding and severe systemic  $\text{O}_2$  desaturation during chest closure, usually indicating a change in the relationship of the intrathoracic contents that results in distortion of the pulmonary arteries or kink in the shunt. Pulmonary edema may develop in the early postoperative period in response to the acute volume overload that accompanies the creation of a large surgical shunt. Measures directed at increasing PVR, such as lowering inspired  $\text{O}_2$  to room air, allowing the  $\text{PaCO}_2$  to rise, and adding PEEP are helpful maneuvers to decrease PBF until the pulmonary circulation can adjust. Decongestive therapy such as diuretics and digoxin may alleviate the manifestations of CHF. Under such circumstances, early extubation is inadvisable.

Pulmonary artery banding is used to restrict PBF in infants whose defects are deemed uncorrectable for either anatomic or physiologic reasons. These patients are generally in CHF with reduced systemic perfusion and excessive PBF. The surgeon places a restrictive band around the main pulmonary artery to reduce PBF. Band placement is very imprecise and requires careful assistance from the anesthesia team to accomplish successfully. Many approaches have been suggested. We place the patient on 21% inspired  $\text{O}_2$  concentration and maintain the  $\text{PaCO}_2$  at 40 mm Hg to simulate the postoperative state. Depending on the malformation, a pulmonary artery band is tightened to achieve hemodynamic (e.g., distal pulmonary artery pressure 50%–25% systemic pressure) or physiologic (e.g.,  $\dot{Q}_p/\dot{Q}_s$  approaching 1) goals. Should the attainment of these objectives produce unacceptable hypoxemia, the band is loosened.

## Anesthesia for Interventional or Diagnostic Cardiac Procedures

Advances in interventional and diagnostic cardiac catheterization techniques are significantly changing the operative and nonoperative approach to the patient with a congenital heart defect. Common interventions in the cardiac

**TABLE 78.11** Common Interventions in the Cardiac Catheterization Laboratory

Device Closures	Coil Embolization
<b>SIMPLE INTERVENTIONS</b>	
Atrial septal defect (ASD)	Decompressing veins
Ventricular septal defect (VSD)	Aortopulmonary (AP) collaterals
Patent ductus arteriosus (PDA)	Surgical shunts
Patent foramen ovale (PFO)	Coronary/atrioventricular fistulas
Balloon valvuloplasty	Balloon angioplasty
Aortic stenosis (AS)	Branch pulmonary artery stenosis
Pulmonary stenosis (PS)	Coarctation of the aorta
<b>COMPLEX INTERVENTIONS</b>	
<b>Hypoplastic Left Heart Syndrome (HLHS)</b>	
<i>After Norwood</i>	
Pulmonary artery stenosis	Angioplasty
Shunt thrombosis	Dilation/thrombectomy
Restrictive ASD	Balloon septostomy
Aortic arch obstruction	Angioplasty
AP collaterals	Coil embolization
<i>Post Glenn/Fontan</i>	
Decompressing veins	Coil embolization
Baffle leaks	Device/coil embolization
Systemic vein stenosis/ thrombosis	Angioplasty/thrombectomy
Right ventricular failure	Creation of fenestration
Exercise intolerance	Closure of fenestration
AP collaterals	Coil embolization
Obstructive Fontan pathway	PA angioplasty, balloon septostomy
Transposition of Great Arteries	Balloon atrial septostomy
<b>Tetralogy of Fallot (TOF)</b>	
Shunt thrombosis	Thrombectomy
Pulmonary artery stenosis	Angioplasty
AP collaterals	Coil occlusion
<b>MISCELLANEOUS INTERVENTIONS</b>	
Severe pulmonary hypertension	Atrial septostomy
ECMO left heart decompression	Atrial septostomy
Stenosis of pulmonary veins	Balloon angioplasty stent
Stenosis/thrombosis of systemic veins	Balloon angioplasty/thrombectomy

ECMO, Extracorporeal membrane oxygenation.

catheterization laboratory are shown in Table 78.11. Nonoperative interventional techniques are being used instead of procedures requiring surgery and CPB for safe closure of secundum ASDs, VSDs, and PDAs. Stenotic aortic and pulmonic valves, recurrent aortic coarctations, and branch pulmonary artery stenoses can be dilated in the catheterization laboratory, avoiding surgical intervention.<sup>330,331</sup>

These techniques shorten the hospital stay and are particularly beneficial to patients with recurrent coarctation and muscular or apical VSDs, who are at a higher risk for operative intervention. Many patients with complex cardiac defects are poor operative candidates. Innovative interventional procedures improve vascular anatomy, reduce pressure loads on ventricles, and decrease the operative risk for these patients. For example, in TOF with hypoplastic pulmonary arteries, balloon angioplasty and vascular stenting procedures create favorable pulmonary artery anatomy and reduce pulmonary artery pressure and right ventricular end-diastolic pressure. Complications are more common during interventional catheterization and include arterial thrombosis, arrhythmias (especially heart block), hemodynamic instability, embolization of devices or coils, bleeding, perforation of the major vessels or heart, and lung reperfusion injuries.<sup>332</sup> Complications are more common in smaller infants, particularly those younger than 6 months of age. Constant vigilance, correction of electrolyte imbalance, maintenance of acid-base status, and appropriate heparinization will mitigate some of the morbidity. Appropriate and early transfusion with deployment of rapid-response ECMO in the resuscitation of an infant in cardiac arrest improves outcome. High-risk patients undergoing diagnostic evaluation of pulmonary artery hypertension in anticipation of heart-lung transplantation also require anesthetic management. Despite the attendant high risks for the procedure in patients with suprasystemic right ventricular pressure, these patients are best managed with general anesthesia and controlled ventilation.

Anesthetic management of interventional or diagnostic procedures in the catheterization laboratory must include the same level of preparation that applies in caring for these patients in the operating room. These patients have the same complex cardiac physiology and, in some cases, greater physiologic complexity and less cardiovascular reserve. Interventional catheterization procedures can impose acute pressure load on the heart during balloon inflation. Large catheters placed across mitral or tricuspid valves create acute valvular regurgitation or, in the case of a small valve orifice, transient valvular stenosis. When catheters are placed across shunts, severe reductions in PBF and marked hypoxemia may occur. The anesthetic plan must consider the specific cardiology objectives of the procedure and the impact of anesthetic management in facilitating or hindering the interventional procedure. In general, the three distinct periods involved in an interventional catheterization are the data acquisition period, the interventional period, and the postprocedural evaluation period.

During the data acquisition period, the cardiologist performs a hemodynamic catheterization to evaluate the need for and extent of the planned intervention. Catheterization data are obtained under normal physiologic conditions—that is, room air and physiologic  $\text{PaCO}_2$ . Increased  $\text{FiO}_2$  or changes in  $\text{PaCO}_2$  may obscure physiologic data. Although some patients may require  $\text{O}_2$  administration if the PBF is such that the administration of room air may lead to life-threatening hypoxia, a discussion with the interventional cardiologist is essential in the care of these children. Ideally a patient would be kept spontaneously ventilating, but this

is impractical. A secured airway allows the anesthesiologist to concentrate on hemodynamic issues. Positive-pressure ventilation also reduces the risk for air embolism; the cardiologist can measure pressures during expiration to obtain the most accurate data. During spontaneous ventilation, a large reduction in intrathoracic pressure can entrain air into vascular sheaths and result in moderate-to-large pulmonary or systemic air emboli. Precise device placement is also facilitated with muscle relaxants that eliminate patient movements and controlled ventilation, thereby reducing the respiratory shifting of cardiac structures. Substantial blood loss and changes in ventricular function occur commonly during the intervention.

In the postprocedural period, the success and physiologic impact of the intervention are evaluated. Blood pressure, mixed venous  $\text{O}_2$  saturation, ventricular end-diastolic pressure, and cardiac output, when available, are used to assess the impact of the intervention. Persistent severe hemodynamic derangement indicates the need for ICU monitoring and respiratory or cardiovascular support.

A brief description of some of the interventional procedures and the associated anesthetic implications follows. The success of these interventions will undoubtedly result in widespread availability and use over the next few years.

## TRANSCATHETER TECHNIQUE FOR ATRIAL SEPTAL DEFECT CLOSURES

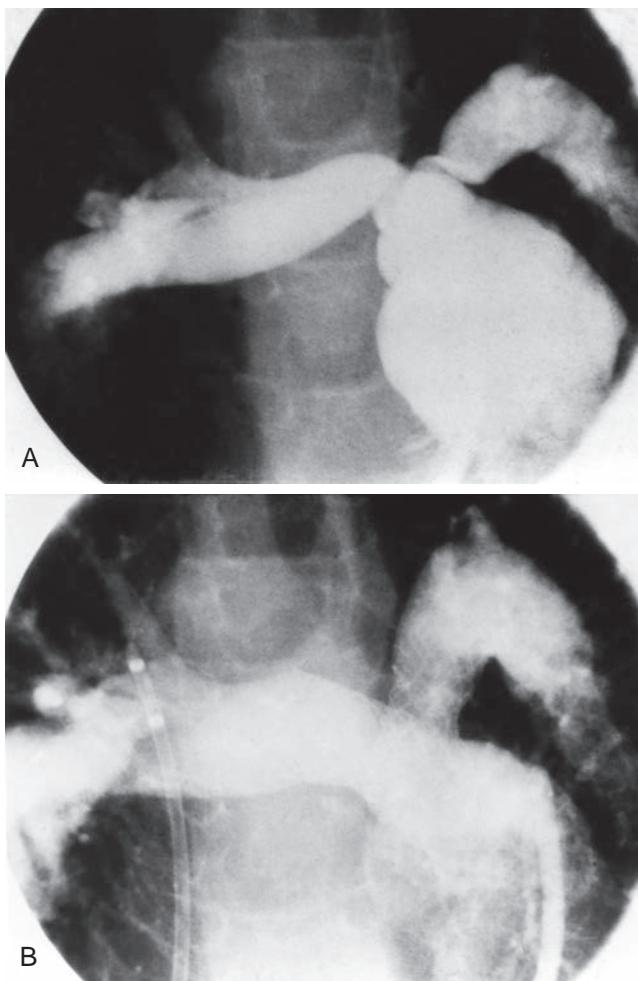
In the transcatheter technique for ASD closures, a collapsed double-umbrella clamshell device is loaded into a large introducer sheath placed through the femoral vein, advanced to the RA, and placed across the ASD into the left atrial chamber. Each side of the device consists of a Dacron mesh patch suspended in six spring-loaded arms that open like an automatic umbrella. Using biplane fluoroscopy and TEE, the catheter is positioned in the LA away from the mitral valve.<sup>333</sup> The sheath is pulled back to open the six distal arms and its Dacron mesh cover into the LA. The sheath and device are then pulled back so the distal arms contact the left atrial septum. Fluoroscopy and TEE or intracardiac echocardiography are used to confirm that the arms are on the left atrial side and do not interfere with mitral valve motion. Once adequately seated, the sheath is pulled farther back to expose the proximal side of the device and the proximal arms, which spring open to engage the right side of the atrial septum. When proper positioning is certain, the device is released.<sup>333</sup> Device closure of secundum ASD is the preferred therapeutic approach. Data continue to support closure of defects of small-to-moderate size (<8–20 mm) in appropriate-size patients with appropriate septal length and device diameter.<sup>334–338</sup> A 2012 review of percutaneous device ASD closure found a major complication rate of 1% to 2.5% (device embolization or erosion, stroke, endocarditis, tamponade, and device thrombus), and a 3.5% to 6% minor complication rate (inflammatory reactions in those with nickel allergy, arrhythmia, access-site complications).<sup>339</sup> Cardiac erosions and heart block can occur in patients who receive a large device for patient size, especially those who have a deficient anterosuperior rim.<sup>340,341</sup> Thrombus is a rare problem that can usually be treated medically, and its incidence appears to be device-dependent.<sup>342</sup>

## TRANSCATHETER VENTRICULAR SEPTAL DEFECT CLOSURES

Most VSDs that are electively closed in the catheterization laboratory are mid-muscular or apical VSDs that are either difficult to close in the operating room or would require a left ventriculotomy. Left ventriculotomies are associated with a high incidence of left ventricular dysfunction and have been relegated to a position as the least desirable surgical option. The preferred therapeutic approach for VSD is surgical closure. Transcatheter closure of muscular VSDs can be performed safely. However, a significant incidence of complications occurs, including heart block, blood loss, and hemodynamic instability.<sup>343,344</sup> Device closure of membranous VSD is in early stages of investigation, and the incidence of complications remains to be determined.<sup>345,346</sup> The transcatheter approach requires a blade atrial septostomy and a retrograde catheter placed through the femoral artery and advanced to the LA. This catheter is pulled across the atrial septum into the RA and is used to guide a superior vena cava catheter (placed through the internal jugular vein) across the ASD into the LA, across the mitral valve, and into the LV. The VSD defect is approached from the left ventricular side. The large sheath containing the double-umbrella clamshell device prevents closure of the mitral valve, resulting in acute mitral regurgitation or, in cases in which the VSD is large or the mitral annulus small, acute severe mitral stenosis. In the latter case, systemic output is decreased and a period of severe hypotension is unavoidable. Judicious use of vasoconstrictors to maintain coronary perfusion may be required during the catheter placement, followed by volume and inotropic resuscitation after the VSD device is deployed. This highly specialized application of the clamshell device is confined to only a few pediatric centers in the United States. A 2015 review and meta-analysis comparing percutaneous versus open surgical closure of perimembranous VSD showed equivalent closure success rates between groups, and no differences in major complications (death, reoperation, need for permanent pacemaker).<sup>347</sup> Patients in the percutaneous closure group were older (median 12 years vs. 5 years in surgical group); blood transfusions and hospital length of stay were shorter in the percutaneous versus the surgical group.

## ANGIOPLASTY OF BRANCH PULMONARY ARTERY STENOSIS

One of the most important areas of interventional catheterization has been the dilation and stenting of hypoplastic or stenotic branch pulmonary arteries. In patients with TOF with hypoplastic pulmonary arteries, pulmonary atresia, or single ventricle with surgically induced peripheral stenoses, the use of balloon angioplasty and stenting procedures creates favorable pulmonary artery anatomy and reduces the risk for subsequent surgical repairs (Fig. 78.16). Peripheral pulmonary artery stenosis is not a surgically amenable lesion and is particularly suited to catheterization and angioplasty. Balloon angioplasty is accomplished by tearing the vascular intima and media, allowing the vessel to remodel and heal with a larger diameter. The balloon is placed across the stenotic lesion so that the middle of the balloon is at the stenosis. The balloon is inflated until



**Fig. 78.16** (A) Severe bilateral branch pulmonary artery stenoses at the distal end of a conduit in a patient with pulmonary trunk atresia and ventricular septal defect. Stents were placed in the right and left pulmonary arteries. (B) Follow-up angiogram in the same projection and magnification showed marked improvement of both right and left stenoses.

the waist of the balloon is eliminated. Ideally, the most stenotic lesions are dilated first to minimize the impact on PBF and cardiac output. When the balloon is inflated, PBF is reduced, right ventricular afterload is increased, and cardiac output falls. In patients with an associated VSD or ASD, right-to-left shunting and desaturation occur with balloon inflation. In patients without a shunt, acute increase in right ventricular afterload can cause systemic hypotension and right ventricular failure. The large vascular sheaths required for these procedures can introduce tricuspid regurgitation, which is poorly tolerated in patients with severe RV hypertension. Occasionally, balloon catheters must be placed across aortopulmonary shunts, significantly reducing PBF.

The procedure is successful in approximately 60% of patients. In an early series, complications included hypotension (40%), pulmonary artery rupture (3%), unilateral reperfusion pulmonary edema (4%), aneurysmal dilation of the dilated pulmonary vessel (8%), death (1.5%), and transient postprocedural right ventricular dysfunction.<sup>348</sup> Improved techniques and patient selection have favorably influenced the results with superior balloon catheters and

stents while significantly reducing serious complications. Anesthetic support minimizes hemodynamic compromise by anticipating changes in blood flow patterns, treating transient hypotension, and providing airway support to minimize the risks associated with pulmonary artery disruption and acute unilateral pulmonary edema.<sup>348</sup>

A unique group of patients are those with Williams syndrome with supravalvular aortic and pulmonary stenosis. Such patients can have multiple areas of severe branch pulmonary artery stenosis, with resultant systemic or suprastemic right ventricular pressures and right ventricular dysfunction. Patients can also have coronary stenosis and develop subendocardial ischemia from hemodynamic disturbances in the setting of biventricular hypertrophy. The presence of supravalvular aortic stenosis, biventricular outflow tract obstruction, and coronary stenosis is associated with increased perioperative risk. Typically, such patients undergo general anesthesia with positive-pressure ventilation and recover in the cardiac ICU for angioplasty of branch pulmonary artery stenosis.<sup>349</sup> Care must be exercised in maintaining SVR, myocardial oxygenation, and contractility. Tachycardia and subendocardial ischemia should be avoided in the presence of ventricular hypertrophy.

## BALLOON VALVULOTOMIES

Balloon valvulotomies conducted in well-compensated infants and children often can be accomplished without anesthetic support. Exceptions include neonates with critical aortic or pulmonary stenosis and patients with significant ventricular dysfunction who exhibit unstable hemodynamics. Balloon valvuloplasty is indicated in valvular pulmonary or aortic stenosis with valvular gradients more than 50 mm Hg. Balloon dilation is effective in most patients, except those with dysplastic valves (e.g., Noonan syndrome); postdilation pulmonary incompetence is anticipated and does not pose a problem in the immediate and intermediate period. Long-term prophylaxis for subacute bacterial endocarditis is needed. Only 8% of patients require repeat interventions. Typically, patients recover in the ICU and may require transfusion depending on hemodynamic stability. Valvular aortic stenosis is associated with poor surgical outcome in the neonatal period. All therapies are palliative, with a high incidence of repeat interventions, and balloon valvuloplasty is often the initial treatment. Residual obstruction or regurgitation is common after balloon dilatation and can require repeat intervention. A real risk exists for damage to the aortic valve and subaortic septum, with the consequence of acute aortic insufficiency and coronary ischemia. Hypotension and bradycardia commonly occur during valvuloplasty, and many centers have a policy of ECMO standby for these high-risk interventions in the catheterization laboratory. Ready availability of a surgical and perfusion team is crucial to a good outcome. Neonates with critical aortic stenosis often require stabilization with inotropes and prostaglandins to maintain systemic perfusion before the procedure. Balloon dilation of recurrent coarctation is often the therapy of choice in older children with recoarctation after surgery. Such patients are often hypertensive. The procedure can be performed with the patient under deep sedation or general anesthesia. In infants after Norwood palliation for HLHS, coarctation can

occur in the distal arch anastomotic site. Catheters placed antegrade via the right side of the heart into the neoaorta can induce hemodynamically significant tricuspid and neoaortic regurgitation, resulting in hemodynamic instability. Careful monitoring and aggressive hemodynamic intervention result in a good outcome.

## COIL EMBOLIZATION

Transcatheter methods can be adapted to occlude undesired vascular structures. Intravascular coils have been used to close PDAs, aortopulmonary collaterals, surgical systemic and pulmonary artery shunts, venous collaterals in single ventricle lesions, coronary fistulas, and some arteriovenous malformations (e.g., vein of Galen malformation). In selected instances, to minimize the risk that coils may escape to threaten vital organ perfusion, cardiologists request the use of general anesthesia with a muscle relaxant.

Depending on the lesion, patients might manifest severe cyanosis, low-output or high-output cardiac failure, or coronary ischemia. Extra care should be exercised in patients with coronary fistulas to maintain myocardial O<sub>2</sub> supply and reduce demand. Materials used for embolization can include surgical gel (Gelfoam), alcohol, and coils. Some of these substances can induce severe allergic reactions with hemodynamic collapse. Antibiotic prophylaxis is mandatory to prevent bacterial endocarditis. Angiography is used to demonstrate successful occlusion of the vascular structure and ascertain appropriate placement.

## VALVE PROSTHESES

Transcatheter bioprosthetic valve replacement of the pulmonary and aortic valves is being performed. The pulmonary valve is a bovine jugular venous valve mounted on a balloon-expandable Cheatham platinum stent. The technique is limited by the maximum size of 22 mm of the bovine jugular venous valve. Percutaneous placement of bioprosthetic valve in the pulmonary position is a reality, and further refinement and miniaturization will lead to its application in aneurysmal right ventricular outflow tract. Current candidates for the implantation of transcatheter pulmonary valve include age of 5 years or older, weight of 30 kg or more, and a conduit diameter of 16 to 22 mm. Candidates have moderate-to-severe pulmonary regurgitation, often with RV dilation or dysfunction and mean right ventricular outflow tract gradients greater than 35 mm Hg. A single-center study comparing transcatheter PVR versus surgical PVR found that patients younger than 17 years of age had better pulmonary valve function following transcatheter versus surgically replaced valves.<sup>350</sup> Transcatheter PVR reduces even significant tricuspid valve regurgitation in patients with RV outflow obstruction and pulmonary regurgitation.<sup>351</sup> Interestingly, a prospective study of transcatheter PVR found significant increases in the size of the pulmonary artery postprocedure; this finding is of unclear significance for patient selection and long-term outcome.<sup>352</sup>

Transcatheter aortic valve replacement continues to be used in the management of adult patients with complex status and aortic stenosis who are not considered surgical candidates because of surgical risk. The use of these devices in pediatrics has been limited. Some authors have described

the use of transcatheter pulmonary valves in the high-pressure circuit with good short-term performance. Complications of the transcatheter valve placements include wire perforation of vessels, conduit rupture, or coronary artery compression.

## EMERGENT PROCEDURES

Emergent interventions such as balloon atrial septostomy to ensure adequate mixing in patients with transposition physiology and in patients who have restrictive ASD with single ventricle physiology are lifesaving and enable planning surgery at a suitable time. The procedure can be performed at the bedside with echocardiography or in the catheterization laboratory with fluoroscopic confirmation of balloon position. Access is by the femoral or umbilical vein, and the balloon catheter is advanced through the foramen ovale into the LA. The balloon is inflated with contrast and pulled back via the septum until a satisfactory ASD is created. If the procedure is successful, the left and right atrial pressures should equalize and adequate mixing should occur. Oxygenation and pulmonary venous drainage should improve. Complications include atrial perforation, laceration of the mitral or tricuspid valves and pulmonary veins, and low cardiac output state. Balloon atrial septostomy is also performed emergently in patients receiving ECMO therapy for left-sided heart decompression.

## ENDOMYOCARDIAL BIOPSY

Typically, endomyocardial biopsies are performed as part of posttransplant surveillance catheterizations at regular intervals to ascertain absence of rejection in patients after orthotopic heart transplantation. Right-sided heart catheterization is usually performed by access of the right internal jugular vein, through which the long sheath and biotome are introduced. Usually five to eight samples are taken. Endomyocardial biopsies are also used to confirm a diagnosis of myocarditis or cardiomyopathy; sedation or general anesthesia is required for smaller children, although older children can undergo this procedure with local anesthesia alone. Children who undergo catheterization during a period of acute rejection are at high risk for malignant arrhythmias during endomyocardial biopsy and might require resuscitation. A clinical history suggestive of an episode of rejection includes fever, gastrointestinal disturbances, and arrhythmias. Complications include perforation, tricuspid valve damage, and the development of coronary-to-right ventricular fistulas.

## CARDIAC CATHETERIZATION OF PATIENTS SUPPORTED BY EXTRACORPOREAL MEMBRANE OXYGENATION

Booth and associates<sup>353</sup> reported on the Boston experience of cardiac catheterization in pediatric patients supported with ECMO. Indications included assessment of surgical repair, left-sided heart decompression, myocarditis or cardiomyopathy, hemodynamic assessment, catheter interventions, and ablation of arrhythmias. The most common interventions were left-sided heart decompression in patients with left atrial hypertension, balloon angioplasty

of the pulmonary arteries, and endomyocardial biopsy. The anesthesiologist coordinates safe transport of the patient on mechanical support with the perfusion and nursing team. The logistics of the transport, availability of surgeon, and blood need to be addressed before the transfer. Anesthesia is provided using isoflurane or sedatives on the ECMO circuit, and paralysis must be achieved before transport. Rest ventilation of the lungs is continued. The anesthesiologist's role is in managing a safe transport and attending to emergency mechanical, cardiorespiratory, and hematologic issues.

At present, hybrid techniques find a niche in lesions in which cardiac surgery is problematic, such as apical muscular or anterior muscular VSDs or in high-risk patients with more complex lesions in which immediate surgery is contraindicated or is associated with significant morbidity and mortality. Close collaboration is required so that a surgical approach is modified to facilitate the subsequent interventional approach. The hybrid approach has been used in the management of HLHS. Stage 1 palliation is performed by creation of an atrial septal communication and stent placement in the ductus arteriosus during catheterization to maintain ductal patency with surgically applied external right and left pulmonary artery bands or transcatheter-placed internal bands.<sup>354,355</sup> A modified Norwood procedure with a bidirectional Glenn anastomosis is performed with CPB during stage 2 palliation.<sup>356</sup> Stage 3 (Fontan operation) is performed entirely by transcatheter techniques.<sup>357</sup> In the current surgical climate, it seems difficult to promote ductal stenting as a method of choice but in patients with contraindications to immediate surgery this provides an attractive bridge.<sup>358</sup>

## Adult Congenital Heart Disease

### EPIDEMIOLOGY AND CLASSIFICATION

The care of adults with CHD is a new and exciting frontier in medicine. Adult congenital heart disease (ACHD) represents a large spectrum of clinical entities ranging from mild to severe and palliated to corrected, with no or multiple adult comorbidities. The incidence of CHD is estimated to be 3 to 6 cases per 1000 live births. Approximately 85% of these patients can be expected to reach adulthood.<sup>359</sup> The prevalence of CHD is rising in both children and adults, with adults representing the largest group.

At the Bethesda conference in 2001, patients with ACHD were categorized into groups of simple, moderate, or great complexity based on medical diagnosis.<sup>359</sup> Anesthesiologists should be aware of the Bethesda task conference recommendations for ACHD in terms of distribution of care for these patients. It is recommended that patients with CHD of great complexity be regularly seen at tertiary care centers that specialize in ACHD.

### CONSIDERATIONS IN THE CARE OF PATIENTS WITH ADULT CONGENITAL HEART DISEASE

Adults with CHD may present with unique anatomy or physiologic sequelae not otherwise encountered in pediatric patients with CHD. Some patients with ACHD may have

had palliative repairs no longer primarily employed for specific diseases today, such as the Mustard or Senning procedure for dextro-transposition of the great arteries (d-TGA). In addition, these patients may not have complete awareness or access to information on medical treatments completed when they were a child. As the number of patients with ACHD increases, so do the chances an anesthesiologist will need to care for one of these patients in an emergent situation. In general, practitioners would want to gather as much information as available in regard to the details of the patient's medical history, surgical repairs, and current functional status.

General considerations include presence of arrhythmias, hypoxemia, pulmonary hypertension, ventricular dysfunction, shunts, thrombosis, and need for antibiotic prophylaxis. Arrhythmias are one of the most common sequelae in adults with CHD. Common arrhythmias occur as the result of atrial dilation and include atrial fibrillation or flutter, which may or may not be hemodynamically significant. A right bundle branch block pattern of the QRS segment of the ECG is common after repair of TOF. In the absence of lung disease, hypoxemia results from a decrease of PBF, either due to obstruction or right-to-left shunting. Strategies to avoid further hypoxemia include adequate hydration, ventilation, and pulmonary perfusion while decreasing PVR or O<sub>2</sub> consumption. It is prudent to determine patient baseline SpO<sub>2</sub> as a reference for the anesthetic. Many patients with ACHD with chronic hypoxemia may require hematocrit values greater than 45% to allow for adequate O<sub>2</sub> delivery; O<sub>2</sub> carrying capacity may be maximized by the administration of packed RBCs. Along with cyanosis, the presence of polycythemia in these patients increases their thromboembolic risk.

The presence of pulmonary hypertension should always be considered when caring for patients with ACHD. Chronic volume overload to the pulmonary vascular bed creates hypertrophy of the arterioles with resultant pulmonary hypertension. Common defects where pulmonary hypertension may be found in childhood include shunt lesions, which, if untreated, result in pulmonary vasoocclusive disease. When hypoxemia is present with these conditions, a high level of suspicion for pulmonary hypertension and possibly Eisenmenger syndrome is necessary. The anesthesiologist should always have a high level of suspicion for the presence of ventricular dysfunction in patients with ACHD. Many CHD defects place a volume or pressure load on the heart that over time may lead to dilated or hypertrophied performance. The careful titration of induction and maintenance agents that maintain ventricular performance is warranted in providing anesthesia care. Shunts of varying size and location may be created in the care of hypoxic patients with CHD in an effort to increase PBF. In many cases, patients rely on the patency of these shunts to supply the lungs with blood and their occlusion could be catastrophic. Likewise, thrombosis of various shunts or cardiac chambers may occur related to altered patterns of blood flow. Therefore, specific anticoagulation strategies may be required to ensure blood flow. The American Heart Association has provided updated guidelines regarding recommendations for prophylaxis against infective endocarditis, and specific guidelines may be found in this chapter (Table 78.12).

**TABLE 78.12** Infective Endocarditis Prophylaxis

Situation	Drug	SINGLE DOSE 30-60 MIN BEFORE DENTAL PROCEDURE	
		Adults	Children
Oral	Amoxicillin	2 g	50 mg/kg
Unable to take oral medication	Ampicillin or	2 g IM/IV	50 mg/kg IM/IV
	Cefazolin/ceftriaxone	1 g IM/IV	50 mg/kg IM/IV
Allergic to penicillins/oral	Cephalexin or	2 g	50 mg/kg IM/IV
	Clindamycin or	600 mg	20 mg/kg IM/IV
	Azithromycin/clarithromycin	500 mg	15 mg/kg
Allergic to penicillins/unable to take oral medication	Cefazolin/ceftriaxone or	1 g IM/IV	50 mg/kg IM/IV
	Clindamycin	600 mg	20 mg/kg

Vancomycin is an alternative for patients who are unable to tolerate a  $\beta$ -lactam or when the infective agent is considered to be methicillin-resistant *Staphylococcus aureus*.

## SPECIFIC LESIONS WITH UNIQUE CONSIDERATIONS FOR ADULT CONGENITAL HEART DISEASE

### Tetralogy of Fallot

TOF consists of four defects of varying physiologic significance: malignant type VSD, varying degrees of right ventricular outflow tract obstruction, right ventricular hypertrophy, and an overriding aorta. The typical clinical significance of this pattern of cardiac anomalies is that of hypoxia as a result of decreased PBF. In the early stages of treatment of TOF the systemic-pulmonary artery shunt (Blalock-Taussig shunt) was used to allow the child to grow, followed by a definitive repair later in life. Many patients up until the 1970s may have had classic Blalock-Taussig shunt or central shunts performed. A mBTS is used today for patients who require augmented PBF but who are not candidates for early complete repair. Most infants undergo complete repair in the first year of life; on occasion, a degree of pulmonary stenosis protects the lung from overcirculation of blood from the VSD while allowing adequate PBF for growth, and these patients may ultimately not require surgical repair.

Adults with TOF may have had any of these potential surgical repairs. The type of repair completed and functional status of the repair should be ascertained. The most common long-term complication after TOF repair is pulmonary insufficiency; cardiac MRI is utilized to follow right ventricular volumes over time to aid in the timing of surgical repair or pulmonary valve replacement.<sup>360</sup> Elevated jugular venous pressures and hepatomegaly should alert the anesthesiologist to right ventricular failure. Other complications of TOF repair include arrhythmias of right ventricular origin or right bundle branch block patterns on the ECG, particularly in the case of previous ventriculotomy. Cyanosis in these patients suggests inadequate PBF.

## Fontan Circulations

In the early 1970s, Fontan and Kreutzer performed a procedure in a patient with tricuspid atresia in an attempt to separate the PBF from the systemic circulation<sup>361</sup>; known now as the Fontan procedure, or total cavopulmonary anastomosis, the goal is to divert deoxygenated venous blood return directly and passively from the systemic venous circulation to the lungs, allowing the single ventricle to pump oxygenated blood to the systemic circulation. This principle of blood diversion is now applied to many types of functionally single-ventricle patients, usually as a series of two to three-staged procedures. Currently, Fontan operations for single-ventricle patients are performed on patients between 2 and 4 years of age, resulting in separation of pulmonary and systemic circulations. However, occasionally, adults present without having undergone a complete separation of circulations. Such patients have variable levels of cyanosis and ventricular dysfunction.

Even with the completion of total cavopulmonary anastomosis, many patients experience a decreased survival beyond 15 years after surgery. Impaired systolic and diastolic ventricular function as well as increased PVR contribute to mortality, and HF therapies to treat two-ventricle patients may not be efficacious in one-ventricle patients.<sup>362</sup> Common causes of death after Fontan procedures include thromboembolism, HF, protein-losing enteropathy, and arrhythmias.<sup>363</sup> When caring for adults with Fontan physiology, the anesthesiologist should be mindful of conditions that may further impair oxygenation and myocardial function. PBF is passive, and any condition that increases PVR, or decreases systemic venous volume, will be poorly tolerated. These patients may also be very sensitive to myocardial depressants. In addition, the initial Fontan procedures included a direct baffle of the atrium to the pulmonary artery, but this was later modified because of complications from atrial dilation and the resulting arrhythmias. Fontan procedures are currently extracardiac, to minimize atrial arrhythmia. Expected O<sub>2</sub> saturation in a patient with Fontan physiology is at least 95%, though it may be lower in a patient with Fontan failure. Chronic anticoagulation for patients who have previously demonstrated, or are at presumed high risk for, thromboembolism is common and must be considered preoperatively.

## Transposition of the Great Arteries

TGA occurs when the aorta arises from the anatomic RV and the pulmonary artery arises from the anatomic LV. In classic d-TGA the two circulations are in parallel and require mixing to be compatible with life. In the 1980s, surgical management of TGA consisted of atrial-level switch procedures—the Mustard or Senning procedure—in which venous return to the heart was redirected at the atrial level through a baffle system. Therefore, highly oxygenated pulmonary venous return was redirected to the RV, which pumped to the aorta and systemic circulation. Systemic deoxygenated blood was directed to the LV, which pumped the blood through the pulmonary artery to the lungs for oxygenation. Long-term complications of this strategy include atrial dilation from baffle obstruction or leak with resultant arrhythmias, sinus node dysfunction, or sudden death. Particularly problematic complications included the systemic right ventricular dysfunction, AV valve regurgitation, subpulmonary stenosis, and pulmonary hypertension.

Today, the arterial switch operation is preferred, in which the aorta with the coronary arteries are attached to the LV and the pulmonary artery is attached to the RV. Complications from the arterial switch operation include regurgitation of the neoaortic valve, myocardial ischemia from coronary ostial stenosis, right or left ventricular outflow tract obstruction, residual intracardiac shunting, and left ventricular dysfunction.

## Pediatric Cardiac Electrophysiology

### DIAGNOSTIC EVALUATION

#### Cardiac Event Monitoring

Most patients with cardiac arrhythmias present with infrequent or episodic symptoms. These symptoms may include chest pain, palpitations, syncope, and presyncope. Trans-telephonic electrocardiographic event monitors may yield documentation of the arrhythmia because they are portable and patient activated.<sup>364</sup>

#### Insertable Cardiac Recorders

Insertable loop recorders implanted subcutaneously allow continuous rhythm monitoring that is stored either when manually activated by a patient or parent or automatically when high or low rate parameters are met.<sup>365</sup> These insertable loop recorders have value in correlating arrhythmias with symptoms when noninvasive means do not make a diagnosis. Typically, loop recorders are inserted under general anesthesia as an outpatient procedure and cause minimal pain.

### RADIOFREQUENCY ABLATION OF ACCESSORY PATHWAYS

Radiofrequency ablation is a nonsurgical approach designed to eliminate atrial or ventricular reentrant tachyarrhythmias. The technique requires pathway mapping and precision ablation of the aberrant pathway, using a radiofrequency ablation catheter. Catheter ablation is offered to patients with refractory arrhythmias that are bothersome and the focus or pathway is amenable to ablation. Supraventricular tachycardias (SVTs) have an incidence of 1 in 250 to 1000 children and usually present later in childhood.<sup>366</sup> Up to 50% of adults with CHD develop SVT.<sup>367</sup> Although right-sided pathways are easier to access, left-sided pathways that require a transseptal puncture have a better cure rate.<sup>368</sup> In pediatrics, the electrophysiology catheters are introduced by femoral venous catheterization and the tips are positioned in the right atrial appendage, the bundle of His area, right ventricular apex, and the coronary sinus. Occasionally, right internal jugular venous access is used for placement of the coronary sinus catheter. Rapid atrial pacing and, occasionally, an isoproterenol infusion are required during the mapping procedure to induce the arrhythmia. An ablation catheter is used to map the substrate, and, subsequently, the pathway is ablated using radiofrequency energy (300-750 kHz). In complex cases or in cases with pathways in the vicinity of the AV node, cryotherapy is used to limit damage to the AV node. Cryotherapy permits a slower burn, and the ability to stop the ablation if transient AV block or lengthening

of the PR interval occurs. General anesthesia is required for ablation procedures in children, as unexpected patient movement may result in catheter dislodgment and damage to normal conducting tissue.

Anesthetic drugs and techniques should aim to maintain circulating catecholamines and avoid suppression of arrhythmogenesis, to aid in identification of the aberrant pathway. Total intravenous anesthesia with propofol or a low-dose volatile anesthetic are equally satisfactory options. Data suggest that modern inhaled anesthetics such as isoflurane and sevoflurane have no significant effects on cardiac conduction in children with SVT and are therefore suitable options.<sup>369,370</sup> There is conflicting evidence on desflurane with more recent data suggesting it may block AV conduction and therefore may not be a good anesthetic in these cases.<sup>371</sup> An increased incidence of postoperative nausea and vomiting (PONV) is reported after these procedures, which is not only distressing but may produce bleeding from the access sites. Both low-dose propofol infusion and low-dose volatile anesthetic may be used along with the bispectral index monitor to maintain a lighter level of anesthesia. To minimize the risk of PONV, two classes of antinausea medications should be administered. Placement of an arterial line is needed for rapid atrial pacing and isoproterenol during the mapping procedure, both of which can cause significant hypotension. Medications that suppress conduction or decrease sympathetic tone, including dexmedetomidine, should be avoided until the end of the procedure.

Severe postablation cardiomyopathy has been described but is very unusual. Presumed causative factors include underlying cardiomyopathy from frequent episodes of SVT, and myocardial O<sub>2</sub> imbalance caused by prolonged periods of rapid atrial pacing and isoproterenol infusions. Other procedure complications include radiation exposure, tamponade, pericarditis, groin hematoma, arterial thrombosis, AV block, systemic embolization, coronary artery dissection, trauma to the mitral and tricuspid valves, and endocarditis.

### Intraatrial Reentrant Tachycardia

Intraatrial reentrant tachycardia (IART) is the most common arrhythmia in CHD and is associated with significant morbidity and mortality. The incidence of IART is highest in patients who have undergone Fontan and atrial switch operations because of atrial incisions, sutures lines, and dilation, and fibrosis caused by long-term hemodynamic changes.<sup>367</sup> Therapeutic options for IART include antiarrhythmic medications, radiofrequency catheter ablation, cryoablation, surgery, and pacing. The Pediatric and Congenital Electrophysiology Society and the Heart Rhythm Society have published comprehensive guidelines for arrhythmia management in ACHD.<sup>372</sup> Careful choice of anesthetic, monitoring, and early management of low cardiac output states, especially in patients with single-ventricle physiology, are important. Prolonged periods of arrhythmia induction during mapping can reduce cardiac output and necessitate inotropic therapy. Cardiac ICU may be indicated for postoperative recovery. Although acute success rates are high at 90%, arrhythmia recurrence is problematic in this population occurring in 34% to 54% of patients. Fontan physiology and older age are risk factors for recurrence.<sup>367,373</sup> As more patients with CHD survive

into adulthood, the incidence of both permanent IART and atrial fibrillation are increasing.<sup>374</sup>

Intraoperative cryoablation within the RA for patients with IART or LA for atrial fibrillation using preoperative and intraoperative mapping can be used successfully. Atrial antitachycardia pacing is an option to terminate treatable tachycardias; a single-center cohort study demonstrated that this technology decreased the need for cardioversion rate in patients with CHD.<sup>375</sup> Atrial antitachycardia pacing has reduced efficacy in patients with L-TGA. In patients who are either unsuitable candidates for catheter ablation or in whom ablation has been unsuccessful, surgical ablation may be successfully combined with repair of CHD.

### Arrhythmias and Sudden Cardiac Death

Certain cardiomyopathies and channelopathies are associated with an increased risk for sudden cardiac death resulting from lethal arrhythmias. The patient usually has a history of syncope, near-syncope, or aborted sudden death. Such patients present for insertion of automated internal cardioverter-defibrillators (AICDs) for either primary or secondary prevention.

### IMPLANTATION OF PACEMAKERS AND DEFIBRILLATORS

Pacemakers are indicated for complete heart block or sinus node dysfunction with symptomatic bradycardia and hemodynamic decompensation. Children usually require general anesthesia with endotracheal intubation. It should be noted that the anesthetic can be associated with worsening bradycardia. Transthoracic pacing pads are applied before induction of anesthesia, and an isoproterenol infusion should be available in case its needed for chronotropy. External transthoracic, esophageal, or emergent transvenous pacing may be necessary until placement of a permanent pacing device is achieved. In small children the pacemaker generator is typically placed in the upper abdomen, and in older children and teenagers it is placed in the subclavicular region. Epicardial leads are used in small children because of inadequate size of the veins and in those in whom transvenous access to the heart is impossible (e.g., the Fontan circulation). Epicardial pacemaker placement usually is performed by a cardiac surgeon, with electrophysiologists readily available to program the device. Adequate peripheral venous access is mandatory in the event of major hemorrhage, and blood should be readily available. A mode of monitoring mechanical capture of electrical pacing activity is also necessary and can include invasive arterial monitoring or pulse plethysmography. Transvenous pacing can be achieved in the operating room with surgical backup or in the cardiac catheterization laboratory by the cardiologists. In the latter situation it is important to address the need for surgical backup during case planning.

AICDs are placed for life-threatening ventricular arrhythmias, which include LQTS, hypertrophic cardiomyopathy, and arrhythmogenic right ventricular dysplasia. Of note, the device is tested after placement, with induction of ventricular fibrillation. It is absolutely essential to have external modes of defibrillation available, as well as antiarrhythmics such as amiodarone, magnesium, and lidocaine, in the event of device failure. These devices are placed with

the patient under general anesthesia with endotracheal intubation and controlled ventilation. Invasive arterial pressure monitoring is typically used. Adequate analgesia can be provided with local infiltration with local anesthetics and short-acting intravenous opioids. Patients are admitted overnight with telemetry monitoring. Appropriate antibiotic therapy is provided for a 24-hour period.

## Advances in Resynchronization Therapy

Bundle branch block or interventricular conduction delay often accompanies HF and some forms of CHD, either preoperatively or postoperatively, and may result in ventricular dysfunction caused by asynchronous myocardial contraction. Biventricular pacing is an attempt to resynchronize ventricular contraction by pacing both ventricles, thereby improving overall ventricular function. In patients with left bundle branch block, cardiac resynchronization therapy counteracts the underlying electrical and mechanical dysynchrony, leading to improved contractility, function, exercise tolerance, and quality of life. Multisite pacing, involving intraoperative placement of atrial and ventricular unipolar epicardial temporary pacing wires, improves cardiac index and systolic blood pressure in the immediate postbypass period.<sup>376</sup> Multisite, temporary pacing may not be indicated or necessary to improve function in low-risk, biventricular repairs<sup>377</sup>; however, despite long-term outcome data, multisite pacing has become standard in many circumstances, including single-ventricle physiology, redo-procedures, or in patients at high risk for morbidity and mortality.

Right bundle branch block is a common outcome after surgery for congenital heart lesions. Right ventricular pressure, volume loading, or both also may be present, with attendant right ventricular enlargement and dyskinesia. Dual-chamber pacing decreases the QRS duration and increases cardiac index; the pacing site producing the most narrow QRS duration is of most benefit.<sup>378,379</sup>

## Anesthesia for Noncardiac Surgery

### INFECTIVE ENDOCARDITIS PROPHYLAXIS: AMERICAN HEART ASSOCIATION GUIDELINES

Guidelines for infective endocarditis prophylaxis were updated by the American College of Cardiology and the American Heart Association in 2008. A detailed discussion of the changes is beyond the scope of this chapter.

Procedures for which prophylaxis for infective endocarditis is recommended include the following<sup>380</sup>:

- Dental procedures involving manipulation of the gingival tissue or periapical region of the teeth or involving perforation of the oral mucosa
- Respiratory procedures involving incision of the respiratory mucosa
- Procedures involving infected skin, skin structure, or musculoskeletal tissue

Prophylaxis is no longer routinely recommended for gastrointestinal and genitourinary procedures. For elective procedures, coexisting enterococcal urinary tract infections should be treated before genitourinary or gastrointestinal procedures; for emergent procedures, in patients at highest risk for infective endocarditis, prophylaxis can be considered.

Conditions for which prophylaxis is recommended for dental procedures include the following (see Table 78.12):

- Prosthetic cardiac valve
- Previous infective endocarditis
- Unrepaired CHD, including palliative shunts and conduits
- Completely repaired CHD with prosthetic material or device within the first 6 months after the procedure
- Repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or device
- Cardiac transplant recipients who develop cardiac valvulopathy

These are guidelines only, and it is prudent practice to consult the child's cardiologist in order to create an individualized plan based on the child's condition, operative procedure, and risk for bacteremia.

### MAGNETIC RESONANCE IMAGING OF THE HEART

A major advantage of MRI is the ability to assess the volume and mass of asymmetric ventricular shapes, especially the RV. The American Society of Anesthesiologists (ASA) has published a practice advisory on anesthetic care for MRI.<sup>381</sup> Apart from the usual considerations of providing general anesthesia in a remote location, the anesthesiologist must be prepared to provide resuscitative care when working in a magnetic field necessitating the use of magnet-safe equipment. Patients with implanted devices and hardware need to be assessed to ensure magnet compatibility and safety. Generally, pacemakers, implanted defibrillators, and aneurysm clips are contraindications to MRI. Coils, stents, and other surgical clips produce interference and imaging artifact but do not constitute a threat to patient safety. In a majority of patients, the scan can be performed as an outpatient procedure.

Patients who are younger, uncooperative, or claustrophobic require sedation or general anesthesia. Good image quality, angiography, and delayed enhancement imaging are aided by breath holds, which may last for more than one minute and require preoxygenation. Typically, if breath holds are required, general endotracheal anesthesia is required and an anesthesia provider is present in the room. However, radiologic advances have allowed many centers to use "free breathing" protocols to avoid the need for breath holds and therefore general anesthesia.<sup>382,383</sup> Such protocols acquire multiple images, then use an algorithm that eliminates the artifact created by respiration. Radiologists are increasingly cognizant of the potential risk of general anesthesia in young children and are adapting protocols to avoid the need for general anesthesia when possible.<sup>384</sup>

Irrespective of anesthetic technique, it is mandatory to maintain continuous monitoring of heart rate, pulse oximetry, capnography, and noninvasive blood pressure. In the

event of hemodynamic compromise, the patient should be removed from the MRI scanner into a safe environment where resuscitation equipment can be safely used. With the development of compatible catheters and devices, MRI is a useful tool in minimizing x-ray exposure, particularly in patients whose CHD necessitates numerous catheterization procedures. Cardiac MRI may be used in combination with fluoroscopy in the catheterization suite to decrease radiation exposure and improve soft tissue visualization in patients with CHD.<sup>385</sup>

## Offsite Anesthesia in Cardiac Surgery Patients

Patients with cardiac disease are no different from any other group of patients who require procedures or investigations in areas outside the operating room. Therefore, anesthesiologists should always be prepared for any eventuality and follow guidelines such as those set out by the ASA. This discussion excludes procedures performed in the cardiac catheterization laboratory as this has been addressed elsewhere. The nature of congenital cardiac surgery will result in a number of patients requiring emergent chest exploration for hemorrhage or to relieve tamponade, or for ECMO cannulation, all of which may take place in the ICU setting. It is obvious that we cannot predict with certainty which patients will have problematic postoperative courses, but the practitioners who have participated in the operative phase will gain an accurate sense of which patients may require possible further exploration or surgery. Accordingly, it is best to plan ahead, and prepare for worst-case scenarios. It is imperative that enough blood and blood products are available to perform surgery at any given time. Successful treatment of emergency situations depends on a team approach to patient care, and thus surgeons, anesthesiologists, intensivists, perfusionists, and operating room nurses must be immediately available. When the decision is made to perform a procedure within the ICU, speed of preparation is of the essence. Drugs, electrolytes, and infusions must be readily available. Emergent preparation includes ensuring that blood is checked, a warmer is ready for use, emergency drugs are present, and the code cart (with internal paddles) is available. The anesthesiologist's role is one of facilitation of the entire procedure including sedation, airway management, patient positioning, preparing the blood, and continuing ongoing volume and pharmacologic resuscitation.

The premature infant with a PDA poses an interesting management problem to cardiac surgery teams because frequently these ill neonates are at hospitals far from major centers where the team is normally assembled. As referenced in an article by Gould and associates,<sup>328</sup> teams have been performing these ductal ligations with great success at hospitals remote from their "home" hospitals. The philosophy is to take the cardiac team to the neonate instead of having these fragile infants transported. In this article, neonates operated on in the "home" hospital NICU were used as the controls, and it was found that the success and complication rates were comparable in the two groups. Thus, from an anesthetic perspective, travel with a full complement of airway equipment and drugs, as described

earlier, with packed red cells being made available at the host hospital. The anesthetic regimen for this procedure comprises a high-dose opioid, muscle relaxant, antibiotic, and a continuation of any preoperative vasoactive infusions. We have found that this is a stable and well-tolerated anesthetic regimen.

The requirement for anesthesia services is ever-widening, and in patients with pediatric heart disease this is also the case. Thus, the patients will require radiologic investigations, including CT, MRI, and nuclear medicine scans; interventional radiology procedures; and gastrointestinal procedures, among others. Before discussion of the patient and the anesthetic, it is important for the practitioners to have a thorough knowledge of the environment into which they are taking the patient with regard to magnetic fields, closest code cart, and the ability to get help quickly if needed. Without going into the specifics of every potential clinical scenario, a few basic points are discussed.

As with any anesthetic procedure, a thorough preoperative evaluation is vital. Most patients with pediatric heart disease have long and complex histories, so this assessment should include a detailed description of their cardiac status, including prior surgeries, catheterization findings, and associated conditions (e.g., neurocognitive function, pulmonary status, renal function). Depending on the patient's underlying condition a recent echocardiogram will give very important clinical details related to overall function, valve pathology, presence or absence of intracardiac shunt, patency of surgical shunts, and presence of pericardial fluid. Although this may be ideal, often the echocardiographic examination may be remote from the anesthetic encounter and thus the clinical history and examination are important. Patients who have had a heart transplant should have a relatively recent echocardiogram, as it will provide vital information that may indicate worsening function in an otherwise asymptomatic patient.

Nothing-by-mouth guidelines deserve special consideration. Many congenital cardiac patients have physiology in which dehydration may be deleterious (e.g., single-ventricle, presence of surgical shunts, unrepaired TOF). In these patients, it is important to allow and encourage oral hydration up until 2 hours before the planned procedure; if this is not possible, intravenous fluids must be used. The anesthetic course will depend on the duration of the planned procedure, the patient's physiology (i.e., spontaneous vs. controlled ventilation), airway management (natural vs. laryngeal mask airway vs. endotracheal tube airway), anesthetic maintenance, travel to and from the procedural area, and maintenance of the patient's temperature. Before leaving the induction area the anesthetic team must be prepared for airway misadventures and even a code situation; thus, the team must travel with auxiliary airway equipment and resuscitative drugs. The very number of these different venues may make it difficult to have an anesthesia machine present in each; however, an anesthetic cart with additional airway equipment, intravenous materials, and resuscitative drugs should be present. The anesthetic that is delivered may vary among practitioners and institutions, but the common details of importance are a thorough knowledge of the patient and the ability to treat expeditiously should any difficulty ensue in a remote venue.

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## KEY POINTS

- Congenital heart disease causes significant alterations in oxygenation, perfusion, and myocardial function after birth, and it can be categorized into hypoxic and normoxic lesions.
- The overall goal of therapy in shock is to treat the underlying cause, return adequate oxygen delivery to the tissues, and remove metabolic products that developed during anaerobic metabolism. It appears that the faster the body returns to adequate perfusion, the better the overall outcome.
- One of the specifics for neonatal resuscitation is the recommendation of positive pressure ventilation (PPV) with room air, unless chest compressions or medications are needed during the resuscitation, then the recommendation is still for PPV with 100% oxygen.
- Pediatric cardiac arrest is not a rare event. At least 16,000 American children (8-20 per 100,000 children per year) suffer a cardiopulmonary arrest each year.
- The four distinct phases of cardiac arrest and cardiopulmonary resuscitation (CPR) interventions are: (1) prearrest, (2) no-flow (untreated cardiac arrest), (3) low-flow (CPR), and (4) post-resuscitation and arrest.
- Acute respiratory distress syndrome (ARDS) diagnostic criteria have been revised recently and are now the Berlin Definition, where ARDS is separated into three mutually exclusive categories based on the degree of hypoxia. Mild is  $\text{PaO}_2/\text{FiO}_2 = 201$  to 300 with positive end-expiratory pressure (PEEP)  $> 5$ , moderate is  $\text{PaO}_2/\text{FiO}_2 = 100$  to 200 with PEEP  $> 5$ , and severe is  $\text{PaO}_2/\text{FiO}_2 < 100$  with PEEP  $> 10$ .
- Traumatic brain injury (TBI) is composed of two components—an initial primary injury owing to direct mechanical deformation of brain parenchyma and a subsequent secondary injury that can develop over hours to days. Secondary injury may be the result of multiple mechanisms including ischemia, excitotoxicity, metabolic failure and eventual apoptosis, cerebral swelling, axonal injury, and inflammation and regeneration.
- A vascular occlusive crisis in the lungs leads to acute chest syndrome (ACS). Acute chest syndrome is the leading cause of death and the second most common complication in sickle cell disease.
- Tumor lysis syndrome is a metabolic crisis precipitated by acute lysis of a large number of tumor cells. Serum uric acid, potassium, and phosphate concentrations are elevated. The elevated phosphate concentrations cause hypocalcemia.
- The role of family in the pediatric intensive care unit (PICU) has evolved over time, and the inclusion of family in the care of their child is now recognized as an important part of critical care.
- Accidents and trauma are the leading causes of death in children 1 to 14 years of age.

## Relationship Between the Intensive Care Unit and the Operating Room

The field of pediatric intensive care may have originated from anesthesia, but these areas have grown apart over time. Due to the extensive training, there are few individuals who cover both disciplines. With more complex patients, it is likely that care will occur both in the operating room and the intensive care unit (ICU). There needs to be excellent communication between the ICU and operating room clinicians to ensure a seamless transition of care. Many institutions require an attending to attending handoff between the ICU and anesthesia for each case. It

is important that this occurs in the preanesthetic as well as the postanesthetic setting. Information regarding current ICU therapy response can simplify a potentially difficult anesthetic. Similarly, understanding the operative and anesthetic course will guide the next several days of management. A complete anesthesia sign-out includes pertinent past medical history, allergies, ease of mask ventilation, induction agents, ease of intubation, decisions regarding extubation, venous and arterial access, blood products, fluid totals, inotropic agents, medications delivered including timing of antibiotics, complications, laboratory values, and most recent blood gas. This information may be available in the anesthetic record; however, a short verbal summary by the anesthesiologist provides a greater amount of practical detail.

## Family Partnered Care in the Pediatric Intensive Care Unit

The family is an important part of the critical care team and needs to be included in shared decision making. In pediatric hospitals, families participate in multidisciplinary rounds with their nurses, respiratory therapists, pharmacists, and physician caring for their child. This does not require more time than traditional rounds and it does not compromise teaching.<sup>1</sup> There has been a significant push to increase family participation in both pediatric and adult ICUs. Family engagement is part of the ICU Liberation ABCDEF Bundle that is directed and supported by the Society of Critical Care Medicine. A great amount of information is available at [www.iculiberation.org](http://www.iculiberation.org). An international multidisciplinary team of experts in neonatal, pediatric and adult critical care recently published Guidelines for Family Centered Care.<sup>2</sup> The guidelines address the need for family presence in the ICU, the need for family support beyond the ICU; goals for communication, use of consult services such as Palliative Care and Ethics, and a means to address the operational and environmental issues in ICUs that prevent family engagement. We see significant family satisfaction with participation in rounds and we believe it likely benefits the team and patient as well.<sup>3-5</sup> We anticipate a point in the future where we do not need to prove to anyone the need to have family involvement.

Giving the family a greater presence in the ICU with more responsibility and autonomy in decision making can increase their anxiety and distress. In addition to the potential development of posttraumatic stress disorder (PTSD) in our patients,<sup>6-8</sup> parents of children admitted to an ICU can incur severe emotional distress.<sup>9</sup> A recent review places the incidence of PTSD in parents of children in the PICU between 10% and 21%, with symptoms of PTSD occurring in up to 84% of families.<sup>10</sup> PTSD can occur no matter how routine the caregivers may view the process. The ICU is a unique and often terrifying experience for families and children. The process of ICU care involves multiple caregivers, changing shifts, and endless physicians. For families in the ICU, there can be a loss of control, significant financial worries, and other factors that affect coping. Helping parents cope with their child's critical illness and these stressors is a central part of intensive care. Parents may display behaviors that out of context may seem abnormal, such as excessive clinginess, intellectualizing the process, blaming others (including their spouses), minimizing, and seeking opinions everywhere (the internet, environmental care, etc.). We must attempt to understand what drives these behaviors to provide optimal care. We must help the parents be parents and educate them about their child's illness. This emphasizes that social workers, psychologists, and child and family therapists are all part of the critical care team.

With the move to family-centered care, we must address the issue of parental presence during invasive procedures and cardiopulmonary resuscitation (CPR) efforts. There is increasing literature that families would like to have the choice to stay during CPR events or invasive procedures and the parents do find benefit to being present.<sup>11-14</sup> We believe that allowing parents to stay during procedures or resuscitation is helpful for the parents coping with the trauma of

a critically ill child. As each PICU addresses this issue there are several things to consider. Caregiver attitudes toward parental presence will need to be addressed, as the likelihood of this event increases over time. The decision to allow parental presence cannot be forced on providers. However, we have seen that resistance to family presence among providers is decreasing over time. A means for declining on the part of the clinician as well as the parent must be available. There must be someone identified who will stay with the family and support them. In our ICUs, this role has been filled by social workers or members of the clergy. For those who are looking for assistance in making the transition to parental presence during CPR, there have been guidelines published from a national consensus conference.<sup>15</sup> Parental presence during invasive procedures may pose a different challenge as these events occur more frequently compared with CPR. In the same manner, someone other than the person performing the procedure should be looking after the family, even for what we believe to be routine procedures. We also must give younger trainees the opportunity to opt out of family presence during procedures.

A final topic that needs to be addressed is the use of palliative care services for our critically ill patients. There is a role for early consultation of palliative care, as we do not believe in restricting its use or support to just those patients who are near to death. We feel that there is a significant benefit to early engagement for children who are at high risk for mortality during their hospitalization, for children with complex diseases, or those where their cognitive and physical abilities following ICU discharge will be significantly different than previously. There are great benefits to palliative care intervention to provide families ongoing support and opportunities to develop coping mechanisms. Many different PICUs have developed automatic triggers for palliative care consultation, so as not to miss opportunities to improve family support. Examples of triggers can be PICU duration, episodes of CPR, prolonged mechanical ventilation, and specific types of surgeries. A review by the IPAL-ICU (Improving Palliative Care in the ICU) Advisory Board in 2014<sup>16</sup> addresses the needs and goals of palliative care integration in the PICU.<sup>1</sup>

## Disclosure of Medical Errors

We believe it is ethically correct to disclosure medical errors to families. However, some clinicians may continue to resist due to concerns regarding litigation. In a survey of 1018 Illinois residents, 27% indicated they would sue, but 38% stated they would recommend the hospital if appropriate disclosure and remediation occurred.<sup>17</sup> The conclusion drawn by the author of the study was that “[p]atients who are confident in their providers' commitment to disclose medical errors are not more litigious and far more forgiving than patients who have no faith in their providers' commitment to disclose.” Explanations of medical errors should come from the senior member of the team to the family. This is usually the current ICU attending, but can be the medical director of the ICU, based on the complexity of the incident and outcome. The discussion should include an explanation of what happened in layman's terms, how it occurred, the repercussions and change of care planned for

the child, and what will be done to prevent a similar error in the future. We find it helpful to have the ICU social worker present to help validate concerns and provide support. The attending remains present until all questions are answered or additional time is scheduled if necessary. Most hospitals will track errors or negative outcomes through a quality assurance program. Depending on the incident, a “root cause analysis” should be performed. Medical errors will occur, but they should also be an opportunity to improve practice quality and prevent future events.

In an ICU setting, there unfortunately will also be a need to cope with death and dying.<sup>18</sup> Palliative care plays an important role when nothing medically can be done for the child. We also find their services exceedingly helpful for children with chronic medical conditions who are anticipated to die during a future admission. With a team approach, we try to minimize pain and suffering for the child and family at the end of life. Caregivers in and ICU must understand when to allow the families choices and support them over what may be their own beliefs and practices—as long as the goal remains to prevent further pain and suffering.<sup>19</sup> The awareness of medical futility is increasing over time. However, with this concept there is a significant interplay with financial, societal, ethical, personal, and religious opinions and feelings. It may be difficult to define futility, but when the pain and suffering of continuing life are more severe than the inevitability of death, care may become futile. However, pain relief and caring support for the child and family can never be classified as futile care.

## Organization of the Pediatric Intensive Care Unit

Medical and nursing directors, hospital administrators, and representatives from pediatric medicine, anesthesia, surgery, and the pediatric subspecialties should be responsible for policy and procedures pertaining to the PICU and should make recommendations regarding personnel staffing, equipment purchases, and structural and design changes within the unit. The medical director oversees the quality of patient care, patient triage, implementation of policy and procedures, in-service education, and coordination of consultants. Physician coverage should be full-time geographic at the resident, fellow, and attending staff level, and should include in-house, full-time coverage at night. The nursing director should have special skills in pediatric intensive care, education, and personnel management. The nursing staff must be trained in all aspects of pediatric critical care and resuscitation. Staffing should be flexible enough to provide one-on-one patient care when necessary. A multidisciplinary in-service program is essential for continuing education and orientation. Other team members include respiratory therapists, physical therapists, nutritionists, social workers, laboratory technologists, pharmacists, and psychiatrists and psychologists for the patients and staff. All medical and support personnel should be encouraged to participate in rounds, educational endeavors, and team meetings whenever possible. There must be adequate workspace around each bed and enough storage space to keep life support equipment within reach. Space for reading, meeting, sleeping, and showering should be available

for the staff. Space should be provided for parents to remain with their children during the day and for parents to sleep overnight. Parents should be encouraged to participate as much as possible in the care of their child. Each bed space should be standardized so that it can be used to provide any level of care. Private rooms are ideal, but if shared rooms are necessary, the distance between beds must be adequate to ensure privacy and minimize nosocomial infection. Isolation rooms should be available within the confines of the unit. Devices for diversion and entertainment should be available for conscious children. Television and computer games are often better than heavy sedation.<sup>20,21</sup> Adequate nurses and nursing involvement at the bedside will prevent potentially life-threatening events. Because sick children require close personal observation, centrally monitored nursing stations have little place in the PICU.

## Cardiovascular System

### STRUCTURAL AND FUNCTIONAL DEVELOPMENT

The shape of the heart is complete by 6 weeks' gestation, but myofibrillar density and maturation increase through the first year of postnatal life. During this time, myocytes engage in rapid protein synthesis and rapid cell growth, which requires a high intracellular concentration of nuclei, mitochondria, and endoplasmic reticulum. The greater number of nonelastic and noncontractile elements makes the neonatal myocardium less compliant, and it contracts less efficiently than the adult myocardium. In the fetus and newborn, the decreased ventricular compliance causes small changes in end-diastolic volume to induce large changes in end-diastolic pressure. In addition, augmentation of stroke volume by the Frank-Starling mechanism is less effective in young children. The newborn is more dependent on heart rate (HR) for maintenance of cardiac output.<sup>22,23</sup> Cardiac output increases only about 15% with volume loading; it increases much more by increasing the HR.<sup>24</sup> This is an important consideration when taking care of the critically ill infant.

### DEVELOPMENT OF THE CIRCULATION

The adult and fetal circulation differs in many ways. The fetal circulation is distinguished by (1) the placenta as the organ of respiration, (2) high pulmonary vascular resistance (PVR), (3) low systemic vascular resistance (SVR), and (4) fetal ventricles that pump in parallel with right ventricular dominance. While the fetus lives in a low oxygen environment, the oxygen content of the blood of the fetus is similar to that of adults (20 mL of oxygen/100 mL of blood) because of a higher concentration of hemoglobin that has high affinity for oxygen. The neonatal circulation has several shunts—the ductus arteriosus, ductus venosus, and foramen ovale—that direct more oxygenated blood to the brain and heart and bypass the lungs. Changes then occur that allow the parallel circulation of the fetus to convert to the series circulation of the adult:

1. With the first breath, expansion of the lung, increased alveolar oxygen, an increase in pH, and neurohumoral

- mediators and nitric oxide (NO) relax the pulmonary vasoconstriction.<sup>25</sup>
- When the placenta separates from the uterine wall, the placental blood vessels constrict, and SVR and left ventricular afterload increase. The decrease in PVR plus increase in SVR raises left atrial pressure above right atrial pressure (RAP) and functionally closes the “flap valve” of the foramen ovale. The foramen ovale may not close anatomically for months to years, if ever. It is patent in at least 15% of adults.<sup>26,27</sup>
  - The decrease in PVR causes flow through the ductus arteriosus to reverse. This exposes the ductus to oxygenated systemic arterial blood, which along with the rapid decrease in prostaglandin E<sub>2</sub> after birth closes the ductus. Anatomic closure of the ductus requires several weeks.
  - The ductus venosus closes passively with removal of the placental circulation and readjustment of portal pressure relative to inferior vena cava pressure.
  - There is a further gradual decline in PVR secondary to structural remodeling of the muscular layer of the pulmonary blood vessels. During fetal life, the central pulmonary vascular bed has a relatively thick muscle layer. After birth, the muscle coat thins and extends to the periphery of the lung—a process that takes months to years to complete.

## DEVELOPMENT OF AUTONOMIC CONTROL OF THE CIRCULATION

The functional integrity of autonomic circulatory control during fetal and perinatal development is still a matter of considerable speculation. The fetal heart has reduced catecholamine stores and increased sensitivity to exogenously administered norepinephrine (NE).

Adrenergic innervation of the human myocardium is complete between 18 and 28 weeks' gestation. Human newborns have low cardiac stores of NE and decreased numbers of sympathetic nerves after birth. Adrenergic responses are apparently present but diminished in newborn humans. In human neonates, the cholinergic system is completely developed at birth, and the heart is sensitive to vagal stimulation. Bradycardia is the probable response to an increase in autonomic tone. The baroreceptor reflex is present but incompletely developed at term in humans. In preterm infants, postural changes elicit no change in HR, suggesting an incomplete or attenuated baroreceptor response.<sup>26</sup> The chemoreceptor response is well developed in utero. The fetal bradycardia that occurs in response to hypoxia is thought to be mediated through chemoreceptors and may be similar to the oxygen-conserving mechanisms of diving animals.<sup>27</sup>

## MYOCARDIAL METABOLISM

Fetal myocardial metabolism differs from that of adults. Relative “hypoxia” is normal in utero, and infant hearts tolerate hypoxia better than the hearts of adults do. This difference may be due in part to high concentrations of glycogen in fetal myocardial tissue and to the ability to more effectively use anaerobic metabolism. Because of the high glycogen stores and the ability to use anaerobic metabolism

efficiently, the fetal/newborn heart is relatively resistant to hypoxia and can be resuscitated more easily if oxygenation and perfusion are reestablished reasonably quickly.

Oxygen consumption increases precipitously after birth, presumably because neonates are required to maintain their own temperature. A full-term infant's oxygen consumption in a neutral thermal environment is approximately 6 mL/kg/min; it increases to 7 and 8 mL/kg/min at 10 days and 4 weeks, respectively.

## Common Cardiovascular Disease States

### CONGENITAL HEART DISEASE

Congenital heart disease causes significant alterations in oxygenation, perfusion, and myocardial function after birth (Box 79.1). These abnormalities can be divided into hypoxic and normoxic lesions. The latter include obstructive lesions of the left side of the heart (mitral valve stenosis, aortic valve stenosis, aortic stenosis, anomalous pulmonary venous return, ventricular septal defect, or patient ductus arteriosus with a right-to-left shunt), whereas hypoxic lesions include tricuspid valve stenosis, pulmonary valve stenosis, pulmonary artery stenosis or aplasia, and the tetralogy of Fallot. Right-sided lesions cause hypoxia if the left-to-right shunting of blood is sufficient to cause congestive heart failure (CHF) and pulmonary edema. Newborns with significant congenital heart disease commonly have either cyanosis or CHF. The degree of dysfunction usually changes during the first few months of life as PVR decreases to adult levels. As PVR decreases, left-to-right shunting of blood usually increases, and the symptoms of CHF become more apparent. Many neonates with a significant ventricular septal defect, which may or may not be observed during the pre-operative workup, have no left-to-right shunting for several weeks after birth; however, induction of alkalosis during surgery can increase shunting. In the newborn, the usual signs and symptoms of CHF include poor feeding, irritability, sweating, tachycardia, tachypnea, decreased peripheral pulses, poor cutaneous perfusion, and hepatomegaly. Many patients with pulmonary edema exhibit tachypnea without retractions. Cyanosis occurs with structural cardiac disease,

### BOX 79.1 Common Congenital Heart Malformations in the Newborn

- Cyanotic congenital heart lesions
  - Tetralogy of Fallot
  - Transposition of the great arteries
  - Hypoplastic left heart syndrome
  - Pulmonary atresia with an intact ventricular septum
  - Single ventricle
  - Total anomalous pulmonary venous return
  - Tricuspid atresia
- Congenital heart lesions manifested as congestive heart failure
  - Ventricular septal defect
  - Patent ductus arteriosus
  - Critical aortic stenosis
  - Coarctation of the aorta

but other causes such as respiratory disease, increased PVR (persistent pulmonary hypertension), and methemoglobinemia must also be considered. Congenital heart disease is diagnosed by physical examination, electrocardiogram (ECG), chest radiograph, and echocardiogram, postnatally and via fetal echocardiography. Cardiac catheterization is occasionally performed as interventional therapy or as a diagnostic tool. Magnetic resonance imaging (MRI) is used to define the anatomy of congenital heart lesions before cardiac surgery. Initial treatment of congenital heart disease is aimed at relieving CHF, improving systemic perfusion, and improving or maintaining pulmonary blood flow. The ductus arteriosus must be maintained open in instances of hypoplastic left heart syndrome, aortic stenosis or atresia, interrupted aortic arch, and symptomatic neonatal coarctation of the aorta. In many cases, infusion of PGE<sub>1</sub> sustains life until definitive surgical correction can be performed.<sup>28</sup>

## ACUTE CIRCULATORY FAILURE IN CHILDREN (SHOCK AND SEPSIS)

### Shock

Shock is the inability to provide adequate oxygen to the tissues that require it. The condition of shock depends on the balance of supply and demand of oxygen. Typically the body delivers excess oxygen to the tissues. Under periods of stress or illness there can be a decrease in supply caused by diminished blood flow or as decreased oxygen in blood. There can also be increased demand or oxygen extraction from the tissues. The content of oxygen in the blood is dependent on the amount bound to hemoglobin and the amount dissolved in plasma. Oxygen content (CaO<sub>2</sub>) (mL/dL) = (1.34g/dL) (SaO<sub>2</sub>) (Hb) + (PaO<sub>2</sub>) (0.003). The normal oxygen content is approximately 20 mL/dL. Delivery of oxygen to the tissues depends on oxygen content and cardiac output. Oxygen delivery (DO<sub>2</sub>) (mL/min) = oxygen content (CaO<sub>2</sub>) × cardiac output (CO) × 0.01. Oxygen consumption (VO<sub>2</sub>) is the demand portion of the equation. Oxygen consumption (VO<sub>2</sub>) is independent of oxygen delivery (VO<sub>2</sub>) above a critical threshold and over a wide range. Below this critical threshold VO<sub>2</sub> is dependent on DO<sub>2</sub>. For infants and young children, VO<sub>2</sub> is estimated at 175 mL/min/m<sup>2</sup>. Oxygen consumption is equal to oxygen delivery multiplied by oxygen extraction (O<sub>2</sub>EX) by the body: VO<sub>2</sub> = DO<sub>2</sub> × O<sub>2</sub>EX. Oxygen extraction O<sub>2</sub>EX is equal to (CaO<sub>2</sub> – CvO<sub>2</sub>)/CaO<sub>2</sub>. CaO<sub>2</sub> is the oxygen content of arterial blood and CvO<sub>2</sub> the oxygen content of venous blood. The difference between oxygen content of arterial and venous blood is predictably 4 to 6 mL/100 mL blood. Initially, as oxygen delivery decreases, the oxygen consumption can remain constant via increased extraction. Below a critical threshold in oxygen delivery, oxygen consumption becomes dependent on delivery. When oxygen to meet metabolic needs of the body cannot be met, nonessential metabolism is decreased or eliminated. Such metabolism includes growth, neurotransmitter synthesis, thermoregulation, and so forth. In this way the remaining oxygen can continue to be substrate for mitochondria. There are organs in the body, such as the kidney, skin, intestines, and skeletal muscle, that receive a high supply of blood relative to their metabolic needs. These organs also have a high proportion of sympathetic nerve innervations that allow for redistribution of blood flow to

organs that with limited oxygen reserves such as the brain and heart.

### Classification of Shock

There are several schemas which clinicians use to classify shock. Further within these classification schemas, disease states can fall into more than one category. One classification schema separates shock into the categories of hypovolemic, cardiogenic, distributive or vasogenic, and extracardiac obstructive.

Hypovolemic shock can be due to hemorrhage from trauma or gastrointestinal (GI) losses from internal bleeding. Nonhemorrhagic hypovolemic shock can be due to external losses of fluid from vomiting, diarrhea, polyuria, and poor fluid intake. Fluid redistribution in cases of burns, trauma, and anaphylaxis can also be a cause.

Cardiogenic shock may be myopathic due to decreased heart function. For adults this may commonly follow myocardial infarction. For children, myocarditis or cardiomyopathy are more common. Other causes of cardiogenic shock include mechanical failure such as valvular regurgitation or obstruction. Significant arrhythmias may result in cardiogenic shock when contractions are so asynchronous they decrease cardiac output.

Extracardiac obstructive shock results from a physical obstruction that prevents adequate forward circulatory flow. Causes include inadequate preload secondary to mediastinal masses, increased intrathoracic pressure from tension pneumothorax, constrictive pericarditis, and cardiac tamponade from pericardial effusions. Pulmonary hypertension, pulmonary embolus, and aortic dissection can cause obstruction to systolic contraction.

Distributive shock is caused by a decrease in SVR and the maldistribution of end-organ blood flow. Cardiac output may be increased in distributive shock, however, blood pressure may remain low due to a very low SVR. Septic causes of distributive shock can be related to bacterial, fungal, viral or rickettsial infections or toxins produced from these infections. Toxic shock syndrome would be an example of toxin-mediated hypotension. Anaphylactic or anaphylactoid reactions are a type of distributive shock. Systemic inflammatory response syndrome (SIRS) may present with distributive shock. Spinal shock can result in distributive shock on a neurogenic basis. Adrenal insufficiency with low circulating hormones results in distributive shock decreased SVR.

### Diagnosis of Shock

Maintaining a high index of suspicion is important to rapidly identify shock in pediatric patients. Volume losses may be readily apparent from the history of present illness. Fever, rash and irritability may point to infection. However, cardiogenic shock may present with vague reports of decreased activity and level of alertness. In addition, if the patient's shock is currently compensated, changes in physical findings may be limited. A child in shock may present initially with tachycardia, cold extremities, and poor capillary refill. Further, in distributive shock, the child may be warm with just an isolated tachycardia. A brief pertinent physical exam should evaluate level of alertness, peripheral perfusion, mucous membranes, pulse rate and quality, respiratory effort, urine output, and blood pressure. In children, blood pressure may be preserved until the degree

of shock has progressed. Hypotension is a sign of late and decompensated shock in children. Metabolic acidosis may not be present on the initial laboratory tests.

### Compensatory Mechanisms

The body applies compensatory mechanisms with the onset of shock to maintain adequate tissue perfusion for as long as possible. There is redistribution of fluid from the intracellular and interstitium to the vascular space. There is a decrease in glomerular filtration to limit renal fluid losses. Renal fluid losses are also limited by the release of aldosterone and vasopressin. There is an increase in sympathetic activity and release of epinephrine. This results in decreased venous capacitance and some preservation of blood pressure. HR is increased as the body tries to maintain cardiac output. There is an increase in cardiac contractility through circulating catecholamines and adrenal stimulation. Increase in sympathetic nerve stimulation shunts blood away from nonvital organs. At the tissue level, transfer of oxygen from hemoglobin is increased by increased red blood cell (RBC) 2, 3-diphosphoglycerate, fever, and tissue acidosis.

### Therapy and Outcomes

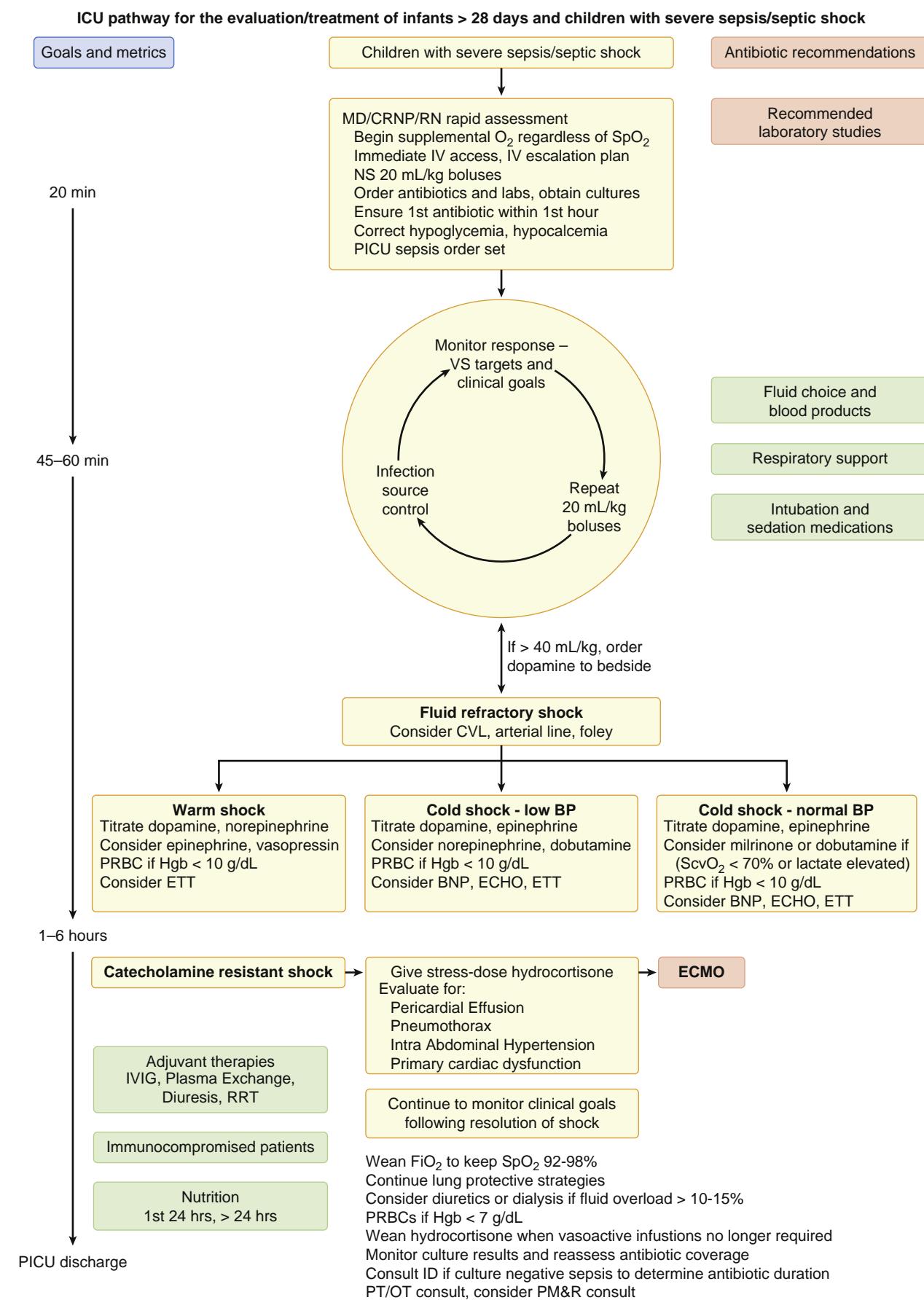
Aggressive therapy to treat pediatric septic shock appears to have resulted in improved outcomes. Therefore therapy for septic shock appears to be a good model for the treatment of shock in general. The overall goal of therapy in shock is to treat the underlying cause, return adequate oxygen delivery to the tissues, and remove metabolic products that developed during anaerobic metabolism. It appears the faster the body returns to adequate perfusion, the better the overall outcome. Many hospitals have developed sepsis pathways based on the data presented as follows that act as guidelines for resuscitation and are readily available to all care providers (Fig. 79.1).

In 1991 Carcillo et al.<sup>29</sup> described a population of 34 children that presented with septic shock to an emergency department. Shock was diagnosed based on hypotension for age, with decreased perfusion, poor peripheral pulses, cool extremities, and tachycardia. Sepsis was defined as a positive blood or tissue culture. Remarkably, within 6 hours of presentation, all the patients had a pulmonary artery catheter placed. The overall mortality for the group was 47%. However, in the nine patients who received more than 40 mL/kg of fluids in the first hour, there was only one death (mortality 11%). The authors point out this patient died with a second episode of sepsis 2 weeks later. In this study, the rapid fluid administration was not associated with an increase in cardiogenic pulmonary edema or ARDS.

In 2001 Rivers et al.<sup>30</sup> published a study in adult patients with septic shock showing early, aggressive, goal directed therapy in the first 6 hours of care improved mortality. There were 263 adults were enrolled; 133 received standard therapy based on clinician discretion. The 130 patients randomized to early goal-directed therapy followed protocols treating hypovolemia and supporting blood pressure with vasoactive agents if necessary. The baseline characteristics of the two groups were similar. The in-hospital mortality was 46.5% in the standard therapy group and 30.5% in early goal-directed therapy group ( $P < .01$ ). Although in adults, this demonstrated the need for early aggressive intervention.

Following the Rivers publication, a task force was formed by members of the Society of Critical Care Medicine to address shock in children. Their work was published in 2002 as "Clinical Practice Parameters for Hemodynamic Support of Pediatric and Neonatal Patients in Septic Shock."<sup>31</sup> Their guidelines were incorporated into the American Heart Association's (AHA) Pediatric Advanced Life Support (PALS) Provider Manual. Their guidelines were translated into Spanish and Portuguese and disseminated widely. The effectiveness of these interventions as well as an 2007 update was published by the same group in 2009.<sup>32</sup> They highlighted significant improvements in mortality in dengue shock syndrome, malaria, and septic shock treated by community physicians using early goal directed therapy.<sup>33-35</sup> The guidelines include rapid recognition of shock and early antibiotic administration and early administration of intravenous (IV) crystalloid. The initial resuscitation should include 20 mL/kg of isotonic saline or colloid pushed as a bolus to over 60 mL/kg until there is an improvement in the patient's perfusion or rales or hepatomegaly develops. The goal is for the initial fluid resuscitation to occur in the first 15 minutes of therapy, and therapy should be initiated even if peripheral IV cannulation attempts fail, by placing and intraosseous (IO) device (Fig. 79.2). The guidelines target therapeutic end points of normal pulses with no difference between peripheral and central; capillary refill  $\leq$  2 seconds; warm extremities, normalization of blood pressure for age, mental status, glucose concentration, ionized calcium concentration; and urine output greater than 1 mL/kg/h. If central venous access is not readily obtained, consideration should be given for placement of an IO line. Cold shock (cold mottled extremities with prolonged capillary refill) should be treated with dopamine up to 10  $\mu$ g/kg/min and then epinephrine 0.05 to 0.3  $\mu$ g/kg/min if there is no improvement. Warm shock (brisk capillary refill) should be treated with NE. Arrangements should be made early to admit the child to an ICU. If shock is not reversed with the inotropic support, hydrocortisone should be considered for catecholamine resistant shock. Recommendations for stabilization in the ICU following the first hour of therapy include monitoring central venous pressure, central venous saturation, and cardiac output. Persistent shock that is resistant to catecholamines should prompt the clinician to rule out pericardial tamponade, pneumothorax, or significantly elevated intra-abdominal pressure that may be compromising circulation. In the absence of a correctible condition, extracorporeal membrane oxygenation (ECMO) should be considered.

There were several new recommendations in the 2007 guidelines that addressed changes in the literature between 2002 and 2007. It was identified that the availability of skilled practitioners to place central venous access could delay the initiation of inotropic support. Therefore, the 2007 guidelines recommended the use of a peripheral IV dopamine or epinephrine if there was delay in obtaining central venous access. Ongoing monitoring of the access site should be performed. It was not recommended to use NE in a peripheral IV, due to risk of extravasation. In the 2002–2007 interval there were several pediatric and adult studies indicating adrenal suppression and increased severity of illness adjusted mortality with the use of etomidate.<sup>36,37</sup> The 2007 guidelines do not



**Fig. 79.1 Sepsis resuscitation pathway.** ECMO, Extracorporeal membrane oxygenation; ETT, endotracheal tube;  $FiO_2$ , fraction of inspired oxygen; ICU, intensive care unit; IV, intravenous; PICU, pediatric intensive care unit; PRBC, packed red blood cells; PT, prothrombin time;  $SpO_2$ , saturation of peripheral oxygen.

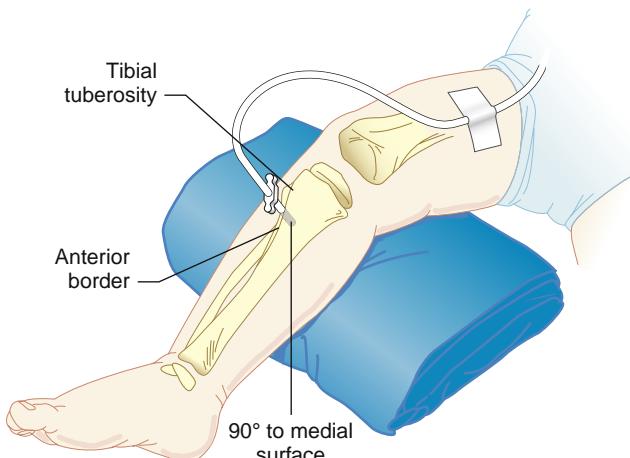


Fig. 79.2 Intraosseous Cannulation Technique.

recommend the use of etomidate unless it is in the format of a randomized controlled trial. Ketamine with atropine was recommended for sedation for invasive procedures in infants and children. However, due to limited experience, ketamine could not be recommended for the newborn population.

The 2007 guidelines<sup>32</sup> recommend titrating therapy to cardiac output and indicate that there are several methods by which cardiac output can be measured. The use of pulmonary arterial catheters has decreased in pediatrics over time, but other methods are available. A good review of monitoring techniques was published by Mtaweh et al. in 2013.<sup>38</sup> Cardiac output can be monitored by newer techniques analyzing the arterial pulse wave, transpulmonary thermodilution, carbon dioxide rebreathing, echocardiography, bio-impedance of the thorax, and ultrasound continuous-wave Doppler. These techniques are less invasive than pulmonary artery catheters. However, many still require validation studies in pediatric, and they may not be available at all centers.

One additional area to be addressed in the 2007 guidelines is in the area of fluid removal.<sup>32</sup> A study published by Goldstein et al. in 2005 in pediatric patients with multiorgan failure, including acute renal failure requiring continuous renal replacement therapy (CRRT), showed improved survival in the group that had a lower percentage of fluid overload at the initiation of CRRT.<sup>39</sup> While supporting the primary premise of fluid resuscitation, the 2007 guidelines offered new recommendation for fluid removal in patients with fluid overload and multiorgan failure.<sup>31</sup> They recommended the use of diuretics, peritoneal dialysis, or CRRT in patients who had been adequately fluid resuscitated but were not able to maintain an even fluid balance through native urine output. Again, it should be noted that peritoneal dialysis and CRRT for pediatric patients may not be available at all centers. However, the association between fluid overload and mortality with acute renal failure has been seen in other studies and will likely be an ongoing issue in pediatric ICU care.

The concern for possible adrenal insufficiency during septic shock needs to be addressed by the clinician caring for the patient. There are certain instances where limited function of the adrenal axis is anticipated. This

would include patients who have recently received glucocorticosteroids, ketoconazole, or etomidate. Further, patients with disease states such as purpura fulminans or those affecting the hypothalamus, pituitary, or adrenal glands will be at increased risk. Patients with adrenal insufficiency need supplemental corticosteroids. However, for children with septic shock but without these factors, it is not clear whether the risk of relative adrenal insufficiency or treatment with systemic steroids alter outcome. Dr. Zimmerman<sup>40</sup> reviewed the adult and limited pediatric literature in 2007 for therapeutic steroid use in sepsis. He highlighted adult studies showing high dose short courses of steroids are associated with decreased survival. Further, data from the CORTICUS trial<sup>41</sup> indicated that low dose steroids as a physiologic replacement during periods of vasopressor resistant shock resolve shock more quickly but there was no change in mortality. In turn, the 2007 guidelines were unchanged from 2002. Hydrocortisone treatment was only recommended for patients with absolute adrenal insufficiency or adrenal-pituitary axis failure and catecholamine-resistant shock. Absolute adrenal insufficiency was defined as peak cortisol concentration of less than 18 µg/dL obtained after corticotropin stimulation.

## Cardiovascular Pharmacology

Pharmacologic support of the circulation includes positive inotropic and chronotropic agents, vasoconstrictors and vasodilators (afterload reduction), and antiarrhythmics (see Chapters 14, 18, and 86). Most currently used drugs have not been adequately tested in children, so dosage recommendations and anticipated effects must be extrapolated from adult doses and clinical experience.

Positive inotropic drugs are used to augment the cardiac output of patients with circulatory failure. Most inotropic agents also affect the HR and vasomotor tone. Tachycardia in a child is usually well tolerated and is frequently beneficial.<sup>42</sup> In a neonate whose ventricles are relatively noncompliant and whose stroke volume is less variable, tachycardia is an important means of augmenting cardiac output. Because drugs that increase the HR or contractility also increase myocardial oxygen consumption, adequate arterial oxygenation and sufficient metabolic substrates are required when these drugs are administered. The cardiovascular response to sympathomimetic amines is attenuated in the presence of severe acidosis and possibly sepsis; higher infusion rates of these drugs are required and need readjustment as the acidosis improves. Commonly used inotropes are listed with brief comments regarding their use in pediatric intensive care are provided in the following paragraphs (Table 79.1).

### EPINEPHRINE

Epinephrine is useful for the treatment of shock in the presence of myocardial dysfunction. Typical starting doses in children are 0.05 to 0.2 µg/kg/min; with escalating doses up to 1 to 2 µg/kg/min, there is profound vasoconstriction in the periphery and abdominal organs to shunt blood to the heart and brain.

**TABLE 79.1** Vasoactive and Inotropic Medications

Drug	Effect	Dose ( $\mu\text{g}/\text{kg}/\text{min}$ )	Inotropy	Chronotropy	Vasodilation	Vasoconstriction
Epinephrine (Adrenalin)	$\alpha, \beta$	0.05-2.0	++	++		++
Isoproterenol (Isuprel)	$\beta_1, \beta_2$	0.05-2.0	++	++	+	
Dopamine (Intropin)	$\delta$	1-3			+Renal splanchnic	
	$\beta > \alpha$	5-15	+	+		+ or -
	$\beta, \alpha$	>15	+	+		+
Milrinone		Bolus: 50 $\mu\text{g}/\text{kg}$ over 15-min period	+		+	
		Infusion: 0.375-0.75				
Norepinephrine	$\alpha >> \beta$	0.05-1.0	Slight+	+		++
Nitroprusside		0.5-10			++	
					Arterial > venous	
Nitroglycerin		1-20			++	

## Dopamine

Dopamine is the most commonly infused inotrope in pediatric patients. Dopamine is the metabolic precursor of both NE and epinephrine. Its effects are dose dependent, with dopaminergic activity at low doses (although these low-dose dopamine effects have not been demonstrated in critically ill children);  $\beta$ -adrenergic activity with intermediate doses 5 to 10  $\mu\text{g}/\text{kg}/\text{min}$  exhibiting chronotropic and inotropic effects; and some  $\alpha$ -adrenergic activity at higher doses, with 10 to 20  $\mu\text{g}/\text{kg}/\text{min}$  exhibiting peripheral vasoconstriction. Young children require higher doses of dopamine than adults do to produce the same effect. In one study, an infusion of 15  $\mu\text{g}/\text{kg}/\text{min}$  was required to increase cardiac output above control levels after cardiac surgery.<sup>43</sup> This may reflect the decreased releasable myocardial stores of NE in immature ventricles. Therefore, in the sick preterm infant there can be decreased dopamine clearance with a much greater vasopressor response than expected.

## Vasopressin

Vasopressin is a pituitary peptide hormone with method of action on the kidney and vasculature. In the kidney, vasopressin controls water reabsorption in the renal tubules, and in the vasculature, it causes vasoconstriction by stimulating smooth muscle V1 receptors. Its clinical applications include GI hemorrhage, central diabetes insipidus (DI), and as a second- or third-line agent to treat hypotension.

## Isoproterenol

Isoproterenol is a synthetic, potent, nonselective  $\beta$ -agonist with strong chronotropic effects with very low affinity to  $\alpha$ -adrenergic receptors, and is usually well tolerated in children. However, high doses of isoproterenol can cause myocardial ischemia.<sup>44</sup> Isoproterenol also induces vasodilation that is responsive to acute volume administration. It is often used for increasing HR in complete heart block, in the immediate postoperative period after cardiac transplantation to improve cardiac output by increasing HR in

the denervated donor heart, and as a potent pulmonary vasodilator during pulmonary hypertensive crisis via  $\beta_2$ -adrenergic receptor activity.

## Dobutamine

Dobutamine provides positive inotropy and afterload reduction,  $\beta$  and  $\alpha$  receptors. Its function is primarily as a inotropic agent but with less vasopressor activity compared with dopamine. It is only used as a continuous infusion of 5 to 20  $\mu\text{g}/\text{kg}/\text{min}$ , and in some studies may increase myocardial oxygen. In children but not in adults it causes tachycardia.<sup>45,46</sup>

## Norepinephrine

NE, a drug with strong  $\alpha$ - and  $\beta$ -agonist effects, has had a resurgence of use in infants and children.<sup>47</sup> Children with nearly normal cardiac function and marked peripheral vasodilation have good responses to this drug. It is especially useful in instances of warm septic shock, anaphylaxis, liver failure, and sympathetic blockade with regional anesthesia. It will increase SVR, but also limits mesenteric blood flow, including hepatic perfusion.

## Milrinone

Milrinone is a selective phosphodiesterase III inhibitor that increases cyclic adenosine monophosphate by inhibiting breakdown. Milrinone has both inotropic and vasodilator effects, without acting on  $\alpha$  and  $\beta$  receptors. This drug has improved the outcome of children who have low cardiac output syndrome after cardiac surgery.<sup>48</sup> The loading dose of milrinone is 25 to 75  $\mu\text{g}/\text{kg}$  administered over a period of 10 minutes; the maintenance infusion rate is 0.25 to 0.75  $\mu\text{g}/\text{kg}/\text{min}$ . Loading doses are often avoided in the ICU setting because of resultant hypotension. Renal failure significantly increases the elimination half-life of this drug.<sup>49,50</sup> Outside the cardiac ICU, milrinone is used for vasoconstricted septic shock and may have a role in the treatment of pulmonary hypertension.

## Levosimendan

Levosimendan is a novel agent that increases the sensitivity of the contractile apparatus to calcium increasing inotropy by binding to cardiac myocyte troponin C. This agent will increase cardiac ejection fraction, while reducing catecholamine dose with minimal effects on blood pressure and HR. In children, the most common indications have been for cardiac failure or post–cardiac surgery, with a loading dose of 612  $\mu\text{g}/\text{kg}$  followed by an infusion of 0.1 to 0.2  $\mu\text{g}/\text{kg}/\text{min}$ .<sup>51,52</sup>

## Nesiritide

Nesiritide is a recombinant form of the human B-type natriuretic peptide, the hormone release from the cardiac ventricles in response to volume overload and increasing mechanical wall stress. The action is on guanylate cyclase with resulting venous and arterial vasodilation. In addition, B-type natriuretic peptide leads to myocardial relaxation (lusitropy) and natriuresis. In children, it has been used to decrease central venous pressure and increase urinary output.<sup>53</sup> Usual dosing suggestions for children and adults: initial 2  $\mu\text{g}/\text{kg}$  bolus followed by a continuous infusion of 0.005 to 0.01  $\mu\text{g}/\text{kg}/\text{min}$ .

## Digitalis

Digitalis is useful for the long-term treatment of myocardial failure in children but may not be effective in neonates.<sup>54</sup> Because of its long half-life and unpredictability, digitalis should be administered cautiously to children who have changing levels of serum potassium, calcium, and pH. In these cases, it is more appropriate to use rapid-acting, titratable inotropic agents.

## Calcium

When serum ionized calcium levels are below normal, administration of calcium produces a positive inotropic effect. If the patient's ionized calcium levels are normal, less marked inotropic effects occur. Low ionized calcium levels most commonly occur in patients with DiGeorge's syndrome, when large volumes of citrate-containing blood products are rapid administered, and in neonates with relatively unstable calcium metabolism. Calcium also has effects on the cardiac conduction system. Rapid administration of calcium can cause severe bradycardia or asystole. This effect may be exaggerated in hypokalemic children or in those receiving digitalis. The vasomotor effects of calcium are controversial, but most reports show an increase in both SVR and PVR when the drug is administered.<sup>55</sup>

## Bicarbonate Therapy

Severe acidosis decreases myocardial function and tissue perfusion. Correction of acidosis with 1 to 2 mEq/kg of sodium bicarbonate is indicated for a pH below 7.20 if ventilation is adequate ( $\text{PCO}_2 < 40$  mm Hg if possible). Treatment is necessary because the circulatory system is refractory to sympathomimetic amines when the pH is less than 7.00. After initial correction of pH, persistence or reappearance of metabolic acidosis suggest a continuing underperfused state and the need for further therapy. Administration of sodium bicarbonate is only a stop-gap measure to improve the response to drugs. Repeat

infusions of sodium bicarbonate can cause hypernatremia and hyperosmolarity. Every 50 mEq of bicarbonate administered produces 1250 mL of  $\text{CO}_2$  when the bicarbonate is fully reacted with acid. Consequently, adequate ventilation must be ensured while the drug is administered to avoid worsening the acidosis. Trishydroxymethylaminomethane (THAM) is an alternative to sodium bicarbonate, but larger volumes of THAM are required to produce the same amount of acid-base correction, which may be a problem in patients who have CHF. THAM does not increase  $\text{PaCO}_2$ .

## Vasodilators

Vasodilators are used to control systemic hypertension, increase cardiac output by decreasing afterload, control pulmonary hypertension, and control cardiac shunting. Vasodilators are an effective treatment of systemic hypertension and increase cardiac output in children with CHF. Treatment of pulmonary hypertension and intracardiac shunting with vasodilators has met with limited success because they decrease both PVR and SVR, which may increase extrapulmonary right-to-right shunting and further reduce pulmonary blood flow.

## Nicardipine

Nicardipine is a dihydropyridine calcium channel-blocking agent used as an IV infusion that has powerful, antihypertensive effects in children. Studies have shown that the rapid onset of action is usually within 1 minute, adding to the profile appropriate for treating severe hypertension. Flynn et al. reports that nicardipine is an effective antihypertensive medication in children ranging in age from 2 to 18 years.<sup>56</sup> In our institution, nicardipine is the drug of choice for hypertensive crisis. Infusion ranges: 0.5 to 1.0  $\mu\text{g}/\text{kg}/\text{min}$  up to 3.0  $\mu\text{g}/\text{kg}/\text{min}$ .

## Sodium Nitroprusside

Sodium nitroprusside relaxes arteriolar and venous smooth muscle, which decreases afterload and preload. The half-life of sodium nitroprusside is only minutes, making it safe to titrate the drug to a desired effect. Nitroprusside is commonly used to control severe systemic hypertension, to provide controlled hypotension to reduce blood loss, and to increase cardiac output in children with low cardiac output syndromes (myocarditis, post–cardiac surgery status).<sup>57</sup> Sodium nitroprusside can generally be used for days without problems, although cyanide and thiocyanate poisoning develops in some children, especially those with renal failure or reduced renal perfusion. Serum thiocyanate levels of 10 mg/dL are associated with weakness, hypoxia, nausea, muscle spasms, and disorientation. When these symptoms occur, nitroprusside administration should be discontinued immediately.

## Hydralazine

Hydralazine is used to control systemic hypertension because it relaxes arterial smooth muscle more than it relaxes veins. Administration of the drug can cause headache, nausea, dizziness, sweating, and tremors. The most important acute side effect is tachycardia, which may increase cardiac output; labetalol, a  $\beta$ -antagonist, can counteract this effect.<sup>58</sup>

## Tolazoline and Phentolamine

These competitive  $\alpha$ -adrenergic blockers have had varied success in the treatment of pulmonary hypertension.<sup>59</sup> However, they are effective in treating the symptoms of pheochromocytoma preoperatively. Serious side effects of these drugs include tachycardia, ventricular arrhythmias, hypotension, and tissue edema.

## Prostaglandin E<sub>1</sub>

PGE<sub>1</sub> acts directly on vascular smooth muscle and has greatly improved the care of neonates with heart disease. At infusion rates of 0.1  $\mu$ g/kg/min, patency of the ductus arteriosus is maintained and a closed ductus reopens in some neonates. The drug is indispensable in the care of patients with ductus-dependent cardiac lesions, such as interrupted aortic arch, critical aortic stenosis, or hypoplastic left heart syndrome, where systemic blood flow is supplied through the ductus arteriosus. It is equally important for the care of patients who have pulmonary atresia or critical pulmonic stenosis.<sup>28</sup> Apnea, fever, and hypotension are common side effects of this drug.

## Nitric Oxide

NO is an endothelium-derived relaxing factor that selectively vasodilates the pulmonary vasculature.<sup>60</sup> When administered by inhalation to patients with pulmonary hypertension, NO reduces PVR. It improves the survival of neonates who have reactive pulmonary hypertension.<sup>61-63</sup> This compound is inactivated by hemoglobin before it reaches the systemic circulation. On rare occasions, NO causes systemic vasodilation or clinically significant methemoglobinemia when administered at 5 to 80 ppm.<sup>62</sup>

## Disorders of Cardiac Rhythm

Sinus tachycardia or an elevated HR for age is not considered an arrhythmia. However, patients with a significantly increased HR may be the most critically ill in the ICU. Causes of tachycardia include hypovolemia, fever, pain, anxiety, CHF, myocardial disease and dysfunction and thyrotoxicosis. With all of these causes, the goal is to treat the underlying disease state and not the tachycardia. For children without underlying heart disease, temporary increases in HR up to 180 to 200 beats/min is well tolerated. This is also not uncommon; children cannot increase their stroke volume so they increase their cardiac output by increasing their HR. Again, the goal is not to specifically control an elevated HR but to treat the cause of the tachycardia. Sinus arrhythmia is a phasic acceleration and slowing of the HR that occurs with respiration. This is not an uncommon finding. It indicates that the patient has a vagal tone greater than sympathetic tone and it can indicate that there is good cardiac reserve. A slow HR or sinus bradycardia is another relatively common heart rhythm seen in the ICU. It is an unremarkable finding in an older teenage patient who is relatively fit. Other potential causes can include increased intracranial pressure (ICP), hyperkalemia, hypothermia, profound hypoxia, and hypothyroidism. These causes should also be investigated. A slow HR is being seen more commonly with the increased use of Dexmedetomidine but can also occur with beta blockers or Digoxin use. Sinus node dysfunction can occur following repair of congenital heart disease in children. Temporary slowing may be treated with

the transcutaneous pacemaker placed during surgery. In the absence of myocardial pacing, if there is complete heart block or a very slow ventricular escape rate, a pacemaker may be needed shortly after the cardiac surgery. Otherwise, some amount of time is given to see if this will resolve.

Normal cardiac conduction starts in the sinus node. The electrical activity propagates through the internodal pathways in the atrium, is delayed in the AV node, it travels through the bundle of His, and then is conducted to the ventricles through the left and right bundle branches. Supraventricular tachycardia (SVT) is an elevated HR occurring at the level of the atrium, the AV node, or both. SVT typically has a narrow QRS morphology. Sinus tachycardia is therefore not a type of SVT but an acceleration of the normal conduction pathways. SVT includes reentrant and non-reentrant tachycardias.

The reentrant tachycardias include AV node reentrant tachycardia (AVNRT), orthodromic reciprocating tachycardia (ORT), and atrial flutter. AVNRT is what is classically thought of as pediatric SVT. The reentrant tachycardias occur due to the presence of an accessory conduction pathway that allows for abnormal electrical conduction in the heart. The presence of the abnormal pathway may be apparent on a standard ECG such as the case of Wolf-Parkinson-White (WPW). Alternatively the abnormal pathway may not appear on an ECG and is described as a concealed pathway. Concealed pathways are non-WPW ORT. In AVNRT, the AV node itself is the area in which the reentrance occurs. In atrial flutter there is a micro-reentrant circuit within the atrial tissue itself. In children, the circuit is typically near the tricuspid valve. In atrial flutter, after the reentrant circuit in the atria, the conduction proceeds through the AV node, where it is slowed. The reentrant circuit is small, and the rates of atrial flutter can be very high. As the conduction is slowed in the AV node, these high rates are not usually conducted to the ventricle. However, if atrial flutter or fibrillation occurs in a patient with WPW, the accessory pathway can allow conduction of the electrical impulse at a rate much greater than through the AV node. This can lead to ventricular tachycardia or fibrillation and can cause sudden death.

The non-reentrant causes of SVT occur due to abnormal automaticity of myocardial tissue. Causes of abnormal automaticity include atrial fibrillation and ectopic atrial tachycardia (EAT). In non-reentrant SVT, the elevated atrial rate is slowed as conduction goes through the AV node. In children, atrial fibrillation is caused by disorganized circuits typically near the pulmonary veins. This rhythm is described as irregularly irregular. EAT is rapid atrial beats that are consecutive and occur without sinus morphology. There can be one focus of the rapid atrial beats. Alternatively, in multifocal or chaotic atrial tachycardia, there can be several different atrial origins. Brief periods of EAT usually do not cause much sequel but can lead to cardiomyopathy if it is prolonged.

Treatment of reentrant SVT is based on whether the patient is clinically unstable or stable. The abnormal reentrant circuit can be interrupted with synchronized cardioversion or other methods. If the patient is unstable, reentrant SVT is treated with synchronized cardioversion with a dose of 0.5 to 1 J/kg. If the patient is stable, there is time to try other therapies. Therapies that increase vagal

tone such as ice to the eyes or a Valsalva maneuver may interrupt the reentrant circuit. The medication adenosine will temporarily block conduction through the AV node. Adenosine can be used to interrupt episodes of reentrant SVT that have a reentrant circuit using the AV node. If the reentrant circuit does not include the AV node adenosine might not stop the tachycardia, but it may be helpful with diagnosis. Following administration of adenosine, there will be a period of sinus pause. Adenosine is metabolized by erythrocytes so it is a short acting medication. Equipment to perform cardioversion should be immediately available when adenosine is given. The initial dose is 0.1 mg/kg, and the dose should be given quickly with a sufficient flush. It is more effective when given centrally if available. If it is not effective at the dose of 0.1 mg/kg, the second dose can be increased to 0.2 mg/kg. Higher doses than this are not likely to be more effective, and if the SVT persists, other medications such as amiodarone, procainamide, or verapamil may be necessary. Amiodarone can block an accessory pathway as well as the AV node. If given too quickly, amiodarone will decrease the blood pressure. For both amiodarone and procainamide, continuous infusions may be necessary after the loading dose. Verapamil will block the AV node for a much longer period of time than adenosine. However, in younger patients (<2 years), verapamil may induce other life-threatening arrhythmias. If a patient has SVT, a cardiology consult should be obtained. This is because an echocardiogram may be beneficial, and depending on the cause, there may be a need for long-term follow-up.

Junctional ectopic tachycardia is caused by abnormal automaticity in an area around the atrioventricular junction. This is not a common pediatric arrhythmia but can occur following repair of congenital heart disease. The most common lesion with which this occurs is tetralogy of Fallot.

Wide complex tachycardias are assumed to arise from the ventricle until proven otherwise. SVT can cause a wide complex tachycardia if there is aberrancy of the conduction through the pathways in the ventricle. However, given the risk of delaying therapy, all wide complex tachycardias should initially be treated as ventricular tachycardia. If there is no pulse, initiate CPR, defibrillate, and follow PALS guidelines. If the patient has a pulse and stable blood pressure, there may be time to consider other therapies. These therapies are cardioversion or use of medications such as adenosine, amiodarone, or procainamide. Ventricular fibrillation is treated with CPR, defibrillation, and then medications following PALS guidelines. Ventricular rhythms should be quickly examined for the possibility of Torsades de Pointes, as giving magnesium will be especially helpful.

In the course of following the continuous rhythm strip of all children in the PICU, common abnormalities may be noted. A prolongation of the PR interval or first degree heart block can occur in otherwise normal children. Typically, these children are asymptomatic. Second-degree heart block occurs as Mobitz Type I and Mobitz Type II. Mobitz Type I is also known as *Wenckebach*. This is a gradual prolongation of the PR interval until a QRS is not seen and then the cycle restarts. This occurs due to delay of the electrical signal in the AV node, and it can be a benign phenomenon. Mobitz Type II is less likely to be a benign phenomenon. The PR interval remains constant, but intermittently there is no QRS or ventricular beat. This phenomenon is evidence

of disease of the His-Purkinje fibers and can progress to complete heart block. Mobitz Type II occurs much less frequently in children as compared with adults. Complete heart block or third-degree AV block is the complete dissociation of atrial and ventricular activity. In complete heart block, the atria contract at a rate greater than the ventricle. Ventricular contraction occurs through ventricular escape. Congenital complete heart block can occur in infants born to mothers who have an autoimmune disorder such as lupus. When there is damage to the conduction pathway during surgery for congenital heart disease, complete heart block can occur. As immediate treatment of complete heart block, the ventricular rate may be increased with IV isoproterenol. When this is ineffective, transthoracic or transvenous pacing will be necessary until definitive therapy can be arranged.

Premature beats are also seen quite frequently in a PICU setting. Premature atrial contractions are usually benign and are caused by automaticity of atrial tissue other than the sinus node. Premature ventricular contractions (PVC) are usually benign with a few considerations. The presence of a central venous catheter touching the heart may cause increased PVCs, and if present, the catheter should be pulled back. Electrolyte abnormalities; typically of potassium, magnesium, and calcium, may cause PVCs. The frequency of PVCs may improve as the electrolytes are corrected. Exogenous catecholamines may cause PVCs, and the frequency of PVCs may improve if the catecholamines can be decreased. Endogenous catecholamines may cause PVCs, and the frequency may be decreased if pain or anxiety is treated.

## HYPERTENSION

Essential hypertension is uncommon in children, but when it occurs, it is often associated with another disease process (Box 79.2) and is frequently difficult to control. The acute onset of severe systemic arterial hypertension is a medical emergency that has the potential of causing cardiovascular decompensation, encephalopathy, seizures, and intracranial hemorrhage. In older children, the neurologic manifestations of hypertension are more likely to precede cardiovascular decompensation. Neonates with severe hypertension are frequently initially found to have CHF. Treatment of hypertension is tailored to the disease process, the absolute degree of hypertension, and the presence of cardiovascular or neurologic symptoms.<sup>64,65</sup>

## Neonatal Resuscitation

Profound changes occur in the cardiovascular and respiratory systems at birth. Failure to successfully make these changes may result in death or central nervous system (CNS) injury. Consequently, someone capable of performing neonatal resuscitation must be present at every delivery. Wasting time finding someone to resuscitate the neonate may be disastrous for the infant. This section discusses the causes and effects of cardiorespiratory insufficiency at birth and the techniques of resuscitation. When possible, the recommendations of the American Academy of Pediatrics have been followed.

## BOX 79.2 Causes of Severe Hypertension in Children

### Renal

- Acute glomerulonephritis (e.g., poststreptococcal, Henoch-Schönlein purpura)
- Hemolytic-uremic syndrome
- Chronic glomerulonephritis (all types)
- Acute and chronic pyelonephritis
- Congenital malformations (dysplasia, hypoplasia, cystic diseases)
- Tumors (e.g., Wilms, leukemic infiltrate)
- Post-renal transplantation status; also rejection
- Oliguric renal failure
- Trauma
- Obstructive uropathy
- After genitourinary surgery
- Blood transfusions in children with azotemia

### Cardiovascular

- Coarctation of the aorta
- Renal artery abnormalities (e.g., stenosis, thrombosis)
- Takayasu's disease

### Endocrine

- Pheochromocytoma
- Neuroblastoma
- Adrenogenital disease
- Cushing syndrome
- Hyperaldosteronism
- Hyperthyroidism
- Hyperparathyroidism

### Iatrogenic

- Intravascular volume overload
- Sympathomimetic administration (e.g., epinephrine, ephedrine)
- Corticosteroid administration
- Rapid intravenous infusion of methyldopa

### Miscellaneous

- Immobilization (e.g., fractures, burns, Guillain-Barré syndrome)
- Hypercalcemia (e.g., hypervitaminosis D, metastatic disease, sarcoidosis, some immobilized patients)
- Hypernatremia
- Stevens-Johnson syndrome
- Increased intracranial pressure (any cause)
- Dysautonomia
- After resuscitation

Guidelines for neonatal resuscitation have been issued by many organizations, including the AHA and the American Academy of Pediatrics.<sup>66</sup>

## INITIAL ASSESSMENT OF THE FETUS AT BIRTH

Initial stabilization should begin with a rapid evaluation of the newborn to determine if the infant is term, breathing, or crying, and has a normal tone (Table 79.2).<sup>66</sup>

## ONGOING ASSESSMENT

Ongoing assessment consists of three signs: HR, respirations, and oxygenation. The preferred method for auscultation of HR is by auscultation. All of these vital signs should be determined within the first 30 seconds.

**TABLE 79.2** Evaluation of the Newborn

Clinical Condition	Intervention
Initial resuscitation	Clear infant airway Warm, dry, stimulate, position Evaluate HR, respirations, color
HR > 100 beats/min, breathing, no cyanosis	Observation
HR > 100 beats/min, but persistent respiratory distress or cyanosis	Clear airway SpO <sub>2</sub> monitoring Consider CPAP
Apnea, gasping, or HR < 100 beats/min	Bag-mask PPV SpO <sub>2</sub> monitoring
After initiation of resuscitation (PPV), HR > 100 beats/min, effective ventilation	Post-resuscitation care
HR < 60 beats/min	Consider intubation Chest compressions Coordinate PPV
HR = 60-100 beats/min	Continue with PPV SpO <sub>2</sub> monitoring

CPAP, Continuous positive airway pressure; HR, heart rate; PPV, positive pressure ventilation; SpO<sub>2</sub>, saturation of peripheral oxygen.

## CLEARING THE AIRWAY

Proper positioning by placing the infant in the sniffing position is recommended, and the practitioner must try to avoid either underextension or hyperextension, both of which will obstruct the airway. Deep sucking should be avoided even in healthy, vigorous newborns, because of risks of vagal-mediated bradycardia.<sup>67</sup> This does not apply to newborns who may have airway obstruction or the depressed infant with meconium (covered later in this section.)

## TEMPERATURE CONTROL

During the initial resuscitation period, the goal temperature for the newborn is normothermia. The initial step is to dry the infant and warm the infant to a goal axillary temperature of 36.5°C. The goal for each neonate is eutherma. Infants wrapped in polyethylene from the neck down will avoid evaporative heat loss. Controlled hypothermia should only be attempted in select tertiary centers within hours after birth in infants with hypoxic-ischemic encephalopathy (HIE).

## OXYGEN

One of the recent changes in neonatal resuscitation in the 2011 Neonatal Resuscitation Program Guidelines is the recommendation of positive pressure ventilation (PPV) with room air, unless chest compressions or medications are needed during the resuscitation then the recommendation are still for PPV with 110% oxygen. It is important to place a preductal (right hand) oximeter probe on the newborn if PPV is initiated. For the preterm infant, oxygen should be blended to goal saturation targets. In summary: (1) Use room air in the baby is cyanotic or needs PPV. (2) If the baby is less than 32 weeks, titrate oxygen (Table 79.3).

**TABLE 79.3** Preterm Infant (<32 Weeks): Titrate Oxygen Using Oxygen Blender to Achieve Target SpO<sub>2</sub>

Time after Birth (min)	Target SpO <sub>2</sub> (%)
1	60-65
2	65-70
3	70-75
4	75-80
5	80-85
10	85-95

SpO<sub>2</sub>, Saturation of peripheral oxygen.

(3) Use 100% oxygen if chest compressions or medications are given, then titrate to targeted SpO<sub>2</sub>. (4) Apply oximeter to right hand (preductal).

## VENTILATION

Breathing usually begins by 30 seconds after birth and is sustained by 90 seconds of age. A few minutes after birth, the respiratory rate (RR) of normal neonates is between 40 and 60 breaths/min. The absence of a pause between inspiration and expiration helps develop and maintain functional residual capacity (FRC). Apnea and bradypnea prolong exhalation, reduce FRC, and cause hypoxia. Causes of apnea and bradypnea include severe acidosis, asphyxia, maternal drugs, infections, and CNS damage. Tachypnea (>60 breaths/min) occurs with hypoxemia, hypovolemia, metabolic and respiratory acidosis, CNS hemorrhage, pulmonary gas leaks, pulmonary disease (e.g., hyaline membrane disease, aspiration syndromes, infections), pulmonary edema, and maternal drugs (e.g., narcotics, alcohol, magnesium, barbiturates).

Recommendations now are that initial breaths should be at 20 cm H<sub>2</sub>O. Ventilation should be performed at 40 to 60 breaths/min with reassessment of HR, color, and breath sounds. In the neonate, rising HR may be the best assessment of adequate ventilation. If gastric distention becomes a problem, hindering compliance, a gastric tube may be placed (8 Fr) to improve compliance. Both sides of the chest should rise equally and simultaneously with inspiration, but the amount of rise should not exceed that associated with the neonate's normal spontaneous breathing. The presence of breath sounds may be misleading because they are well transmitted within the neonate's small chest. A difference in breath sounds between the two sides of the chest should raise suspicion of endobronchial intubation, pneumothorax, atelectasis, or a congenital anomaly of the lung. The presence of loud breath sounds over the stomach suggests esophageal intubation or a tracheoesophageal fistula. If ventilation is adequate, the neonate will become pink, initiate rhythmic breathing, and have a normal HR.

Because most asphyxiated neonates have no lung disease, they can be effectively ventilated with peak airway pressures lower than 25 cm H<sub>2</sub>O, even for the first few breaths. Those with stiff lungs (e.g., erythroblastosis fetalis, congenital anomalies of the lung, pulmonary edema, severe meconium aspiration, diaphragmatic hernia) may require

higher inspiratory pressure to ventilate their lungs and are more likely to have pulmonary gas leaks. To reduce this likelihood, the lungs should first be ventilated with an inspiratory pressure of 15 to 20 cm H<sub>2</sub>O and inspiratory rate of 150 to 200 breaths/min. If low-pressure (low-volume), high-rate ventilation does not improve the oxygenation, higher pressure and volume may be required. Failure to adequately ventilate the lungs at birth may worsen hypoxemia and lead to CNS damage or even death. If PaO<sub>2</sub> exceeds 70 to 80 mm Hg or SaO<sub>2</sub> exceeds 94%, the inspired oxygen concentration should be reduced (if increased concentrations of oxygen are used) until SaO<sub>2</sub> and PaO<sub>2</sub> are normal for age. Oxygenation is maintained at the low range of normal in neonates 34 weeks' or less gestation to avoid the retinopathy of prematurity.<sup>68</sup> The neonate's HR should be monitored continuously during endotracheal intubation because the process of tracheal intubation may cause arrhythmias in hypoxic neonates.

If the practitioner is having difficulty with bag mask ventilation or fails intubation, a laryngeal mask airway (LMA) should be considered.<sup>69,70</sup>

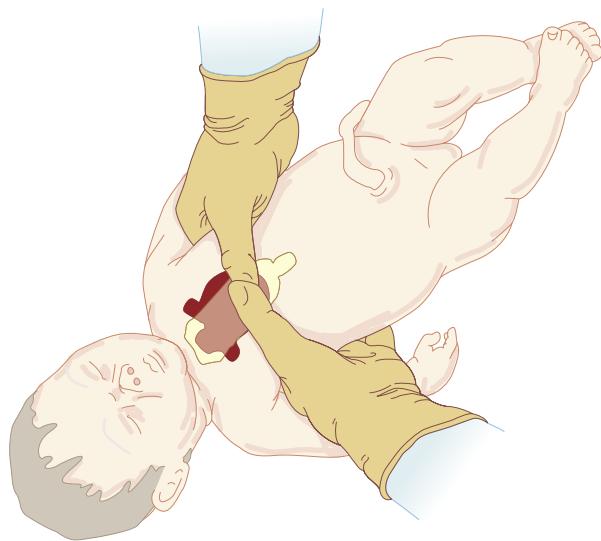
## PNEUMOTHORAX

Pneumothorax occurs in 1% of all vaginal deliveries, in 10% of meconium-stained neonates, and in 2% to 3% of neonates who require mechanical ventilation in the delivery room. The hemithorax containing free air is usually hyperexpanded and moves poorly with ventilation. The point of maximum cardiac impulse is shifted toward the side without the pneumothorax. Heart tones may be muffled.

If a small, high-intensity cold light is placed directly on the skin of the neonate's chest, the involved side of the chest will glow if a pneumothorax is present.<sup>71</sup> Pneumothoraces are relieved by needle or chest tube drainage.

## ENDOTRACHEAL INTUBATION

The head should be placed in a neutral or "sniffing" position during bag-and-mask ventilation and tracheal intubation. An appropriately sized endotracheal tube (ETT) is inserted and its tip is placed 1 to 2 cm below the vocal cords, depending on the size of the neonate. Usually, this means that the distance from the tip of the tube to the gums is 7, 8, 9, or 10 cm in 1-, 2-, 3-, and 4-kg infants. A small gas leak should be present between the ETT and trachea when the ventilation pressure is 15 to 25 cm H<sub>2</sub>O. This usually entails the use of a 2.5-mm (internal diameter) tube for neonates weighing less than 1.5 kg, a 3.0-mm tube for those between 1.5 and 2.5 kg, and a 3.5-mm tube for those weighing more than 2.5 kg. Successful tracheal intubation is confirmed by observing the ETT pass through the vocal cords, by observing bilateral chest movement with each mechanical inspiration, and by observing condensation in the ETT during exhalation. Breath sounds should be much louder over the chest than over the abdomen, and the skin color, HR, and SaO<sub>2</sub> should improve with positive-pressure ventilation. Carbon dioxide should be present during exhalation. However, the small tidal volumes and low pulmonary blood flow of some infants at birth may make it difficult to use capnography effectively.



**Fig. 79.3 Neonatal chest compression.** For simplification, ventilation is not shown. (From Gregory GA. Resuscitation of the newborn. *Anesthesiology*. 1975;43:225.)

## CARDIAC COMPRESSIONS

Place both thumbs on the sternum and allow the fingers to support the back (Fig. 79.3). Compress the sternum to approximately one-third the depth of the chest. Three compressions should be performed with a breath in place of the fourth compression for an effective compression rate of 90 compressions and 30 breaths/min. HR should be evaluated every 45 to 60 seconds, and if after adequate ventilation and compressions for 60 seconds the HR is still less than 60 beats/min, then medications should be considered.

## MEDICATIONS

Resuscitation with medications are needed only for the infant that is critically depressed or presents with significant anomalies leading to cardiovascular depression. There should be a quick reference drug list designed for each delivery room for easy access for these rare occasions, and should help with dosing based on an estimated weight of the infant at birth. IV route of administration is the preferred for administration of resuscitation medications; however, IO and umbilical venous catheters can be placed rapidly by trained individuals and may be life-saving.

### Epinephrine

The primary medication used in the resuscitation of a newborn is epinephrine, and should be given if the infant's HR is less than 60 bpm, 45 to 60 seconds after the initiation of PPV and chest compressions. The recommended dose is 0.1 to 0.3 mL/kg of 1:10,000 concentration; (0.01-0.03 mg/kg), followed by a 1 mL flush of saline. While IV administration is preferable, if venous access is not obtained, it is appropriate to give epinephrine via the ETT. In this instances the practitioner, should give a higher dose of Epinephrine: 0.5 to 1 mL/kg of 1:10,000 concentration; (0.05-0.1 mg/kg). Epinephrine can be repeated every five minutes, as needed, while re-evaluating HR every 45 to 60 seconds.

### Naloxone

Naloxone (Narcan) is not recommended as an initial response to respiratory distress in neonatal resuscitation.<sup>66,72</sup> Neonates should be supported on PPV, even in women who have received narcotics less than four hours prior to delivery. However, if respiratory depression continues, naloxone can be considered. In addition, naloxone should be avoided in an infant whose mother has a history of narcotic dependence due to the risk of seizures from withdrawal.

## DETECTION OF HYPOVOLEMIA

Hypovolemia is detected by measuring arterial blood pressure and by physical examination (i.e., skin color, perfusion, capillary refill time, pulse volume, and extremity temperature).

CVP measurements are useful in detecting hypovolemia and in determining the adequacy of fluid replacement. The venous pressure of normal neonates is 2 to 8 cm H<sub>2</sub>O. If CVP is less than 2 cm H<sub>2</sub>O, hypovolemia should be suspected.

## TREATMENT OF HYPOVOLEMIA

Treatment of hypovolemia requires expansion of intravascular volume with blood and crystalloid. Albumin may also be used, but evidence of its effectiveness is limited. If it is suspected that the neonate will be hypovolemic at birth, Rh-negative type O packed RBCs should be available in the delivery room before the neonate is born.<sup>73</sup> Crystalloid and blood should be titrated in 10 mL/kg and given slowly over 10 minutes, if hemodynamics allow, to limit the risk of intraventricular hemorrhage.

Occasionally, enormous volumes of blood and fluid are required to raise arterial blood pressure to normal. At times, more than 50% of the blood volume (85 mL/kg in term neonates and 100 mL/kg in preterm neonates) must be replaced, especially when the placenta is transected or abruptly during birth. In most cases, less than 10 to 20 mL/kg of volume restores mean arterial pressure to normal.

## OTHER CAUSES OF HYPOTENSION

Hypoglycemia, hypocalcemia, and hypermagnesemia also cause hypotension in neonates. Hypotension induced by alcohol or magnesium intoxication usually responds to blood volume expansion or dopamine, or to both. Hypermagnesemic neonates generally respond to 100 to 200 mg/kg of calcium gluconate administered over a 5-minute period.<sup>66</sup>

## MECONIUM

Meconium stained amniotic fluid (MSAF) when aspirated into the lungs during delivery or in utero can cause serious lung injury and respiratory distress syndrome (RDS). Most cases of meconium aspiration occur in utero; therefore, endotracheal intubation to suction the airway to remove MSAF should only occur if the neonate is distress: absent or depressed respirations, HR less than 100 bpm, or poor muscle tone.<sup>66,74,75</sup> A depressed MSAF stained infant should be

intubated as soon as possible following delivery. Suctioning is accomplished through an ETT, and if there is a significant amount of MSAF or the infant remains in extremis, they should be transferred directly to the neonatal ICU.

## COLOR

Essentially all neonates have a blue-tinged cast to their skin at birth. By 60 seconds of age, most of them are entirely pink, except for their hands and feet, which remain blue. If central cyanosis persists beyond 90 seconds of age, asphyxia, low cardiac output, pulmonary edema, methemoglobinemia, polycythemia, congenital heart disease, arrhythmias, and pulmonary disorders (e.g., respiratory distress, airway obstruction, hypoplastic lungs, diaphragmatic hernia) should be considered, especially if the infant remains cyanotic despite oxygen and controlled ventilation. Neonates who are pale at birth are often asphyxiated, hypovolemic, acidotic, or anemic, or they have congenital heart disease. A neonate whose skin is entirely pink within 2 minutes of birth may be intoxicated with alcohol or magnesium or may be alkalic (pH > 7.50). Rubrous neonates are usually polycythemic.

## RESUSCITATION EQUIPMENT

Resuscitation beds should allow positioning of the neonate's head below the level of the lungs to promote drainage of lung fluid and reduce the likelihood of aspirating gastric contents. A servo-controlled infrared heater should be used to maintain the neonate's temperature between 36°C and 37°C, unless there is evidence of asphyxia. If asphyxia is noted, body temperature should be reduced to 34°C to 35°C for brain protection. A suction device should be available and should allow the suction pressure to be varied; pressures below -100 mm Hg should not be used.

Equipment required for tracheal intubation includes 0 and 00 straight laryngoscope blades; a pencil-type laryngoscope handle; 2.5-, 3.0-, and 3.5-mm ETTs; and a suction catheter that easily fits through each size tube. The ventilation system must permit ventilatory rates of at least 150 breaths/min and make it possible to maintain positive end expiratory pressure (PEEP). One-way valves can stick in the closed position, especially when high gas flow and high RRs are used. The modified Jackson-Rees or Ayres system works well when appropriately trained people use it. Overexpansion of the lungs with large tidal volumes injures the lungs and activates inflammatory processes that may cause chronic lung disease. Gentle inflation of the lung is less injurious to the lung. Airway inflation pressures should be measured continuously during assisted or controlled ventilation in the delivery room, and excessive pressures and tidal volumes should be avoided. As in any critical care situation, patient care should be guided by information. Consequently, blood gas and pH measurements are mandatory, and the results of these tests must be available within 10 minutes of drawing the blood sample. Umbilical arterial catheters are useful for measuring arterial blood pressure and withdrawing blood for blood gas analysis and pH. They can also be used to infuse emergency fluids. Arterial oxygen saturation ( $\text{SaO}_2$ ) can be measured immediately after birth by attaching a pulse oximeter to a hand or foot.<sup>76</sup>

Pulse oximeters permit rapid detection of changes in oxygenation and rapid reduction of fraction of inspired oxygen ( $\text{FiO}_2$ ). The normal  $\text{SaO}_2$  of neonates is usually 87% to 95%, which is associated with a  $\text{PaO}_2$  of 55 to 70 mm Hg.

## PEDIATRIC CARDIAC ARREST AND RESUSCITATION

Pediatric cardiac arrest is not a rare event. At least 16,000 American children (8-20/100,000 children/year) suffer a cardiopulmonary arrest each year.<sup>77-81</sup> More than half of these cardiac arrests probably occur in-hospital.<sup>77-82</sup> With advances in resuscitation science and implementation techniques, survival from pediatric cardiac arrest has improved substantially over the past 25 years.<sup>83</sup>

Outcomes from pediatric cardiac arrest have improved significantly over the past 20 years. For example, survival to discharge from pediatric in-hospital cardiac arrest has increased from less than 10% in the 1980s<sup>84,85</sup> to greater than 25% in the 21st century. Of the pediatric patients that survive to hospital discharge, nearly three quarters will have favorable neurologic function defined by specific pediatric cerebral outcome measures and quality of life indicators.<sup>83,86-88</sup> Factors that influence outcome from pediatric cardiac arrest include (1) the pre-existing condition of the child; (2) the environment in which the arrest occurs; (3) the initial ECG rhythm detected; (4) the duration of no-flow time (the time during an arrest without spontaneous circulation or CPR); (5) the quality of the life-supporting therapies provided during the resuscitation; and (6) the quality of the life-supporting therapies during postresuscitation.

Not surprisingly, outcomes after pediatric out-of-hospital arrests are much worse than those after in-hospital arrests.<sup>78,79,89-97</sup> This may be due to the fact that there is a prolonged period of no flow in out-of-hospital arrests, where many of the pediatric cardiac arrests are not witnessed and only 30% of children are provided with bystander CPR. As a result of these factors, less than 10% of cases of pediatric out-of-hospital cardiac arrest (OHCA) survive to hospital discharge, and for those that do survive, severe neurological injury is common. These findings are especially troublesome, given that bystander CPR more than doubles patient survival rates in adults.<sup>98</sup> An exciting prospective, nationwide, population-based cohort study from Japan similarly demonstrates more than doubling of survival rates for children who have OHCA and receive bystander CPR either with conventional CPR (with rescue breathing) or chest compression only CPR compared with no bystander CPR.<sup>99</sup> The same study then further stratifies outcomes for OHCA into "cardiac" and "noncardiac" causes for arrest, and defines the relative value of rescue breathing during CPR by bystanders. Pediatric patients who have OHCA with noncardiac causes and receive bystander conventional CPR (including rescue breathing) had an association with higher frequency of favorable neurologic outcomes at 1 month after arrest compared with compression-only bystander CPR or no bystander CPR. For pediatric arrests defined as "cardiac" in nature, bystander CPR (conventional or compression-only) was associated with a higher rate of favorable neurologic outcomes 1 month after arrest compared with no bystander CPR. Interestingly, the two types of bystander CPR (conventional or compression-only)

seemed to be similarly effective for pediatric cardiac arrests with cardiac causes, consistent with animal and adult studies.<sup>99</sup>

Survival outcomes after in-hospital cardiac arrest are higher in the pediatric population compared with adults; 27% of children survive to hospital discharge compared with only 17% of adults.<sup>83</sup> For both children and adults, outcomes are better after arrhythmogenic arrests, ventricular fibrillation (VF)/ventricular tachycardia (VT). Importantly, pediatric in-hospital arrests are less commonly caused by arrhythmias (10% of pediatric arrests vs. 25% of adult arrests), and approximately one-third of children and adults with these arrhythmogenic arrests survive to hospital discharge. Interestingly, the superior pediatric survival rate following in-hospital cardiac arrest reflects a substantially higher survival rate among children with asystole or pulseless electrical activity (PEA) compared with adults (24% vs. 11%). Further investigations have shown that the superior survival rate seen in children is mostly attributable to a much better survival rate among infants and preschool age children compared with older children.<sup>87</sup> Although speculative, the higher survival rates in children may be due to improved coronary and cerebral blood flow (CBF) during CPR because of increased chest compliance in these younger arrest victims, with improved aortic diastolic pressure and venous return.<sup>100,101</sup> In addition, survival of pediatric patients from an in-hospital cardiac arrest is more likely in hospitals staffed with dedicated pediatric physicians.<sup>102</sup>

## Phases of Resuscitation

The four distinct phases of cardiac arrest and CPR interventions are (1) prearrest, (2) no flow (untreated cardiac arrest), (3) low flow (CPR), and (4) postresuscitation/arrest. Interventions to improve outcome of pediatric cardiac arrest should optimize therapies targeted to the time and phase of CPR, as suggested in Table 79.4.

### PREARREST

The prearrest phase refers to any relevant preexisting conditions of the child (e.g., neurologic, cardiac, respiratory, or metabolic problems) and precipitating events (e.g., respiratory failure or shock), uncoupling metabolic delivery and metabolic demand. Pediatric patients who suffer an in-hospital cardiac arrest often have changes in their physiological status in the hours leading up to their arrest event.<sup>103,104</sup> Therefore, interventions during the prearrest phase focus on preventing the cardiac arrest, with special attention to early recognition and targeted treatment of respiratory failure and shock. Early recognition plays a key role in identifying a prearrest state in children, who unlike adults may be able to mount a prolonged physiologic response to a worsening clinical picture. Medical emergency teams (METs; also known as *rapid response teams*) are in-hospital emergency teams designed specifically for this purpose. Front-line providers, and even parents, are encouraged to initiate evaluation by METs based on physiologic protocol driven parameters or even intuition. Patients are assessed by the METs, and those at high risk of clinical decompensation

**TABLE 79.4** Phases of Cardiac Arrest and Resuscitation

Phase	Interventions
Pearrest phase (protect)	Optimize patient monitoring and rapid emergency response Recognize and treat respiratory failure or shock to prevent cardiac arrest
Arrest (no-flow) phase (preserve)	Minimize interval to BLS and ACLS Organize response with clear leadership Minimize interval to defibrillation, when indicated
Low-flow (CPR) phase (resuscitate)	Push hard, push fast Allow full chest recoil Minimized interruptions in compressions Avoid overventilation Titrate CPR to optimize myocardial blood flow (coronary perfusion pressures and exhaled CO <sub>2</sub> ) Consider adjuncts to improve vital organ perfusion during CPR Consider ECMO if standard CPR/ALS not promptly successful
Post-resuscitation phase: short-term	Optimize cardiac output and cerebral blood flow Treat arrhythmias, if indicated Avoid hyperglycemia, hyperthermia, hyperventilation Debrief to improve future responses to emergencies
Postresuscitation phase: long-term rehabilitation (regenerate)	Early intervention with occupational and physical therapy Bioengineering and technology interface Possible future role for stem cell transplantation

ACLS, Advanced cardiac life support; ALS, advanced life support; BLS, basic life support; CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation.

are transferred to a pediatric ICU if necessary, with the goal to prevent progression to full cardiac arrest or to decrease the response time to initiation of advanced life support, thereby limiting the no-flow state. Implementation of METs decreases the frequency of cardiac arrests compared with retrospective control periods before MET initiation.<sup>105-107</sup> While early recognition protocols cannot identify all children at risk for cardiac arrest, it seems reasonable to assume that transferring critically ill children to an ICU early in their disease process for better monitoring and more aggressive interventions can improve resuscitative care and clinical outcomes. The caveat is that prearrest states must be identified to initiate monitoring and interventions that may inhibit the progression to an arrest. While a significant amount of research dollars and resources are spent on the other phases of cardiac arrest, particular focus on the prearrest state may yield the greatest improvement in survival and neurologic outcomes.

### NO FLOW/LOW FLOW

#### Airway-Breathing-Circulation or Circulation-Airway-Breathing

For OHCA victims, “compression-only” CPR has been associated with improved outcomes.<sup>108,109</sup> This is now the recommended modality for emergency medical service dispatcher

instructing bystander CPR.<sup>110</sup> In a recent Japanese study, children with OHCA due to a primary cardiac etiology displayed an equivalent survival rate between compression-only CPR and classic CPR with rescue breaths. However, only 29% of patients had a cardiac cause of OHCA. Those with noncardiac etiology in the overall cohort had a significantly worse survival rate with compression-only CPR, as compared with classic CPR with rescue breaths.<sup>111</sup> Additionally, in another nationwide Japanese OHCA registry study, compression-only CPR was superior to no bystander CPR at all but not to conventional CPR.<sup>112</sup> In a recent American OHCA registry study, children who received conventional bystander CPR with chest compressions and rescue breaths had improved rates of overall survival and survival with favorable outcomes as compared with those who did not receive CPR, whereas those receiving compression-only CPR did not fare any better than children not receiving CPR.<sup>113</sup> Thus compression-only CPR is not recommended for children in either the inpatient or out-of-hospital setting, except in situations in which “rescuers are unwilling or unable to deliver breaths.”<sup>114</sup>

Regardless, the prioritization of initial interventions during CPR has shifted from airway-breathing-circulation (“A-B-C”) to circulation-airway-breathing (“C-A-B”) in order to prevent harmful delays in the initiation of chest compressions and due to the relative complexity of the tasks involved in providing assisted ventilation. This is endorsed by both the 2010 and 2015 AHA BLS Guidelines.<sup>114,115</sup> However, a 2015 International Liaison Committee on Resuscitation consensus statement identified a paucity of pediatric-specific evidence to support this recommendation.<sup>116</sup> In our opinion, the approach is physiologically sound, especially given the association of delayed chest compression initiation with poor outcomes. With that said, the pediatric provider must consider the predominance of asphyxia and hypoxemia as precursors to cardiac arrest.<sup>83,117</sup> This is especially true in the ICU and operating room, where personnel and other resources frequently allow for simultaneous circulatory support with high-quality chest compressions as well as the provision of assisted ventilations by experienced personnel.

In order to improve outcomes from pediatric cardiac arrest, it is imperative to shorten the no-flow phase of untreated cardiac arrest. To that end, it is important to monitor high-risk patients to allow early recognition of the cardiac arrest and prompt initiation of basic and advanced life support. Effective CPR optimizes coronary perfusion pressure (by elevating aortic diastolic pressure relative to RAP) and cardiac output to critical organs to support vital organ viability (by elevating mean aortic pressure) during the low flow phase. Important tenets of basic life support are *push hard, push fast, allow full chest recoil between compressions, and minimize interruptions of chest compression*. The myocardium receives blood flow from the aortic root, mainly during diastole, via the coronary arteries. When the heart arrests and no blood flows through the aorta, coronary blood flow ceases. However, during chest compressions, aortic pressure rises at the same time as RAP and with the subsequent decompression phase of chest compressions, the RAP falls faster and lower than the aortic pressure, which generates a pressure gradient that perfuses the heart with oxygenated

blood. Therefore, full elastic recoil (release) is critical to create a pressure difference between the aortic root and the right atrium. A CPP below 15 mm Hg during CPR is a poor prognostic factor for ROSC. Achieving optimal coronary perfusion pressure, exhaled carbon dioxide concentration, and cardiac output during the low flow phase of CPR is consistently associated with an improved chance for return of spontaneous circulation (ROSC) and improved short- and long-term outcome in mature animal and human studies.<sup>118-125</sup> There is a critical need for research evaluating goal directed CPR, both in immature animal models and pediatric patients. Other measures essential for truncating the no-flow phase during VF and pulseless VT are rapid detection and prompt defibrillation. Clearly, CPR alone is inadequate for successful resuscitation from these arrhythmias. For cardiac arrests resulting from asphyxia and/or ischemia, provision of adequate myocardial perfusion and myocardial oxygen delivery are the critical elements for ROSC.

## POSTARREST/RESUSCITATION

The postarrest/resuscitation phase includes coordinated, skilled management of the immediate post-resuscitation stage, the next few hours to days, and long-term rehabilitation. The immediate post-resuscitation stage is a high-risk period for ventricular arrhythmias and other reperfusion injuries. Goals of interventions implemented during the immediate post-resuscitation stage and the next few days include adequate tissue oxygen delivery, treatment of post-resuscitation myocardial dysfunction, and minimizing post-resuscitation tissue injury (e.g., preventing post-resuscitation hyperthermia and hypoglycemia; and, perhaps initiating post-resuscitation therapeutic hypothermia, preventing hyperglycemia and avoiding hyperoxia). This post-arrest/resuscitation phase may have the greatest potential for innovative advances in the understanding of cell injury (excitotoxicity, oxidative stress, metabolic stress) and cell death (apoptosis and necrosis), ultimately leading to novel molecular-targeted interventions. The rehabilitation stage concentrates on salvage of injured cells, and support for reengineering of reflex and voluntary communications of these cell and organ systems to improve long-term functional outcome.

The specific phase of resuscitation dictates the focus of care. Interventions that improve outcome during one phase may be deleterious during another. For instance, intense vasoconstriction during the low flow phase of cardiac arrest improves coronary perfusion pressure and the probability of ROSC. The same intense vasoconstriction during the post-resuscitation phase increases left ventricular afterload and may worsen myocardial strain and dysfunction. Current understanding of the physiology of cardiac arrest and recovery allows us to only crudely manipulate blood pressure, oxygen delivery and consumption, body temperature, and other physiologic parameters in our attempts to optimize outcome. Future strategies likely will take advantage of increasing knowledge of cellular injury, thrombosis, reperfusion, mediator cascades, cellular markers of injury and recovery, and transplantation technology, including stem cells.

## Interventions During the Cardiac Arrest (No Flow) and Cardiopulmonary Resuscitation (Low Flow)

### AIRWAY AND BREATHING

During CPR, cardiac output and pulmonary blood flow are ~10% to 25% of that during normal sinus rhythm; therefore, a lower minute ventilation is necessary for adequate gas exchange from the blood traversing the pulmonary circulation. Animal and adult data indicate that overventilation ("overventilation" from exuberant rescue breathing) during CPR is common and can substantially compromise venous return and subsequently cardiac output.<sup>126-128</sup> These detrimental hemodynamic effects are compounded when one considers the effect of interruptions in CPR to provide airway management and rescue breathing and may contribute to worse survival outcomes.<sup>129-132</sup> While overventilation is problematic, in light of the fact that most pediatric arrests are asphyxial in nature, immediate initiation of *adequate* ventilation is still important. The difference between arrhythmogenic and asphyxial arrests lies in the physiology. In animal models of sudden VF cardiac arrest, acceptable PaO<sub>2</sub> and PaCO<sub>2</sub> persist for 4 to 8 minutes during chest compressions without rescue breathing.<sup>133,134</sup> This is in part because aortic oxygen and carbon dioxide concentrations at the onset of the arrest do not vary much from the prearrest state with no blood flow and minimal aortic oxygen consumption. The lungs act as a reservoir of oxygen during the low-flow state of CPR; therefore, adequate oxygenation and ventilation can continue without rescue breathing. Several retrospective studies of witnessed VF cardiac arrest in adults have also shown that outcomes are similar after bystander-initiated CPR with either chest compressions alone or chest compressions plus rescue breathing.<sup>135</sup> However, during asphyxial arrest, peripheral and pulmonary blood flow continues during the prearrest, state resulting in significant arterial and venous oxygen desaturation, elevated lactate levels, and depletion of the pulmonary oxygen reserve. Therefore, at the onset of CPR, there is substantial arterial hypoxemia and resulting acidemia. In this circumstance, rescue breathing with controlled ventilation can be a life-saving maneuver. In contrast, the adverse hemodynamic effects from overventilation during CPR combined with possible interruptions in chest compressions to open the airway and deliver rescue breathing are a lethal combination in certain circumstances such as VT/VF arrests. In short, the resuscitation technique should be titrated to the physiology of the patient to optimize patient outcome.

### CIRCULATION: OPTIMIZING BLOOD FLOW DURING LOW FLOW CARDIOPULMONARY RESUSCITATION: PUSH HARD, PUSH FAST

When the heart arrests, no blood flows to the aorta and coronary blood flow ceases immediately.<sup>135</sup> At that point, provision of high quality CPR (PUSH HARD, PUSH FAST) is vital to reestablish coronary flow. The goal during CPR is to

maximize the myocardial perfusion pressure (MPP). Related by the following equation: MPP = aortic diastolic blood pressure (AoDP) minus RAP, myocardial blood flow improves as the gradient between AoDP and RAP increases. During downward compression phase, aortic pressure rises at the same time as RAP with little change in the MPP. However, during the decompression phase of chest compressions, the RAP falls faster and lower than the aortic pressure, which generates a pressure gradient perfusing the heart with oxygenated blood during this artificial period of "diastole." Several animal and human studies have demonstrated, in both VT/VF and asphyxial models, the importance of establishing MPP as a predictor for short-term survival outcome (ROSC).<sup>124,136-139</sup> Because there is no flow without chest compressions, it is important to minimize interruptions in chest compressions. To allow good venous return in the decompression phase of external cardiac massage, it is also important to allow full chest recoil and to avoid overventilation (preventing adequate venous return because of increased intrathoracic pressure).

Based on the provided equation, MPP can be improved by strategies that increase the pressure gradient between the aorta and the right atrium. As an example, the inspiratory impedance threshold device (ITD) is a small, disposable valve that can be connected directly to the tracheal tube or face mask to augment negative intrathoracic pressure during the inspiratory phase of spontaneous breathing and the decompression phase of CPR by impeding airflow into the lungs. Application in animal and adult human trials of CPR has established the ability of the ITD to improve vital organ perfusion pressures and myocardial blood flow<sup>140-145</sup>; however, in the only randomized trial during adult CPR, mortality benefit was limited to the subgroup of patients with PEA.<sup>145</sup> Additional evidence that augmentation of negative intrathoracic pressure can improve perfusion pressures during CPR comes from the active compression-decompression device (ACD). The ACD is a handheld device that is fixed to the anterior chest of the victim by means of suction similar to a household plunger that can be used to apply active decompression forces during the release phase, thereby creating a vacuum within the thorax. By actively pulling during the decompression phase, blood is drawn back into the heart by the negative pressure.<sup>146</sup> Animal and adult studies have demonstrated that the combination of ACD with ITD act in concert to further improve perfusion pressures during CPR compared with ACD alone.<sup>142</sup> In the end, while novel interventions such as the ITD and ACD are promising adjuncts to improve blood flow during CPR, the basic tenants of PUSH HARD, PUSH FAST, ALLOW FULL CHEST WALL RELEASE, MINIMIZE INTERRUPTIONS, and DON'T OVERVENTILATE are still the dominate factors to improve blood flow during CPR and chance of survival.

### CHEST COMPRESSION DEPTH

The pediatric chest compression depth recommendation of at least one-third anterior-posterior chest depth (approximately 4 cm in infants and 5 cm in children) is based largely upon expert clinical consensus, using data extrapolated from animal, adult, and limited pediatric data. In a small study of six infants, chest compressions targeted to one half

anterior-posterior chest depth resulted in improved systolic blood pressures, compared with those targeted at one-third anterior-posterior chest depth.<sup>147</sup> While only a small series with qualitatively estimated chest compression depths, this is the first study to collect actual data from children supporting the existing chest compression depth guidelines. On the contrary, two recent studies using computer automated tomography (CT)<sup>148,149</sup> suggest that depth recommendations based on a relative (%) anterior-posterior chest compression depth are deeper than that recommended for adults, and that a depth of one half anterior-posterior chest depth will result in direct compression to the point of fully emptying the heart and requisite shifting of heart because of inadequate AP diameter reserve in most children. Future studies that collect data from actual children and that associate quantitatively measured chest compression depths with short- and long-term clinical outcomes (arterial blood pressure, end tidal carbon dioxide, ROSC, survival) are needed.

## COMPRESSION/VENTILATION RATIOS

The amount of ventilation provided during CPR should match, but not exceed, perfusion and should be titrated to the amount of circulation during the specific phase of resuscitation, as well as the metabolic demand of the tissues. Therefore, during the low flow state of CPR when the amount of cardiac output is roughly 10% to 25% of normal, less ventilation is needed.<sup>150</sup> However, the best ratio of compressions to ventilations in pediatric patients is largely unknown and depends on many factors, including the compression rate, the tidal volume, the blood flow generated by compressions, and the time that compressions are interrupted to perform ventilation. Recent evidence demonstrates that a compression/ventilation ratio of 15:2 delivers the same minute ventilation and increases the number of delivered chest compressions by 48% compared with CPR at a compression/ventilation ratio of 5:1 in a simulated pediatric arrest model.<sup>151,152</sup> This is important because when chest compressions cease, the aortic pressure rapidly decreases and coronary perfusion pressure falls precipitously, thereby decreasing myocardial oxygen delivery.<sup>135</sup> Increasing the ratio of compressions to ventilations minimizes these interruptions, thus increasing coronary blood flow. The benefits of PPV (increased arterial content of oxygen and carbon dioxide elimination) must be balanced against the adverse consequence of decreased circulation. These findings are in part the reason the AHA now recommends a pediatric compression/ventilation ratio of 15:2.

## DUTY CYCLE

In a model of human adult cardiac arrest, cardiac output and coronary blood flow are optimized when chest compressions last for 30% of the total cycle time (approximately 1:2 ratio of time in compression to time in relaxation).<sup>153</sup> As the duration of CPR increases, the optimal duty cycle may increase to 50%. In a juvenile swine model, a relaxation period of 250 to 300 milliseconds (duty cycle of 40%-50% at a compression rate of 120/min) correlates with improved cerebral perfusion pressures (CPPs) compared with shorter duty cycles of 30%.<sup>154</sup>

## CIRCUMFERENTIAL VERSUS FOCAL STERNAL COMPRESSIONS

In adult and animal models of cardiac arrest, circumferential (vest) CPR has been demonstrated to dramatically improve CPR hemodynamics.<sup>155</sup> In smaller infants, it is often possible to encircle the chest with both hands and depress the sternum with the thumbs, while compressing the thorax circumferentially (thoracic squeeze). In an infant animal model of CPR, this “two-thumb” method of compression with thoracic squeeze resulted in higher systolic and diastolic blood pressures and a higher pulse pressure than traditional two-finger compression of the sternum.<sup>156</sup> Although not rigorously studied, our clinical experience indicates that it is very difficult to attain adequate chest compression force and adequate aortic pressures with the two-finger technique, so we fully support the AHA Guidelines for health care providers to perform CPR on infants with the two-thumb-encircling hands technique.<sup>157</sup>

## OPEN-CHEST CARDIOPULMONARY RESUSCITATION

In animal models, high quality standard, closed-chest CPR generates myocardial blood flow that is greater than 50% of normal, CBF that is approximately 50% of normal, and cardiac output ~10% to 25% of normal.<sup>135,155,158,159</sup> By contrast, open-chest CPR can generate myocardial and CBF that approaches normal. Although open-chest massage improves coronary perfusion pressure and increases the chance of successful defibrillation in animals and humans,<sup>160-162</sup> performing a thoracotomy to allow open-chest CPR is impractical in many situations. A retrospective review of 27 cases of CPR following pediatric blunt trauma (15 with open-chest CPR and 12 with closed-chest CPR) demonstrated that open-chest CPR increased hospital cost without altering rates of ROSC or survival to discharge. However, survival in both groups was 0%, indicating that the population may have been too severely injured or too late in the process to benefit from this aggressive therapy.<sup>163</sup> Open-chest CPR is often provided to children after open-heart cardiac surgery and sternotomy. Earlier institution of open-chest CPR may warrant reconsideration in selected special resuscitation circumstances.

## MEDICATIONS USED TO TREAT CARDIAC ARREST

While animal studies have indicated that epinephrine can improve initial resuscitation success after both asphyxial and VF cardiac arrests, there are no prospective studies to support the use of epinephrine or any other medication to improve survival outcome from pediatric cardiac arrest. A variety of medications are used during pediatric resuscitation attempts, including vasopressors (epinephrine and vasopressin), antiarrhythmics (amiodarone and lidocaine), and other drugs such as calcium chloride and sodium bicarbonate. Each will be discussed separately as follows.

### Vasopressors

Epinephrine (adrenaline) is an endogenous catecholamine with potent  $\alpha$ - and  $\beta$ -adrenergic stimulating properties. The

$\alpha$ -adrenergic action (vasoconstriction) increases systemic and PVR. The resultant higher aortic diastolic blood pressure improves coronary perfusion pressure and myocardial blood flow, even though it reduces global cardiac output during CPR; as noted previously, adequacy of myocardial blood flow is a critical determinant of ROSC. Epinephrine also increases CBF during good quality CPR because peripheral vasoconstriction directs a greater proportion of flow to the cerebral circulation.<sup>164-166</sup> However, recent evidence suggests that epinephrine can decrease local cerebral microcirculatory blood flow at a time when global cerebral flow is increased.<sup>167</sup> The  $\beta$ -adrenergic effect increases myocardial contractility and HR, and relaxes smooth muscle in the skeletal muscle vascular bed and bronchi; however, the  $\beta$ -adrenergic effects are not observed in the peripheral vascular beds secondary to the high dose used in cardiac arrest. Epinephrine also increases the vigor and intensity of VF, increasing the likelihood of successful defibrillation. High-dose epinephrine (0.05-0.2 mg/kg) improves myocardial and CBF during CPR more than standard-dose epinephrine (0.01-0.02 mg/kg) in animal models of cardiac arrest and may increase the incidence of initial ROSC.<sup>168,169</sup> However, prospective and retrospective studies have indicated that the use of high-dose epinephrine in adults or children does not improve survival and may be associated with worse neurologic outcome.<sup>170,171</sup> A randomized, blinded, controlled trial of rescue high-dose epinephrine versus standard-dose epinephrine after failed initial standard dose epinephrine in pediatric in-hospital cardiac arrest demonstrated a worse 24-hour survival in the high-dose epinephrine group (1 of 27 survivors vs. 6 of 23 survivors,  $P < .05$ ).<sup>172</sup> Based on these clinical studies, high-dose epinephrine cannot be recommended routinely for either initial or rescue therapy. Importantly, these studies indicate that high-dose epinephrine can worsen a patient's post-resuscitation hemodynamic condition and likelihood of survival.

*Vasopressin* is a long-acting endogenous hormone that acts at specific receptors to mediate systemic vasoconstriction ( $V_1$  receptor) and reabsorption of water in the renal tubule ( $V_2$  receptor). Vasoconstrictive properties are most intense in the skeletal muscle and skin vascular beds. Unlike epinephrine, vasopressin is not a pulmonary vasoconstrictor. In experimental models of cardiac arrest, vasopressin increases blood flow to the heart and brain and improves long-term survival compared with epinephrine. However, vasopressin can decrease splanchnic blood flow during and following CPR and can increase afterload in the post-resuscitation period placing further strain on the left ventricle.<sup>158,173-176</sup> Adult randomized, controlled trials suggest that outcomes are similar after use of vasopressin or epinephrine during CPR.<sup>177,178</sup> During pediatric arrest, a case series of four children who received vasopressin during six prolonged cardiac arrest events suggested that the use of bolus vasopressin may result in ROSC when standard medications have failed.<sup>179</sup> However, a more recent retrospective study of 1293 consecutive pediatric arrests from the National Registry of CPR (NPCRP) found that vasopressin use, while infrequent (administered in only 5% of events), was associated with a lower likelihood of ROSC. Therefore, it is unlikely that vasopressin will replace epinephrine as a first-line agent in pediatric cardiac arrest. However, the available data suggest that its use in conjunction with

epinephrine may deserve further investigation, especially in prolonged arrest unresponsive to initial epinephrine resuscitation.

### Antiarrhythmic Medications

**Calcium.** Calcium is used frequently in cases of pediatric cardiac arrest, despite the lack of evidence for efficacy. In the absence of a documented clinical indication (i.e., hypocalcemia, calcium channel blocker overdose, hypermagnesemia, or hyperkalemia), administration of calcium does not improve outcomes from cardiac arrest.<sup>180-188</sup> To the contrary, three pediatric studies have suggested a potential for harm, as routine calcium administration was associated with decreased survival rates and / or worse neurological outcomes.<sup>180-188</sup> Despite limited clinical data to support the use of calcium during CPR, it is reasonable to consider calcium administration during CPR for cardiac arrest patients at high risk of hypocalcemia (e.g., renal failure, shock associated with massive transfusion, etc.).

**Buffer Solutions.** There are no randomized controlled studies in children examining the use of sodium bicarbonate for management of pediatric cardiac arrest. Two randomized controlled studies have examined the value of sodium bicarbonate in the management of adult cardiac arrest<sup>189</sup> and in neonates with respiratory arrest in the delivery room.<sup>190</sup> Neither study was associated with improved survival. In fact, one multicenter retrospective in-hospital pediatric study found that sodium bicarbonate administered during cardiac arrest was associated with decreased survival, even after controlling for age, gender and first documented cardiac rhythm.<sup>187</sup> Therefore, during pediatric cardiac arrest resuscitation, the routine use of sodium bicarbonate is not recommended. Clinical trials involving critically ill adults with severe metabolic acidosis do not demonstrate a beneficial effect of sodium bicarbonate on hemodynamics despite correction of acidosis.<sup>191-192</sup> This is somewhat surprising in light of data that severe acidosis may depress the action of catecholamines and worsen myocardial function.<sup>193,194</sup> Nevertheless, the common use of sodium bicarbonate during CPR is not supported by clinical data. Pediatric patients with implanted cardiac pacemakers may have an increased threshold for myocardial electrical stimulation when acidotic<sup>195</sup>; therefore, administration of bicarbonate or another buffer is appropriate for management of severe documented acidosis in these children. Administration of sodium bicarbonate also is indicated in the patient with a tricyclic antidepressant overdose, hyperkalemia, hypermagnesemia, or sodium channel blocker poisoning. The buffering action of bicarbonate occurs when a hydrogen cation and a bicarbonate anion combine to form carbon dioxide and water. Carbon dioxide must be cleared through adequate minute ventilation; thus, if ventilation is impaired during sodium bicarbonate administration, carbon dioxide buildup may negate the buffering effect of bicarbonate. Because carbon dioxide readily penetrates cell membranes, intracellular acidosis may paradoxically increase after sodium bicarbonate administration without adequate ventilation. Therefore, bicarbonate should not be used for management of respiratory acidosis.

Unlike sodium bicarbonate, tromethamine (THAM) buffers excess protons without generating carbon dioxide; in

fact, carbon dioxide is consumed following THAM administration. In a patient with impaired minute ventilation, tromethamine may be preferable when buffering is necessary to mitigate severe acidosis. Tromethamine undergoes renal elimination, and renal insufficiency may be a relative contraindication to its use. Carbicarb, an equimolar combination of sodium bicarbonate and sodium carbonate, is another buffering solution that generates less carbon dioxide than sodium bicarbonate. In a canine model of cardiac arrest comparing animals given normal saline, sodium bicarbonate, THAM, or Carbicarb, the animals given any buffer solution had a higher rate of ROSC than the animals given normal saline. In the animals given sodium bicarbonate or Carbicarb, the interval to ROSC was significantly shorter than in animals given normal saline. However, at the end of the 6-hour study period, all resuscitated animals were in a deep coma, so no inferences regarding meaningful survival can be drawn.<sup>196</sup> It is premature to recommend either THAM or Carbicarb during CPR at this time.

## POST-RESUSCITATION INTERVENTIONS

### Temperature Management

Two seminal articles<sup>197,198</sup> have established that induced hypothermia (32°C-34°C) could improve outcome for comatose adults after resuscitation from VF cardiac arrest. In both randomized, controlled trials, the inclusion criteria were patients older than 18 years who were persistently comatose after successful resuscitation from nontraumatic VF.<sup>199,200</sup> However, in a recent randomized control trial with unconscious adult survivors of OHCA, a targeted temperature of 33°C did not confer a benefit as compared with the targeted temperature of 36°C.<sup>201</sup> Interpretation and extrapolation of these studies to children is difficult; however, fever within the first 48 hours following cardiac arrest, brain trauma, stroke, and ischemia is associated with poor neurologic outcome. Emerging neonatal trials of selective brain cooling and systemic cooling show promise in neonatal HIE, suggesting that induced hypothermia may improve outcomes.<sup>202,203</sup> The efficacy of therapeutic hypothermia following pediatric cardiac arrest is being evaluated in a randomized controlled trial ([clinicaltrials.gov](https://clinicaltrials.gov) identifier NCT00880087); THAPCA: Therapeutic Hypothermia After Pediatric Cardiac Arrest ([www.thapca.org](http://www.thapca.org)). At a minimum, it is advisable to avoid hyperthermia in children following CPR. Using an approach of “therapeutic normothermia” with scheduled administration of antipyretic medications and the use of external cooling devices, while monitoring core temperature, may be necessary to prevent hyperthermia in this population. Notably, preventing hyperthermia is not easy. Many children become hyperthermic post-arrest despite the intent to prevent hypothermia.<sup>198</sup>

### Glucose Control

Both hyperglycemia and hypoglycemia following cardiac arrest is associated with worse neurologic outcome.<sup>204-207</sup> While it seems intuitive that hypoglycemia would be associated with worse neurologic outcome, whether hyperglycemia per se is harmful or is simply a marker of the severity of the stress hormone response from prolonged ischemia is not clear. A recent randomized control trial suggests

that tight glycemic control in critically ill children had no effect on major clinical outcomes, but was associated with a higher incidence of hypoglycemia.<sup>208</sup> In summary, there is insufficient evidence to formulate a strong recommendation on the management of hyperglycemia in children with ROSC following cardiac arrest. If hyperglycemia is treated following ROSC in pediatric patients, blood glucose concentrations should be carefully monitored to avoid hypoglycemia.

### Blood Pressure Management

A patient with ROSC may have substantial variability in blood pressure following cardiac arrest. Postarrest/resuscitation myocardial dysfunction is very common and is often associated with hypotension (discussed later).<sup>199,200,209-218</sup> In addition, hypertension may occur, especially if the patient receives vasoactive infusions for postarrest myocardial dysfunction. Optimization of blood pressure postarrest is critical to maintain adequate perfusion pressure to vital organs that may have already been injured from the “no flow” and “low blood flow” states during initial cardiac arrest and CPR. Cerebral blood flow in healthy patients is tightly controlled over a wide range of mean arterial blood pressure via cerebral neurovascular bundle (autoregulation); however, adults resuscitated from cardiac arrest have demonstrated impaired autoregulation of CBF, and this may also be the case in children.<sup>219</sup> Dysautoregulation of the cerebral neurovascular bundle following cardiac arrest may limit the brain’s ability to regulate excessive blood flow and microvascular perfusion pressure, thereby leading to reperfusion injury during systemic hypertension. However, in animal models, brief induced hypertension following resuscitation results in improved neurologic outcome compared with normotensive reperfusion.<sup>220,221</sup> Conversely, systemic hypotension may perpetuate neurologic metabolic crisis following ischemic injury by uncoupling bioenergetic demand and delivery. Therefore, a practical approach to blood pressure management following cardiac arrest is to attempt to minimize blood pressure variability in this high-risk period following resuscitation.

## Post-resuscitation Myocardial Dysfunction

Postarrest myocardial stunning and arterial hypotension occur commonly after successful resuscitation in both animals and humans.<sup>199,200,209-218</sup> Animal studies demonstrate that postarrest myocardial stunning is a global phenomenon with biventricular systolic and diastolic dysfunction. Postarrest myocardial stunning is pathophysiologically and physiologically similar to sepsis-related myocardial dysfunction and postcardiopulmonary bypass myocardial dysfunction, including increases in inflammatory mediators and NO production.<sup>212,215,218,216</sup> Because cardiac function is essential to reperfusion following cardiac arrest, management of postarrest myocardial dysfunction may be important to improving survival. The classes of agents used to maintain circulatory function (i.e., inotropes, vasopressors, and vasodilators) must be carefully titrated during the post-resuscitation phase to the patient’s cardiovascular physiology. Although the optimal

management of post–cardiac arrest hypotension and myocardial dysfunction has not been established, data suggest that aggressive hemodynamic support may improve outcomes. Controlled trials in animal models have shown that dobutamine, milrinone, levosimendan can effectively ameliorate post–cardiac arrest myocardial dysfunction.<sup>209,210,222,223</sup> In clinical observational studies, fluid resuscitation has been provided for patients with hypotension and concomitant low central venous pressure, and various vasoactive infusions, including epinephrine, dobutamine, and dopamine, have been used to treat the myocardial dysfunction syndrome.<sup>199,200,213–217</sup> In the end, optimal use of these agents involves close goal-directed titration, and the use of invasive hemodynamic monitoring may be appropriate. General critical care principles suggest that appropriate therapeutic goals are adequate blood pressures and adequate oxygen delivery. However, the definition of “adequate” is elusive. Reasonable interventions for vasodilatory shock with low central venous pressure include fluid resuscitation and vasoactive infusions. Appropriate considerations for left ventricular myocardial dysfunction include euvoolemia, inotropic infusions, and afterload reduction.

## NEUROMONITORING

Continuous neuromonitoring and goal-directed intervention following cardiac arrest is an exciting frontier with great promise in improving neurologic outcomes post–cardiac arrest.<sup>224</sup> Continuous electroencephalogram (cEEG) monitoring is an increasingly instituted modality for neuromonitoring of critically ill patients, especially to diagnose nonconvulsive seizures (NCS) and seizures in patient’s receiving muscle relaxants. cEEG monitoring is noninvasive, performed at the bedside, and permits continuous assessment of cortical function. Interpretation of continuous electroencephalogram (EEG) is usually performed by a neurologist from a remote location, and not bedside critical care physicians. However, advances in quantitative EEG tools may allow bedside caregivers to identify important electrographic events, such as seizures or abrupt background changes, to potentially permit real-time analysis and intervention.<sup>225</sup> In a prospective study of cEEG in children, NCS were detected in 39% (12 of 31) children following cardiac arrest.<sup>226</sup> In a partially overlapping cohort of 19 children, NCS were common in children undergoing therapeutic hypothermia after cardiac arrest.<sup>226</sup> NCS seems to be a common occurrence following cardiac arrests in children. Although the relationship of NCS to worse outcomes has not been established in pediatric patients following cardiac arrest, it has been associated with worse outcomes among critically ill adults and neonates.<sup>227–233</sup> We believe that cEEG should be considered for children post–cardiac arrest and that patients with NCS (especially status epilepticus with NCS) should be treated with anticonvulsant medication. Further study is warranted to better establish frequency of NCS and potential benefit in outcomes with anticonvulsant therapy.

Oxidative injury may be greatest in the early phases of post–resuscitation therapy following cardiac arrest.<sup>234</sup> Interestingly, the use of 100% oxygen (compared with room air) during and immediately following resuscitation

in animal models may potentiate oxidative injury to key mitochondrial enzymes (pyruvate dehydrogenase or manganese superoxide) or mitochondrial lipids (cardiolipin), and is associated with worse neurologic outcomes.<sup>235–238</sup> Experimental protocols in large animals using peripheral pulse-oximetry to titrate oxygenation in the post–resuscitation phase can reduce post–resuscitation hyperoxia and significantly improve neuropathology and neurobehavioral outcomes.<sup>239</sup> Consistent with these experimental findings, arterial hyperoxia ( $\text{PaO}_2 \geq 300 \text{ mm Hg}$ ) was independently associated with in-hospital mortality compared with either hypoxia or normoxia in an observational study among critically ill adult patients admitted to the ICU within 24 hours of a cardiac arrest.<sup>240</sup> We believe it is prudent to titrate oxygenation during and following pediatric cardiac arrest. Although the optimal  $\text{SpO}_2$  is not known, we recommend titration of  $\text{FiO}_2$  to the lowest amount necessary to assure  $\text{SpO}_2 > 94\%$ . Perhaps the future of post–arrest care will include more aggressive neurocritical care monitoring, such as near infrared spectroscopy, cerebral microdialysis,  $\text{PbtO}_2$ , CBF, and even bedside analysis of mitochondrial dysfunction.

## QUALITY OF CARDIOPULMONARY RESUSCITATION

Despite evidence-based guidelines, extensive provider training, and provider credentialing in resuscitation medicine, the quality of CPR is typically poor. CPR guidelines recommend target values for selected CPR parameters related to rate and depth of chest compressions and ventilations, avoidance of CPR-free intervals, and complete release of sternal pressure between compressions.<sup>241</sup> Slow compression rates, inadequate depth of compression, and substantial pauses are the norm. An approach to *Push Hard, Push Fast, Minimize Interruptions, Allow Full Chest Recoil, and Don’t Overventilate* can markedly improve myocardial, cerebral, and systemic perfusion, and will likely improve outcomes.<sup>131</sup> Quality of post–resuscitative management has also been demonstrated to be critically important to improve resuscitation survival outcomes.<sup>213</sup> Measuring the quality of CPR and avoiding overventilation during cardiac arrest resuscitation have recently been reemphasized by consensus of the International Liaison Committee on Resuscitation and the AHA.<sup>242</sup> Although the correct amount, timing, intensity, and duration of ventilation that is required during CPR is controversial, there is no controversy that measurement and titration of the amount of ventilation to the amount of blood perfusion are desirable. Thus additional technology that is safe, accurate, and practical would improve detection and feedback of the “quality of CPR.”

Recent technology has been developed that monitors quality of CPR by force sensors and accelerometers, and can provide verbal feedback to the CPR administrator regarding the frequency and depth of chest compressions and the volume of ventilations. Recent pediatric data illustrates that intensive training and real-time corrective feedback can help chest compression quality approach age-specific AHA CPR guideline targets.<sup>243–245</sup> Moreover, improvements in post–resuscitation care can improve resuscitation survival outcomes.<sup>213</sup>

## EXTRACORPOREAL MEMBRANE OXYGENATION-CARDIOPULMONARY RESUSCITATION

The use of extracorporeal membrane life-saving (ECLS) devices as a rescue therapy for refractory cardiac arrest (ECPR) is an exciting topic in resuscitation science. In children with medical or surgical cardiac diseases, ECPR has been shown to improve survival to hospital discharge<sup>246</sup> and can be effective after even greater than 50 minutes of CPR.<sup>247</sup> However, at this time, observational data has not consistently demonstrated a survival benefit of ECPR compared with conventional CPR across broad populations.<sup>248,249</sup> Children with primary cardiac disease may have a survival advantage, due to these disease processes being amenable to a bridge with ECLS—whether to recovery, surgery, or transplantation. There may be an underlying advantage for these patients as well, stemming from predominantly single-organ failure compared with patients with noncardiac etiologies of cardiac arrest, allowing for a greater chance of full recovery after resuscitation.<sup>250</sup> Importantly, in these observational studies, ECPR is used as a rescue therapy in patients who likely would have died with continued conventional resuscitation efforts.<sup>250</sup> In fact, in a GWTG-R study that looked at both cardiac and noncardiac patients with greater than 10 minutes of CPR, those who received ECPR had improved survival and favorable neurologic outcome at discharge.<sup>251</sup> A lack of survival advantage, even when controlling for confounding factors, is flawed by the nature of these studies.<sup>252</sup> In the absence of randomized controlled trials that specifically compare early initiation of ECPR and conventional CPR, it is probably reasonable to consider ECPR as a rescue therapy in patients with potentially reversible underlying disease processes. However, as noted in PALS guidelines, any reasonable chance of success requires a setting with “existing ECMO protocols, expertise, and equipment,”<sup>253</sup> and dedicated teams that train for efficient cannulation under difficult circumstances. Therefore, timely, quality E-CPR may be an exciting adjuvant to conventional CPR for pediatric patients. Future frontiers will define patient populations and optimize the clinical approach to extracorporeal support; however, clinicians providing CPR should consider E-CPR early in the course of a resuscitation not responding to conventional CPR. Perhaps after failure to attain ROSC within 5 minutes, clinicians should ask themselves: (1) does the patient have a potentially reversible process, (2) would ECMO be a “bridge” to a potentially good outcome, and (3) do we have the personnel and resources to provide ECMO promptly? If the answer to all three are “yes,” prompt implementation of E-CPR should be considered. We believe that patients arriving with a witnessed arrest with immediate initiation of CPR and evidence of quality CPR should be considered E-CPR candidates.

## Ventricular Fibrillation and Ventricular Tachycardia in Children

Pediatric VF, or VT, has been an underappreciated pediatric problem. Recent studies indicate that VF and VT (i.e., shockable rhythms) occur in 27% of in-hospital cardiac arrests

at some time during the resuscitation.<sup>254</sup> In a population of pediatric cardiac ICU patients, as many as 41% of arrests were associated with VF or VT.<sup>255</sup> According to the National Registry of Cardiopulmonary Resuscitation (NRCPR) database, 10% of children with in-hospital cardiac arrest had an initial rhythm of VF/VT. In all, 27% of the children had VF/VT at some time during the resuscitation.<sup>254</sup> The incidence of VF varies by setting and age.<sup>256</sup> In special circumstances, such as tricyclic antidepressant overdose, cardiomyopathy, post–cardiac surgery, and prolonged QT syndromes, VF and pulseless VT are more likely. The treatment of choice for short-duration VF is prompt defibrillation. In general, the mortality rate increases by 7% to 10% per minute of delay to defibrillation. Because VF must be considered before defibrillation can be provided, early determination of the rhythm by ECG is critical. An attitude that VF is rare in children can be a self-fulfilling prophecy with a uniformly fatal outcome. The recommended defibrillation dose is 2 J/kg, but the data supporting this recommendation are not optimal and are based on old monophasic defibrillators. In the mid-1970s, authoritative sources recommended starting doses of 60 to 200 J for all children. Because of concerns for myocardial damage and animal data suggesting that shock doses ranging from 0.5 to 1 J/kg were adequate for defibrillation in a variety of species, Gutgesell et al. evaluated the efficacy of their strategy to defibrillate with 2 J/kg monophasic shocks.<sup>257</sup> Seventy-one transthoracic defibrillations in 27 children were evaluated. Shocks within 10 J of 2 J/kg resulted in successful defibrillation (i.e., termination of fibrillation) in 91% of defibrillation attempts. More recent data demonstrate that an initial shock dose of 2 J/kg terminates fibrillation in less than 60% of children, suggesting that a higher dose may be needed.<sup>93,258-260</sup> Interestingly, retrospective observational NRCPR data demonstrate that higher initial doses of 4 J/kg were associated with worse short-term survival (i.e., immediate survival of the cardiac arrest event with a spontaneous rhythm). Despite 5 decades of clinical experience with pediatric defibrillation, the optimal dose remains unknown.

## ANTIARRHYTHMIC MEDICATIONS: LIDOCAINE AND AMIODARONE

Administration of antiarrhythmic medications should never delay administration of shocks to a patient with VF. However, after an unsuccessful attempt at electrical defibrillation, medications to increase the effectiveness of defibrillation should be considered. Epinephrine is the current first-line medication for both pediatric and adult patients in VF. If epinephrine and a subsequent repeat attempt to defibrillate are unsuccessful, lidocaine or amiodarone should be considered.

Lidocaine traditionally has been recommended for shock-resistant VF in adults and children. However, only amiodarone improved survival to hospital admission in the setting of shock-resistant VF compared with placebo.<sup>261</sup> In another study of shock-resistant out-of-hospital VF, patients receiving amiodarone had a higher rate of survival to hospital admission than patients receiving lidocaine.<sup>262</sup> Neither study included children. Because there is moderate experience with amiodarone use as an antiarrhythmic agent in children and because of the adult studies, it is rational to use amiodarone similarly in children with shock-resistant VF/VT.

The recommended dosage is 5 mg/kg by rapid IV bolus. There are no published comparisons of antiarrhythmic medications for pediatric refractory VF. Although extrapolation of adult data and electrophysiologic mechanistic information suggest that amiodarone may be preferable for pediatric shock-resistant VF, the optimal choice is not clear.

## PEDIATRIC AUTOMATED EXTERNAL DEFIBRILLATORS

Automated external defibrillators (AEDs) have improved adult survival from VF.<sup>263,264</sup> AEDs are recommended for use in children 8 years or older with cardiac arrest.<sup>157,265</sup> The available data suggest that some AEDs can accurately diagnose VF in children of all ages, but many AEDs are limited because the defibrillation pads and energy dosage are geared for adults. Adapters having smaller defibrillation pads that dampen the amount of energy delivered have been developed as attachments to adult AEDs, allowing their use in children. However, it is important that the AED diagnostic algorithm is sensitive and specific for pediatric VF and VT. The diagnostic algorithms from several AED manufacturers have been tested for such sensitivity and specificity and therefore can be reasonably used in younger children.

## WHEN SHOULD CARDIOPULMONARY RESUSCITATION BE DISCONTINUED?

Several factors determine the likelihood of survival after cardiac arrest including the mechanism of the arrest (e.g., traumatic, asphyxial, progression from circulatory shock), location (e.g., in-hospital or out-of-hospital), response (i.e., witnessed or unwitnessed, with or without bystander CPR), underlying pathophysiology (i.e. cardiomyopathy, congenital defect, drug toxicity or metabolic derangement), and the potential reversibility of underlying diseases. These factors should all be considered before deciding to terminate resuscitative efforts. Continuation of CPR has been traditionally considered futile beyond 15 minutes of CPR or when more than 2 doses of epinephrine are needed.<sup>266</sup> Presumably in part because of improvements in CPR quality and post-resuscitation care, improved outcomes from in-hospital CPR efforts beyond 15 minutes or 2 doses of epinephrine are increasingly the norm.<sup>83,86</sup> The potential for excellent outcomes despite prolonged CPR has been highlighted by the ECPR data noted above.<sup>267-271</sup> Conversely, the decision to discontinue CPR prematurely is final and cannot be rescinded. In the first decade of the 21st century, there is no simple answer to the important clinical question: when should CPR be discontinued?

## Respiratory System

### STRUCTURAL AND FUNCTIONAL DEVELOPMENT: AGE-DEPENDENT VARIABLES

#### Airways and Alveoli

The lungs appear in the fourth to eighth weeks of gestation. At this time, the lung buds divide into the mainstem

bronchi; by 6 weeks all subsegmental bronchi are present; and by 16 weeks, the number of airway generations is similar to that of adults. When airway development is complete, the terminal airways remodel and multiply to form a cluster of large saccules, or alveolar precursors, that can support gas exchange. True alveoli appear before and after birth, and the respiratory saccules are thin and septate during postnatal growth.

At birth, children have approximately 24 million alveoli; by 8 years of age, the number has increased to 300 million (Table 79.5). After that, further lung growth is primarily the result of increased alveolar size. There is less elastic tissue in the neonatal lung than in the lungs of adults, and the elastin extends only to the alveolar duct. By 18 years of age, elastin extends to the alveolus and is at its maximum. It then slowly decreases over the next 5 decades. Lung compliance is integrally related to the amount of elastin; hence, compliance peaks in adolescence. It is lower in the very young and the very old. Airways close in the tidal volume range until about 5 years of age.

#### Pulmonary Circulation

The main axial arteries of the lungs are present at 14 weeks' gestation. By 20 weeks' gestation, the pattern of branching is similar to that of adults, and collateral supernumerary vessels are present. During fetal life, additional arteries develop to accompany the respiratory airways and saccules. Bronchial arteries appear between the 9th and 12th weeks of gestation. The arterial wall develops a fine elastic lamina by 12 weeks' gestation, and muscle cells are present as early as 14 weeks of gestation. By 19 weeks, the elastic tissue extends to the seventh generation of arterial branching, and muscularization extends distally. In the fetus, muscularization of the arteries ends at a more proximal level than in children and adults. The muscularized arteries have thicker walls than arteries of similar size in adults. The pulmonary arteries are actively constricted until the latter part of gestation. In the fetal lamb, pulmonary blood flow is only 3.5% of the combined ventricular output at 0.4 to 0.7 of gestation and is just 7% near term. Immediately after birth, pulmonary blood flow increases to near adult levels. Development of the pulmonary venous system mirrors that of the arterial system. The pulmonary arteries continue to develop after birth; new artery formation follows airway branching up to about 19 months of age, and supernumerary arteries continue to grow until 8 years of age. As alveolar size increases, the acinar branching pattern becomes more extensive and complex. The arterial structure also changes as preexisting arteries increase in size; the thickness of the muscular arteries decreases to adult levels during the first year of life.

#### Biochemical Development

By 24 weeks of gestation, the alveolar cuboidal epithelium flattens, and type I pneumocytes become the lining and supporting cells for the alveoli. The larger type II cells, which manufacture and store surfactant, also develop at this time. Surfactant initially appears at 23 to 24 weeks' gestation in humans and increases in concentration during the last 10 weeks of gestational life.<sup>68</sup> Surfactant is released into the alveoli at about 36 weeks' gestation, thus making normal extrauterine life possible.

**TABLE 79.5** Age-dependent Respiratory Variables: Normal Values

	<b>Newborn</b>	<b>6 months</b>	<b>12 months</b>	<b>3 years</b>	<b>5 years</b>	<b>12 years</b>	<b>Adult</b>
Respiratory rate (breaths/min)	50 ± 10	30 ± 5	24 ± 6	24 ± 6	23 ± 5	18 ± 5	12 ± 3
Tidal volume (mL)	21	45	78	112	270	480	575
Minute ventilation (L/min)	1.05	1.35	1.78	2.46	5.5	6.2	6.4
Alveolar ventilation (mL/min)	385	—	1245	1760	1800	3000	3100
Dead space–tidal volume ratio	0.3	0.3	0.3	0.3	0.3	0.3	0.3
Oxygen consumption (mL/kg/min)	6 ± 1.0	5 ± 0.9	5.2 ± 0.9	—	6.0 ± 1.1	3.3 ± 0.6	3.4 ± 0.6
Vital capacity (mL)	120	—	—	870	1160	3100	4000
Functional residual capacity (mL)	80	—	—	490	680	1970	3000
Total lung capacity (mL)	160	—	—	1100	1500	4000	6000
Closing volume as percentage of vital capacity	—	—	—	—	20	8	4
Number of alveoli (saccules) × 10 <sup>6</sup>	30	112	129	257	280	—	300
Specific compliance: CL/FRC (mL/cm H <sub>2</sub> O/L)	0.04	0.038	—	—	0.06	—	0.05
Specific conductance of small airways (mL/s/cm H <sub>2</sub> O/g)	0.02	—	3.1	1.7	0.12	8.2	13.4
Hematocrit	55 ± 7	37 ± 3	35 ± 2.5	40 ± 3	40 ± 2	42 ± 2	43-48
pH <sub>a</sub>	7.30 ± 7.40	—	7.35-7.45	—	—	—	7.35-7.45
PaCO <sub>2</sub> (mm Hg)	30-35	—	30-40	—	—	—	30-40
PaO <sub>2</sub> (mm Hg)	60-90	—	80-100	—	—	—	80-100

From O'Rourke PP, Crone RK. The respiratory system. In: Gregory G, ed. *Pediatric Anesthesia*. 2nd ed. New York: Churchill Livingstone; 1989:63.

### Respiratory Transition: Placenta to Lung

By approximately 24 weeks' gestation, the lungs are capable of extrauterine gas exchange. However, several important circulatory and mechanical changes must occur immediately after birth for pulmonary gas exchange to be adequate. Ventilation begins to match perfusion within the first hours of life. Initially, there is right-to-left intrapulmonary shunting through atelectatic areas of the lung, as well as left-to-right shunting through the ductus arteriosus and some right-to-left shunting through the foramen ovale. The resultant PaO<sub>2</sub> of 50 to 70 mm Hg indicates a right-to-left shunt that is three times that of normal adults. Transition from fetal to neonatal respiration and circulation is dynamic. Postnatally, the pulmonary vascular bed remains constricted if it is exposed to acidosis, cold, or hypoxia. If pulmonary artery constriction occurs, right-to-left shunting of desaturated blood through the foramen ovale and ductus arteriosus increases and consequently reduces pulmonary blood flow. Maintenance of this active pulmonary vasoconstriction is called persistent pulmonary hypertension of the newborn or persistent fetal circulation.

### Mechanics of Breathing

For ventilation of the lungs, the respiratory muscles must overcome the lung's static-elastic and dynamic-resistive

forces. Changes in these opposing forces during postnatal development affect lung volume, the pattern of respiration, and the work of breathing.

### Lung Compliance Versus Age

Lung compliance changes with age because of the changing alveolar structure, amount of elastin, and amount of surfactant. At birth, compliance is low because alveolar precursors have thick walls and decreased amounts of elastin. A deficiency of surfactant (e.g., hyaline membrane disease) further decreases lung compliance. The improved lung compliance occurring over the first years of life is the result of continued development of alveoli and elastin.

### Chest Wall

The chest wall of infants is very compliant because their ribs are cartilaginous. Because of the box-like configuration of an infant thorax, there is less elastic recoil than there is with the dorsoventrally flattened thoracic cage of adults. Adults have a high proportion of slow-twitch, high-oxidative, fatigue-resistant fibers in their diaphragm and intercostal muscles. Whereas adults have 65% of these fibers in the intercostal muscles and 60% in the diaphragmatic muscles, neonates have only 19% to 46% of these

fibers in their intercostal muscles and 10% to 25% in the diaphragm.<sup>70</sup> Consequently, infants are more vulnerable to muscle fatigue and decreased stability of the chest wall. The net effect of the compliant chest wall and the poorly compliant lungs is alveolar collapse and lower resting lung volume (FRC). Despite this tendency for lung collapse, a child maintains a large dynamic FRC via rapid RRs, laryngeal breaking, and stabilization of the chest wall with increased intercostal tone during exhalation.

### Upper Airway

The upper airways of children and adults have several anatomic differences that affect their ability to maintain a patent airway. The more anterior and cephalad position of the larynx in children makes the “sniffing position” ideal for mask ventilation and endotracheal intubation. Extreme neck extension can actually obstruct the airway. The narrowest part of the adult airway is the vocal cords. Up to the age of 5 years, the narrowest portion of a child’s airway is at the cricoid cartilage, because the posterior larynx is positioned more cephalad than the anterior larynx, which causes the cricoid ring to be an ellipse rather than a circle. By 5 years of age, the posterior larynx has descended to the adult level.<sup>272</sup> An ETT that passes easily through the vocal cords of a young child may cause ischemic damage to the distal airway. The cricoid narrowing and very pliant tracheal cartilage provide an adequate seal around an uncuffed ETT. Children younger than 5 years rarely require a cuffed ETT, although some practitioners use cuffed tubes regularly in these patients.<sup>273</sup>

### Closing Capacity

The elastic properties of the lung closely correlate with closing capacity. Closing volume is the lung volume at which the terminal airways close and gas is trapped behind the closed airways. Large closing volumes increase dead space ventilation, which leads to atelectasis and right-to-left shunting of blood. Elastic tissues help keep the airways open, so the greater the elastic stroma in the small airways, the lower the lung volume required to close small, noncartilaginous airways. Closing volume is small in late adolescence and relatively large in the elderly and the very young. Children overcome the complications of large closing volumes and secondary atelectasis by breathing rapidly, by constant activity, and by crying. Closing volume becomes a significant problem in infants who are inactive, sedated, or anesthetized.

### Resistive Forces

Neonates have small airways with high resistance or low conductance (conductance = 1/resistance). The diameter of the small airways does not significantly increase until about 5 years of age; hence, young children have elevated airway resistance at baseline and are particularly vulnerable to diseases that cause further narrowing of the airways (i.e., smooth muscle constriction, airway edema/inflammation). The normal high airway resistance of neonates and young children helps maintain FRC.

### Control of Breathing

The newborn’s respiratory control is unique. Hypoxia initially increases ventilation for a short time. This increase

is followed by a sustained decrease in ventilation.<sup>77</sup> The response is more exaggerated in preterm neonates. In full-term infants, it disappears after several weeks. Periodic breathing is also more common in infants, particularly preterm infants, and is probably due to inadequate development of the medullary respiratory centers.

### Oxygen Transport: Oxygen Loading and Unloading

Fetal hemoglobin has low levels of 2,3-diphosphoglycerate and an oxygen half-saturation pressure of hemoglobin (P<sub>50</sub>) of 18 mm Hg, which is much lower than the 27 mm Hg in adults. This lower P<sub>50</sub> allows the fetus to load more oxygen at low placental oxygen tension, but it makes unloading oxygen in tissues more difficult. Three to 6 months after birth, fetal hemoglobin has been replaced with adult hemoglobin. The increased oxygen content of fetal hemoglobin and the increased fetal hemoglobin concentration are advantageous to the fetus because it allows an oxygen content of 20 mL of oxygen/100 mL of blood to be delivered to the brain and heart. This is the same oxygen content that adults have when breathing room air. The oxygen concentration of neonates at birth is 6 to 8 mL/kg/min. It decreases to 5 to 6 mL/kg/min over the first year of life. The decreased ventilation-perfusion ratio, the decreased P<sup>63</sup> of fetal hemoglobin, and the progressive anemia characteristic of infants can make it difficult to deliver adequate oxygen during the first few months of life. Infants compensate by having a cardiac output of approximately 250 mL/kg/min for the first 4 to 5 months of life.

## RESPIRATORY FAILURE

Respiratory failure is the inability of the lungs to adequately oxygenate and remove CO<sub>2</sub> from pulmonary arterial blood. There are many causes of respiratory failure, including a low environmental oxygen concentration, parenchymal lung disease, and pulmonary vascular disease. A complete history of the severity and chronicity of the respiratory problem helps formulate a differential diagnosis and an approach to treatment. Specific data should include a history of prematurity, previous airway instrumentation, previous mechanical ventilation, nonpulmonary organ dysfunction, and a family history of respiratory disease. A detailed feeding history and up-to-date growth chart may provide valuable information because growth failure may increase the need for oxygen. Usually, 1% to 2% of the total oxygen consumed is used for breathing. During respiratory illnesses, as much as 50% of the total oxygen consumption may be used for breathing. Infants and children with respiratory failure often have intercostal and suprasternal retractions, signs that the work of breathing and oxygen consumption are increased. Patients grunt during expiration in an attempt to maintain FRC. Most infants and children have tachypnea, which also helps maintain FRC by decreasing the time for exhalation. Less energy is required to breath rapidly and shallowly than to take deep breaths. Infants with respiratory failure often have cyanotic lips, skin, and mucous membranes. However, it is often difficult to recognize skin color changes unless the PaO<sub>2</sub> is below 70 mm Hg. Symmetry of chest movement should be noted. Differences in movement may indicate pneumothorax or

blockage of a bronchus. The small thoracic volume allows easy transmission of breath sounds from one side to the other. Breath sound may be normal, even when pneumothorax is present. Abdominal distention can dramatically impede breathing in infants and young children.

## MONITORING OF RESPIRATORY FUNCTION

An arterial blood gas is considered the gold standard to measure oxygenation, as  $\text{PaO}_2$  is measured directly from blood. The percent oxygen saturation of hemoglobin can be measured directly or calculated from  $\text{PaO}_2$ , pH,  $\text{PaCO}_2$ , and temperature. Venous and capillary blood gases do not predict  $\text{PaO}_2$ . Use of arterial lines has decreased in pediatric ICUs over time.<sup>274</sup> Pulse oximeters are ubiquitous. Pulse oximeters can provide continuous estimations of  $\text{SaO}_2$  when the saturation is less than 97%. This is due to the shape of the oxygen dissociation curve. Pulse oximeters pass at least two wavelengths of light through the patient and the change in the absorbance of light is compared with an algorithm that produces the oxygen saturation. In the saturation range of 91 to 97%, pulse oximeters have been shown to read higher than measured arterial saturations by approximately 1%.<sup>275</sup> However, in the saturation range of 76% to 90%, pulse oximeters read higher than measured arterial saturations by approximately 5% with very wide confidence intervals.<sup>275</sup> Pulse oximeters may also have poorer performance when there is decreased perfusion to the extremity with the sensor. Lastly, most pulse oximeters have difficulty detecting abnormal forms of hemoglobin, such as methemoglobin or carboxyhemoglobin, and will produce erroneous results in their presence.

Umbilical artery cannulation is common in neonates, so those caring for such children can obtain arterial blood and continuously measure arterial blood pressure. These catheters are relatively simple to insert and reasonably easy to maintain.<sup>276-278</sup> The tip of the catheter ideally should be at or just above the level of the aortic bifurcation and below the level of the renal arteries (L2). Once the child's condition is stable, a peripheral artery catheter should be inserted and the umbilical artery catheter should be removed. All intraarterial catheters have the potential to cause distal thromboembolic disease. Care must be taken to flush arterial catheters gently to prevent cerebral or cardiac emboli. With proper insertion and maintenance, serious complications of arterial lines are rare. They have been shown to be relatively safe for short term use.<sup>279</sup> Although arteries that are cannulated for a long time may develop thrombosis in a small study by Ergaz et al. all of the infants that developed thrombosis had spontaneous resolution with sequela.<sup>280</sup>

$\text{PaCO}_2$  is used as a measure of ventilation. An arterial blood gas may be the gold standard,  $\text{PaCO}_2$  obtained from capillary or venous blood gases can provide valuable information.  $\text{CO}_2$  values obtained from capnography or transcutaneous  $\text{CO}_2$  (TCOM) can provide continuous information in a manner similar to pulse oximeters.<sup>281</sup> Capnographs produce a waveform displaying exhaled  $\text{CO}_2$  that can be either time-based or volumetric. Time-based capnography is much more common. Capnographs can either be an aspirating or nonaspirating system. An aspirating system takes gas from the ventilator circuit and measure the  $\text{CO}_2$ . A nonaspirating system has an exhalation chamber placed in

line with the ventilator circuit. The system uses an infrared light source and detector which measures the exhaled  $\text{CO}_2$ . There is a great amount of information that can come from capnography, including the end-tidal  $\text{CO}_2$  (ET $\text{CO}_2$ ) value, RR, dead space calculations, cardiac output, and detection of obstruction of the airways.

For time-based capnography, the plateau of the slope will always be lower than  $\text{PaCO}_2$ . Elevations in ET $\text{CO}_2$  must be investigated as they signal a change in ventilation. For individuals with healthy lungs, this ET $\text{CO}_2$  to  $\text{PaCO}_2$  gradient is usually 2 to 5 mm Hg. The gradient increases with increased dead space, abnormalities in the pulmonary vasculature, decreased cardiac output, and pulmonary over distension. ET $\text{CO}_2$  from capnography can be used clinically to calculate the approximate alveolar dead space by the alveolar dead space fraction (AVDSF).  $\text{AVDSF} = (\text{PaCO}_2 - \text{ETCO}_2)/\text{PaCO}_2$ . AVDSF is a reasonable indicator of alveolar dead space<sup>282</sup> and has been shown in several pediatric patients with acute hypoxic respiratory failure to be associated with mortality.<sup>283-285</sup> Other valuable information is available from the waveform produced by time-based capnography. As an example, a rising upslope to the exhalation phase can indicate obstructive airways disease. Time-based capnography is more accurate with slower RRs and when there is a minimal leak around the ETT.

Volumetric capnography traces the  $\text{CO}_2$  concentration against the exhaled volume and is appearing as a feature on some ventilators. Free-standing monitors that provide the same measure are also available. Volumetric capnography provides direct information for dead space calculations. Clinically volumetric capnography is helpful in setting the optimal PEEP. In this way, PEEP can be titrated to balance improved oxygenation through alveolar recruitment and decreased dead space by not causing overdistension. Volumetric capnography can also be used to demonstrate a response to bronchodilator therapy.

In circumstances such as high frequency ventilation (HFV), the use of transcutaneous  $\text{CO}_2$  monitoring (TCOM) provides a continuous measure of ventilation. The TCOM module heats the skin underneath a small sensor. There is increased diffusion of  $\text{CO}_2$  across the skin as the capillary bed dilates from the heat. The diffused  $\text{CO}_2$  is then measured. When the TCOM is first set up, it should be calibrated against a capillary or arterial blood gas. There can be drift of calibration over time, but newer modules have improved stability. A recent study by Bhalla et al. demonstrated that transcutaneous  $\text{CO}_2$  monitoring provides an acceptable estimate of  $\text{PaCO}_2$ , even with low cardiac output or increased subcutaneous tissue.<sup>281</sup> In their study, it did not perform well in patients with cyanotic heart disease.

The effort of breathing with or without a ventilator can be obtained by the objective measurement value of the pressure-rate-product (PRP). The pressure measure by a balloon-tipped catheter placed into the distal third of the esophagus can be used as a surrogate for pleural pressure. The PRP is the change in esophageal pressure (Pes) multiplied by the RR.  $\text{PRP} = \text{Pes} \times \text{RR}$ . The PRP has been used as an objective measure of effort of breathing in studies: before and after extubation,<sup>286,287</sup> with PEEP and obstructed airways disease,<sup>277</sup> evaluating increasing inspiratory load;<sup>278</sup> pressure-rate product and phase angle as measures of acute inspiratory upper airway obstruction in rhesus monkeys,

evaluating effectiveness of high-flow nasal cannula,<sup>288,289</sup> and evaluating effectiveness of noninvasive ventilation (NIV) in infants.<sup>290</sup> Some ventilators can measure esophageal pressure, or it can be obtained with separate devices. We have found that the accuracy of PRP measurements is sensitive to the volume of air used to fill the esophageal catheter.<sup>291</sup> In addition to measuring the PRP, the esophageal pressure is very important in measuring the pressure across the lungs or the transpulmonary pressures. Many adult studies are appearing demonstrating the benefits of titrating ventilator settings to trans-pulmonary pressure for patients with acute respiratory distress syndrome (ARDS).<sup>292-294</sup> The transpulmonary pressure may have particular benefit in patients who are obese and requiring mechanical ventilation for respiratory failure,<sup>295-298</sup> where the decreased compliance of the chest wall may cause practitioners to limit ventilator pressures. For adult medicine, the field of esophageal pressure monitoring and the titration of mechanical ventilation to transpulmonary pressure has recently grown significantly. The need for and goals of this type of monitoring can be best summarized in a few review articles,<sup>299,300</sup> including one from the PleUral pressure working Group (PLUG-Acute Respiratory Failure section of the European Society of Intensive Care Medicine).<sup>301</sup>

The phase of breathing or the synchrony between movement of the abdomen and the chest wall can be measured with respiratory inductance plethysmography (RIP).<sup>302</sup> This noninvasive measure uses elastic bands placed around the abdomen and chest. Movement of the abdomen and chest changes the inductance of a small wire in the bands. Movement of the abdomen relative to the chest can be presented graphically or measured as the phase angle. When there is obstruction to breathing, such as with upper airway obstruction, there is a lag in the movement of the abdomen and chest wall, which is identified as an increasing phase angle. The phase angle obtained by RIP is an objective measure of the degree of upper airway obstruction<sup>278,302,303</sup> and can be used to evaluate the effectiveness of therapy.<sup>304-306</sup> This is a valuable tool for research in the area of causes and treatment of upper airway obstruction, as there is great interobserver variability in the clinician's assessment of this process.<sup>307</sup> RIP can easily be measured with free-standing devices and may have an increased role in future pediatric studies.

A great deal of information on the respiratory effort of patients receiving mechanical ventilation can be obtained from respiratory spirometry. Spirometry can display flow-volume loops, pressure-volume loops, in addition to graphs of flow-time, pressure-time, and volume-time. The characteristic shape of some respiratory flow-volume loops can help with the diagnosis of various respiratory diseases. There is a classic scooped out appearance to the exhalation portion of a flow-volume curve with obstructive lung disease. The pressure-volume loops obtained on the ventilator can be used to increase PEEP to keep lung tissue recruited above an area of potential atelectasis. This can be seen graphically as a lower inflection point on the inspiratory curve. This is where the curve moves from a flat area to an area of maximal compliance where there is the greatest change in volume for a given change in pressure. There is also an upper inflection point on pressure volume loops where overdistension of the lungs can be identified if the inspiratory pressure or volume is too great. The pressure-volume curve with

over-distension looks like a bird's beak and ventilator settings should be reduced.

There are multiple noninvasive techniques that can provide additional information on the patient's respiratory status. Radiologic evaluation of the nasopharynx, neck, and thorax can provide meaningful information regarding the cause and severity of the respiratory dysfunction. Fluoroscopy can be used to evaluate the airways and movement of the diaphragm in an uncooperative child. Electrical impedance tomography (EIT) is a noninvasive technique that does not use ionizing radiation that can provide information on regional lung ventilation. The technique uses electrodes placed on the chest wall to measure the electrical conductivity and impedance of the lung to form a tomographic image. The images are used to determine which areas of the lungs have atelectasis, normal ventilation, or overdistension. At the moment, there is much more adult data showing uses of and management strategies with EIT,<sup>308-311</sup> as compared with pediatrics.<sup>312-314</sup> However, as more companies produce the machines and more adult manuscripts are published, we expect there will be an increased use of EIT in pediatric mechanical ventilation monitoring. Finally, there is a rapid growth of point of care ultrasound use in pediatrics. This has multiple benefits for the patient, as it can be provided at the bedside and does not use ionizing radiation. Lung ultrasound offers the ability to identify pneumothorax, alveolar consolidation, pneumonia, atelectasis, pulmonary edema, pleural effusions, and diaphragm movements and thickness. There are an increasing number of pediatric manuscripts identifying the benefits of lung ultrasound.<sup>315-318</sup> In the near future, ultrasound diaphragm thickness and how it changes over time may be used to guide mechanical ventilation strategies and help predict extubation success.<sup>319-322</sup>

## RESPIRATORY FAILURE

The cause of respiratory failure depends to some degree on the age of the patient. Newborn respiratory failure is often the result of congenital anomalies and immaturity of the lungs and their blood vessels. Congenital anomalies can include airway malformations, dysgenesis or malfunction of the lung or nonpulmonary organs, and abnormalities of the pulmonary vessels. Lesions of immaturity include apnea of prematurity, hyaline membrane disease, and abnormalities of surfactant production and secretion. During the perinatal period, neonates are subject to infections and stress. Persistent pulmonary hypertension can complicate neonatal pulmonary and nonpulmonary problems. These and other important causes of respiratory failure in the newborn are listed in Table 79.6. A wide variety of disorders cause respiratory failure in older children (Box 79.3). Regardless of the specific cause, respiratory failure can be categorized as hypoventilation syndromes in patients with normal lungs, intrinsic alveolar and interstitial disease, and obstructive airway disease.

## HYPVENTILATION SYNDROMES IN CHILDREN WITH NORMAL LUNGS

Causes of hypoventilation include neuromuscular disease, central hypoventilation, and structural/anatomic impairment of lung expansion (i.e., upper airway obstruction,

**TABLE 79.6** Causes of Neonatal Respiratory Distress

Location	Congenital Abnormalities	Developmental Immaturity	Specific Neonatal Stress
Impaired control of ventilation	Central nervous system dysgenesis Ondine's curse	Apnea of prematurity Intracranial hemorrhage	Drug intoxication (note maternal drugs) Sepsis Central nervous system infection Seizures
Neuromuscular disorders	Congenital myopathies		High cervical cord injuries
Structural impairment	Thoracic deformities Lung hypoplasia Diaphragmatic hernia Potter syndrome Abdominal malfunction Gastroschisis Omphalocele		Severe abdominal distention Pneumothorax or other leak
Airway obstruction	Choanal atresia		Massive meconium aspiration
Upper airway	Pierre Robin syndrome Laryngeal web/cleft Congenital tracheal/laryngeal stenosis Recurrent laryngeal palsy Hemangioma Lymphangioma		Vocal cord paralysis is secondary to myelodysplasia
Lower airway	Tracheoesophageal fistula Lobar emphysema		Meconium/blood aspiration
Alveolar disorders		Respiratory distress syndrome	Bronchopulmonary dysplasia

massive abdominal distention). These clinical conditions are characterized by inadequate lung expansion, secondary atelectasis, intrapulmonary right-to-left shunting, and systemic hypoxia. Atelectasis and the secondary reduction in FRC increase the work of breathing. The child's response to the increased work of breathing and lower lung volumes is to breathe faster with a smaller tidal volume. This pattern of breathing eventually increases the amount of atelectasis and shunting. As a result, children with intrinsically normal lungs and hypoventilation syndromes exhibit tachypnea, small tidal volumes, increased work of breathing, and cyanosis. Chest radiographs reveal small lung volumes and miliary or lobar atelectasis. Positive-pressure ventilation and PEEP quickly reverse the pathologic processes.

### Primary Pulmonary Alveolar or Interstitial Disorders

Intrinsic lung disease involving the alveoli or pulmonary interstitium decreases lung compliance and increases airway closure, both of which cause atelectasis and increase the work of breathing. Edema or inflammation of the alveoli or fibrosis of the interstitium decreases lung compliance. The stiffer lung requires a greater negative intrapleural pressure for air movement, thereby increasing the work of breathing and the risk for pneumothorax.

### Obstructive Airway Disease

Airway obstruction can be extrinsic or intrinsic. Intrinsic small airway obstruction commonly occurs with bronchiolitis, bronchopneumonia, asthma, and bronchopulmonary dysplasia (BPD). Airway obstruction decreases conductance and increases airway resistance and the work of breathing. Partial obstruction impedes expiration more than inspiration and causes gas trapping or regional emphysema. Complete airway obstruction results in atelectasis and

right-to-left shunting of blood within the lung. Patients with disease of the small airways usually have a mixture of total and partial airway obstruction and inhomogeneous collapse and overdistention of the lung. The areas of collapse cause intrapulmonary right-to-left shunting of blood, and the overdistended areas increase the amount of dead space. If the entire lung is overdistended, compliance is decreased and the work of breathing is increased. The clinical and radiographic picture varies with the different degrees of collapse and overdistention of the lung. In summary, all causes of respiratory failure share similar pathophysiology: atelectasis and decreased FRC with intrapulmonary right-to-left shunting of blood or alveolar overdistention with increased dead space and decreased CO<sub>2</sub> elimination, or both. The increased work of breathing associated with all forms of respiratory dysfunction can cause fatigue and a breathing pattern that further complicates the initial process. It may also lead to apnea, hypoxia, and cardiac arrest in young children if the increased work of breathing is not quickly detected and treated.

### RESPIRATORY CARE

A patient's FiO<sub>2</sub> can be increased by a number of means including nasal cannula or mask. The FiO<sub>2</sub> can be increased up to approximately 40% with nasal cannula oxygen at 5 L flow/min. However, this high rate of flow can become uncomfortable. As room air is entrained around the cannula during inspiration the FiO<sub>2</sub> cannot be increased further with nasal cannula. It should be noted that the size of the patient correlates with the inspiratory volume with each breath. The larger the patient, the greater inspiratory volume is relative to flow from the cannula and the greater volume of room air that is entrained. In turn, the smaller a patient the less room air is entrained and there may be a greater impact on FiO<sub>2</sub>.

### BOX 79.3 Causes of Respiratory Failure in Children

1. Impaired control of ventilation
  - Head trauma
  - Intracranial hemorrhage
  - Increase intracranial pressure secondary to tumor, edema, hydrocephalus, Reye syndrome
  - Central nervous system infections
  - Drug intoxication
  - Status epilepticus
2. Neuromuscular disorders
  - High cervical cord injury
  - Poliomyelitis
  - Guillain-Barré syndrome
  - Neurodegenerative disease (e.g., Werdnig-Hoffman syndrome)
  - Muscular dystrophies and myopathies
  - Myasthenia gravis
  - Botulism
  - Tetanus
  - Phrenic nerve injury
3. Structural impairment
  - Severe kyphoscoliosis
  - Flail chest
  - Large intrathoracic tumor
  - Pneumothorax or pneumomediastinum
  - Large pleural effusion, hemothorax, empyema
  - Severe abdominal distention
  - Severe obesity (pickwickian syndrome)
4. Airway obstruction
  - Upper airway
  - Congenital anomalies
  - Tumor, intrinsic or extrinsic
  - Epiglottitis
  - Croup (laryngotracheobronchitis)
  - Foreign body
  - Postintubation edema, granulation tissue, or scarring
  - Vocal cord paralysis
  - Burns
  - Vascular ring
  - Lower airway
  - Asthma
  - Bronchiolitis
  - Foreign body
  - Lobar emphysema
  - Cystic fibrosis
5. Alveolar disorders, pneumonia
  - Infectious: bacteria, virus, fungus, *Pneumocystis* species
  - Chemical: aspiration, hydrocarbon, smoke inhalation
  - Pulmonary edema: cardiogenic, near-drowning, capillary leak syndrome
6. Massive atelectasis
7. Oxygen toxicity
8. Pulmonary confusion
9. Pulmonary hemorrhage

The  $\text{FiO}_2$  can be increased further with a properly fitted face mask. The open holes of a venture or simple face mask allow for greater entrainment of room air as compared with a non-rebreather face mask that has no holes. A  $\text{FiO}_2$  approaching 1.0 can be obtained with a non-rebreather face mask with an oxygen reservoir and one-way valve. Patients with respiratory distress while on the pediatric ward may temporarily require a non-rebreather mask at high flows. If there is no significant improvement to immediate interventions, arrangements should be made to transfer the patient to the PICU. Non-rebreathing mask systems can be humidified for comfort, but they don't provide any positive pressure to the airways.

High flow humidified nasal cannula (HFHNC) oxygen can provide a higher  $\text{FiO}_2$  and is more easily tolerated as compared with standard nasal cannula. The gas in HFHNC is heated to body temperature and near completely humidified with water vapor. HFHNC can be delivered with flow rates in pediatrics up to 2 L/kg/min. HFHNC has been shown in a number of studies to decrease the effort of breathing in critically ill children.<sup>323-325</sup> HFHNC has been used frequently to support patients with bronchiolitis.<sup>324-328</sup> Weiler et al. demonstrated that the lowest effort of breathing for toddlers with bronchiolitis was at greater than 1.5 L/kg/min of flow.<sup>324</sup> It is unclear whether the significant benefits of HFHNC come from washing out carbon dioxide from the airways,<sup>329,330</sup> from the generation of positive pressure,<sup>331</sup> or from increases in end expiratory lung volumes.<sup>332</sup> The potential for complications exists with higher gas flow rates. Air leak syndrome was reported in three patients by Hegde et al.<sup>333</sup> As the use of HFHNC increases, other problems may be identified. Given that the amount of  $\text{FiO}_2$  delivered approaches 1.0, HFHNC outside of an ED or ICU setting should be used with caution. The high degree of respiratory support provided can mask a significant degree of respiratory distress.

However, with appropriate monitoring and protocols, it is possible to provide HFHNC on a general ward to specific populations such as stable patients with bronchiolitis. Franklin et al.<sup>326</sup> recently published a study of children younger than 12 months of age with bronchiolitis. The use of HFHNC significantly reduced the risk of escalation of care (12%) as compared with regular nasal cannula (23%).

NIV can be supplied with continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP). This is typically delivered with a tight fitting nasal or face mask that allows for the development of positive airway pressure. Most modern ventilators can be set to deliver this therapy, but specific free-standing BiPAP machines are more often used. BiPAP therapy is best for short-term use and in patients who have the ability to cough and protect their airway. It is not an absolute that the patient initiates every breath as a back-up rate can be set. However, if the patient is completely reliant on the rate set on the machine, intubation should be considered. Other indications for conversion from BiPAP to endotracheal intubation include pressure related tissue breakdown on the face from constantly wearing the mask and the need to initiate enteral feedings, as patients are typically NPO on BiPAP, increasing pressure settings on the BiPAP machine.

CPAP reduces the patient's work of breathing by providing airway pressure, reducing atelectasis, decreasing dead space, and improving the balance of ventilation to perfusion. An initial CPAP pressure is typically 4 to 6 mm Hg and is then increased as needed and as the patient tolerates the therapy. Given that the feeling of positive airway pressure is a bit foreign, starting with lower pressures and increasing gives the patient a chance to adapt. We typically start patients on CPAP therapy for several minutes even if they will ultimately receive BiPAP. For BiPAP, the expiratory

pressure is also initially at 4 to 6 mm Hg and the inspiratory pressure is set at 4 to 6 mm Hg above that. The inspiratory and expiratory pressures are adjusted, as well as the rise time to inspiratory flow. All of these changes can help the patients tolerate therapy. Given the tight seal, a  $\text{FiO}_2$  of 1.0 can be delivered. With use of the full face mask, patients are at risk for aspiration if they vomit. BiPAP therapy is being used in status asthmaticus,<sup>334,335</sup> and it may provide a more effective means of delivering aerosolized medication. The use of BiPAP therapy for this indication may increase over time as it is being recommended in current guidelines.<sup>336,337</sup> BiPAP can also be used as an ongoing therapy for chronic respiratory failure for such things as central hypoventilation or restrictive lung disease. These patients may be able to receive their therapy at home and are typically followed by the hospital's pulmonary service.

The size of ETT required should be selected carefully. One formula that estimates the appropriately sized tube for children older than 2 years is  $(\text{age} + 16)/4$ . This formula provides the internal diameter of the appropriately sized ETT. The correct size should have a slight air leak when a positive pressure of 20 to 30 cm  $\text{H}_2\text{O}$  is applied. Serious life-long laryngeal and subglottic damage can result from using inappropriately large ETTs, particularly in children with inflammatory lesions of the upper airway such as laryngotracheobronchitis. Because of the more flexible tracheal cartilage and the relative subglottic narrowing of children, uncuffed ETTs generally provide an adequate seal in those younger than 5 years. However, if the patient has lung disease that requires high ventilation pressure, a cuffed tube is more appropriate. Small cuffed ETTs are frequently used in the ICU in younger patients,<sup>338</sup> but care should be taken to ensure that there is a small leak of air at 25 to 30 cm  $\text{H}_2\text{O}$ . Cuffed tubes will usually eliminate the air leak around an ETT, but overinflation of the cuff may occlude venous flow and injure the airway. There are presently no data on the long-term safety of using cuffed ETTs in young children. However, there has been work by Khemani et al.<sup>339</sup> that showed risk factors associated with the development of postextubation subglottic upper airway obstruction included low cuff leak volume or high preextubation leak pressure. We should take care to make sure that ETT cuffs are appropriately inflated.

With endotracheal intubation, it is important to correctly position the ETT. If correctly positioned, chest movements should be symmetric, and breath sounds should be equal when auscultated in the axillae. An electronic or colorimetric  $\text{CO}_2$  detection system helps confirm whether the ETT is in the trachea or the esophagus.<sup>340</sup> If the double lines on the ETT are at the level of the vocal cords, the ETT is usually in the correct position. Another way to correctly position the ETT is to advance it into the right mainstem bronchus and listen for breath sounds in the left axilla. Breath sounds will be diminished. Withdraw the ETT slowly. When breath sounds are heard on the left, pull the tube out an additional 1 to 2 cm, depending on the size of the child. If the breath sounds are equal, fix the tube in place. The tip of the ETT should be midway between the vocal cords and the carina on the chest radiograph. In small infants, the distance between the carina and the vocal cords is very short. It is easy to inadvertently place the ETT in the right mainstem bronchus in small infants because of this short distance. Flexion

of the head moves the ETT into the airway. Extension moves it toward the vocal cords. Turning the head to the side may obstruct the tip of the ETT if it comes in contact with the tracheal wall, which may cause  $\text{CO}_2$  retention or hypoxemia, or both (unpublished data). It is common to leave a child's trachea intubated for 2 weeks or longer before performing a tracheostomy. This is possible with proper humidification of the inspired gases, improved endotracheal suctioning and monitoring ( $\text{SaO}_2$ ), and excellent nursing care. Everyone caring for the child must be constantly alert to the possibility that the ETT will become obstructed by secretions or that accidental extubation or mainstem bronchus intubation will occur. Tracheostomy is indicated when children require a long-term artificial airway for mechanical ventilation, for endotracheal suctioning, or to bypass an upper airway obstruction. Accidental dislodgement of the tracheostomy tube before the tract is well healed can be life threatening. Reinsertion of a tracheostomy tube during the first 72 hours after insertion can be very difficult and can create false passages that can make it impossible to ventilate the lungs or can cause pneumothorax.

Intubation and mechanical ventilation can provide significant elevations in airway pressure as compared with NIV and a  $\text{FiO}_2$  of 1.0. There can be regional variation to the mode of mechanical ventilation chosen, but there is likely a greater use of pressure controlled ventilation rather than volume controlled ventilation in pediatric ICUs. However, as there are no studies looking at outcomes with mode of ventilation, we cannot recommend one mode over another. With pressure-controlled ventilation, pressure is set and the tidal volume may change as the pulmonary compliance changes. With volume-controlled ventilation, tidal volume is set, and the pressure needed to deliver that may change as the pulmonary compliance changes. These are likely the two main modes of mechanical ventilation in pediatric ICUs. For the majority of intubated children who have reasonable pulmonary compliance, there are little differences between the two modes. One potential advantage of pressure-controlled ventilation for patients who are sicker with poorer pulmonary compliance is that most ventilators in this mode use a decelerating inspiratory flow pattern. This means that the flow of gas is greatest early in inspiration and then decelerates to zero flow when the peak pressure is achieved. This can result in the delivery of a larger tidal volume for a lower peak pressure as compared with the same pressure that might be required in a tidal volume mode.

There are additional modes available on modern ventilators that may have benefit for patients with lung injury. The names of the modes will differ between the ventilator manufacturers. Many will have a mode where a desired tidal volume is guaranteed and the lowest pressure necessary to achieve that is used. Terms usually given to define this mode are *pressure-regulated volume control* and *volume guarantee*. These modes may reduce the pressure used, but they work best when the patient is well sedated and not competing with the ventilator.

Neurally adjusted ventilatory assist is a newer method of triggering ventilator synchrony available on the Servo-i ventilators by Maquet. This uses a small esophageal probe that can sense the electrical activity of the diaphragm and use that activity to synchronize the ventilator. The potential benefits of improved triggering such as improved

comfort, lower ventilator settings, and increased minute ventilation have been shown in some studies.<sup>341,342</sup> Some degree of expertise is necessary with the mode, as the electrical activity of the heart can also cause auto-triggering of the ventilator.<sup>343</sup>

Airway pressure release ventilation (APRV) is a mode of mechanical ventilation that is less common than pressure control or volume control. There is adult data that was recently published by Zhou et al.<sup>344</sup> that early use of APRV can reduce length of mechanical ventilation. As we do know, however, children are just little adults. Lal-gudi et al.<sup>345</sup> recently published the results of a randomized controlled trial of APRV in children with ARDS. The trial was stopped early for increased mortality in the APRV arm. There are few published pediatric studies using this mode,<sup>346-349</sup> and its benefits and limitations continue to be explored. Like other modes of ventilation, its use appears to be regional, and some will only consider this as rescue therapy when patients fail conventional ventilation.

To describe its use, APRV is essentially CPAP with brief, intermittent release coupled with spontaneous ventilation. The high CPAP level (Phigh) maintains alveolar recruitment and aids in oxygenation over a period of time (Thigh), and the timed release to a low pressure (Plow) minimizes resistance to expiratory flow and carbon dioxide removal. In addition, the patient is able to spontaneous breath during all phases, Phigh and Plow, potentially allowing for improved pulmonary mechanics and gas exchange. APRV differs from other modes of ventilation because it relies on an intermittent decrease in airway pressure, instead of an increase in airway pressure to maintain an open lung strategy for ventilation. Therefore, the release time (Tlow) should be set long enough to allow for an adequate tidal volume (6-8 mL/kg), but short enough to avoid alveolar collapse and atelectrauma. In summary, the operator-controlled parameters in APRV are: Phigh, Thigh, Plow, Tlow, and  $\text{FiO}_2$ . Recommendations for implementing APRV are limited in pediatrics, and thus extrapolated from adult recommendations.<sup>350</sup> Plow is initially set a zero. Phigh can be set by several methods such plateau pressures or 75% of peak inspiratory pressure; however, when transitioning from conventional modes of ventilation, Phigh is often determined by  $mP_{AW}$  pressure formula where the  $mP_{AW}$  is set 2 to 3 cm H<sub>2</sub>O above conventional  $mP_{AW}$ :  $(\text{Phigh} \times \text{Thigh}) + (\text{Plow} \times \text{Tlow}) / (\text{Thigh} + \text{Tlow})$ . To determine Thigh and Tlow, first determine the total cycle time according to a normal RR range for the patient's age (i.e., a RR of 20 yields a total cycle time of 3 seconds). Thigh will be the total cycle time minus a Tlow of 0.2 to 0.6 seconds, initially starting at 0.4 seconds (i.e., total cycle time of 3 seconds yields a Thigh of 2.6 seconds and Tlow of 0.4 seconds), or Number of cycles (RR) = 60 seconds/(Thigh + Tlow). Transitioning to APRV, like transitioning to HFOV, will take time for optimal lung recruitment. After several hours, if the patient continues to have severe hypoxemia, Thigh can be increased to aid in oxygenation. Once established Plow and Tlow usually do not require further changes; however, as lung compliance improves, Phigh and Thigh can be decreased and increased, respectively, to wean a patient toward a target of a continual CPAP of 5 to 6 cm H<sub>2</sub>O in preparation for extubation. APRV may be advantageous to other modes of advanced mechanical ventilation because of

the patient's ability to breathe spontaneously throughout the entire ventilatory cycle improving respiratory mechanics and reducing the need for sedation and neuromuscular blockade. However, some authors are concerned that there may be a higher incidence of cyclic alveolar collapse during airway release leading to a greater degree of atelectrauma, as compared with HFOV.<sup>346,347</sup>

High frequency oscillatory ventilation (HFOV) is being used in pediatrics as a rescue therapy for acute lung injury (ALI) or ARDS. HFOV is a subset of HFV. Use of HFOV was first described by Lunkemheimer in 1972.<sup>351</sup> A 1994 publication by Arnold et al.<sup>352</sup> is the only multicenter randomized trial of HFOV. This study showed lower use of oxygen supplementation in the HFOV group at 30 days. There have been other pediatric studies showing positive benefit of HFOV such as a single center prospective study by Samransamruajkit et al.<sup>353</sup> and a single center retrospective study by Babbitt et al.<sup>354</sup> The conclusion that could be drawn by many studies with HFOV in pediatrics is that for disease processes with significant mortality, rescue therapy with HFOV may be appropriate and may show improved outcomes. In some of the most critically ill patients with a very high mortality such as immune compromised children with ARDS, the response to HFOV has been used as diagnostic criteria to identify survivors from nonsurvivors.<sup>347,355</sup> Early use of HFOV has been shown to decrease mortality in patients who have undergone hematopoietic cell transplant who have developed severe pediatric ARDS.<sup>356</sup> There is some adult data using HFOV from large randomized trials. The OSCAR trial<sup>357</sup> was a negative study and the OSCILLATE Trial<sup>357</sup> was stopped early for a potential increase mortality in the HFOV group. It is unclear whether these findings can be translated to pediatric patients. The disease processes and the condition of our patients can be very different as compared with adults. Bateman et al.<sup>358</sup> used a propensity score model to reanalyze results from the Randomized Evaluation of Sedation Titration for Respiratory Failure (RESTORE) Study.<sup>359</sup> Using their adjusted models, they found that early use of HFOV was associated with longer mechanical ventilation. There also was no mortality benefit to the use of HFOV. Given the results of the adult studies as well as those from Bateman et al.,<sup>358</sup> it is unclear if the motivation would be present to perform a multicenter HFOV trial in pediatrics. There may continue to be other indications for HFOV in pediatrics, such as air leak syndrome or congenital diaphragmatic hernia.

To describe its use, HFV is a type of mechanical ventilation where the RR of the ventilator is much greater than a normal physiologic rate. Maintaining the same minute ventilation these ventilation modes produce tidal volumes that are very small. There are several different methods, but most commonly used in pediatrics is the HFOV. This type of ventilator houses a piston that is attached to semi-rigid connecting tubing which attaches to the ETT. This circuit can be pressurized to a set mean airway pressure (MAP). The piston then oscillates up to 840 times a minute, creating small positive and negative respiratory cycles. The MAP is higher as compared with conventional ventilation, and this prevents atelectasis as well as shear forces from opening and closing alveoli with each respiratory cycle. The  $\text{FiO}_2$  is set as in a conventional ventilator. The frequency of oscillation of the piston is adjusted to remove carbon dioxide