CONGENITAL HEART DEFECTS AND SUPRAVENTRICULAR TACHYCARDIA IN CHILDREN

Donald B. Wiest, Pharm.D., BCPS; and Walter E. Uber, Pharm.D.

Reviewed by Marcia L. Buck, Pharm.D., FCCP; Mindi S. Miller, Pharm.D., BCPS; and
Glen T. Schumock, Pharm.D., MBA, FCCP, BCPS

Learning Objectives

1. Account for the differences in the fetal circulation and the circulatory changes that occur at birth as they relate to the physical assessment of congenital heart defects.
2. Develop an understanding of the anatomy and physiology associated with uncorrected, palliated, and corrected congenital heart defects.
3. Design pharmacological treatment plans needed for preoperative, postoperative, and long-term management of various congenital heart defects.
4. Describe the anatomy, physiology, and potential complications associated with corrected versus uncorrected congenital heart defects.
5. Based on the clinical features and electrocardiogram findings, distinguish between atrioventricular reentrant tachycardia and atrioventricular nodal reentrant tachycardia.
6. Design a pharmaceutical care plan for the management of acute and chronic supraventricular tachycardia in infants and children.

Introduction

In the United States, about 150,000 babies are born each year with birth defects. The parents of 1 out of every 28 newborns will receive this frightening news. The number one type of birth defect is congenital heart defects (CHDs). In the United States, more than 32,000 babies (1 out of 125–150) are born each year with heart defects. To put this in perspective, 1 in every 800–1000 babies are born with Down syndrome. When considering all birth defects, those affecting the cardiovascular system have the greatest effect on infant mortality. During the first year of life about one-third of infants born with CHDs become critically ill and either die or receive surgical treatment. The associated social and personal costs, morbidity, and disability from CHDs are difficult to measure. As an indicator, in the United States, between 1988 and 1990 more than 2.7 million days of hospital care were provided to children with CHDs.

The specialty of pediatric cardiology began its evolution in the early 1930s as a result of investigations into the mysteries of birth defects. Dr. Helen Taussig, at Johns Hopkins University, began to characterize the clinical and fluoroscopic findings of congenitally malformed hearts in the 1930s. In 1938, Dr. Robert E. Gross, of the Children's Hospital in Boston, successfully ligated the patent ductus arteriosus (PDA). This single accomplishment ushered in the era of surgery for CHDs. The specialty of pediatric cardiology has evolved to include not only CHDs but all diseases that may affect a child's heart (e.g., arrhythmias or acquired heart disease).

Since the 1930s, virtually all aspects of pediatric cardiology have witnessed remarkable discoveries and innovations. Congenital heart defects may be diagnosed in utero as early as the second trimester (12–24 weeks) with fetal echocardiography, allowing informed counseling of parents and delivery at a tertiary medical center where the neonate's heart disease will be managed. Treatment of many structural problems can now be corrected during cardiac catheterization, limiting the need for surgery for many cardiac defects. Cardiac ultrasound, color-flow Doppler, and magnetic resonance imaging have made diagnostic cardiac catheterization almost unnecessary. The pharmacological manipulation with prostaglandin E_1 (PGE_1) has markedly changed the potential for interventions for babies with many serious structural heart malformations.

The impact of these innovations has been lower mortality and the enhanced comfort of planned operations to replace desperate attempts at emergency palliations. Neonatal cardiac surgery has progressed from a rare, high-risk procedure to a commonly used strategy. Today, the correction of basic CHDs, such as PDA or a ventricular septal defect (VSD), carries a mortality rate of less than 2%.

Abbreviations in this Chapter

AP	Accessory pathway	HLHS	Hypoplastic left heart syndrome
ASD	Atrial septal defect	PDA	Patent ductus arteriosus
AV	Atrioventricular	PGE_1	Prostaglandin E_1
AVNRT	Atrioventricular nodal reentrant tachycardia	PVR	Pulmonary vascular resistance
		RFA	Radiofrequency ablation
AVRT	Atrioventricular reentrant tachycardia	SVR	Systemic vascular resistance
BT	Blalock-Taussig	SVT	Supraventricular tachycardia
CHD	Congenital heart defect	TAPVR	Total anomalous pulmonary venous return
CHF	Congestive heart failure		
CoA	Coarctation of the aorta	TOF	Tetralogy of Fallot
D-TGA	Complete transposition of the great arteries	VSD	Ventricular septal defect
		WPW	Wolff-Parkinson-White Syndrome
ECG	Electrocardiogram		

Thirty years ago, a complex CHD, such as complete transposition of the great arteries (D-TGA), was universally fatal. Today, survival is 97% after surgical correction. Pediatric heart transplantation has evolved to become the final modality for patients with an inoperable CHD or terminal cardiomyopathy unresponsive to standard therapy.

Pediatric arrhythmia management has seen similar discoveries and innovations. The most common form of arrhythmia encountered in infancy and childhood is supraventricular tachycardia (SVT). Before 1989, the management of SVT fell into one of three categories: 1) vagal maneuvers for hemodynamically stable SVT attacks; 2) antiarrhythmic drug therapy for SVT that was hemodynamically unstable or unresponsive to vagal maneuvers; and 3) cardiac arrhythmia surgery for severely refractory SVT.

Since the mid-1980s, we have learned that antiarrhythmic therapy carries proarrhythmic risks not only for adults but also for children, especially when using class I and class III antiarrhythmic drugs. To reduce the risks associated with antiarrhythmic drug therapy, radiofrequency ablation (RFA), first used in 1989 in children with SVT, has undergone multiple technological advances and has emerged as the standard treatment for children with chronic SVT. Today, arrhythmia diagnosis and RFA therapy can be performed during a single procedure, providing a cure and sparing the child from the risks of a lifetime of antiarrhythmic drug therapy.

This chapter reviews CHDs and SVT in children. These two disease states cover the majority of patients on a pediatric cardiology service. The section on CHDs focuses on structural defects, hemodynamic consequences after birth, and surgical management. Pharmacological management strategies used in the preoperative, postoperative, and long-term management of these patients is reviewed. The section on SVT focuses on mechanisms and diagnosis, pharmacological management, and RFA. In order for the pharmacist to provide care for children with CHDs or SVT and their families, an understanding of perinatal circulation, the pathophysiology of various disorders, and available treatment options is necessary.

Perinatal Circulation

An understanding of the fetal, transitional (fetal to neonatal), and neonatal adaptations in circulation is important when evaluating the pediatric cardiovascular system. Congenital heart defects are frequently evident with the circulatory changes that occur at birth. Signs and symptoms include cyanosis, congestive heart failure (CHF), shock, asymptomatic heart murmur, and arrhythmia. The patient's age at recognition and the accompanying symptoms depend on the nature and severity of the anatomic defect and the urgency with which assessment and intervention is necessary. Neonates who become symptomatic in the first 3 days of life often have CHDs (e.g., D-TGA) for which the transitional changes in circulation are profoundly unfavorable. Other neonates become symptomatic between 4 and 14 days after birth when the closure of the ductus arteriosus occurs (e.g., tetralogy of Fallot [TOF]), and symptoms appear even later in infants with complex CHDs.

Fetal Circulation

The structural elements of the fetal myocardium are unique. Early fetal myocytes undergo cellular replication or hyperplasia (i.e., increase in number), whereas adult myocytes hypertrophy or increase in size. The fetal heart is much stiffer, being composed of 60% noncontractile elements, which results in impaired relaxation relative to the adult's heart. The fetal heart is unable to increase stroke volume due to stiff wall compliance. Preload is also limited in the fetus as a result of ventricular constraint due to a compressed thoracic cavity, lungs, and pericardium.

In the fetus, the gas exchange organ is the placenta, and its vascular connections are in a parallel arrangement with other organs, remote from the pulmonary circulation (Figure 1-1). The course of the fetal circulation can be

Gersony WM. Major advances in pediatric cardiology in the 20th century: II. Therapeutics. J Pediatr 2001;139:328–33.

described as starting with the umbilical vein from the placenta. As fetal blood passes through the placenta, the umbilical venous blood achieves its maximum oxygen saturation of 85%–90%. About 50% of the umbilical venous blood bypasses the liver through the ductus venosus entering the inferior vena cava, with the remainder perfusing the liver. Blood in the inferior vena cava enters the right atrium, with two-thirds flowing across the foramen ovale into the left atrium and, subsequently, the left ventricle. The myocardial and cerebral circulations are perfused by the left ventricle using the most highly oxygenated blood. The remaining one-third of the blood from the inferior vena cava mixes with deoxygenated blood from the superior vena cava and flows into the right ventricle. The high pulmonary vascular resistance (PVR) causes about 85% of the blood ejected by the right ventricle to be shunted through the ductus arteriosus and enter the descending aorta to return through the umbilical arteries and back to the placenta. The systolic pressures within the ventricles are equal, with both chambers pumping to the systemic circulation. Thus, the fetal circulation delivers the most oxygenated blood to the organs in greatest demand (heart and brain) and deoxygenated blood back to the placenta for waste disposal and oxygen replenishment.

Circulatory Adaptations at Birth

With birth, the function of gas exchange is transferred from the placenta to the lungs. The arterial and venous circuits become separate, eliminating the need for the fetal shunts (ductus venosus, foramen ovale, and ductus arteriosus) (Figure 1-1). With the first breath, the lungs begin to function as the respiratory center, decreasing pulmonary artery resistance and increasing pulmonary artery blood flow as a result of increased oxygen tension. Pulmonary vascular resistance continues to decrease as right ventricular pressures approach adult values by 10 days of age. With the clamping of the umbilical cord, systemic vascular resistance (SVR) increases, resulting in increased pulmonary venous return, which increases left atrial pressure and left ventricular afterload. The increases in left atrial pressure lead to flap closure of the foramen ovale, which is the shunt between the right and left atrium, by 3 months of age. Through both mechanical and chemical means, the ductus arteriosus begins to close by 10–15 hours of age and is fully closed by 2–3 weeks of age in healthy full-term infants. Factors that prolong the time to ductus closure include hypoxia, acidosis, and when a ductal dependent CHD is present (e.g., D-TGA, pulmonary atresia, or hypoplastic left heart syndrome).

The infant with a ductal-dependent CHD will typically exhibit symptoms during the first week of life. Hemodynamically significant VSDs without associated anomalies rarely present before 2–4 weeks of age. Atrial septal defects (ASDs) seldom manifest during infancy. The hemodynamics of each CHD may be dependent or incompatible with the fetal or adult circulation. During the adaptation phase at birth, the neonate may not be overtly symptomatic, possibly leading to a missed diagnosis and discharge from the nursery. However, if the CHD is an obstructive lesion, such as hypoplastic left heart syndrome, the patient may exhibit signs of cyanosis, respiratory failure, or shock. Thus, the patient's age at time of diagnosis provides significant information on the nature of the cardiac anomaly and the urgency of care indicated.
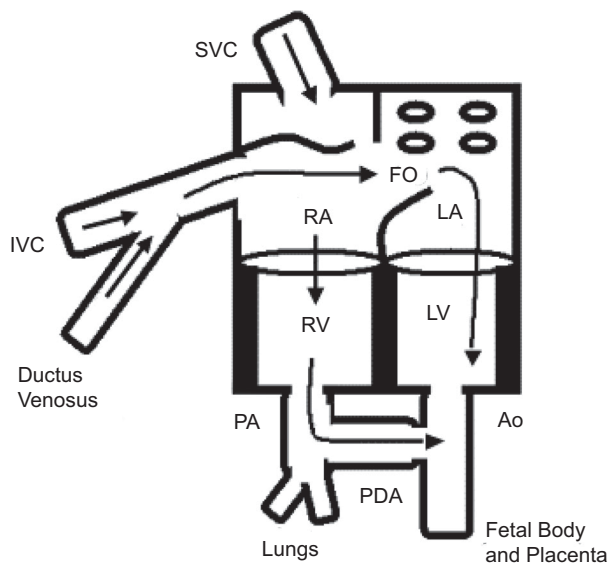

Figure 1-1. Schematic representation of the fetal heart.
The most deoxygenated blood drains from the superior vena cava (SVC) and is directed toward the tricuspid valve, into the body of the right ventricle and down the patent ductus arteriosus (PDA), descending aorta (Ao), and to the placental circulation to pick up oxygen. Ductus venosus blood carries the most richly oxygenated blood and is directed across the foramen oval (FO) so that the left ventricle (LV) can eject this blood into the coronary and cerebral circulations, which arise proximal to the patent ductus arteriosus. Relatively little flow is directed to the lungs. The unique structures of the ductus venosus, foramen ovale, and ductus arteriosus in conjunction with high pulmonary vascular resistance and very low placental vascular resistance dictate these adaptive and beneficial flow patterns.
IVC = inferior vena cava; LA = left atrium; PA = pulmonary artery.
Reprinted with permission from Elsevier. Rychik J. Frontiers in fetal cardiovascular disease. Pediatr Clin North Am 2004;51:1489–1502.

Congenital Heart Defects

A CHD refers to structural or functional abnormalities of the heart that are present at birth. In the United States, the incidence of CHDs is 4–8 cases per 1000 live births (range: 4–50 per 1000 live births). The variations reported in the literature are primarily related to clinicians' ability to detect small lesions such as small VSDs. About 40% of CHDs are diagnosed in the first year of life. More than one-third of these infants undergo corrective or palliative surgery during the first year of life.

Congenital heart defects are the most common form of birth defect and the leading cause of birth defect-related

Mitchell SC, Korones SB, Berendes HW. Congenital heart disease in 56,109 births. Circulation 1971;43:323–32.

Hoffman JI, Kaplan S. The incidence of congenital heart disease. J Am Coll Cardiol 2002;39:1890–900.

deaths. Cardiac malformations account for about 10% of infant mortality and almost all pediatric cardiac-related deaths. The most common lethal CHD in the neonatal period is hypoplastic left heart syndrome (HLHS), a ductal-dependent lesion that is uniformly fatal if untreated.

The cause of CHDs is unknown in most instances. The majority are probably multifactorial with a combination of genetic and environmental factors involved. A few CHDs appear to have a higher association with chromosomal abnormalities, such as the association of complete atrioventricular (AV) septal defect with Down syndrome, truncus arteriosus or interrupted aortic arch with DiGeorge syndrome, and long QT syndrome with sudden death in otherwise healthy individuals. Maternal infection with rubella virus (German measles) can cause birth defects if contracted during the first 3 months of pregnancy. Many drugs—including isotretinoin, lithium, warfarin, valproic acid, phenytoin, and carbamazepine—taken during pregnancy will increase the risk of CHDs. Diabetes, phenylketonuria, and alcohol consumption during pregnancy also increase the risk of CHDs.

Because of therapeutic advances during the past 30 years in diagnosis and treatment of CHDs in infants and children, patients are now surviving well into adulthood. In the United States, the population of adults with CHDs is estimated to be about 1 million, increasing at a rate of 5% per year. Because many of these adult patients are at risk for high complication rates, premature death, and arrhythmias, they should be examined every 12–24 months by cardiologists with expertise in adult CHDs. Current estimates are that between 320,000 and 600,000 adults with moderate or complex CHDs are in need of this specialized care now. Unfortunately, only a handful of adult cardiologists have received adequate training to provide competent care in this area. Pharmacists specializing in adult cardiology will face a similar or greater challenge when managing adult patients with CHDs. Understanding the anatomy, physiology, and potential complications associated with uncorrected and corrected CHDs is the foundation that one must have before considering any pharmaceutical care plan. Research and training programs are desperately needed to meet the medical needs of this growing population.

Several classifications have been used to characterize CHD lesions. The classification system used in this chapter divides various CHDs into three categories: left-to-right shunts, cyanotic heart lesions, and obstructive lesions.

Left-to-right Shunts

Left-to-right shunts (e.g., ASD, VSD, PDA, and complete AV septal defect) compose a group of defects where saturated blood from the left atrium, left ventricle, or aorta crosses directly to the right atrium, right ventricle, or the pulmonary artery. These normally acyanotic defects result in increased pulmonary blood flow as well as increased right and left ventricular pressure and volume overload, depending on the particular defect. Unrepaired defects can result in right-to-left shunting with cyanosis

secondary to developing pulmonary hypertension, which may be irreversible.

These defects can occur with other complex CHDs. In these instances, the direction and amount of shunting will be determined by the hemodynamics of the defect. In addition, creation (e.g., ASD) or maintenance (e.g., PDA) of some of these defects may be vital to survival in patients with other complex CHDs until palliative or corrective procedures can be performed.

The following section focuses specifically on VSD and PDA as the primary defect. The role of these defects in the presence of other complex CHDs is discussed later.

Ventricular Septal Defect

Ventricular septal defect is the most common CHD in infants and children, accounting for 20%–30% of all CHDs. Ventricular septal defects frequently occur in conjunction with other complex CHDs, but can be found as isolated defects in 30% of patients. Ventricular septal defects are classified into four types based on their location. Perimembranous VSDs located on the membranous septum are the most common type, occurring in about 70% of patients. Muscular VSDs, located on the muscular septum, occur in 20% of patients and carry the highest potential for spontaneous closure. Supracristal VSDs, located in the right ventricular outflow tract, account for 5% of defects and are associated with aortic valve prolapse. Inlet VSDs are located under the mitral and tricuspid valves and account for the remaining 5% of defects.

The pathophysiology and presentation in patients with isolated VSDs depend on the location and size of the defect as well as the degree of PVR in relation to SVR. Large VSDs have less resistance to flow and allow increased shunting from left to right. As PVR decreases over the first several weeks of life, left-to-right shunting and pulmonary blood flow is increased. These patients are usually diagnosed at 4–6 weeks in CHF with tachypnea, tachycardia, and failure to thrive. If allowed to persist over time, irreversible developing pulmonary hypertension will develop with cyanosis secondary to reversal of shunting from right to left. Supracristal VSDs can be complicated by moderate to severe aortic insufficiency. Small VSDs can produce only trivial shunts and no manifestation of symptoms. Small VSDs, especially those located in the muscular septum, can close spontaneously with no further sequelae. Large VSDs (e.g., inlet VSDs) are not usually amenable to spontaneous closure.

Echocardiography is used to confirm the diagnosis of a VSD, demonstrating the presence and location of the defect, the magnitude and direction of the shunt, as well as other associated defects, if present. Cardiac catheterization is usually not required unless patients are suspected of having significant pulmonary vascular disease where quantification of pulmonary artery pressures is required.

Initial management of VSD is based on control of systems to allow for growth and prevention of adverse outcomes (e.g., pulmonary hypertension, ventricular dysfunction). Asymptomatic patients with small VSDs generally require no further intervention. In patients with

Moodie DS. Adult congenital heart disease. Curr Opin Cardiol 1994;9:137–42.

large defects and CHF symptoms, pharmacological management can be used to control symptoms and promote growth, with subsequent surgical closure during childhood. In patients who fail to thrive, surgical correction with patch closure of the VSD is required. In addition, patients with large defects and developing pulmonary hypertension require surgical closure by age 1 to prevent irreversible pulmonary hypertension. Operative mortality with VSD repair is less than 5%. Overall, outcomes with VSD closure depend on the coexistence of other CHDs. The long-term prognosis in patients with isolated VSDs requiring repair is excellent.

Patent Ductus Arteriosus

Patent ductus arteriosus is a persistent communication by the ductus arteriosus between the pulmonary artery at the bifurcation and the aorta just distal to the left subclavian takeoff. It accounts for 8%–10% of all CHDs with a female predilection of 2:1. Risk factors for persistent PDA include pregnancies complicated by perinatal hypoxemia, or maternal rubella, and neonates born prematurely or at high altitudes. In 90% of cases, PDA occurs as an isolated defect.

The pathophysiology and presentation in patients with isolated PDA depend on age at presentation, size of defect, and PVR in relation to SVR. In premature infants, PDAs are structurally normal and will spontaneously close in most instances. Conversely, PDAs in term infants are structurally abnormal and will rarely close spontaneously. Patients with small PDAs may be asymptomatic with little shunting and have normal growth and development. Moderate to large PDAs will have increased left-to-right shunting, which may be further enhanced as PVR decreases over the first several weeks of life, resulting in increased pulmonary blood flow and evidence of left atrial and left ventricular volume overload. Over time, this may lead to significant dilation and development of atrial arrhythmias and left ventricular dysfunction. Large PDAs can result in the development of irreversible pulmonary hypertension and cyanosis secondary to reversal of shunting from right to left. Patients with large PDAs can manifest CHF symptoms in infancy, whereas patients with moderate PDAs can manifest symptoms in childhood or even as adults.

A continuous "machinery-like" murmur heard in the left chest is highly suspicious for the presence of a PDA. Echocardiography is used to confirm the diagnosis of a PDA, amount of shunting, left atrial and ventricular size, and potential presence of other CHDs. Cardiac catheterization is rarely needed for diagnosis but is frequently used for device deployment for percutaneous PDA closure.

Management strategies used for PDA closure are based primarily on the age of the patient and the size of the defect. In premature infants where spontaneous closure does not occur, pharmacological closure with indomethacin is the primary method used. Patients at increased risk for adverse effects from pharmacological closure or with documented pharmacological failure may require surgical intervention. In other patients, closure should be performed by a catheter-directed device or surgical ligation at the earliest possible convenience. Coil or device occlusion is the option of choice in most instances in patients with PDAs less than

8 mm. Complete closure has been demonstrated in more than 85% of patients, with mortality rates less than 1%. Surgical closure can achieve better success rates, but is associated with increased morbidity. Surgical closure is reserved for patients with larger defects (greater than 8 mm), where no interventional services are available, or with multiple CHDs requiring corrective surgery. Patent ductus closure to reduce endocarditis risk in asymptomatic patients with small defects remains controversial.

Patients with unrepaired PDAs are at an increased risk for endocarditis, aneurysm formation with rupture, CHF, and pulmonary hypertension. The mortality rate is 33% by age 40 and 66% by age 60. With a successful repair before onset of the above sequelae, an excellent patient outcome with a normal life span is expected. Follow-up echocardiography will be necessary after the repair to assess for potential recanalization.

Cyanotic Heart Lesions

Tetralogy of Fallot, transposition of the great arteries, tricuspid atresia, total anomalous pulmonary venous return (TAPVR), and truncus arteriosus make up the majority of cyanotic heart lesions in which desaturated blood enters the systemic circulation, resulting in cyanosis. These are complex lesions, each associated with multiple anatomic defects of varying degrees that result in different scenarios, which will affect their initial manifestation, initial management, and subsequent surgical repair.

Improvements in surgical techniques, intra-operative strategies, and intensive postoperative management have dramatically improved outcomes for patients with cyanotic heart lesions. In addition, complete surgical correction can now be performed in the neonatal period to restore normal or near-normal physiology. Refinements in operative and other management techniques continue to be developed to reduce long-term complications associated with increased morbidity and mortality. The following section focuses specifically on two defects: TOF and transposition of the great arteries.

Tetralogy of Fallot

Tetralogy of Fallot is probably the most-studied cyanotic CHD, with more than 40 years of surgical follow-up. It accounts for up to 10% of all CHDs and is the most common cyanotic heart defect encountered after the first year of life. Tetralogy of Fallot has four characteristic features (Figure 1-2), which include large nonrestrictive VSD; right ventricular outflow tract obstruction secondary to subvalvular (infundibular), valvular, supravalvular, and/or pulmonary branch stenosis; aorta overriding the ventricular septum; and right ventricular hypertrophy. Other associated abnormalities may include a right aortic arch (20%–25%), ASD (10%), coronary anomalies (10%), and aortopulmonary collaterals.

The pathophysiology of TOF is primarily determined by the amount of right ventricular outflow tract obstruction, which determines the amount of pulmonary blood flow and shunting across the VSD. In patients with mild obstruction, flow across the VSD is left to right, resulting in increased pulmonary blood flow with symptoms of CHF and increased risk for pulmonary hypertension. Patients with
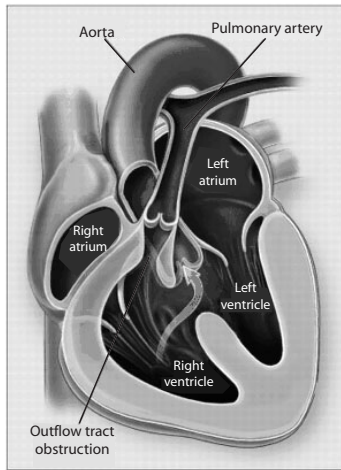
Figure 1-2. Tetralogy of Fallot.
Tetralogy of Fallot is characterized by a large ventricular septal defect, an aorta that overrides the left and right ventricles, obstruction of the right ventricular outflow tract, and right ventricular hypertrophy. With substantial obstruction of the right ventricular outflow tract, blood is shunted through the ventricular septal defect from right to left (arrow). Reprinted with permission from the Massachusetts Medical Society. Brickner ME, Hillis LD, Lange RA. Congenital heart disease in adults— second of two parts. N Engl J Med 2000;342:334–42.
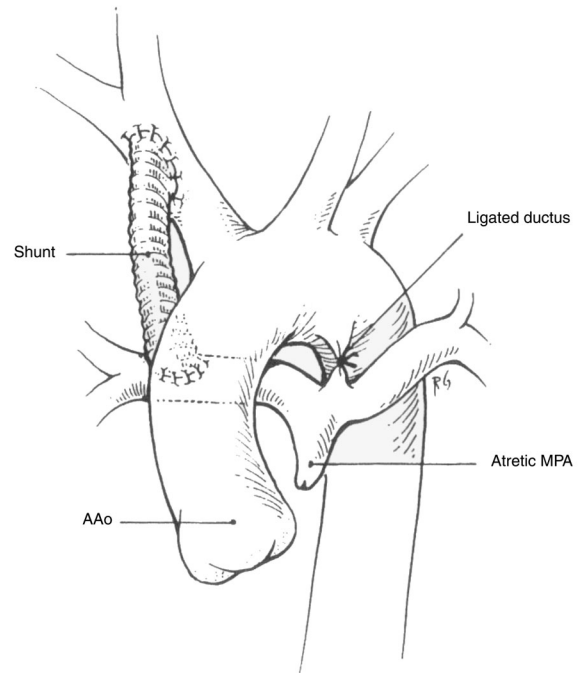

Figure 1-3. Modified Blalock-Taussig shunt.
Note the atretic main pulmonary artery (MPA) and the ligated ductus arteriosus (ductus). A Gore-Tex tube graft (shunt) is sewn side-to-side between the innominate artery and the right pulmonary artery. Size of the tube graft (3.5 mm, 4.0 mm, or 5.0 mm) is chosen at surgery depending on patient size and caliber of pulmonary artery. Some surgeons perform the shunt through a median sternotomy and others choose a lateral thoracotomy; cardiopulmonary bypass is usually not required.
Reprinted with permission from Elsevier. Waldman LD, Wernly JA. Cyanotic congenital heart disease with decreased pulmonary blood flow in children. Pediatr Clin North Am 1999;46:385–404.

severe obstruction will have profound reduction in pulmonary blood flow, with significant right-to-left shunting across the VSD, resulting in hypoxemia and cyanosis. In situations where severe stenosis exists, pulmonary blood flow can be ductal-dependent and require pharmacological manipulation with PGE_1 to maintain ductal patency until palliative or corrective surgery can be performed. Patients with moderate obstruction can exhibit a balance with enough obstruction to prohibit pulmonary overcirculation and CHF and with little shunting across the VSD, resulting in minimal to mild hypoxemia. These patients may be asymptomatic initially but will manifest symptoms as right ventricular hypertrophy and right ventricular outflow tract obstruction progress.

The majority of patients with TOF will present with cyanosis during the first year of life. Hypoxic "tet" spells associated with reduction in an already compromised pulmonary blood flow may be seen in the first few years of life. Other symptoms include dyspnea and decreased exercise tolerance. Growth retardation can also be present. Evidence of clubbing may be seen in older children.

Echocardiography is primarily used to diagnose TOF, demonstrating presence of an overriding aorta, right ventricular hypertrophy, the level and severity of the right ventricular outflow tract obstruction, location and presence of shunting at the VSD, size of the pulmonary artery and branches, and presence of other associated abnormalities. Cardiac catheterization can be used to confirm the diagnosis and obtain other information, including identification of coronary anatomy.

Surgical correction is required to improve long-term outcome and quality of life in patients with TOF. Previous surgical approaches used a staged repair strategy that involved palliation in infancy with a systemic to pulmonary shunt (e.g., modified Blalock-Taussig [BT] shunt; see Figure 1-3) to improve pulmonary blood flow and symptoms, with complete correction performed later in childhood. Advances in neonatal and infant heart surgery coupled with potential complications associated with shunt placement have prompted many centers to advocate complete correction as the primary operation for TOF. At present, mortality with complete surgical correction is reported to be less than 3%. Palliative surgery is now reserved for severely ill patients with lesions not amenable to complete repair.

Complete surgical correction requires closure of VSD with relief of the right ventricular outflow tract obstruction (Figure 1-4). The VSD is usually closed using a Dacron or pericardial patch. Techniques used to relieve right ventricular outflow tract obstruction depend specifically on the extent of obstruction (subvalvar, valvar, or supravalvar). Pulmonary valvotomy, resection of infundibular muscle bundles, placement of a right ventricular outflow tract or trans-annular patch, and placement of prosthetic pulmonic

Blalock A, Taussig HB. The surgical treatment of malformations of the heart in which there is pulmonary stenosis or pulmonary atresia. J Am Med Assoc 1945;128:189–92.

valve or valved conduit may be required to provide sufficient relief of right ventricular outflow tract obstruction. Anomalous origin of the left anterior descending coronary artery from the right coronary artery, which crosses the right ventricular outflow tract to the left ventricle, has been described in up to 10% of patients and can increase risk for transection if not recognized before right ventricular outflow tract augmentation. Angioplasty and/or patch augmentation of pulmonary arteries may be required for sufficient relief of stenosis. Last, concurrent defects (e.g., ASD) should be addressed and repaired, if possible, at the time of correction.

Surgically corrected versus uncorrected TOF, as well as complications associated with surgical repair, clearly influence long-term outcomes. Adults with uncorrected TOF exhibit dyspnea and decreased exercise tolerance. Other complications potentially include erythrocytosis,

hyperviscosity, coagulopathy, stroke, and infection (e.g., endocarditis). Outcomes in uncorrected TOF are poor, with a survival of 66% at 1 year, 40% at 3 years, and decreasing to 3% at 40 years. In comparison, corrected TOF has demonstrated significant improvement with survival reported at 32 and 36 years of 86% and 85%, respectively. Comparison of survival in patients with corrected TOF versus healthy age-matched controls without CHD demonstrates a reduction in overall survival in TOF patients (86% vs. 96%, respectively, at 32 years).

The majority of patients are asymptomatic after surgical correction of TOF on follow-up. However, 10%–15% of patients may exhibit symptoms at 20 years. These symptoms are associated with developing arrhythmias and right ventricular dysfunction, which may be linked to sudden death in corrected TOF patients. Development of right ventricular dysfunction is felt to be secondary to either
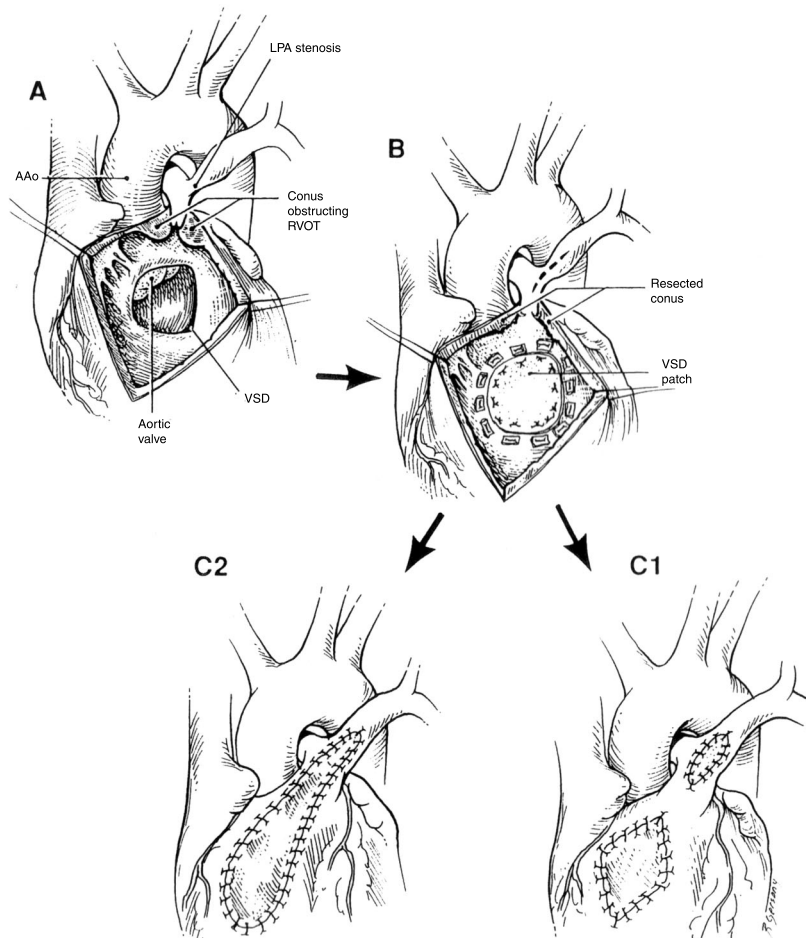

Figure 1-4. Repair of tetralogy of Fallot.
A: The anterior RV wall has been incised for exposure. The VSD is seen as well as part of the aortic valve on the left ventricular side of the VSD. Note the dilated ascending aorta, the small MPA, and the obstructing muscle in the RVOT under the pulmonary valve. B: The VSD has been closed with a Dacron patch. Pledgets were used to buttress the sutures carefully placed so as to avoid damage to the conduction system. The obstructing subpulmonary muscle has been incised and resected. For completion of the repair, two alternatives are depicted; use of an RV-to-PA conduit is not shown. C1: After a pulmonary valvotomy, the pulmonary anulus has been measured and found to be adequate. Patches have been placed to enlarge the MPA and LPA, as well as the RV outflow tract area, but the pulmonary anulus and valve function are preserved. C2: The pulmonary anulus is judged too small, and a transannular patch is placed from RV outflow tract to branch pulmonary artery. This relieves the obstruction but leaves the child with pulmonary regurgitation.
AAo = ascending aorta; LPA = left pulmonary artery; MPA = main pulmonary artery; PA = pulmonary artery; RV = right ventricle; RVOT = right ventricular outflow tract; and VSD = ventricular septal defect.
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residual or recurrent right ventricular outflow tract obstruction or pulmonary insufficiency created with some forms of TOF repair (e.g., using trans-annular patch). Significant pulmonary insufficiency with chronic right ventricular volume overload may lead to slow deterioration in right ventricular function. Development of ventricular and atrial arrhythmias can be a result of hemodynamic problems related to pulmonary insufficiency and/or incisions to the myocardium. Atrial fibrillation/flutter is a significant cause of morbidity. Nonsustained ventricular arrhythmias have been reported in 60% of patients with sustained ventricular tachycardia reported infrequently. Sudden death has been reported to be 0.5%–6% over 30 years.

Strategies to improve outcomes and survival in patients with complications after TOF correction include repair or replacement of pulmonary valve and management of arrhythmias with pharmacological and/or catheter/surgical ablation. Repair or replacement of the pulmonary valve has improved exercise capacity and can improve right ventricular function. Surgical timing continues to be a critical issue necessitating intervention before the onset of irreversible changes in right ventricular function. Tricuspid valve repair may be required in cases where moderate to severe tricuspid insufficiency exists. Patients with arrhythmias should undergo hemodynamic assessment with correction of residual defects if present. Surgical ablation may be considered simultaneously in patients requiring surgical repair. Catheter-directed ablation can be performed in patients with no evidence of hemodynamic lesions. Pharmacological intervention with antiarrhythmic drugs can be useful. Automatic implantable cardioverter defibrillator placement can be considered in patients with previous episodes of near-sudden death.

Strategies to decrease the development of complications after surgical correction for TOF are evolving. Modifications in approaches to the management of right ventricular outflow tract obstruction are being developed. These include using a limited right ventricular incision for patch augmentation of right ventricular outflow tract and/or the pulmonary annulus instead of the generous use of trans-annular patching. These techniques attempt to maintain competency of the pulmonary valve and to reduce development of pulmonary insufficiency and right ventricular dysfunction long term.

Transposition of the Great Arteries

Transposition of the great arteries accounts for 5% of all CHDs and exhibits a male predilection of 2:1. Transposition of the great arteries can be divided into two types: D-TGA and corrected transposition of the great arteries. D-transposition of the great arteries is the more common type and is the most common cardiac cause of cyanosis in neonates. The characteristic feature that describes D-TGA is the presence of ventriculoarterial discordance (aorta arises from the right ventricle and main pulmonary artery arises from the left ventricle, Figure 1-5A). Other associated defects with D-TGA include PDA, patent foramen ovale, ASD, and VSD with or without pulmonary stenosis. Corrected transposition of the great arteries has both AV and
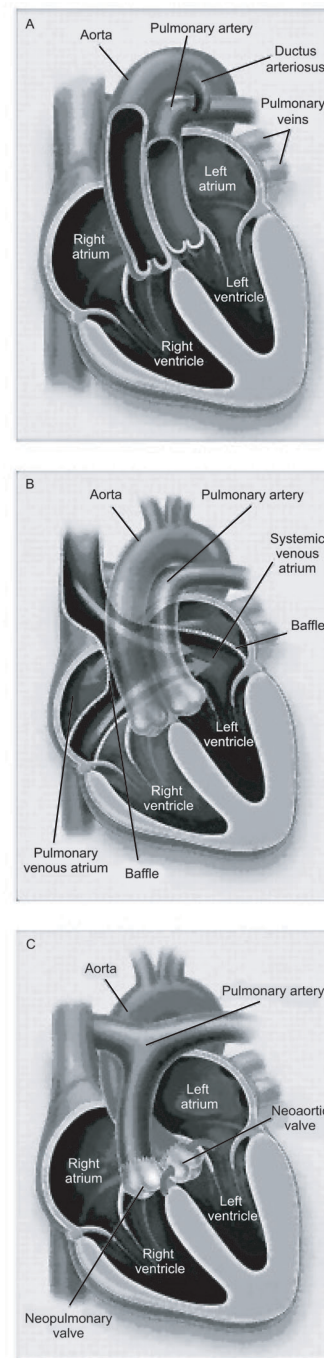

Figure 1-5. Transposition and switching of the great arteries.
In D-transposition of the great arteries (complete transposition) (Panel A), systemic venous blood returns to the right atrium, from which it goes to the right ventricle and then to the aorta. Pulmonary venous blood returns to the left atrium, from which it goes to the left ventricle and then to the pulmonary artery. Survival is possible only if there is a communication between the two circuits, such as a patent ductus arteriosus. With the "atrial switch" operation (Panel B), a pericardial baffle is created in the atria, so that blood returning from the systemic venous circulation is directed into the left ventricle and then the pulmonary artery (blue arrows), whereas blood returning from the pulmonary venous circulation is directed into the right ventricle and then the aorta (red arrow). With the "arterial switch" operation (Panel C), the pulmonary artery and ascending aorta are transected above the semilunar valves and coronary arteries, then switched (neoaortic and neopulmonary valves).
Reprinted with permission from the Massachusetts Medical Society. Brickner ME, Hillis LD, Lange RA. Congenital heart disease in adults— second of two parts. N Engl J Med 2000;342:334–42.

ventriculoarterial discordance. It is infrequently encountered and is not discussed further.

The pathophysiology of D-TGA results from the complete separation of the pulmonary and systemic circuits. Instead of acting in series, the systemic and pulmonary circuits act in parallel (i.e., oxygenated blood is continuously circulated to the lungs with deoxygenated blood circulated to the body). Oxygenation of systemic blood is totally dependent on shunting from other associated defects to allow for mixing of oxygenated and deoxygenated blood. If shunting is inadequate, oxygen delivery to tissues is impaired and, if not corrected, results in hypoxemia, acidosis, multiorgan impairment, and eventually death.

"Simple transposition" makes up about two-thirds of patients who present with D-TGA. These patients have no defects other than a PDA and a patent foramen ovale at the time of birth, and are initially stable. The presence of a PDA assists in the delivery of deoxygenated blood to the lungs, whereas the patent foramen ovale provides access for oxygenated blood to reach the systemic circulation. As the PDA begins to close, cyanosis and tachypnea ensue. Pharmacological manipulation with PGE_1 to maintain ductal patency may be vital for survival. If the patent foramen ovale is restrictive, balloon atrial septostomy may be required to improve left-to-right shunting.

Patients with an ASD or VSD may have continued mixing after PDA closure, which can delay onset of cyanosis. Left-to-right shunting is predominant across the ASD, which improves shunting for systemic oxygenation. Some amount of right-to-left shunting also exists. In many instances, ASDs, whether congenital or created with balloon atrial septostomy, may have sufficient bidirectional flow, allowing discontinuation of PGE_1. In patients with D-TGA, the VSD, if present, will shunt right to left due to lower left ventricular pressure than right ventricular pressure secondary to the anatomic location of the pulmonary artery. The amount of shunting will depend on the amount of concurrent pulmonary stenosis that frequently exists with a VSD. Patients with only minimal pulmonary stenosis may have cyanosis with signs of CHF secondary to a large right-to-left shunt. Patients with mild to moderate pulmonary stenosis may exhibit a balanced circulation and be stable, requiring no immediate intervention. Patients with severe pulmonary stenosis will have dramatically reduced pulmonary blood flow, variable shunting (i.e., little to no right-to-left or even left-to-right), and severe cyanosis.

Echocardiography, the standard diagnostic test for D-TGA, demonstrates the presence of the main pulmonary artery arising from the left ventricle, aorta from the right ventricle, presence and direction of shunt from a patent foramen ovale, ASD, VSD, and/or the PDA, and the presence and severity of pulmonary stenosis. Echocardiography can also assist in the evaluation of a therapeutic response by PGE_1 on the PDA. Cardiac catheterization is reserved for defining coronary anatomy and performing balloon atrial septostomy.

Initial palliation with balloon atrial septostomy may be required to improve left-to-right shunting and delivery of oxygenated blood systemically. This is performed percutaneously by placing a balloon catheter across a patent foramen ovale or restrictive ASD with subsequent inflation and pullback creating a larger atrial septal communication. This procedure may allow stabilization and/or improvement in the patient's condition until time of complete correction.

Today, the arterial switch operation is the technique of choice for complete correction in patients with D-TGA (Figure 1-5C). The procedure entails the transection of the aorta and main pulmonary artery above the aortic and pulmonary valve, respectively. The coronary arteries are then translocated to what is now the neo-aortic root (i.e., residual pulmonary artery and pulmonary valve connected to left ventricle). The neo-pulmonary root (i.e., residual aorta and aortic valve connected to the right ventricle) is then reconstructed with attachment of the main pulmonary artery. Finally, the aorta is attached to the neo-aortic root. Closures of any existing defects (e.g., ASD, VSD, or PDA) are also addressed at the time of correction. This procedure leaves the patient with virtually normal anatomy and physiology with the exception that the aortic valve is now the functional pulmonary valve and the pulmonary valve is now the functional aortic valve. Operative mortality with the arterial switch procedure in the neonatal period is now less than 5%.

Pulmonary vascular resistance decreases within the first few weeks of life, resulting in left ventricular deconditioning in D-TGA. The arterial switch operation should be performed within the first 2–3 weeks of life; otherwise, left ventricular function may be insufficient to handle systemic afterload. Risks associated with arterial switch are increased after 30 days of life and may be prohibitive after 40 days. Patients with D-TGA, VSD, and significant pulmonary stenosis are not candidates for arterial switch because the pulmonary valve will become the functional aortic valve, leaving the patient with aortic stenosis. These patients will require alternative forms of operative correction (e.g., Mustard, Figure 1-5B.).

The outcome in patients with D-TGA without correction is poor, with a mortality rate of 90% within 6 months. Complete correction with an arterial switch has a 10-year survival of greater than 90% and greater than 95% for patients in New York Heart Association class I. Patients exhibit normal growth and development, with a good quality of life. Re-operation associated with the arterial switch procedure is less than 15% at 10 years and has been primarily related to relief of right ventricular outflow tract obstruction. Aortic insufficiency (10%) and aortic root enlargement have been noted. The effect of coronary reimplantation in the development of atherosclerosis remains to be seen.

Obstructive Lesions

Patients with lesions obstructing right or left ventricular outflow may be asymptomatic or exhibit cyanosis and/or cardiogenic shock depending on the level of obstruction.

Jatene AD, Fontes VF, Paulista PP, et al. Anatomic correction of transposition of the great vessels. J Thorac Cardiovasc Surg 1976;72:364–70.

Castaneda AR, Norwood WI, Jonas RA, et al. Transposition of the great arteries and intact ventricular septum: anatomical repair in the neonate. Ann Thorac Surg 1984;38:438–43.

Lesions associated with right-sided obstruction include pulmonary stenosis and pulmonary atresia. Lesions commonly associated with left-sided obstruction include aortic stenosis, subaortic stenosis, complete interruption of aortic arch, coarctation of the aorta (CoA), and HLHS. Because of the complexity of lesions in surgical and pharmacological management, this section focuses specifically on CoA and HLHS.

Coarctation of the Aorta

Coarctation of the aorta accounts for 6%–8% of all CHDs and is characterized as a narrowing of the aorta that occurs, in most instances, just distal to the takeoff of the left subclavian artery. Coarctation of the aorta typically manifests as a discrete ridge or shelf around the site of PDA attachment, or in some instances, as a long-segment hypoplasia of the aortic arch. The exact mechanism for the development of CoA is not known, but may include reduction in flow through the aortic isthmus in utero, or presence of aberrant ductal tissue leading to obstruction. Coarctation of the aorta is more commonly manifested in males (2–5:1) and is associated with other forms of complex CHD in 50% of cases, some of which include bicuspid aortic valve (20%–85%), VSD, PDA, mitral stenosis, and/or mitral regurgitation. In addition, CoA is also associated with other syndromes (e.g., Turner syndrome), which influences prognosis.

In patients with CoA, pathophysiology is influenced by age, the severity of obstruction, and the presence of other forms of CHD. In utero, the ductus arteriosus supplies blood flow to the lower half of the body and begins to close within hours of birth. In patients with severe CoA, PDA closure leads to hypoperfusion of distal tissues, resulting in acidosis and subsequent shock with renal and hepatic impairment. Increased left ventricular afterload resulting in ventricular dysfunction can lead to cardiogenic shock. Presence of a VSD can further worsen congestion secondary to increased left-to-right shunting. Patients with severe CoA will present as neonates within the first few weeks of life with severe CHF, tachypnea, poor growth, and in some instances profound circulatory shock. Other findings can include decreased pulses and blood pressure with cyanosis in the lower extremities.

Patients with isolated CoA and mild to moderate obstruction can manifest no sequelae for many years, or they may be asymptomatic, with upper extremity hypertension and/or a systolic ejection murmur being the only presenting sign. Older children may complain of headache, dizziness, palpitations, chest pain, and lower extremity weakness or claudication. Blood pressure in the lower extremities is reduced, with femoral pulses being weak and delayed or even absent. A systolic ejection murmur can be heard at the left sternal border or the back. The presence of a systolic murmur at the base can indicate the presence of a bicuspid aortic valve. The murmur may be continuous if collateral vessels are present. In children older than 5–6 years, chest x-ray may reveal rib notching of the third through the eighth rib secondary to erosion by intercostal collaterals.

Diagnostic findings by clinical examination are confirmed by echocardiography, which demonstrates the presence, site, and length of narrowing with CoA, as well as the gradient to flow. In addition, the presence or absence of a PDA, anatomy of the ascending and transverse aortic arch, and existence of other CHDs can be identified. Magnetic resonance imaging can be useful in older patients where echocardiography fails to demonstrate anatomy. Cardiac catheterization is not routinely used in the initial evaluation of CoA but may play an important role in treatment.

Initial treatment in neonates with severe CoA focuses on restoring ductal blood flow immediately with PGE_1 and providing adequate resuscitation to reverse acidosis and improve end-organ function (e.g., kidney or hepatic). Emergent surgical intervention may be required in instances where the PDA is unresponsive. Once stabilization is achieved, surgical correction is carried out. Beyond the neonatal period, elective repair is optimally performed in the first 3–10 years of life to decrease the risk of residual hypertension and other cardiovascular diseases as an adult.

Surgical techniques for CoA repair include resection with end-to-end anastomosis, patch aortoplasty with prosthetic material or a subclavian flap, and interposition grafts. Resection with end-to-end anastomosis was first performed in 1944. As implied, the aorta is cross-clamped above and below the level of coarctation. The coarctation is then resected with subsequent reapproximation of the two ends. The advantage of this technique is that the obstructing portion is completely resected. Ductal and other tissue are removed in an attempt to reduce the chance of restenosis. Disadvantages with resection include potential loss of spinal and intercostal arteries and potential restenosis at the circumferential anastomosis. Improvements in suture and anastomosis techniques have reduced the restenosis rates associated with the use of end-to-end anastomosis. Thus, the end-to-end method is the technique of choice for surgical repair of CoA. Operative mortality in patients with isolated CoA is less than 2%. However, in patients with other associated defects, surgical mortality can be increased.

Of significance is the development of rebound hypertension seen immediately postcoarctectomy. The hypertension is secondary to baroreceptor-mediated increases in sympathetic activity and reflex vasospasm in vascular beds distal to CoA. Postcoarctectomy syndrome has also been reported. Characterized by mesenteric arteritis secondary to increased flow and pressure, it can result in abdominal pain, distention, vomiting, decreased bowel sounds, and rarely an acute abdomen requiring surgical intervention. Postoperative hypertension and early feeding can increase the risk of postcoarctectomy syndrome. Therefore, aggressive management of blood pressure in patients after CoA repair is required in the acute postoperative period. In addition, a delay in feeding for at least 2 days has been advocated. Other rare surgical complications include injuries to the recurrent laryngeal nerve (e.g., hoarseness), phrenic nerve (e.g., paralyzed diaphragm), thoracic duct (e.g., chylothorax), and spinal cord (e.g., paralysis).

Crafoord C, Nylin G. Congenital coarctation of the aorta and its surgical treatment. J Thorac Surg 1945;14:347–61.

The recent introduction of balloon angioplasty with possible stent deployment in the treatment of native and recurrent CoA is of significant interest. However, controversy concerning the rate of restenosis and aneurysm formation prevents consensus on the use of this technique. This is the case in the management of infants born with (native) CoA. Neonates and infants with native CoA have a high rate of restenosis after balloon angioplasty. Therefore, this technique is felt to be palliative and is only used in high-risk patients for stabilization before a surgical correction. In children, results have been more favorable. In adolescents and adults, this technique has been viewed by many as a reasonable alternative to surgical intervention, especially in patients where stent deployment can be used. However, questions about long-term patency and aneurysm rates compared with surgical intervention have led to varying opinions and institutional practice. Surgical repair in patients with recurrent CoA can be extremely difficult, with increased morbidity and mortality (5%–20%), and may still carry a recurrence rate of up to 20%. In this instance, balloon angioplasty with or without stent deployment can be considered as a first-line intervention. Late follow-up in one series demonstrated that 72% of patients with successful dilatation did not require further intervention over a 12-year period. Further studies with long-term follow-up are needed to clearly define the role of this technique in managing CoA.

Without correction, CoA significantly limits long-term survival. In untreated infants with CHF, the 1-year mortality rate may be up to 84%. Overall, the mean life expectancy is 35 years of age with a 75%–80% mortality rate by age 50 and 90% by age 60. Two-thirds of patients with uncorrected CoA will have CHF after age 40.

Survival with corrected CoA has dramatically improved over the years, with an overall survival rate of 91% at 10 years, 84% at 20 years, and 72% at 30 years. Age at the time of repair appears to have a significant impact on survival. Repair in childhood is associated with a survival of 89% and 83% at 15 and 25 years, respectively. By comparison, patients with CoA repair at 20–40 years of age had a 25-year survival rate of 75%, and patients older than 40 years with CoA repair had a survival rate of 50%. Functional capacity of the heart is excellent, with 97%–98% of long-term survivors in New York Heart Association class I.

Long-term complications include the development of aortic aneurysms, endocarditis, coronary artery disease, residual or recurrent hypertension, aortic stenosis, and recurrence of CoA. Recurrent hypertension is common and, like survival, appears to be related to age at the time of repair. If CoA repair is performed during childhood, the prevalence of recurrent hypertension is 10%, 50%, and 75% at 5, 20, and 25 years post-repair, respectively. In comparison, 50% of patients who undergo CoA repair after age 40 will have residual hypertension postoperatively, with many of the remaining patients experiencing hypertension with exercise. The prevalence of hypertension appears to increase over the length of follow-up.

Significant aortic stenosis related to the increased incidence of congenital bicuspid aortic valve with CoA may be seen in up to two-thirds of patients and may require subsequent aortic valve replacement (10%). This condition may be associated with an increased incidence for development of aortic aneurysm/dissection and CHF and account for 20% of late deaths in this patient population.

Recurrence/restenosis of CoA has occurred in 3%–41% of patients. Recurrence appears to correlate inversely with age, with younger patients demonstrating higher rates of restenosis. Balloon angioplasty with or without stent deployment appears, at this time, to be the treatment of choice.

Hypoplastic Left Heart Syndrome

Hypoplastic left heart syndrome accounts for less than 1% of all CHDs. It is the most common defect, causing death within the first year of life. This syndrome encompasses a group of cardiac abnormalities in which the left ventricle fails to form or is severely undersized and nonfunctional. In most instances, there is also atresia of the mitral and aortic valves, as well as the ascending aorta, transverse arch, and descending aorta. Of interest is the fact that the majority of babies are otherwise healthy, with a low incidence of other associated noncardiac defects.

The pathophysiology of HLHS is determined by the absence of a functional left ventricle and other left-sided structural abnormalities. This results in the inability of pulmonary venous blood to be delivered by the left side of the heart to the systemic circulation. Instead, pulmonary venous blood enters the left atrium and passes through an intra-atrial communication (e.g., ASD or patent foramen ovale) to the right atrium where it mixes with superior and inferior vena caval blood. Blood then crosses the tricuspid valve into the right ventricle and out the pulmonary valve to the main pulmonary artery. It is here that blood either proceeds into the branch pulmonary arteries or crosses the PDA supplying the aorta with retrograde flow into the transverse arch, ascending aorta, and coronary arteries, as well as antegrade down the descending aorta. This leaves the right ventricle to supply both the pulmonary and systemic circuits.

Ductal patency, size of the intra-atrial communication, and PVR in relation to SVR are the main determinants of systemic blood flow after birth and ultimately dictates when and how these patients will present. Ductal patency is vital to maintain systemic blood flow. As the PDA closes, systemic blood flow decreases resulting in systemic hypoperfusion and multiorgan dysfunction. Pulmonary blood flow increases resulting in overcirculation and congestion. Patients with restrictive ASD/patent foramen ovale or in rare instances TAPVR will have significant obstruction of the pulmonary venous circulation. This obstruction results in pulmonary venous and pulmonary artery hypertension with profound hemodynamic compromise. Pulmonary hypertension may also be persistent postcorrection, which substantially increases the risk involved in any palliation procedure. In instances where the PDA remains open, PVR decreases after several days, decreasing the amount of right-to-left shunting and resulting in increased pulmonary blood flow with subsequent reduction in systemic blood flow.

Patients with HLHS appear normal immediately after birth in most instances. The majority of patients will present

24–48 hours postbirth with tachypnea, respiratory distress, and acidosis with progression to profound shock. When the PDA remains open, patients will present several days later with pulmonary congestion. Patients with restrictive pulmonary venous outflow often present within the first 24 hours of life with respiratory distress from pulmonary congestion.

Today, the diagnosis of HLHS is often made in utero using fetal echocardiography. Echocardiography is also the method of choice to confirm clinical findings of HLHS after birth in instances where the diagnosis was not established in the prenatal period. Cardiac catheterization is rarely required. Documentation of anatomic and physiologic characteristics using echocardiography is extremely important in determining prognosis, initial management strategies, and surgical options. Important characteristics include the following: right ventricular function; tricuspid valve competence; evidence of pulmonary stenosis or regurgitation; size and patency of the mitral valve, aortic valve, and ASD/patent foramen ovale; evidence of TAPVR; size of the aorta and PDA; and absence or nature of existing left ventricle.

Initial management in HLHS focuses on restoration of systemic flow and adequate resuscitation to improve end-organ function. Prostaglandin E_1 is initiated to restore ductal-patency critical for systemic flow. Mechanical ventilation and other pharmacological drugs may also be required to improve hemodynamics. A key element in managing these patients is the balance of flow across the PDA needed to maintain adequate systemic and pulmonary blood flow. Manipulation of SVR and PVR is often required to maintain this balance. Pulmonary overcirculation may require an adjustment in ventilation (e.g., hypoventilation) and oxygenation (e.g., decrease fraction of inspired oxygen) to increase PVR, thereby increasing right-to-left shunt across the PDA and improving systemic flow and perfusion. Pulmonary venous outflow obstruction secondary to a restrictive ASD/patent foramen ovale or obstructive TAPVR will require emergent intervention with balloon atrial septostomy or surgery.

Surgical options for HLHS include three-stage palliative reconstruction (i.e., Norwood, hemi-Fontan/bidirectional Glenn, and fenestrated Fontan) or cardiac transplantation. The classic Norwood operation as the initial stage repair for HLHS was first reported in 1980. The operation was designed to provide unobstructed coronary and systemic flow, relieve pulmonary venous outflow obstruction, and provide adequate but not excessive pulmonary blood flow. This was accomplished in three steps: 1) creation of a neo-aorta off the right ventricle by detaching the branch pulmonary arteries from the main pulmonary artery followed by connection of the main pulmonary artery to the proximal aorta with further reconstruction of the ascending, transverse arch, and descending aorta to relieve systemic outflow obstruction; 2) atrial septectomy to allow free flow of pulmonary venous blood from the left atrium to the right

atrium; and 3) reconnection of the branch pulmonary arteries with the placement of a modified BT shunt (i.e., innominate artery to pulmonary artery shunt) (Figure 1-6). The right ventricle now serves as the single ventricle providing both systemic and pulmonary blood flow. The amount of pulmonary blood flow is controlled by the size of the shunt used. Optimal timing for performing the Norwood operation appears to be after adequate resuscitation and reduction in PVR, allowing the smallest sized shunt to be placed (3 days to 3 weeks of life).

Operative survival of 68%–83% has been reported after a Norwood operation. Risk factors associated with poor outcome after a Norwood operation are low birth weight (less than 2.5 kg), small ascending aorta (less than 3 mm), and older age (14–30 days) at time of operation. Risk factor stratification, refinements in operative technique, and other improvements in neonatal heart surgery have improved operative outcome over time in recent series. The highest risk for mortality after a Norwood operation continues to be during the first month of life. The exact reason is unclear but may be related to poor myocardial blood flow and/or difficulty in maintaining proper balance of pulmonary to systemic flow through the BT shunt.

A recent modification to the Norwood operation using a direct right ventricular to pulmonary artery connection instead of a BT shunt has been advocated (Figure 1-7). The right ventricle to pulmonary artery conduit is thought to provide more stable hemodynamics in the early postoperative period with regard to systemic and pulmonary artery flow. In addition, the right ventricle to pulmonary conduit reduces the amount of diastolic run-off seen with BT shunts, resulting in a higher diastolic blood pressure which may increase myocardial perfusion. Early operative survival with right ventricle to pulmonary artery conduits appear to be similar to that reported with using BT shunts in small, single-center series. Larger studies will be needed to fully evaluate this technique.

The functional single ventricle is exposed to increased volume conditions both before and after initial palliation secondary to receiving both systemic and pulmonary venous return. If left unchanged, this would eventually result in significant dysfunction and progress to ventricular failure. Initial palliative procedures do not normalize arterial oxygen saturation secondary to continued mixing of saturated and desaturated blood. Therefore, patients who survive a Norwood operation will require further staged correction to completely separate systemic and pulmonary venous circuits to relieve cyanosis and decrease volume overload on the functional single ventricle. The Fontan procedure, first reported in 1971 for palliation of tricuspid atresia, continues to be the primary surgical technique for complete palliation in patients with HLHS. The procedure involves diversion of superior and inferior vena cava blood flow directly to the pulmonary circuit and, in essence, bypassing the functional single ventricle. The functional single ventricle continues to serve as the pump for both the

Norwood WI, Kirklin JK, Sanders SP. Hypoplastic left heart syndrome: experience with palliative surgery. Am J Cardiol 1980;45:87–92.

Sano S, Ishino K, Kawada M, et al. Right ventricle-pulmonary artery shunt in first-stage palliation of hypoplastic left heart syndrome. J Thorac Cardiovasc Surg 2003;126:504–10.

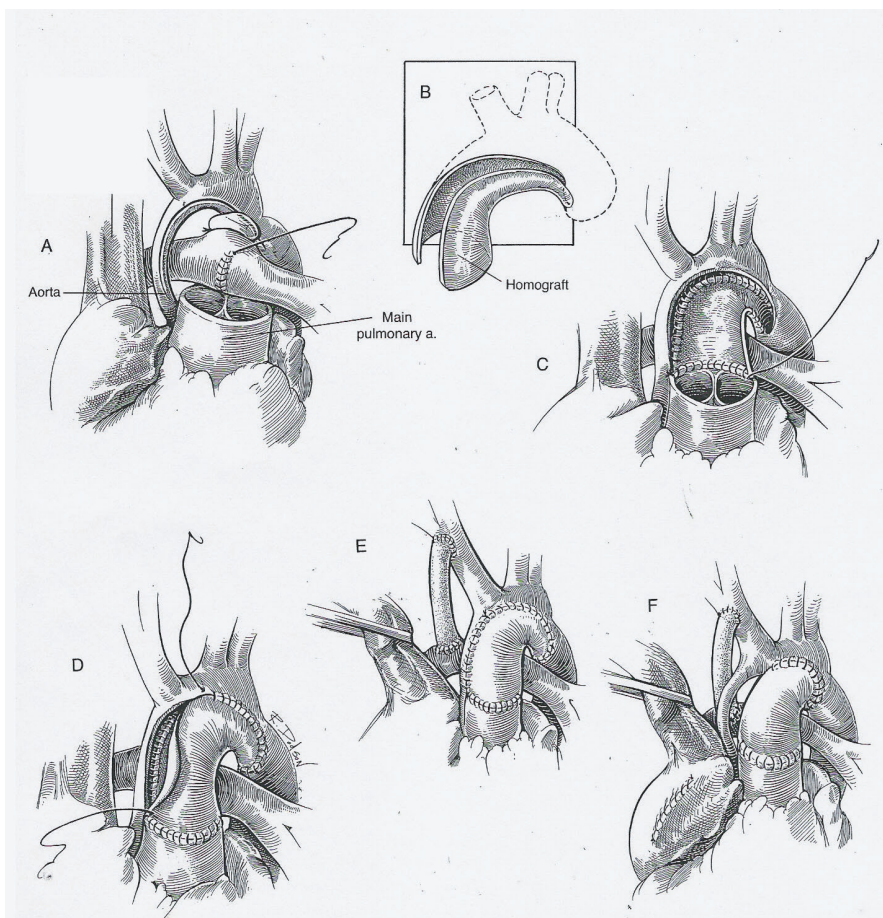Fontan F, Baudet E. Surgical repair of tricuspid atresia. Thorax 1971;26:240–8.

Figure 1-6. Technique of the Norwood operation.
Current techniques for first-stage palliation of the hypoplastic left heart syndrome. A: Incisions used for the procedures, incorporating a cuff of arterial wall allograft. The distal divided mean pulmonary artery may be closed by direct suture or with a patch. B: Dimensions of the cuff of the arterial wall allograft. C: The arterial wall allograft is used to supplement the anastomosis between the proximal divided main pulmonary artery and the ascending aorta, aortic arch, and proximal descending aorta. D-E: The procedure is completed by an atrial septectomy and a 3.5-mm modified right Blalock shunt. F: When the ascending aorta is particularly small, and alternative procedure involves placement of a complete tube of arterial graft. The tiny ascending aorta may be left in situ, as indicated, or implanted into the side of the neoaorta.
Reprinted with permission from Elsevier. Castaneda AR, Jonas RA, Mayer JE. Hypoplastic left heart syndrome. In: Castaneda AR, Jonas RA, Mayer JE, et al, eds. Cardiac Surgery of the Neonate and Infant. Philadelphia: W.B. Saunders, 1994:371.

systemic and pulmonary circuit, but now central venous pressure becomes the driving force to propel blood across the pulmonary circuit. Separation of the pulmonary and systemic circuits eliminates mixing, relieves cyanosis, and decreases volume overload by eliminating systemic venous return to the functional single ventricle, potentially improving long-term performance.

In recent years, several modifications to the Fontan procedure have been made. Three modifications responsible for improved patient selection and survival include the cavopulmonary anastomosis, creation of a baffled fenestration, and an intermittent stage procedure (e.g., bidirectional Glenn anastomosis or hemi-Fontan). The cavopulmonary anastomosis is performed by division of the superior vena cava, with anastomosis to the right pulmonary artery in an end-to-side fashion ensuring bidirectional flow into both the right and left pulmonary artery. Inferior vena cava blood flow is subsequently diverted to the right pulmonary artery with bidirectional flow using either an intra-atrial lateral tunnel approach or an extra-cardiac conduit (Figure 1-8). Both strategies use techniques to improve flow dynamics, which enhances efficiency and reduces stasis in the Fontan conduit. Both strategies may also help protect the right atria from high pressure and subsequent dilation.

Cardiopulmonary bypass induces an inflammatory response, resulting in a transient elevation in PVR and myocardial dysfunction. This response is extremely

de Leval MR, Kilner P, Gewillig M, et al. Total cavopulmonary connection: a logical alternative to atriopulmonary connection for complex Fontan operations. Experimental studies and early clinical experience. J Thorac Cardiovasc Surg 1988;96:682–95.

Bridges ND, Lock JE, Castaneda AR. Baffle fenestration with subsequent transcatheter closure: modification of the Fontan operation for patients at increased risk. Circulation 1990;82:1681–9.

Bridges ND, Jonas RA, Mayer JE, et al. Bidirectional cavopulmonary anastomosis as interim palliation for high-risk Fontan candidates: early results. Circulation 1990;82(suppl 5):IV170–6.
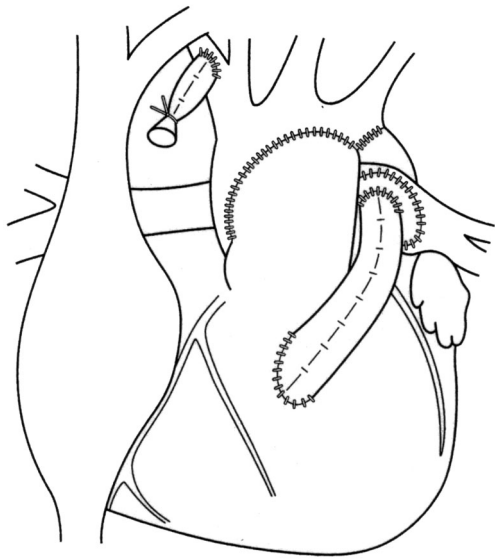
Figure 1-7. Right ventricle-pulmonary artery conduit.
After completion of aortic reconstruction and atrial septectomy, proximal anastomosis of the RV-PA shunt was performed with the heart beating.
PA = pulmonary artery; RV = right ventricle.
Reprinted with permission from Elsevier. Sano S, Ishino K, Kawada M, et al. Right ventricle-pulmonary artery shunt in first-stage palliation of hypoplastic left heart syndrome. J Thorac Cardiovasc Surg 2003;126:504–10.

problematic in patients during the acute postoperative period after Fontan palliation. Creation of a baffled fenestration in the Fontan conduit allows for a small right-to-left shunt, resulting in reduced central venous pressure, improved ventricular preload, and improved cardiac output with only minor decreases in systemic saturation. Use of a fenestration allows for recovery from the inflammatory insult with reduction in PVR and improvement in ventricular function. The fenestration may be closed later via an occlusion device in the catheterization laboratory or with snare closure tunneled to the subcutaneous tissue placed at time of surgery.

An intermittent procedure is now advocated between the time of initial palliation and completion of the Fontan to minimize risk factors (e.g., ventricular hypertrophy and dilation secondary to palliative shunt) and improve outcome. A bidirectional Glenn shunt is performed by anastomosis of the superior vena cava to the right pulmonary artery in an end-to-side fashion allowing flow down both the right and left pulmonary artery (Figure 1-9). The superior vena cava entry into the right atrium is then closed. The hemi-Fontan operation creates a baffle that diverts superior vena caval blood to the pulmonary arteries but maintains continuity between the superior vena cava and the right atrium allowing easier transition to a lateral tunnel Fontan completion. Both procedures produce the same
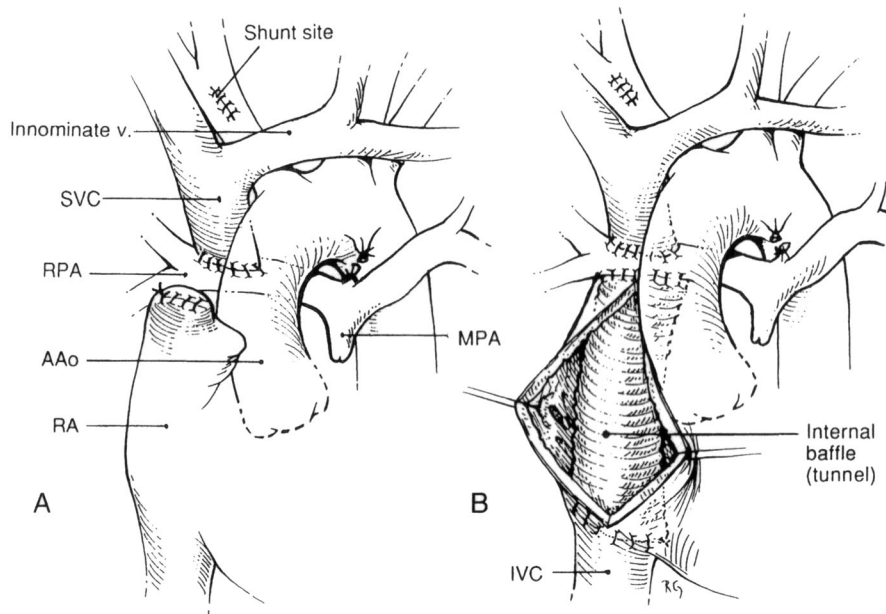

Figure 1-8. Cavopulmonary anastomosis and Fontan procedure.
A: The cavopulmonary anastomosis (hemi-Fontan). The SVC has been transected well above the junction with the RA, thereby avoiding damage to the SA node and nodal artery. The previous systemic-pulmonary shunt has been excised. That part of the SVC remaining with the RA is over sewn. A wide anastomosis is created between the distal part of the SVC and the top of the RPA. De-oxygenated blood from the head and arms (40% of total systemic venous return) is thereby delivered directly—without admixture—to the pulmonary arteries in continuity. Note the atretic MPA. B: Completion of the Fontan connection. The SVC already communicates exclusively with the pulmonary arteries. The RA is opened and an internal baffle tunnels the IVC blood through the RA to the dome of the atrium where the tunnel is connected to the undersurface of the RPA. When completed, all systemic venous return is channeled (not pumped) to the lungs and the heart receives only oxygenated blood for delivery to the aorta. Sometimes a small hole is placed in the baffle for decompression; at a later time, this can be closed surgically or per catheter.
AAo = ascending aorta; Inn Vn = innominate vein; IVC = inferior vena cava; MPA = main pulmonary artery; RA = right atrium; RPA = right pulmonary artery; and SVC = superior vena cava.
Reprinted with permission from Elsevier. Waldman LD, Wernly JA. Cyanotic congenital heart disease with decreased pulmonary blood flow in children. Pediatr Clin North Am 1999;46:385–404.

physiologic feature in that superior vena cava blood flow is diverted to the lungs while inferior vena cava blood returns directly to the heart. These operations provide adequate relief of cyanosis, promote adequate growth of pulmonary arteries, reduce ventricular volume preserving function, and limit development of systemic AV valve insufficiency, all of which will lead to successful Fontan completion.

Other improvements in cardiopulmonary bypass techniques have also led to improvements in outcomes in patients after Fontan completion. Minimizing the inflammatory response using modified ultrafiltration and aprotinin has decreased morbidity, with improved myocardial and pulmonary function in patients post-Fontan completion. Improved postoperative intensive care management plays a significant role in survival in the acute postoperative period.

Most pediatric cardiothoracic centers will proceed with a bidirectional Glenn/hemi-Fontan operation at 4–6 months followed by a fenestrated Fontan completion around 2–3 years of age. The operative survival after a second- and third-stage reconstruction is greater than 97% and 88%, respectively.

The first successful neonatal cardiac transplant was performed in 1985. Subsequently, cardiac transplantation has been advocated by some pediatric cardiothoracic centers as the surgical procedure of choice in patients with HLHS. The distinct advantage of this approach would be to restore normal cardiovascular physiology, rather than a staged approach with dependence on single ventricle physiology. A major limitation is the shortage of donor hearts resulting in a high percentage of patients (25%–31%) dying while awaiting transplantation. In addition, cardiac transplantation is not without long-term challenges. With improvement in outcomes using staged palliation in HLHS, most centers use cardiac transplantation in patients with HLHS who are not candidates for subsequent stage palliation after a Norwood operation (e.g., systemic ventricular dysfunction) or those with a failing Fontan who meet criteria for transplantation.

Untreated, HLHS is usually fatal during the first month of life. After staged palliation, the reported actuarial survival is about 72%–80% at 1 month, 60%–67% at 1 year, 54%–58% at 5 years, and 40% at 10 years. Reported causes of inter-stage and late mortality include recurrent arch obstruction, pleural effusions, sepsis, respiratory infections, right ventricular failure, and sudden death. An increased incidence of sudden death (4%–15%) appears to occur in patients between the Norwood and second-stage operation. Possible explanations for this increased incidence are dysrhythmia, ventricular dysfunction, aspiration, viral infection, and altered baroreceptor reflexes. Whether improved modifications will decrease the incidence of sudden death is unknown at this time.

Patients with HLHS after Fontan completion appear to perform similarly to other patients with single ventricle physiology (e.g., tricuspid atresia) with 80%–90% of patients in New York Heart Association class I or II. Right ventricle function and other anatomic factors (e.g., tricuspid valve) do not appear to be limitations. Long-term follow-up
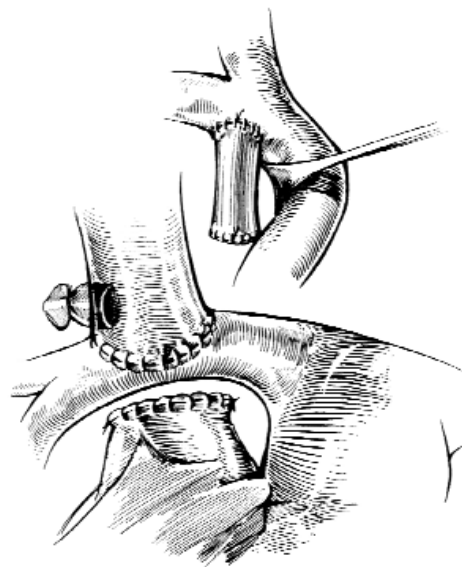

Figure 1-9. Bidirectional Glenn shunt.
The superior vena cava-to-right pulmonary artery anastomosis is completed with running absorbable suture.
Reprinted with permission from Elsevier. Castaneda AR, Jonas RA, Mayer JE, et al. Single ventricle with tricuspid atresia. In: Castaneda AR, Jonas RA, Mayer JE, et al, eds. Cardiac Surgery of the Neonate and Infant. Philadelphia: W.B. Saunders, 1994:262.

is needed to assess if these patients will have a higher incidence of single right ventricle dysfunction compared with those with a single functioning left ventricle.

Morbidity in patients undergoing a staged repair for HLHS includes arrhythmias, pulmonary artery occlusion, chronic pleural effusions, pulmonary hypertension, and cardiomyopathy. Long-term complications in patients with HLHS post-Fontan correction are associated with deteriorating ventricular function secondary to chronic elevation in central venous pressure and vascular resistance. These include atrial fibrillation/flutter, thromboembolism, obstruction of Fontan circuit, protein losing enteropathy, and chronic CHF.

Development of atrial fibrillation/flutter is problematic and is felt to be related to atrial incisions and suture lines made at the time of repair, as well as increasing right atrial pressure and size. Patients can present with hemodynamic deterioration requiring immediate intervention. Echocardiography should be performed to rule out obstruction and evidence of thrombus. Anticoagulation should also be initiated before attempted cardioversion and may be required long term in patients with evidence of obstruction or thrombosis. A large percentage of patients will be refractory to antiarrhythmic drugs and require catheter-directed or surgical ablation.

Thromboembolism can be a devastating complication. Risks associated with thromboembolism include atrial arrhythmias and right atrial dilation, or patients with ventricular dysfunction. Intervention with thrombolytics or

Bailey LL, Nehlsen-Cannarella SL, Doroshow RW, et al. Cardiac allotransplantation in newborns as therapy for hypoplastic left heart syndrome. N Engl J Med 1986;315:949–63.

surgical removal may be required. Long-term anticoagulation is required in patients with HLHS post-Fontan correction.

Patients with partial obstruction of their Fontan conduit can present with decreased exercise tolerance, atrial arrhythmias, and/or right-sided heart failure. Total occlusion usually results in sudden death. Surgical revision for obstruction of the Fontan conduit is usually required.

Protein-losing enteropathy is possibly due to elevated central venous pressures resulting in bowel edema with luminal protein loss. The frequency of protein losing enteropathy appears to increase with time and is refractory to most treatments. Revising the Fontan conduit may be entertained if evidence of obstruction exists. Resolution of refractory protein-losing enteropathy has been seen in patients with chronic CHF after cardiac transplantation. Chronic CHF manifests in patients with profound systemic ventricular dysfunction. In patients refractory to pharmacological management, cardiac transplantation may be indicated.

The reported incidence and severity of long-term side effects may be weighted toward early experiences with Fontan palliation and may not account for recent modifications. It is hoped that the improvements seen with short and intermediate survival will transmit into sustained increases in long-term survival and reduced complications.

Patient survival with HLHS after cardiac transplantation in infancy is compelling. Outcomes at Loma Linda Medical Center have demonstrated survival rates of 91% at 1 month, 84% at 1 year, 76% at 5 years, and 70% at 7 years. Registry data from the International Society of Heart and Lung Transplantation in 2004 recorded an improvement in survival in patients who received cardiac transplantation at less than 1 year of age, with about 85% survival at 1 month, 75% at 1 year, 70% survival at 5 years, and 65% at 9 years. However, long-term complications (i.e., acute rejection and transplant coronary artery disease leading to graft dysfunction, graft loss, and need for re-transplantation), as well as adverse effects associated with immunosuppressive drugs (e.g., opportunistic infections, malignancy, hypertension, diabetes, renal dysfunction, hypercholesterolemia), continue to hamper long-term outcomes.

Pharmacological Management

Surgical correction or palliation is the definitive treatment for most patients with CHD. However, pharmacological therapy continues to play a vital role in the stabilization, resuscitation, and prophylaxis and treatment of long-term complications. The role of the pharmacist in implementing effective pharmacological treatments in patients with CHD is complex. This role requires the ability to integrate knowledge about the anatomy and physiology of uncorrected and corrected CHDs, existing (e.g., other noncardiac congenital defects) or acquired (e.g., inflammatory response to cardiopulmonary bypass, or infection) disease states, and potential complications with knowledge of pharmaceutical care to design proper treatment regimens. The following discussion addresses pharmacological issues involved in preoperative,

postoperative, and long-term management of patients to limit complications and improve patient outcome.

The first preoperative priority is to reestablish a balanced circulatory flow to allow for adequate oxygenation and tissue perfusion. Depending on the CHD, this requires restoration of at least one of the following: pulmonary blood flow, systemic blood flow, or inter-circulatory mixing.

The majority of CHD disorders that present during infancy are dependent on a PDA to maintain adequate pulmonary blood flow (e.g., TOF with severe right ventricular outflow tract obstruction, tricuspid atresia, critical pulmonary stenosis, or pulmonary atresia), systemic blood flow (e.g., critical aortic stenosis, severe CoA, HLHS, and truncus with interrupted aortic arch), or inter-circulatory mixing (e.g., D-TGA). Patients with ductal closure will usually present during the first several days of life and may be critically ill with severe cyanosis and/or cardiogenic shock and multiorgan dysfunction (e.g., kidney or hepatic).

Prostaglandin E_1 (alprostadil) is the drug of choice to restore ductal flow. Endogenous PGE_1 production by the placenta and in ductal tissue is vital in maintaining ductal patency in utero. After birth, loss of placental PGE_1 and increased pulmonary blood flow promotes ductal closure. Administration of alprostadil restores or maintains ductal patency by directly causing relaxation of ductal and vascular smooth muscle resulting in vasodilation. Response is usually immediate with improved oxygenation and tissue perfusion. Response failure may indicate an incorrect diagnosis, ductal unresponsiveness or absence, or an obstruction to pulmonary venous flow (e.g., obstructive TAPVR, and HLHS with restrictive ASD). Alprostadil is initiated as a continuous intravenous infusion at 0.025–0.1 mcg/kg/minute and then titrated once therapeutic effect is achieved to the lowest effective dose to maintain ductal patency (e.g., 0.02–0.03 mcg/kg/minute) to minimize adverse effects. The most frequent dose-related adverse effects are apnea, hypotension, and tachycardia. These effects are seen most often seen in infants weighing less than 2 kg. All patients on alprostadil require continuous cardiac and respiratory monitoring. Patients should have a separate intravenous access in case of hypotension to allow administration of fluid boluses, if required, for resuscitation. In patients requiring transport to a specialized care facility, elective intubation with mechanical ventilation for potential apnea episodes should be considered. In instances when apnea occurs, intubation with mechanical ventilation may be warranted until palliative or definitive correction is performed.

For isolated persistent PDA resulting in pulmonary congestion and left ventricular volume overload, the opposite approach to ductal management is indicated. Pharmacological closure with indomethacin is the primary method used for ductal closure in premature infants with isolated persistent PDA. Indomethacin works by inhibiting production of PGE, thereby allowing the ductus to close. Dosing of indomethacin is dependent on postnatal age and renal function. Patients need to be monitored closely for adverse effects secondary to indomethacin administration

Boucek MM, Edwards LB, Keck BM, Trulock EP, Taylor DO, Hertz MI. Registry for the International Society for Heart and Lung Transplantation: seventh official pediatric report—2004. J Heart Lung Transplant 2004;23:933–47.

(e.g., renal dysfunction, or gastrointestinal bleeding). Patients at high risk for adverse effects or with documented pharmacological failure should not receive indomethacin and, therefore, may require surgical intervention.

Significant hemodynamic compromise can be seen on initial presentation or with postsurgical intervention. Hemodynamic support may be required secondary to profound hypoxemia and hypoperfusion resulting in acidosis and ventricular dysfunction. Myocardial function can be impaired after cardiopulmonary bypass for many reasons, some of which include an inflammatory response due to cytokine release with cardiopulmonary bypass, ischemia and reperfusion injury, inadequate myocardial protection, and need for ventriculotomy (e.g., TOF with transannular patch). Volume resuscitation, inotropic support, and correction of metabolic acidosis with sodium bicarbonate may be required for initial stabilization.

Volume resuscitation is the initial treatment for hypoperfusion states due to intravascular volume depletion or where higher filling pressures are desired (e.g., ventricular noncompliance secondary to myocardial edema or significant ventricular hypertrophy). Fluid boluses using 0.9% sodium chloride, 5% albumin, or other colloidal expanders if indicated (e.g., packed red blood cells and fresh frozen plasma) may be given intravenously at 10–20 mL/kg increments until an adequate response is achieved. This is determined by improvement in systemic arterial pressure, arterial and venous saturation, or peripheral perfusion (e.g., skin color and temperature, pulses), renal function (e.g., urine output, serum creatinine, and blood urea nitrogen), with a reduction in heart rate and normalization of core body temperature, acid/base balance, and other end-organ function (e.g., liver).

If initial resuscitation fails or volume overload with pulmonary congestion is present, inotropic drugs may be used. Dopamine, an endogenous catecholamine, shows dose-dependent effects on the dopaminergic, β_1- and α_1-receptors. At a low dose (2–3 mcg/kg/minute), the dopaminergic effects predominate resulting in increases renal and mesenteric blood flow. At intermediate doses (3–10 mcg/kg/minute), the β_1-receptor effects predominate, resulting in an increased inotropic effect and improvement in myocardial contractility. At doses greater than 10 mcg/kg/minute, the α_1-receptor effects predominate, resulting in increased vasoconstriction. In most instances, dopamine doses less than 10 mcg/kg/minute improve myocardial contractility by increasing stroke volume, cardiac output, mean arterial pressure, and urine output, with a relatively low incidence of adverse effects. Interpatient variability requires individualized dosing. Adverse effects include tachycardia, arrhythmias, increased myocardial oxygen demand/consumption, and increased PVR.

Milrinone, a phosphodiesterase III inhibitor, increases intracellular cyclic adenosine monophosphate concentrations resulting in enhanced myocardial contractility. In addition, increased intracellular cyclic adenosine monophosphate concentrations in vascular smooth muscle result in smooth muscle relaxation and decreases SVR. The net effect is positive inotropy with systemic and pulmonary vasodilation. It improves myocardial function without increasing myocardial oxygen demand and has a lower risk of inducing arrhythmias compared with catecholamine drugs. Milrinone has also improved diastolic relaxation. Milrinone used in conjunction with catecholamines can provide a synergistic effect on improving myocardial function. Milrinone is beneficial in the postoperative period for a patient who has reduced cardiac function and increased diastolic dysfunction secondary to myocardial edema with increased PVR. When inotropic support is needed in patients after congenital heart surgery, our practice is to use milrinone at an average dose of 0.5 mcg/kg/minute (range: 0.25–0.75 mcg/kg/minute) in combination with dopamine. Milrinone, either alone or in combination with catecholamines (e.g., dobutamine), can also be used in patients with end-stage CHF who require inotropic support to maintain adequate hemodynamics while awaiting cardiac transplantation. Side effects associated with milrinone use are hypotension and arrhythmias. Unlike catecholamine agents, milrinone possesses a longer elimination half-life (3–4 hours), which may be problematic in patients exhibiting side effects, specifically hypotension. Milrinone is also eliminated renally and can accumulate in patients with decreased renal function necessitating a dosage adjustment (0.2–0.3 mcg/kg/minute).

Dobutamine, a synthetic catecholamine, predominately stimulates β_1-receptors on the myocardium. At low doses, it possesses weak effects on α_1- and β_1-receptors. At higher doses, however, stimulation of β_2-receptors results in vasodilation. The net effect is potent inotropic activity with some afterload reduction at higher doses. Usual doses of dobutamine range from 2 to 10 mcg/kg/minute. Doses as high as 20 mcg/kg/minute have been used. In the authors' experience, problems with tachycardia, arrhythmias, and tachyphylaxis coupled with the more favorable effects of milrinone have limited the use of dobutamine in postoperative cardiac patients. Dobutamine can also be used in patients with end-stage CHF requiring inotropic support to maintain adequate hemodynamics while awaiting cardiac transplantation.

Epinephrine, also an endogenous catecholamine, stimulates α_2-, β_1-, and β_2-receptors in a dose-dependent fashion. At low doses (0.01–0.05 mcg/kg/minute) of epinephrine, β_1- and β_2-receptor effects predominate over α_1-receptor effects. At higher doses (0.05–1 mcg/kg/minute), β_1- and α_1-receptor effects predominate. The net effect is, at low doses, epinephrine increases mean arterial pressure and cardiac output with a reduction in SVR and pulmonary capillary wedge pressure. At high doses, epinephrine increases mean arterial pressure, cardiac output, SVR, and pulmonary capillary wedge pressure. Epinephrine is a potent inotrope; however, its potential side effect profile is problematic. Side effects include tachycardia, exacerbation of supraventricular and ventricular arrhythmias, increased myocardial oxygen demand, and increased afterload at higher doses. In addition, epinephrine can induce hyperglycemia and metabolic acidosis. In our experience, epinephrine is used as a third-line drug behind dopamine and milrinone, and it is used in the short term to augment cardiac output and blood pressure.

Recently, vasopressin (antidiuretic hormone) has been used to treat profound vasodilatory shock after cardiac surgery. Vasopressin stimulates the V_1-receptor, which

causes vasoconstriction in patients with arterial hypotension. Normally, vasopressin exhibits little vasoconstrictor effect in hemodynamically normal patients. However, in instances where arterial pressure is threatened, vasopressin is an important endogenous vasopressor. Vasopressin levels may be inappropriately low in patients with vasodilatory shock after cardiopulmonary bypass or other systemic inflammatory response syndrome states. Administration in small doses (0.0003–0.002 units/kg/minute) by continuous intravenous infusion in pediatric patients improves blood pressure and allows reduction in exogenous catecholamine requirements. Other advantages of vasopressin are its effectiveness in the presence of metabolic acidosis, improvement in myocardial oxygen delivery without increasing consumption, and potential for reducing pulmonary vasoconstriction when compared with catecholamines. Vasopressin is presently used in conjunction with catecholamines and inotropic drugs in the management of vasodilatory shock. Side effects to consider include coronary and mesenteric ischemia (uncommon at doses used in vasodilatory shock), limb ischemia, free water resorption, decreased urine output, water intoxication, and hyponatremia.

Methylprednisolone administered at 10 mg/kg intravenously about 8 hours before and immediately before initiation of cardiopulmonary bypass may be used in specific cases (e.g., neonatal surgery and single ventricle repair) to blunt the inflammatory response, limit postoperative myocardial dysfunction, and limit pulmonary vascular reactivity associated with cardiopulmonary bypass. Methylprednisolone has also been given in the immediate postoperative period in unstable patients who exhibit an exaggerated or continued inflammatory response.

Aprotinin, a serine protease inhibitor, is also used to reduce the inflammatory response and improve myocardial and pulmonary function in patients undergoing cardiopulmonary bypass. Although it is not totally clear, aprotinin's effect on the coagulation system is felt to be due to inhibition of plasmin, kallikrein, and trypsin in a dose-related fashion causing inhibition of fibrinolysis and contact activation, with preservation of platelet function. This results in a reduction in blood loss and the need for transfusion of blood components during cardiac surgery. In addition, aprotinin may attenuate the inflammatory response to cardiopulmonary bypass by regulating cytokine release and leukocyte activation.

Using aprotinin decreases morbidity and mortality in various pediatric populations undergoing cardiac surgery (e.g., Norwood or Fontan). Aprotinin is given intra-operatively in patients with a body surface area of less than or equal to 1.16 m² as follows: 240 mg/m² (maximum dose: 280 mg) intravenously as a loading dose, 240 mg/m² (maximum dose: 280 mg) in priming volume of bypass pump, and 56 mg/m²/hour (maximum dose: 70 mg/hour) as a continuous intravenous infusion during surgery. In patients with a body surface area of greater than 1.16 m², aprotinin is dosed as follows: 280 mg/m² (maximum dose: 280 mg) intravenously as a loading dose, 280 mg/m² (maximum dose: 280 mg) in priming volume of bypass pump, and 70 mg/m²/hour (maximum dose: 70 mg/hour) as a continuous intravenous infusion during surgery. All patients must receive a test dose of aprotinin 0.1 mg/kg (maximum dose: 1.4 mg) intravenously before full dosing to assess the potential for an allergic reaction. This is important in re-operative patients who may have had previous exposure to aprotinin.

Postoperatively, triiodothyronine can be administered in patients requiring aggressive hemodynamic support with continued poor function. Thyroid hormones, specifically triiodothyronine, have a direct impact on the cardiovascular system including effects on heart rate, cardiac output, and systemic vascular resistance. Triiodothyronine decreases SVR and increases cardiac contractility and chronotropy, resulting in an increase in cardiac output. Thyroid hormone concentrations may be suppressed in patients with critical illness and after surgical procedures. Triiodothyronine stores may even be depleted post-cardiopulmonary bypass. Triiodothyronine replacement has augmented cardiac function and may allow weaning of inotropic support in pediatric patients with low cardiac output states after cardiac surgery. Triiodothyronine as a single intravenous dose of 2 mcg/kg/day, followed by 1 mcg/kg/day for up to 12 days, has been used.

In isolated instances, systemic blood pressure may be elevated preoperatively or in the initial postoperative period, resulting in increased afterload and decreased cardiac output. Intravenous vasodilators such as nitroprusside or nitroglycerin can be effective in reducing afterload and improving cardiac output in these patients. Nitroprusside is a potent arterial/venous vasodilator with quick onset and offset allowing for rapid titration. Doses range from 0.5 to 5 mcg/kg/minute as a continuous intravenous infusion. Side effects include hypotension and cyanide and thiocyanate toxicity. The latter two side effects are associated with patients who receive increased doses for longer time periods (longer than 48 hours) or who have renal (thiocyanate toxicity) or hepatic (cyanide toxicity) insufficiency. Though not as effective as nitroprusside, nitroglycerin may be used as an alternative in patients with elevated blood pressure. Dose regimens used in this population are 0.5–5 mcg/kg/minute as a continuous intravenous infusion. In addition, nitroglycerin can be used in patients in instances where coronary perfusion is in question (e.g., D-TGA after arterial switch). Side effects with nitroglycerin include hypotension and headache. Tachyphylaxis can be seen with prolonged use.

Chronic CHF is a potential long-term complication in patients with a CHD, especially in those requiring single ventricle palliations (e.g., tricuspid atresia, pulmonary atresia, and HLHS). Definitive trials addressing pharmacological management in pediatric patients with chronic CHF lag significantly behind their adult counterparts. In addition, differences in structural anatomy and physiology, resulting in the development of CHF in the pediatric population compared with adult patients, often inhibit extrapolation of various treatment regimens used in adults to the pediatric population. Hence, specific heart failure regimens considered standard in adult patients are only beginning to make their way into the pediatric arena.

At this time, pharmacological therapy primarily focuses on using digoxin, loop diuretics, and afterload reduction with angiotensin-converting enzyme inhibitors. Digoxin, a

cardiac glycoside, continues to be used in chronic management of pediatric CHF. It acts as a positive inotrope to increase myocardial contractility resulting in the improvement in symptoms. Doses are age-dependent secondary to changes in pharmacokinetic parameters with increasing age. Its narrow therapeutic index requires close follow-up to avoid toxicity. Furosemide, 1–2 mg/kg/dose administered every 6–24 hours, is effective in managing edema and improving symptoms, in most instances, in pediatric CHF. Close monitoring of electrolyte concentrations (e.g., potassium and magnesium) will be required to prevent depletion and potential side effects.

Angiotensin-converting enzyme inhibitors, as in adults, have now become a cornerstone in managing heart failure in pediatric patients. Of the angiotensin-converting enzyme inhibitors available today, captopril and enalapril are the most studied and, therefore, the most used in this population. In neonates, captopril is initiated at 0.05–0.1 mg/kg/dose orally every 8–24 hours and slowly titrated to effect or a dose of 0.5 mg/kg/dose orally every 6–24 hours. In infants and children, a starting dose of 0.1–0.3 mg/kg/dose orally every 6–8 hours with titration to effect or a maximum total dose of 6 mg/kg/day. Enalapril is initiated at 0.1 mg/kg/day orally divided every 12 hours or daily and titrated to effect or a maximum dose of 0.5 mg/kg/day. Side effects include hypotension, hyperkalemia, angioedema, and renal dysfunction.

β-Blockers (e.g., metoprolol and carvedilol) and/or spironolactone are useful in relieving symptoms and improving survival in adult patients. Experience with these drugs in pediatric patients with CHF is beginning to evolve. Some patients will continue to progress to end-stage heart failure with adequate medical management. In these patients, cardiac transplantation may be indicated. In isolated instances, intravenous inotropic drugs (e.g., dobutamine and milrinone) and/or mechanical support (e.g., intra-aortic balloon pump and extracorporeal membrane oxygenation) may be required as a bridge to transplantation. The role of nesiritide in managing acute decompensated heart failure in pediatric CHF has not been studied.

Hypertension is another complication that can present after infancy and, in particular, in patients after coarctectomy for CoA. Antihypertensive drugs may be required before surgery and initially postoperatively. β-Blockers (propranolol 1–5 mg/kg/day orally divided every 6–8 hours; atenolol 0.8–1.5 mg/kg/day orally once a day) and angiotensin-converting enzyme inhibitors (e.g., captopril and enalapril) are drugs of choice for treating preoperative hypertension in these patients. In the initial postoperative period, esmolol (50–1000 mcg/kg/minute intravenously as a continuous infusion) and/or nitroprusside may be required to control rebound hypertension, with subsequent conversion to oral drugs in patients who require continued management.

Hypercyanotic spells (i.e., "tet spells") experienced in some patients with TOF can be problematic. These spells are characterized by increases in agitation or irritability, tachypnea, hyperpnea, and profound cyanosis. Severe spells can result in unconsciousness, seizures, cerebrovascular accidents, and, in rare instances, death. Propranolol at 1–2 mg/kg/dose given orally every 6 hours has been used

prophylactically in patients to decrease the frequency and severity of hypoxic spells. Treatment strategies are targeted at increasing pulmonary blood flow either by reducing right ventricular outflow tract obstruction or increasing SVR. Initial efforts should be made to calm the infant or child and to hold the child in a knee-to-chest position over the shoulder. Treatment with oxygen, sedation (e.g., morphine 0.05–0.1 mg/kg/dose intravenously), and volume expansion may be necessary. Phenylephrine, a direct-acting α_1-agonist, may be used in persistent cases. Phenylephrine at 5–20 mcg/kg/dose given intravenously at a bolus 10–15-minute intervals or by continuous infusion intravenously at 0.1–0.5 mcg/kg/minute will cause systemic vasoconstriction. This will increase SVR, resulting in increased pulmonary blood flow secondary to reduction in right-to-left shunting through the VSD. In rare instances, intubation with mechanical ventilation and surgical intervention may be required.

Preoperative and postoperative arrhythmias most commonly include SVT. Antiarrhythmic drugs (e.g., adenosine, digoxin, β-blockade, procainamide, amiodarone, and flecainide) may be needed to abort and/or suppress further arrhythmic activity (see Cardiac Rhythm Disorders section for further details). Junctional ectopic tachycardia is an arrhythmia that occurs rarely in the acute postoperative period. This arrhythmia may be life-threatening and is difficult to eradicate. Rapid junctional ectopic tachycardia can cause profound hemodynamic instability and, if uncontrolled, will produce profound ventricular dysfunction and death. Therapies used include mechanical ventilation, sedation and paralysis, hypothermia (e.g., 33–35°C), elimination of catecholamines and other myocardial irritants if possible, and overdrive pacing. Antiarrhythmic drugs used to treat junctional ectopic tachycardia include esmolol (25–300 mcg/kg/minute intravenously as a continuous infusion), amiodarone (5–10 mg/kg intravenously given over 1 hour followed by a continuous infusion at 5–15 mcg/kg/minute), and procainamide (5–15 mg/kg intravenously as a loading dose given over 15–60 minutes followed by a continuous infusion at 20–80 mcg/kg/minute).

Long-term atrial fibrillation/flutter is the most common arrhythmia and may be problematic. Patients with reduced ventricular function can develop hemodynamic deterioration requiring immediate intervention. Evidence of thrombus formation must be excluded and anticoagulation should be initiated before cardioversion in most instances. Patients can become refractory to antiarrhythmic drugs, necessitating ablation. Automated implantable cardioverter defibrillator placement should be considered in patients with previous episodes of near sudden death.

Mechanical ventilation is used in patients with impending respiratory failure, as well as in postoperative patients, to improve and maintain oxygenation and ventilation. Mechanical ventilation is also used in certain patients with CHD to manipulate the pulmonary circuit, and to achieve a balance in pulmonary and systemic blood flow in preoperative patients with ductal dependent blood flow and in postoperative patients with systemic to pulmonary artery shunts (e.g., HLHS post-Norwood).

Inhaled nitric oxide, a selective pulmonary vasodilator, is administered through the ventilatory circuit in patients with

pulmonary hypertension refractory to conventional pharmacological and ventilatory management. Endogenous nitric oxide is formed by the vascular endothelium from L-arginine and oxygen catalyzed by nitric oxide synthase. It subsequently acts on vascular smooth muscle to cause vasodilation via the cyclic guanosine monophosphate-dependent pathway. Patients can exhibit pulmonary vascular endothelial dysfunction and decreased pulmonary blood flow after cardiopulmonary bypass. This can result in transient impaired production of nitric oxide and development of pulmonary hypertension with hemodynamic compensation in the acute postoperative period in some patients. In this setting, inhaled nitric oxide has been beneficial in reducing pulmonary vascular resistance and pulmonary artery pressure while improving hemodynamics in patients with reactive pulmonary hypertension after cardiac surgery. When given exogenously through the ventilator circuit, nitric oxide is delivered directly to the blood vessels in the lungs. Rapid inactivation by hemoglobin prohibits systemic exposure and, therefore, accounts for its selectivity in the pulmonary vasculature without causing systemic hypotension. Inhaled nitric oxide is usually administered at 1–80 ppm. Patients should be titrated to the lowest possible dose to maintain efficacy and reduce toxicity.

Patients need to be monitored closely for the potential development of methemoglobinemia and nitrogen dioxide toxicity while receiving inhaled nitric oxide. In instances where methemoglobinemia develops, methylene blue (1–2 mg/kg/dose intravenously) can be given. Caution must be taken to avoid discontinuation or abrupt withdrawal of inhaled nitric oxide until the pathologic insult has resolved to avoid development of a rebound pulmonary hypertensive crisis. In patients being weaned from inhaled nitric oxide, rebound pulmonary hypertension associated with nitric oxide withdrawal has been experienced. This may be secondary to reduced production of endogenous nitric oxide as well as reduction in cyclic guanosine monophosphate with discontinuation of inhaled nitric oxide. Phosphodiesterase V is responsible for the breakdown of cyclic guanosine monophosphate in lung tissue. The phosphodiesterase V inhibitor sildenafil, at 0.25–0.35 mg/kg given every 4–8 hours, has been effective in blunting rebound pulmonary hypertension, allowing successful withdrawal of inhaled nitric oxide. Sildenafil can be used for intermediate and long-term management of pulmonary hypertension and also act synergistically with inhaled nitric oxide in refractory patients. Adverse effects include hypotension secondary to systemic vasodilation.

Continuous intravenous sedation with lorazepam (0.1 mg/kg/hour) or midazolam (0.1 mg/kg/hour) and paralysis with vecuronium (0.1 mg/kg/hour) or cisatracurium (3 mcg/kg/minute) may be required to assist with mechanical ventilation. In neonates with evidence of intraventricular hemorrhage and/or seizures, anticonvulsant drugs may be initiated. Continuous sedation/paralysis is used with mechanical ventilation to induce hypoventilation in patients with pulmonary overcirculation to reduce

pulmonary blood flow and improve systemic flow through the PDA (e.g., HLHS).

In many instances, significant renal dysfunction is present initially secondary to hypoperfusion and shock. Drugs must be evaluated and dose adjusted to avoid adverse effects and maintain efficacy as renal function improves. Patients can develop volume overload secondary to CHF and fluid retention with PGE_1 administration. Diuretic therapy (e.g., furosemide 1–2 mg/kg/dose intravenously every 6–12 hours) is used to assist in volume management. Postoperative patients can become volume-overloaded secondary to capillary leak syndrome, which can be induced by the inflammatory effects of cardiopulmonary bypass. These patients can become refractory to intermittent loop diuretics and require a thiazide diuretic (e.g., metolazone 0.2–0.4 mg/kg/day orally divided every 12–24 hours, chlorothiazide 5 mg/kg/dose intravenously every 6–12 hours) and/or continuous intravenous infusion of loop diuretics (e.g., furosemide 0.1–0.4 mg/kg/hour) to augment urine output. Close monitoring of electrolytes (e.g., sodium, chloride, potassium, magnesium, and calcium) to avoid depletion and adverse events (e.g., arrhythmias) will be required with aggressive diuretics use.

Hepatic insufficiency from shock will result in decreased hepatic drug metabolism and elimination, requiring careful dosage adjustment of certain drugs. In addition, coagulopathy can be present secondary to decreased production of vitamin K clotting factors. Vitamin K (1–2 mg subcutaneously or intravenously) is frequently used in conjunction with administration of other clotting factors to control or minimize the risk of bleeding. Stress ulcer prophylaxis with a histamine type-2 blocking drug, such as ranitidine (2–4 mg/kg/day intravenously divided every 8–12 hours, maximum 50 mg/dose) or sucralfate (25 mg/kg/dose orally every 6 hours, maximum 1 g/dose) is initiated to reduce risk of gastrointestinal bleeding.

Nutrition support is important in patients with CHD. Many will present as newborns with high caloric requirements, whereas others will present later with failure to thrive. Patients with ductal-dependent lesions, premature infants, and infants with indwelling umbilical artery catheters are at an increased risk for developing necrotizing enterocolitis secondary to reduced mesenteric flow. To reduce the risk of necrotizing enterocolitis, parenteral nutrition may be used until palliation/correction is performed and umbilical artery lines are removed before starting enteral nutrition.

Anticoagulation will be required in patients with CHD after various operative procedures, including BT shunts, mechanical valve replacement, bidirectional Glenn shunt, hemi-Fontan, Fontan, and Norwood procedures. Anticoagulation strategies used in these patients differ depending on institutional practice. Consensus guidelines addressing immediate and long-term anticoagulation for various congenital heart procedures were recently published. Recommendations for acute anticoagulation for the above procedures are with unfractionated heparin (e.g., 10–25 units/kg/hour intravenously as a continuous infusion)

Monagle P, Chan A, Massicotte P, Chalmers E, Michelson AD. Antithrombotic therapy in children: the seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004;126(suppl 3):645S–87S.

titrated to a therapeutic level of anticoagulation by activated partial thromboplastin time with the exception of bidirectional Glenn/hemi-Fontan conduits where there is no consensus.

Recommendations for long-term prophylaxis with BT shunts are either aspirin (5 mg/kg/dose orally every day) or no treatment. Mechanical valve anticoagulation guidelines recommend warfarin (e.g., initial dose of 0.2 mg/kg orally every day, maximum initial dose of 5 mg/day) with target international normalized ratios recommended for use in adult patients (aortic valve: 2–3, mitral valve: 2.5–3.5). Patients at high risk or with documented previous thrombosis can use aspirin (6–20 mg/kg/day orally every day, maximum dose: 81 mg/day) in addition to warfarin. No consensus for prophylaxis with bidirectional Glenn and hemi-Fontan conduits was stated. Fontan patients require either aspirin (5 mg/kg orally every day) or warfarin (e.g., initial dose of 0.2 mg/kg orally every day, maximum initial dose of 5 mg/day) with target international normalized ratios of 2–3.

In the authors' experience, unfractionated heparin is started initially postoperatively when hemostasis has been achieved (about 6–8 hours after surgery) at a dose of 12 units/kg/hour intravenously by continuous infusion and titrated to a therapeutic activated partial thromboplastin time; heparin is continued until all intra-cardiac lines and epicardial pacing wires have been removed. In patients who have undergone a BT shunt, bidirectional Glenn, hemi-Fontan, Fontan, or Norwood operation, heparin is discontinued with conversion to aspirin at 5–10 mg/kg/day orally. Patients with post-mechanical valve replacement are transitioned to warfarin, with heparin being discontinued when international normalized ratio values are above 2.0. International normalized ratios are subsequently maintained according to adult guidelines for warfarin anticoagulation based on the type and location of the valve (aortic valve: 2–3, mitral valve: 2.5–3.5).

Thromboembolism is a devastating long-term complication. Patients with atrial arrhythmias, evidence of thrombus or with previous history of thrombosis, or severe ventricular dysfunction will require long-term anticoagulation with warfarin with target international normalized ratios of 2–2.5. Close monitoring is required to maintain adequate anticoagulation and reduce the bleeding risk. Thrombolytic intervention (e.g., alteplase 0.1–0.5 mg/kg/hour intravenously as a continuous infusion) is sometimes used in episodes of acute thrombosis. Risk of bleeding and embolization of residual thrombus must be carefully considered.

A sepsis evaluation should be completed with antibiotic drugs initiated (ampicillin 50–200 mg/kg/day intravenously divided every 6–12 hours with either cefotaxime 50 mg/kg intravenously every 8–12 hours or gentamicin 2–2.5 mg/kg/dose intravenously every 8–12 hours) where infection is suspected. Preoperative antibiotic drugs (cefazolin 25 mg/kg intravenously) are given before skin incision in the operating room and then immediately after cardiopulmonary bypass. Prophylactic antibiotic drugs (cefazolin 25 mg/kg intravenously every 8 hours) are continued for 48 hours postsurgery for sternal/thoracotomy wound prophylaxis and then discontinued.

Neonates who undergo congenital heart surgery requiring cardiopulmonary bypass (e.g., HLHS) can experience a significant inflammatory response resulting in profound third-spacing of fluid into the tissues including the heart and surrounding tissues. This can result in the development of myocardial edema and reduced ventricular function. In addition, profound tissue edema also occurs, which can prevent the ability to close the sternum and skin secondary to the creation of tamponade-like physiology secondary to extrinsic compression of structures on the heart. These patients will return from the operating room with an open chest with silastic closure and will need to receive preemptive antibiotic drug coverage (vancomycin 10–15 mg/kg intravenously every 8–12 hours and gentamicin 2–2.5 mg/kg intravenously every 8–12 hours). These drugs should be closely followed because of potential changes in renal function in this critically ill population. Antibiotic drugs are continued until 48 hours after sternal closure if cultures obtained at the time of closure are negative. Positive cultures will require longer therapy (7–14 days post-closure), with antibiotic drugs directed at the isolated organism.

Nosocomial infections such as ventilator-associated pneumonia should be treated with appropriate antibiotic drugs. Endocarditis prophylaxis, in accordance with guidelines from the American Heart Association, is recommended in all patients with CHD with the exception of patients with isolated secundum ASDs and in patients with surgically repaired ASD, VSD, and PDA without a residual defect at greater than 6 months.

Cardiac Rhythm Disorders

Arrhythmias result from disorders of impulse generation (e.g., automaticity or triggered depolarization), disorders of impulse conduction (e.g., conduction block or reentry circuit), or any combination of either disorder. Almost any type of arrhythmia can occur and result as a consequence of cardiac or systemic disease or as a primary disorder in an otherwise healthy child. The majority of children who are diagnosed with arrhythmias have structurally normal hearts. Advances in surgical and medical management for children with a CHD have resulted in improved survival. However, these children may be at risk for developing postoperative (early or late) arrhythmias. About 90% of children will have an audible heart murmur at some point during their childhood, with a 60% incidence reported in healthy newborns. Benign arrhythmias, such as premature atrial contractions and sinus pause in healthy full-term neonates, are common. Premature ventricular contractions are frequently observed in normal infants through adolescence with a reported prevalence of 10%–35%. Most premature ventricular contractions are idiopathic, easily suppressed with exercise, and self-limited. Sinus arrhythmia is another frequently benign arrhythmia commonly seen in adolescents.

Frommelt MA. Differential diagnosis and approach to a heart murmur in term infants. Pediatr Clin North Am 2004;51:1023–32.

Sinus arrhythmia is frequently due to the normal diving reflex changes in heart rate associated with respiration.

Although many diagnostic tools are available to distinguish the innocent murmur from the pathologic one, a thorough medical history is the first step in evaluating a child with an arrhythmia. The medical history should include maternal history, pregnancy and perinatal course, heritable syndromes, drug use, and growth and development. An accurate feeding history of the infant is also important. Feeding difficulties with associated tachypnea and diaphoresis are common manifestations of CHF, resulting from a CHD and/or arrhythmia. An appreciation for the unique features that a child displays, as well as knowledge of age-appropriate parameters for blood pressure, heart rate, PR interval and QRS duration, is essential for an accurate diagnosis.

Symptoms of arrhythmias are determined largely by effects on cardiac output, the presence or absence of heart disease, and the patient's age. Classic symptoms (e.g., palpitations, heart racing, and dizziness) of an arrhythmia described by adults may not be seen in children until the age of 5 years or older. Infants exhibit nonspecific symptoms, such as periods of lethargy, fussiness, or poor feeding. An arrhythmia can go unrecognized for hours or days if hemodynamic compromise is minimal. In the presence of hemodynamic compromise (e.g., CHD), signs of CHF can develop rapidly leading to hypotension, shock, and possibly death. In an adolescent, symptoms of an arrhythmia can be described as chest discomfort, fast heart rate, or dizziness. In rare cases, syncope and/or cardiac arrest can occur.

Supraventricular Tachycardia

Supraventricular tachycardia is the most common arrhythmia in children. Supraventricular tachycardia is a tachyarrhythmia that originates above the bundle of His. It implies the presence of a rapid heart rate (generally 200–300 beats/minute) that is paroxysmal (i.e., abrupt onset and termination) or nonparoxysmal, with or without the presence of a P wave. Supraventricular tachycardia is mediated by an accessory pathway (AP) that may be concealed or evident on a surface electrocardiogram (ECG). Accessory pathways are anomalous bands of conducting tissue between the atrium and ventricle. Most APs conduct in an antegrade manner from atrium to ventricle or in a retrograde manner in the opposite direction.

The prevalence of SVT is estimated to be between 1 in 25,000 and 1 in 250 children. Although there are 16 different mechanisms responsible for SVT (e.g., ectopic atrial tachycardia, junctional ectopic tachycardia, and atrial fibrillation) in children, many of the mechanisms are rare and have characteristic features that allow for rapid recognition. This discussion focuses on the two most common mechanisms in children: atrioventricular reentrant tachycardia (AVRT) and atrioventricular nodal reentrant tachycardia (AVNRT). Despite fundamental differences, both are paroxysmal reciprocating tachycardias that use anatomically discrete antegrade and retrograde APs. Atrioventricular reentrant tachycardia and AVNRT are both reentry arrhythmias that have the presence of a pathologic circus movement of an electrical impulse(s) around an anatomic loop (e.g., Wolff-Parkinson-White [WPW]

syndrome, AV node). Reentry may precipitate various supraventricular and ventricular arrhythmias.

The prevalence of these two mechanisms varies with patient age. About 90% of infant SVT is attributed to AVRT, with males being affected more often than females. The first episode of infant SVT occurs during the first year of life in 50%–60% of patients with the majority presenting by 2–3 months of age. In many infants, SVT will spontaneously resolve by 6–12 months of age, but 30% or more of these infants will have recurrence later in life (at a mean age of 8 years). In patients with SVT older than 5 years, there is a 78% chance that episodes of SVT will continue. With advancing age, AVNRT becomes more prevalent and approaches a prevalence of 15%–20% in the teenage years. Mortality from SVT in children is reported to be 1% in patients with a CHD and 0.25% in patients with normal anatomy.

Atrioventricular Reentrant Tachycardia

The most common form of AVRT involves antegrade conduction (from atrium to ventricle), also referred to as orthodromic, through the AV node and retrograde conduction up the AP to the atria. When there is antegrade AP conduction during sinus rhythm, ventricular pre-excitation occurs due to early activation of the ventricle through the AP. A frequently encountered type of orthodromic AVRT is WPW Syndrome, which is found in 22%–50% of children with SVT. The ECG signature of WPW syndrome during sinus rhythm reveals ventricular pre-excitation from the sinus impulse conducting through the AP (e.g., Kent bundle) resulting in a delta wave (i.e., slurred upstroke into the QRS complex) before the sinus impulse has passed through the AV node. During orthodromic AVRT (e.g., WPW syndrome), an atrial or ventricular depolarization initiates a reentry circuit in which the impulse travels antegrade fashion over the AV node, bundle of His, and bundle branches to the ventricles and then retrograde fashion up the AP to the atrium. No delta wave is seen during the tachycardia because the ventricles are depolarized through the normal AV conduction system. Retrograde P waves typically occur during the T wave, making the visibility of the P wave on ECG variable between individuals (Figure 1-10). A 1:1 relationship between atria and ventricles exists, with rates ranging from 220 to 280 beats/minute in the infant compared with 180 to 240 beats/minute in older children. After conversion to sinus rhythm, the QRS morphology displays the delta wave again. In patients with an AP that conducts only retrograde, its presences is not revealed on the standard ECG during sinus rhythm and is commonly called a "concealed" pathway. Among patients with AVRT, about 50% have a concealed AP.

Patients with WPW syndrome have an increased risk of atrial fibrillation, which also increases with age. Sudden death, cardiac arrest, and ventricular fibrillation have all been reported as the presenting sign in patients with undiagnosed and/or asymptomatic WPW syndrome. Ventricular fibrillation can be the presenting arrhythmia, and the consequences of a "missed" sudden death in children are obviously devastating. The lifetime risk for sudden cardiac death in patients with WPW Syndrome is 3%–4%. Asymptomatic patients with WPW syndrome have the same risk profile as symptomatic patients.
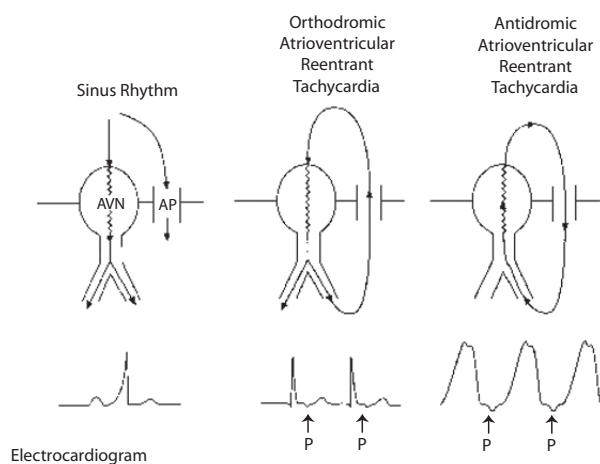
Sinus Rhythm   Orthodromic Atrioventricular Reentrant Tachycardia   Antidromic Atrioventricular Reentrant Tachycardia

Electrocardiogram

Figure 1-10. Mechanism of atrioventricular reentrant tachycardia in patients with the Wolff-Parkinson-White syndrome.

During sinus rhythm the slurred initial portion of the QRS or delta wave is due to early activation of part of the ventricles through rapid anterograde conduction over the accessory pathway (AP). During orthodromic atrioventricular reentrant tachycardia, no delta wave is seen because all anterograde conduction is over the atrioventricular node (AVN) and through the normal His-Purkinje system. Retrograde P waves are visible shortly after each QRS. During antidromic atrioventricular reentrant tachycardia, there is maximal preexcitation with wide, bizarre QRS complexes, because ventricular activation results entirely from anterograde conduction over the accessory pathway.

Reprinted with permission from the Massachusetts Medical Society. Ganz LI, Friedman PL. Supraventricular tachycardia. N Engl J Med 1995;332:162–73.

Atrioventricular Nodal Reentrant Tachycardia

Atrioventricular nodal reentrant tachycardia is the second most common type of SVT in children and is rarely seen in infants, but it appears with increasing frequency during early childhood and adolescence. These age-related findings are possibly the result of maturational changes known to occur in AV node physiology. Following surgical repair of a CHD, AVNRT is the third most common type of SVT after AP and intra-atrial reentry tachycardias. Atrioventricular nodal reentrant tachycardia is distinguished from AVRT in that dual pathways exist within or in close (i.e., perinodal) proximity of the AV node. The ECG during normal sinus rhythm is without pre-excitation (i.e., no delta wave). Abrupt changes in the PR interval during sinus rhythm are suggestive of dual AV node physiology. Typically, conduction proceeds antegrade down a slow pathway and retrograde up the AV node fast pathway (i.e., slow-fast AVNRT) to create the reentry circuit. On the ECG, the retrograde P waves are typically hidden within the QRS complex. Occasionally, the P wave can be seen just before the end of the QRS complex forming a pseudo s-wave in leads II and III. Heart rates are slower than in WPW syndrome and can range from 120 to 280 beats/minute, reflecting the influence of autonomic tone on this form of SVT. Bundle branch block should not affect the rate because the bundle branches are not involved in the reentrant circuit.

Acute Management

The management of children with acute SVT is dependent on presentation and severity of symptoms. When a life-threatening situation exists, such as unconsciousness or cardiovascular collapse, the ABCs of resuscitation (airway, breathing, circulation) must be followed. Once the airway is secured and assisted ventilation provided, attention can be focused on circulation. If no contraindications exist, all patients are initially treated with vagal maneuvers or adenosine.

Vagal maneuvers can be used while preparing a patient for drug therapy or electrical cardioversion. Inducing the diving reflex by placing an ice bag to the face is thought to be the most effective method in infants and young children with success rates of 30%–60%. In older children, the Valsalva maneuver may be effective by having the child forcibly exhale with a closed glottis, nose, and mouth. Another Valsalva technique suggested is having the child blow through a straw. Either method results in increased intrathoracic pressure, which decreases venous return to the heart and increases venous pressure, causing a reflex slowing of the heart rate. Carotid sinus massage may also be effective. The carotid sinus, located at the bifurcation of the common carotid artery, is supplied with sensory nerve endings of the sinus branch of the vagus nerve. When the carotid sinus is massaged, it causes vessel distention along with increased blood pressure, which results in reflex vasodilation and slowing of the heart rate. Applying external ocular pressure to produce a vagal response can lead to retinal detachment and is not recommended. Success rates of vagal maneuvers are variable and depend on the patient's level of cooperation. When a vagal maneuver is attempted, the patient's rhythm should be continuously monitored.

Adenosine is the drug of choice in any age group for tachycardias involving the AV node. Adenosine's advantages include a short elimination half-life (less than 10 seconds) and minimal or absent negative inotropic effects. Adenosine is an endogenous nucleoside with A_1-receptor agonist activity. Adenosine's electrophysiologic properties result in depression of sinus node automaticity, shortened atrial myocyte action potential and refractory period, slowed AV nodal conduction, and suppressed catecholamine-induced-triggered activity. Adenosine breaks the orthodromic circuit probably by direct action on AV nodal adenosine receptors.

Adenosine is administered by intravenous bolus through a vessel close to the heart using a starting dose of 100 mcg/kg followed immediately with a 5–10 mL normal saline flush. Because of adenosine's rapid metabolism in the vascular endothelium and erythrocytes, it must be administered as a rapid intravenous bolus. If the initial dose is ineffective, additional doses can be given by increasing the initial dose by 50–100 mcg/kg every 1–2 minutes until a maximum dose of 350 mcg/kg is reached. Successful cardioversion with adenosine in children ranges from 72% to 77%. A lower success rate (i.e., 60%–68%) has been reported in children younger than 1 year. Proposed explanations include the use of smaller gauge catheters, which limit rapid delivery of adenosine to the AV node, or AV nodes of infants may be more resistant to adenosine. In about 28% of children, recurrence of SVT will occur within seconds after successful termination by adenosine. If adenosine is not successful, it may be useful in diagnosing

primary atrial tachycardias during the brief time AV conduction is interrupted.

The effects of adenosine are antagonized by methylxanthines (i.e., theobromine, caffeine, and theophylline), which decrease the effect of adenosine by blocking adenosine receptors. Patients who are receiving antagonists will require either large doses of adenosine or an alternative drug. Dipyridamole is an adenosine uptake inhibitor and will prolong the effects of adenosine. Smaller doses of adenosine should be used in patients receiving dipyridamole. The use of adenosine in patients receiving verapamil, digoxin, or carbamazepine may increase the degree of heart block, which has been associated with ventricular fibrillation on rare occasions, warranting significantly smaller doses of adenosine or alternative methods of SVT conversion. Dosage adjustment is also necessary in pediatric patients with heart transplants who have a denervation-induced super sensitivity to adenosine. Adenosine is contraindicated in patients who have active bronchospasm, sick sinus syndrome (unless paced), and second- or third-degree heart block.

The incidence of adverse effects from adenosine range from 10% to 22% and are usually transient (2–3 minutes). The primary adverse effects include dizziness, facial flushing, nausea, chest pain, and dyspnea. Rare, more serious adverse effects include atrial fibrillation and flutter, ventricular fibrillation and flutter, asystole with fatal outcomes, and both fatal and nonfatal myocardial infarction. Continuous monitoring of blood pressure and an ECG are essential during adenosine administration.

Although digoxin has been used in both acute and chronic treatment of SVT, issues remain concerning slow response, lack of efficacy, and whether it is safe in children with WPW syndrome (i.e., pre-excitation). In as many as one-third of patients with WPW Syndrome, digoxin may shorten the antegrade refractory period pathway. In atrial tachyarrhythmias, this would result in a more rapid ventricular rate and an increased risk of sudden death. Recommendations have been made to avoid digoxin altogether because of effective alternative modes of therapy. Using oral or intramuscular digoxin is not recommended because of variable absorption. When AV nodal blocking drugs are not successful in terminating SVT, or the patient is hemodynamically unstable, synchronized electrical cardioversion while the patient is adequately sedated should be used. Synchronized direct current cardioversion is the recommended treatment for any patient with life-threatening symptoms. Synchronized cardioversion should be performed with an energy output of 0.5–1 Joule/kg, with the output doubled to a maximum of 5–6 Joule/kg until the treatment is effective.

If electrical cardioversion is not recommended, feasible, or successful, intravenous procainamide (5 mg/kg over 5 minutes, may repeat to a maximum loading dose of 15 mg/kg) or amiodarone (5 mg/kg over 20–60 minutes) should be considered. Procainamide and amiodarone both prolong the QT interval and should not be used concurrently. Verapamil should be used with extreme caution in infants younger than 1 year because of the potential to cause refractory hypotension and cardiac arrest. Verapamil (0.1 mg/kg intravenously over 2 minutes) can be useful in children older than 1 year when adenosine is ineffective or SVT rapidly recurs. Verapamil has a longer duration of action, which may be an advantage in preventing immediate recurrence. The primary disadvantage of verapamil is the propensity for hypotension. Verapamil should be given by slow intravenous infusion while the heart rate and blood pressure are monitored. In older children, verapamil has the same adverse effects as in adult patients, which include wide QRS-complex tachycardia, atrial fibrillation with an antegrade conducting AP (i.e., blocking the AV node may increase ventricular rate via AP), and significant hemodynamic compromise.

The pharmacist should recognize that all antiarrhythmic drugs used in the management of pediatric SVT, with the exception of digoxin, have negative inotropic effects. These drugs can cause significant hypotension and induce potentially life-threatening proarrhythmic events. The importance of having resuscitation equipment readily available when attempting pharmacological or electrical cardioversion in any patient cannot be overstated.

Chronic Management

Options available for long-term management of SVT include antiarrhythmic therapy, vagal maneuvers, and RFA. Long-term management of SVT is based on age, severity of symptoms, natural history of SVT, and the risks and benefits of each option. For newborns and infants, pharmacological therapy is advised for up to 1 year of life because recognition of recurrence of SVT may be difficult for many parents. For school-aged children with normal cardiac anatomy and minimal symptoms during SVT, an effective vagal maneuver is the only treatment required. For the remainder of children, antiarrhythmic drug treatment or RFA will be indicated. Which antiarrhythmic drug or combination of drugs actually improves patient outcomes is difficult to assess due to the absence of placebo-controlled trials in the prophylactic management of SVT during infancy and childhood. Long-term antiarrhythmic drug treatment is intended to prevent further episodes of SVT or decrease the severity of symptoms during a recurrence.

In newborns and infants, AVRT predominates as the type of SVT, with WPW Syndrome accounting for the mechanism in 20%–50%. For concealed AVNRT, digoxin (dosage is age dependent), a β-blocker, or both are generally considered first-line therapy. The goal is to modify conduction through the AV node. Oral digoxin is frequently used after the first episode of SVT or when the tachycardia is associated with signs of cardiac failure. Digoxin serum concentrations (0.8–2 ng/mL, International system of units = 1.0–2.6 µmol/L) should be monitored especially in cases of SVT recurrence, dose adjustment, declining renal function, clinical symptoms of toxicity, or abnormal ECG findings. Caution should be exercised in patients receiving digoxin during electrical cardioversion or during calcium infusion, both of which can induce ventricular fibrillation. Success rates for digoxin as single-drug therapy in preventing further attacks of SVT range from 40% to 75%. Propranolol (class II antiarrhythmic drug, nonselective β-blocker) has been widely used and is administered orally in a dose range of 1–4 mg/kg/day divided 3–4 times/day. Propranolol carries the risk of hypotension, bradycardia,

bronchospasm, and central nervous system effects due to its lipophilic properties. Atenolol (class II antiarrhythmic drug, cardioselective β-blocker) has increased in popularity due to the advantages of once-daily dosing (initial dosing 0.5–1 mg/kg/day with a maximum of 2 mg/kg/day) and fewer central nervous system effects due to its hydrophilic properties. Success rates for β-blockers in preventing recurrence of SVT have been reported to range from 50% to 90% of children treated. Digoxin and calcium-channel blockers (e.g., verapamil) should not be used in patients with WPW syndrome as both may shorten the effective refractory period of the AP. Acceptable first-line drug therapy for WPW syndrome is propranolol or atenolol. In patients having their initial episode of SVT at or before 2–3 months of age, antiarrhythmic drug therapy is usually weaned after 6–12 months with monitoring for recurrence. However, in older children, spontaneous cessation of SVT is rare. For these patients, chronic antiarrhythmic drug therapy can be used until RFA is indicated.

For SVT refractory to first-line drug therapy, other antiarrhythmic drugs such as flecainide, sotalol, and amiodarone can be effective. Flecainide or sotalol should be considered second-line treatment. Both drugs are equivalent in their risk profile. Amiodarone is primarily used as last-line treatment in case of refractoriness to flecainide or sotalol or life-threatening arrhythmias. The proarrhythmic potential of these drugs is concerning and is highest in children with a CHD, but it must also be considered in patients with structurally normal hearts. The natural history of childhood SVT is often a relatively benign course, and the prognosis for many of these children is excellent. A cautious risk-benefit analysis is essential every time antiarrhythmic drug treatment is considered. It would be disastrous for an otherwise healthy child with SVT to die because of a proarrhythmic event.

Flecainide is a class Ic antiarrhythmic drug that has local anesthetic- (sodium channel blocking activity) and membrane-stabilizing activity. Flecainide decreases conduction in all parts of the heart with the greatest effect on the His-Purkinje system (ventricular conduction velocity is decreased). Effects on AV nodal and intra-atrial conduction are affected to a lesser extent than ventricular conduction. The efficacy of flecainide in preventing recurrence of SVT in children is about 72%. Flecainide predominately increases the retrograde refractoriness of the AP in patients with SVT. Oral absorption is almost complete. Flecainide is 10%–50% renally eliminated, with the remainder metabolized through the liver to one active and one inactive metabolite. The elimination half-life of flecainide is age dependent, with the longest half-life of 29 hours at birth and decreasing to 6 hours by 1 year of age. In children 1–12 years of age, the half-life is about 8 hours and increases to 12 hours in adolescents. Flecainide serum concentrations should be maintained at 0.2–0.5 mcg/mL (International system of units = 0.4–1 µmol/L) up to 0.8 mcg/mL (International system of units = 1.6 µmol/L). Steady-state trough serum concentrations should be obtained after dosage adjustment, declining renal or hepatic function, or worsening cardiovascular status. Initiation of flecainide should be on an inpatient basis, with close monitoring by continuous ECG and supervised by a pediatric cardiologist for a minimum of 3 days. For children younger than 6 months, the initial dose of flecainide is 50 mg/m^2 orally divided 2–3 times/day. For children 6 months or older, the initial dose of flecainide is 100 mg/m^2 orally divided 2–3 times/day with a maximum dose of 200 mg/m^2/day. Changes in dosage may lead to disproportionate increases in plasma levels. Electrocardiograms and trough flecainide levels should be obtained at steady-state after dosage adjustment. Amiodarone can increase flecainide levels 2-fold if the flecainide dose is not reduced by 50%. Propranolol and cimetidine will increase flecainide levels by 20%–30%. Flecainide will increase digoxin levels by 15%–20%. Milk may inhibit absorption in infants, and reduction in dosage should be considered when milk is removed from the diet. Flecainide is associated with a risk of potentially dangerous proarrhythmic events in up to 7.5% of children treated. In a large multicenter trial, the frequency of proarrhythmia was similar in children with a CHD and those with normal hearts. However, cardiac arrest and sudden death predominated in children with a CHD. Three children with no risk factors other than SVT experienced cardiac arrest. Proarrhythmia could not be related to excessive dosage or plasma concentrations.

Sotalol is a class III antiarrhythmic drug with β-blocking properties. The β-blocking properties of sotalol are weak, resulting in negative inotropic effect that is of little clinical significance. The efficacy of sotalol in preventing recurrence of SVT has ranged from 79% to 94% in infants and children. The electrophysiologic effects of sotalol are prolongation of atrial and ventricular action potentials. Sotalol increases the effective refractory periods of atrial and ventricular muscle and APs in both the antegrade and retrograde directions in patients with SVT. The prolonged repolarization leads to an increase in the QT duration, which is dose dependent. The risk of torsades de pointes progressively increases with QT prolongation. Using sotalol concurrently with other drugs that prolong the QT interval, such as class I and class III antiarrhythmic drugs, tricyclic antidepressant drugs, and some macrolide antibiotic drugs, is not recommended. Patients must be monitored by continuous ECG during treatment initiation or dosage adjustment. Sotalol oral absorption is 90%–100% complete, and it has minimal protein binding and is not metabolized. Sotalol is primarily eliminated unchanged in the urine and therefore requires dose adjustment in conditions of renal impairment. The pharmacokinetics of sotalol are linear and correlate with body surface area and creatinine clearance. The terminal elimination half-life of sotalol in children is about 9.5 hours. The pharmacodynamics (i.e., β-blocking effect, QT and R-R interval) of sotalol are also linear, increasing in a dose-dependent fashion. For children 2 years or older, treatment should be initiated with an oral dose of 30 mg/m^2 3 times/day (90 mg/m^2 total daily dose) titrating to a maximum of 60 mg/m^2/dose. Titration should be guided on clinical response, heart rate, and QTc. At least 36 hours should separate dose increments to attain steady-state plasma concentrations in patients with normal renal function. For children younger than age 2, the sotalol dose is adjusted based on age and body surface area. Sotalol shares the same proarrhythmia effects as flecainide,

including torsades de pointes. Proarrhythmia has been documented in 10% of children treated with oral sotalol. Proarrhythmic events occurred in most instances within a few days of initiating sotalol treatment, was not dose related, and occurred with similar frequency in patients with and without a CHD. In-hospital treatment initiation and dose titration is warranted for all children under the supervision of a pediatric cardiologist.

Amiodarone is a class III antiarrhythmic drug that possesses activity in all four Vaughn-Williams classes. Oral amiodarone is generally reserved as the last drug used in the management of refractory SVT. Success rates in preventing recurrence of SVT in children have been consistently high, ranging from 84% to 93%. The electrophysiologic effects of amiodarone are similar to sotalol, which prolongs the action potential and refractoriness of all cardiac cells. These effects are reflected in a decreased sinus rate of 15%–20% and prolonged PR and QT intervals of about 10%. Amiodarone has a low negative inotropic effect and can be used safely in patients with decreased cardiac contractility. Amiodarone shows considerable interindividual variation in response. Absorption of oral amiodarone is variable, with a bioavailability of about 50%. Because amiodarone is highly lipophilic, measuring serum drug concentrations is of minimum value and correlates poorly with drug effect. The terminal elimination half-life of amiodarone is 6–8 weeks. Oral amiodarone is initiated with a loading dose of 10–15 mg/kg/day divided into one or two dosages and given daily for 4–15 days depending on response. If patients do not respond after 10 days, many clinicians will increase the loading dose to 15 mg/kg/day. Once arrhythmia control is achieved, the dose is reduced to 5 or 10 mg/kg/day (i.e., 5 mg/kg/day reduction from loading dose) given 1 time/day and continued for 2–3 months. If arrhythmia control continues, the dose is gradually tapered to the lowest effective dose. Onset of action can be as soon as 2–3 days, but generally takes 1–3 weeks even when patients receive loading doses. Elimination of amiodarone is by hepatic metabolism and biliary excretion. One active metabolite, desethylamiodarone, has been identified. There are no current recommendations for altering dosage in patients with hepatic insufficiency.

Amiodarone has an extensive list of possible adverse effects, some of which include proarrhythmia (e.g., torsades de pointes, AV block, bradycardia, ventricular fibrillation, and asystole), hypertension, hypotension, hepatotoxicity, hyper- or hypothyroidism, corneal deposits, keratopathy, skin rash, peripheral neuropathy, photosensitivity, blue skin discoloration, and central nervous system and gastrointestinal adverse effects. The incidence of adverse effects in children is unrelated to dosage and ranges from 8% to 29%. The incidence of adverse effects from amiodarone appears to be lower in children than in adults and becomes more frequent with advancing age. For patients refractory to amiodarone therapy, combinations of sotalol and flecainide or amiodarone and propranolol have been effective.

The recognition of potentially harmful effects and increased risk of sudden death with some antiarrhythmic drugs has led to a decline in their use and the subsequent widespread application of RFA. Radiofrequency catheter ablation was introduced in the 1990s and has completely revolutionized the management of SVT. After 2 decades of development and refinement, technology has provided the ability to accurately map the tachycardia, allowing precise endocardial ablation of the pathway responsible for the disease mechanism. This ablation has provided a much better outlook and a curative treatment option for children with recurrent SVT. For infants who continue to have frequent recurrences of SVT with severe hemodynamic compromise despite aggressive antiarrhythmic management, RFA may be considered as a therapeutic option.

Radiofrequency catheter ablation is performed in the cardiac catheterization or electrophysiology laboratory with percutaneously inserted electrode catheters to map the arrhythmia substrate and an ablation catheter to create a strategically placed thermal lesion(s) that interrupts impulse conduction through the substrate. Typical lesion dimensions are 3–5 mm in diameter and depth. Acute RFA success for AVRT and AVNRT is demonstrated by elimination of conduction over the targeted tissue and the inability to re-induce the SVT after the procedure.

Radiofrequency catheter ablation of the anatomical substrate is an attractive alternative to drug therapy, with a rate of permanent cessation of the tachycardia of up to 81%–97% dependent on the type of SVT and on the institution's experience. Results in children with structurally normal hearts are comparable to those achieved in adults. Major complications have occurred in 2.6% of cases that include second- and third-degree AV block, perforation/pericardial effusion, thromboembolic events, brachial plexus injury, and pneumothorax.

Despite the clear advantages of this procedure, it should be performed only with unquestionable indication. The long-term morphologic and electrophysiologic sequelae on the growing atrial and ventricular myocardium are still unknown. Indications for RFA include the following: medically recalcitrant tachycardias, life-threatening arrhythmias, adverse antiarrhythmic drug effects, tachycardia-induced cardiomyopathy, pending cardiac surgery, and patient choice. With newer technology, the indications for RFA have become broader, with use in more complex arrhythmias such as atrial flutter and ventricular tachycardia.

Radiofrequency catheter ablation is now the accepted standard of treatment in managing pediatric patients with symptomatic tachyarrhythmias. In addition, RFA has significantly reduced the risk of life-threatening arrhythmias in asymptomatic patients with WPW syndrome. The decision-making process for using prophylactic RFA in high-risk children should be determined by balancing risks and benefits. Ablation is associated with several hazards in children: general anesthesia, electrophysiological testing, and the ablation procedure itself. Some pediatric heart centers now advocate using RFA as the primary treatment of SVT in children as young as 1–4 years of age.

Ferguson JD, DiMarco JP. Contemporary management of paroxysmal supraventricular tachycardia. Circulation 2003;107:1096–9.

Campbell RM, Strieper MJ, Frias PA, et. al. Current status of radiofrequency ablation for common pediatric supraventricular tachycardias. J Pediatr 2002;140:150–5.

Conclusion

Of all birth defects, CHDs continue to carry the highest rate of infant mortality. Congenital heart defects can range from isolated simple defects in which patients may be asymptomatic for several years to more complex CHDs where patients acutely decompensate shortly after birth and are at substantial risk for increased morbidity and mortality. Improvements in surgical and noninvasive techniques, intra-operative strategies, and intensive postoperative management have dramatically improved patient outcomes with CHDs. In addition, complete surgical correction may now be performed in the neonatal period to restore normal or near-normal physiology. Implementation of effective pharmacological treatments is complex and requires integration of knowledge about the anatomy and physiology of uncorrected and corrected CHDs, other disease states, and potential complications with knowledge of pharmaceutical care to design proper treatment regimens. The population of adults with CHDs continues to increase, with many of these patients at high risk for long-term complications, premature death, and arrhythmias. Specialized care is now needed to meet the medical needs of this growing population.

For SVT, the acute management is generally straightforward. In newborns and infants, long-term pharmacological therapy for the first year of life is generally accepted as the treatment of choice due to the favorable prognosis for this age group. In school-aged children and adolescents with symptomatic SVT, chronic antiarrhythmic drug therapy is indicated, which carries the potential risk of proarrhythmic events. To reduce these risks, RFA has become a therapeutic option, providing a cure and sparing the child from the risks of a lifetime of antiarrhythmic drug therapy.

Annotated Bibliography

1. Pappone C, Manguso F, Santinelli R, et al. Radiofrequency ablation in children with asymptomatic Wolff-Parkinson-White syndrome. N Engl J Med 2004;351:1197–205.

    Although pharmacists are infrequently involved in the decision for arrhythmia ablation, they should be knowledgeable concerning available therapy that may improve patient outcomes. Prophylactic ablation improves outcome in high-risk adults with asymptomatic ventricular preexcitation (92% arrhythmia risk reduction). This randomized study compared radiofrequency ablation of accessory pathways with no ablation in 47 asymptomatic children (range: 5–12 years) with Wolff-Parkinson-White (WPW) syndrome. The primary end point was the frequency of life-threatening arrhythmias during follow-up. All patients with reproducible induction of atrioventricular (AV) reciprocating tachycardia or atrial fibrillation were considered at high risk and randomly assigned to the ablation (n=20) or control group (n=27). During follow-up (median duration: 34 months), one child (5%) in the ablation group and 12 (44%) in the control group had arrhythmic events (two had ventricular fibrillation and one died). The number of high-risk patients to treat with ablation to prevent arrhythmic events was 2.0. The findings support ablation as an appropriate intervention that markedly reduces the risk of life-threatening arrhythmias in children.

2. Gollob MH, Green MS, Tang AS, et al. Identification of a gene responsible for familial Wolff-Parkinson-White syndrome. N Engl J Med 2001;344:1823–31.

    The identification of the genetic defect in WPW syndrome has important implications both for elucidating the pathogenesis and for future management of the disease. A study was undertaken in 70 members of two families. A total of 31 members (23 from family one and 13 from the other) had WPW syndrome. Affected members had ventricular preexcitation and cardiac hypertrophy. The investigators identified a missing mutation in the gene that encodes the $\gamma 2$ regulatory subunit of adenosine monphosphate-activated protein kinase (PRKAG2). The mutation results in glutamine for arginine substitution at the 302 residue in the protein. The identification of an AMP-activated protein kinase provides the first information of the pathways that regulate embryonic development of the AV conduction system and its function in the adult heart. Future therapies for these patients may include genetic and pharmacogenomic strategies that could replace electronic pacemakers.

3. Pfammatter J, Pavlovic M, Bauersfeld U. Impact of curative ablation on pharmacological management in children with reentrant supraventricular tachycardias. Int J Cardiol 2004;94:279–82.

    Radiofrequency catheter ablation as a curative treatment has become the standard of care for children with recurrent supraventricular tachycardia (SVT). The focus of this study was the impact of ablation therapy on pharmacological management of SVTs. The number of SVT episodes, acute drug conversions, and chronic antiarrhythmic drug treatments prescribed were compared for two time periods, 1989–1994 (primary drug treatment) and 1995–2000 (primary ablative therapy). The study included 88 patients, with 40 in the 1989 group and 48 in the 1995 group. When comparing the 1989 group with the 1995 group, the number of acute drug conversions decreased from 1.1/patient to 0.2/patient, episodes of SVT fell from 3.7 to 2, and chronic antiarrhythmic drug treatment decreased from 15 months/patient to 4.6 months/patient. With the use of ablation as first-line therapy for recurrent SVT, the use of acute and chronic antiarrhythmic drug treatment was decreased in older children.

4. Hoffman JI, Kaplan S, Liberthson RR. Prevalence of congenital heart disease. Am Heart J 2004;147:425–39.

    To assess the medical, social, and economic impact of congenital heart defects (CHDs), an accurate estimation of the number of children born with CHD who reach adulthood is needed. To answer this question, the expected number of infants with CHD born in each 5-year period since 1940 was estimated from birth rates and incidence of CHD. The survival rates with or without treatment were estimated from the natural history and treatment results of CHD. From 1940 to 2002, about 3 million children were born with CHD. If all of these children were treated, there would be 750,000 survivors with simple CHD (e.g., ventricular septal defect [VSD], atrial septal defect [ASD], patent ductus arteriosus [PDA]), 400,000 with moderate CHD, and 180,000 with severe CHD (e.g., any cyanotic heart lesion). This estimate excludes 3 million patients with bicuspid aortic valves. Survival in each group, without treatment, would be about 53%, 55%, and 17%, respectively. This study concludes that

the survival of patients with CHD is improving, with larger numbers of patients expected to reach adulthood. The number of health care professionals that need to be trained in managing adults with CHD is considerable.

5. Freedom RM, Lock J, Bricker JT. Pediatric cardiology and cardiovascular surgery: 1950–2000. Circulation 2000;102:IV58–68.

This review focuses on major achievements in pediatric cardiology and cardiac surgery during the past 50 years. The background highlights older techniques that were important in paving the way to future milestones, including ligation of PDA, subclavian artery to pulmonary artery shunt, pulmonary valvotomy, atrial septectomy, and repair of coarctation. Major advances chronicled over this time frame include a more detailed understanding of physiological and anatomical aspects of fetal circulation and congenital heart disease, advances in diagnostic techniques (e.g., echocardiography), pharmacological management (e.g., prostaglandin E_1 [PGE_1]), surgical procedures (e.g., cardiopulmonary bypass, deep hypothermia, arterial switch, Fontan, Norwood, and cardiac transplantation), and catheter-based techniques (e.g., balloon valvuloplasty, balloon atrial septostomy, balloon angioplasty with endovascular stent placement, device closure of PDA, and various atrial and ventricular septal defects). Other advances include outcome (e.g., standards of practice and training) and prevention (e.g., environmental and genetic factors) strategies, which have led to dramatic improvements in virtually all aspects of pediatric cardiovascular medicine and surgery.

6. Wessel DL. Managing low cardiac output syndrome after congenital heart surgery. Crit Care Med 2001;29(suppl 10):S220–30.

Causes of persistent low cardiac output states after congenital heart surgery can include residual or undiagnosed structural lesions. Cardiopulmonary bypass can also be a key component in causing myocardial dysfunction. Inflammatory response with cardiopulmonary bypass, myocardial ischemia and reperfusion injury, inadequate myocardial protection, and need for surgical ventriculotomy can result in the development of myocardial edema, decreased myocardial compliance, and increased pulmonary vascular resistance, which can contribute to myocardial dysfunction. Anticipation and prompt intervention is paramount to avoid morbidity and the need for mechanical support (e.g., extracorporeal membrane oxygenation). Nonpharmacological modalities discussed in the treatment of low output states include preserved (e.g., patent foramen ovale) or surgically created (e.g., fenestration) shunts and cardiac pacing. Pharmacological modalities discussed are volume resuscitation, inotropic drugs (e.g., dopamine, dobutamine, epinephrine, and milrinone), afterload reduction (e.g., nitroprusside, nitroglycerin, and angiotensin-converting enzyme inhibitors), pulmonary vasodilators (e.g., inhaled nitric oxide, and sildenafil), and antiinflammatory drugs (e.g., corticosteroids). The merit and indications for using mechanical support are also discussed.