SECTION VI

Adult Congenital Heart Disease

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CHAPTER 29

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Atrial Septal Defect and Patent Foramen Ovale

I. INTRODUCTION

A. Atrial septal defects (ASDs) constitute approximately 5% to 10% of congenital heart disease. Excluding bicuspid aortic valve and mitral valve prolapse, ASD is the most common form of congenital heart defect found among adults and is the most common acyanotic shunt lesion in adults as well.

B. Often, an atrial communication may go unrecognized into adulthood because the clinical symptoms and physical manifestations can be subtle.

C. Although survival into adulthood is the rule, the overall life expectancy is decreased in patients with an unrepaired ASD. Long-term exposure to chronic right heart volume overload can have deleterious effects, such as atrial arrhythmias, pulmonary vascular disease, and right heart failure. These clinical findings are directly related to patient age, with almost all patients becoming symptomatic by the fifth or sixth decade. The presence of an atrial communication is also a potential source of paradoxical embolus.

D. A patent foramen ovale (PFO) is a specific form of interatrial communication caused by incomplete closure of the foramen ovale after birth. PFOs are present in 25% to 30% of the general population. The prevalence of PFO in patients with cryptogenic stroke is approximately 40% to 50%.

E. Atrial septal aneurysms are congenital outpouchings of the atrial septum, near the fossa ovalis. These can perforate, resulting in an ASD with left-to-right shunting of blood. Atrial septal aneurysms can be detected in up to 10% of patients undergoing echocardiography and in up to 30% of patients with cryptogenic stroke, generally with a concomitant PFO.

II. ANATOMY AND EMBRYOLOGY.

The primitive atrium is first partitioned into right and left atria by growth of the septum primum—a thin, crescent-shaped membrane that grows from the roof of the primitive atrium toward the endocardial cushions located between the atria and ventricles. An atrial communication initially persists as the foramen primum, composed of the free edge of the septum primum and the endocardial cushions. Before closure of the foramen primum, fenestrations develop in the septum primum that coalesce to form the ostium secundum. As the septum primum then fuses with the endocardial cushions, the ostium secundum maintains a right-to-left atrial flow that is important in the fetal circulation. **Failure of this fusion results in the development of a primum ASD**. A second septum, the septum secundum, then forms to the right of the septum primum, growing toward the endocardial cushions and usually closing the ostium secundum. **Failure to close the ostium secundum results in the formation of a secundum ASD**.

The septum secundum forms an incomplete partition of the atria, leaving a foramen ovale (i.e., fossa ovalis). The remaining septum primum tissue on the left atrial (LA) side

becomes a flap valve, or valve of the foramen ovale, and allows for the continued right-to-left shunting in the fetal circulation. At birth, when LA pressure increases, the septum primum flap closes and eventually fuses to anatomically seal the atrial septum. A "true ASD" results from a deficiency in septal development or from resorption of atrial tissue, whereas a **PFO results from failure of this septum primum flap to adequately seal the fossa ovalis**. At autopsy, a "probe-patent" PFO remains in 25% to 30% of patients.

During development, if there is overabundant or weakened septal tissue, the septum becomes very mobile. This can be visualized during echocardiography, and the degree of excursion can be measured. If the maximal excursion of the interatrial septum is **15 mm or more**, this abnormality is called an **atrial septal aneurysm**. If the amount of septal excursion is < 15 mm, it is referred to as a redundant atrial septum.

ATRIAL SEPTAL DEFECTS

I. ASD TYPES (Fig. 29.1)

A. Ostium secundum defects or **secundum ASDs** constitute the most common type, accounting for 70% to 75% of ASDs. This defect, a true defect of the atrial septum, is located in the midportion of the atrial septum, within or including the fossa ovalis. Defects result from a deficient septum primum or an abnormally large foramen secundum. This type of ASD is two times more common in female patients. Isolated secundum ASD has been associated with mitral valve prolapse and other forms of congenital heart disease. It may also be associated with rheumatic mitral stenosis (i.e., Lutembacher syndrome).

B. Ostium primum defects or **primum ASDs** account for 15% to 20% of ASDs and are part of the spectrum of atrioventricular (AV) septal defects (also known as AV canal defects or endocardial cushion defects). These defects occur in the inferior–anterior portion of the atrial septum and are frequently associated with a cleft in the anterior leaflet of the mitral valve, leading to varying degrees of mitral regurgitation. In their complete form, they include a large ventricular septal defect and a common

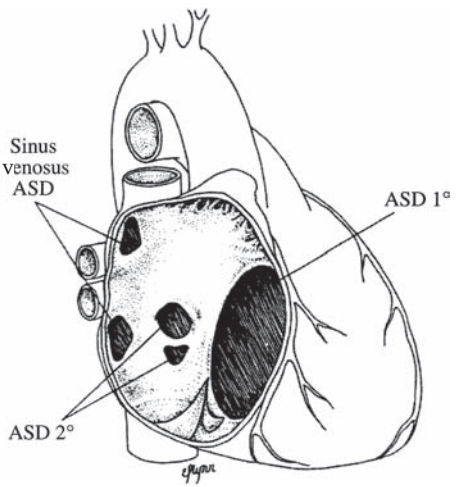

FIGURE 29.1 Diagrammatic representation of common atrial septal defects. ASD, atrial septal defect; 1°, primum; 2°, secundum. Reproduced from Fyler DC, ed. *Nadas Pediatric Cardiology.* Philadelphia, PA: Hanley & Belfus; 1992, with permission.

AV valve. Depending on the severity of dysfunction of the mitral valve, these patients may become symptomatic at a young age. This defect in the inlet septum is the most common ASD associated with Down's syndrome.

C. Sinoseptal defects constitute the remaining 5% to 10% of septal defects. Distinct from the true ASDs described previously, these lesions involve the portion of the atrial wall derived from the sinus venosus (i.e., there is no direct communication between the right and left atria). **Sinus venosus defects** are typically at the orifice of the superior vena cava (SVC) at the junction of the right atrium or, less frequently, in the region of the inferior vena cava (IVC). These sinus venosus defects are frequently associated with partial anomalous pulmonary venous drainage of the right pulmonary veins and require a high index of suspicion for diagnosis because they are generally not visualized by standard transthoracic echocardiography (TTE). Transesophageal echocardiography (TEE) is generally required for visualization in adults. Magnetic resonance imaging (MRI) or computed tomography may also be used for diagnosis. These defects should be considered in any patient with unexplained right atrial (RA) or right ventricular (RV) dilation. An uncommon sinoseptal defect is the partially or completely **unroofed coronary sinus**, which is located inferior and slightly anterior to the fossa ovalis. These defects are commonly associated with other forms of congenital heart disease, such as complete AV septal defect, or can be associated with an absence of coronary sinus and a left SVC that drains into the left atrium.

II. PATHOPHYSIOLOGY. The magnitude and direction of the shunt through the ASD depend on the size of the defect as well as the diastolic filling properties of the ventricles. Any condition that causes reduced left ventricular (LV) compliance, such as LV hypertrophy or LV scar, or increased LA pressure, such as mitral stenosis, will increase the degree of left-to-right shunting. Conversely, conditions that cause reduced RV compliance, such as pulmonary hypertension or pulmonary stenosis, or increased RA pressure, such as tricuspid stenosis, will reduce the degree of left-to-right shunting and, in some instances, even lead to shunt reversal. In general, the ASD must be at least 10 mm in its greatest dimension to cause a significant shunt, although this can be hard to measure, as most ASDs are not circular. A left-to-right shunt is considered significant when the ratio of pulmonary-to-systemic blood flow, or shunt fraction (Q_p/Q_s), is > 1.5:1.0 or when right heart chamber dilation is present.

III. CLINICAL MANIFESTATIONS. The clinical presentation of a patient with an ASD results from the effects of long-term left-to-right shunting and subsequent volume loading of the right heart. The age at which the symptoms occur is variable and does not necessarily depend on the size of the defect.

A. Exercise intolerance with **fatigue** and **dyspnea** may occur, but it is frequently not appreciated by the patient until after the defect has been closed. Late findings include **supraventricular arrhythmias**, such as atrial fibrillation or flutter, severe irreversible **pulmonary vascular disease**, and, eventually, **right heart failure**. Occasionally, a **paradoxical embolus** causing a stroke or transient ischemic attack (TIA) is the first clue to an ASD.

B. The physical findings may include a hyperdynamic cardiac impulse, the characteristic **widely or fixed split second heart sound**, and a **soft systolic murmur at the second left intercostal space** due to increased flow across the pulmonary valve. If the shunt is more than a shunt fraction (Q_p/Q_s) of 2.5:1, there may be a diastolic murmur secondary to increased flow across the tricuspid valve. A loud P_2 component of the second heart sound indicates the presence of pulmonary hypertension, which can affect up to 20% of patients; if cyanosis is present, this generally suggests advanced pulmonary hypertension with reversal of shunt flow (**Eisenmenger syndrome**). An important clue to the presence of Eisenmenger syndrome is an oxygen saturation that does not significantly improve with supplemental oxygen.

Another physical examination finding that may be encountered is a holosystolic murmur characteristic of mitral regurgitation, which is often heard in a patient with a primum ASD.

IV. LABORATORY EXAMINATION

A. Electrocardiogram (ECG). The ECG can provide clues to the possibility of an ASD. The rhythm may be sinus, but may also be atrial fibrillation or atrial flutter. Inverted P waves in the inferior leads suggest an absent or nonfunctional sinus node, as may be seen with a sinus venosus defect.

1. **Secundum ASD**
   - **(a)** RSR' pattern in lead V_1
   - **(b)** QRS duration < 0.11 seconds (incomplete right bundle branch block)
   - **(c)** Right-axis deviation
   - **(d)** RV hypertrophy
   - **(e)** First-degree AV block (20%)
   - **(f)** RA enlargement (about 50%) with a prominent P wave in lead II
2. **Primum ASD**
   - **(a)** RSR' pattern in lead V_1
   - **(b)** Left-axis deviation
   - **(c)** First-degree AV block, classically seen with right bundle branch block and left anterior fascicular block

B. Chest radiography may reveal cardiomegaly due to right heart enlargement. With large left-to-right shunts, the central pulmonary arteries and vascular markings may appear prominent. In the setting of advanced pulmonary vascular disease, however, the pulmonary arteries may appear large but have oligemic peripheral lung fields, so-called vascular pruning.

V. DIAGNOSTIC STUDIES

A. Echocardiography is the primary means by which an ASD is diagnosed. TTE can document the size of the defect as well as the direction of the shunt flow and occasionally the location of the pulmonary veins in the younger patient. In the adult, transesophageal studies are generally required for a full anatomic assessment. An ASD should be suspected when right-sided chamber enlargement is noted on echocardiography and no other cause is identified.

1. Typical transthoracic views for imaging an ASD include the parasternal short-axis view, the apical four-chamber view, and the subcostal coronal and sagittal views. Findings include RA and RV enlargement, which indicate a functionally important defect. An estimate of RV pressure should be made via the jet of tricuspid insufficiency, and evidence for RV pressure and volume overload should be noted via observation of septal motion in systole and diastole, respectively. Evidence of left-to-right (or right-to-left) shunting across the defect should be demonstrated using color Doppler techniques. Evidence of RA and RV enlargement in the absence of an obvious cause on echocardiography, such as tricuspid regurgitation or an ASD, should prompt a search for a sinus venosus defect and/or partial anomalous pulmonary venous drainage. Intravenous contrast (i.e., agitated saline) and TTE can identify a shunt, but TEE is usually required to demonstrate a sinus venosus defect. Of note, in isolated partial anomalous pulmonary venous return, the intravenous contrast study will be negative.
2. TEE is usually required in the adult patient for further anatomic definition and to determine whether the defect is amenable to percutaneous closure. Contrast studies with agitated saline are helpful in confirming the presence and location of atrial shunting. The midesophageal four-chamber and bicaval views are preferred, with injection of agitated saline through an upper extremity vein. Injection into the left arm may be particularly helpful to establish the presence of a

persistent left SVC that drains into the coronary sinus or directly into the left atrium. In the diagnosis of a sinus venosus defect, care must be taken to evaluate the location of the pulmonary veins for evidence of anomalous drainage.

B. Cardiac catheterization is typically not required for diagnostic purposes except to assess pulmonary pressures and resistance, to assess for coronary artery disease before planned surgical closure in the adult patient, or as part of a planned transcatheter device closure. Right heart catheterization can be performed in most cases using a standard end-hole catheter. The lateral camera is helpful in directing the catheter posterior before advancing across the ASD. Our standard is to perform a complete right heart catheterization, including oximetry measurements and hemodynamic assessment.

1. Oximetry samples obtained during catheterization demonstrate a step-up within the right atrium due to shunting across the defect. Careful interrogation of innominate vein saturation and SVC saturation is important to exclude a step-up at the SVC level that would support the existence of associated partial anomalous pulmonary venous drainage. Desaturation in the left atrium systemically confirms right-to-left shunting and should prompt further investigation of RV and pulmonary artery pressures. Other diagnoses producing a similar picture include large ventricular septal defects with tricuspid regurgitation, partial or complete AV canal defects, or systemic arteriovenous fistulas.

   The significance of the defect can be assessed by calculating the **shunt fraction (Q_p/Q_s)**, which is the ratio of pulmonary blood flow (Q_p) to systemic blood flow (Q_s). Oximetry values, obtained during right heart catheterization and used previously to determine if a step-up is present, can be helpful for shunt calculation as follows:

$$Q_p/Q_s = \frac{\text{aortic saturation} - \text{mixed venous saturation}}{\text{pulmonary vein saturation} - \text{pulmonary artery saturation}}$$

   The mixed venous saturation is obtained in the setting of an ASD by multiplying the SVC saturation by 3, adding the IVC saturation, and then dividing the sum by 4. If the pulmonary vein saturation is not directly measured, it can be assumed in the absence of considerable lung disease to be 95%.

2. Hemodynamic assessment may reveal modest elevations in RV and pulmonary artery pressures. An important assessment is comparison of pulmonary artery pressure with systemic pressure and measurement of pulmonary vascular resistance. If pulmonary pressures are elevated, the response to oxygen or other vasodilators should be assessed. Alternatively, the ASD can be balloon occluded with assessment of hemodynamics to ensure that closure is safe. Examples of the usual catheterization findings with and without pulmonary vascular disease are illustrated in Figure 29.2.

   Using a derivative of Ohm's law, $P = Q \times R$, an ASD will increase the flow (Q) to the lungs, and, therefore, increase the pulmonary pressure (P) without a significant change in resistance (R). Findings that may preclude eventual ASD closure include one or more of the following: pulmonary vascular resistance more than one-half of the systemic vascular resistance or an indexed pulmonary vascular resistance > 7 Wood units/m^2.

3. Angiography is typically not necessary for diagnostic purposes. Some transcatheter closure device protocols include angiography, typically performed in the right pulmonary vein or levophase from a main pulmonary artery injection in the left anterior oblique and cranial projections. This may be an important way to confirm the absence of additional defects, such as partial anomalous pulmonary venous drainage, before proceeding with transcatheter device closure.

C. Cardiac MRI can be helpful, as it can provide additional information beyond echocardiography. MRI provides an excellent assessment of RV size and function,

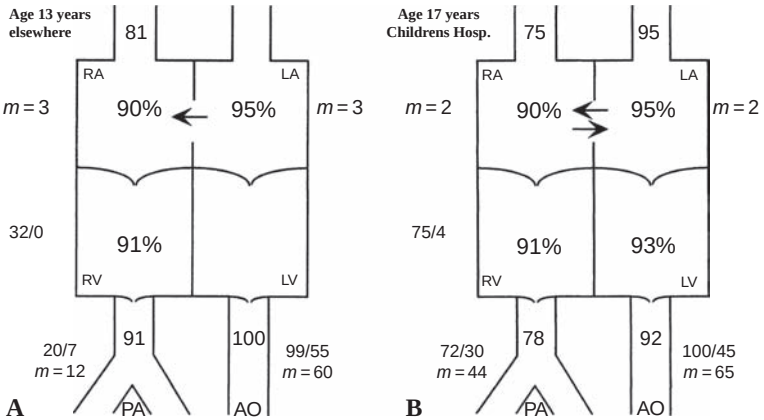

FIGURE 29.2 Catheterization data derived from two studies of the same female patient. The data obtained at age 13 (A) were interpreted as compatible with a small atrial septal defect of insufficient size to require closure. Some years later, she had developed pulmonary vascular obstructive disease (B) and was no longer shunting enough to recommend surgery. Death occurred 5 years later. AO, aorta; LA, left atrium; LV, left ventricle; PA, pulmonary artery; RA, right atrium; RV, right ventricle; numeric values within the schematic, oxygen saturation (%); numeric values outside the schematic, pressure (mm Hg). Adapted from Fyler DC, ed. *Nadas Pediatric Cardiology*. Philadelphia, PA: Hanley & Belfus; 1992.

especially if views obtained with echocardiography are not diagnostic. MRI is also excellent at determining the location of the pulmonary veins as well as calculating ventricular volumes and shunt fraction.

VI. TREATMENT. Medical intervention is typically not required preoperatively, because many patients are asymptomatic. Congestive symptoms may be improved with standard diuretic therapy. Rhythm disturbances such as atrial fibrillation require attention with respect to rate control and anticoagulation. Endocarditis antibiotic prophylaxis during dental procedures is not required in the setting of an isolated ASD before surgery, but it is warranted for 6 months after surgical or device closure (AHA/ACC class IIa).

A. Surgical or transcatheter therapy. The mainstay of therapy is closure of the defect by surgical or transcatheter techniques. Because of the reduced life expectancy associated with an unrepaired ASD, closure is recommended at diagnosis if there is evidence of a hemodynamically significant shunt ($Q_p/Q_s \geq 1.5:1$), evidence of right heart dilation, and evidence of probable paradoxical embolism or associated symptoms. In the setting of pulmonary hypertension, pulmonary reactivity to vasodilators should be documented and a net left-to-right shunt demonstrated during catheterization before consideration for closure. Alternatively, the defect can be temporarily balloon occluded at the time of catheterization, and the hemodynamic effects are directly measured. Situations in which ASD closure should not be pursued are listed in Table 29.1 and include advanced pulmonary hypertension (Eisenmenger syndrome) and severe LV dysfunction with elevated LA pressure.

B. Primary surgical closure has been the standard approach for many years. Generally, surgical closure is the treatment of choice for ostium primum and sinus venosus defects. Patients with secundum ASDs and anatomy that is not amenable to percutaneous closure (ASD diameter > 35 mm; inadequate septal rims to permit device deployment; or close proximity to AV valves, coronary sinus, or venae cavae) are

TABLE 29.1 Conditions Where Atrial Septal Defect Closure Is Not Favored

Defect is too small to be hemodynamically significant
Pulmonary hypertension is too advanced
Severe LV dysfunction, where ASD is acting as a "pop-off" valve for the left ventricle
In most cases where ASD is diagnosed in pregnancy, closure can be postponed until 6 months after delivery

ASD, atrial septal defect; LV, left ventricular.

also candidates for open surgical closure. Depending on the defect size and location, the secundum ASD can be closed by primary suture or, if needed, by the use of an autologous pericardial or synthetic patch. Ostium primum defects require patch closure as well as repair of the likely cleft mitral valve. Repair of sinus venosus defects is technically more challenging, as the pulmonary veins often have anomalous drainage and require rerouting.

1. Important preoperative risk factors include older age at operation, presence of atrial fibrillation, and elevated pulmonary pressure and resistance.
2. Postoperatively, patients are at risk for heart block, which is a significant complication in these cases. They are also at risk for postpericardiotomy syndrome, more so than after other surgery for congenital defects. Atrial arrhythmias may persist in short-term and long-term follow-ups because the RA and RV sizes may take time to return to normal, so anticoagulation is often recommended for several months after surgery. In some centers, prophylactic β-adrenergic blockade is advocated empirically for 3 to 6 months after surgery.

C. Transcatheter closure of a secundum ASD has become an attractive alternative to surgical closure and is now considered the treatment of choice. Any patient with an isolated secundum ASD may be suitable for transcatheter closure, which is generally assisted with TEE or intracardiac echocardiography in addition to fluoroscopy. Catheter closure decreases hospital length of stay, avoids surgical wounds and their possible complications, and significantly speeds up postprocedure recovery. With the devices available today, defects with a resting diameter of < 35 mm may be considered. In general, the gently stretched diameter of the defect is approximately 6 to 8 mm greater than the resting diameter. The defect must be located centrally with adequate room for the device to be positioned, without interference of other intracardiac structures such as the AV valves, coronary sinus, or pulmonary veins. The US Food and Drug Administration (FDA) has approved two devices for the closure of secundum ASDs: the Amplatzer Septal Occluder (AGA Medical Corporation, Golden Valley, MN) approved in December 2001 and the Helex Septal Occluder (WL Gore & Associates, Flagstaff, AZ) approved in August 2006. Studies have proved the safety and efficacy of catheter-based closure of a secundum ASD compared with surgical closure. The Amplatzer device consists of two disks made of Nitinol wire mesh filled with polyester fabric and separated by a narrower waist, which is appropriately fitted by balloon sizing. It is inserted percutaneously through a 6F to 12F sheath, depending on the device size required. The Helex device is also disklike and consists of expanded polytetrafluoroethylene (ePTFE) patch material supported by a single Nitinol wire frame. Major complications, such as cardiac perforation or device embolization, occur very rarely (generally fewer than 1% of cases), and successful closure of the defect is achieved in up to 95% of all patients. After closure, antiplatelet therapy, frequently aspirin and clopidogrel, is prescribed for a minimum of 6 months, after which time the device is generally believed to have endothelialized.

VII. PROGNOSIS. Hemodynamically significant ASDs are associated with increased morbidity and mortality. Long-term outcomes can be improved by closing these defects, especially if performed early in life. Atrial arrhythmias are common, especially in older patients, and are the result of long-standing atrial stretch. Arrhythmias, particularly atrial flutter and fibrillation, contribute to a significant portion of the morbidity and mortality of older patients, particularly the risk of systemic embolization and the resultant stroke. It has been demonstrated that age at the time of surgical repair is inversely related to the risk of subsequent atrial fibrillation or flutter after repair and argues for earlier closure. Some have advocated for consideration of a concomitant ablation procedure in high-risk patients, but the available data do not generally support this.

The functional capacity of patients frequently improves after closure of the ASD, and often they do not realize how severely their functional capacity had been affected until after the defect is closed. In addition, improvements in LV filling and systemic cardiac output are seen rapidly after defect closure. Reduced RA and RV volumes can be seen within 24 hours and continue to improve over the course of the first year following closure.

PFO AND ATRIAL SEPTAL ANEURYSM

I. PATHOPHYSIOLOGY. PFO can result in transient right-to-left shunting of blood flow, usually when RA pressure exceeds LA pressure such as during coughing or straining. These defects generally do not cause significant hemodynamic derangements. The clinical importance of an atrial septal aneurysm or a PFO is its impact on the risk of stroke. PFO features that increase the risk of a paradoxical embolus include large tunnel lengths (≥ 4 mm), high mobility of the valve of the foramen ovale, a well-formed eustachian valve, and a resting right-to-left shunt.

II. CLINICAL MANIFESTATIONS. Generally these defects are asymptomatic, most often coming to attention in patients with cryptogenic (unexplained) stroke. PFO is more common in patients with cryptogenic stroke than in the general population, but PFO alone has not been shown to be an independent risk factor for cryptogenic stroke. There are now accumulating data to suggest that an isolated PFO is not associated with an increased risk of recurrent ischemic stroke. The data in patients with both a PFO and an ASD are conflicting but suggest increased risk of recurrent stroke when both lesions are present. PFO should be suspected in young patients who sustain a stroke, as more than one-half of stroke patients younger than 45 years have a PFO. Other less common clinical associations with PFO include migraine headaches, platypnea–orthodeoxia syndrome, and decompression illness in divers and those who work in high altitudes.

III. DIAGNOSTIC STUDIES. **Echocardiography** can easily differentiate between an ASD and a PFO if the interatrial septum is well visualized. If this is not possible via a transthoracic approach, a TEE may be necessary. A simple way to determine if a shunt is present is the "**bubble study**," which is the injection of agitated saline via an upper extremity vein. If shunting is not present at rest, the patient can perform a Valsalva maneuver, which augments right-to-left shunt. If bubbles can be seen in the left atrium or the left ventricle within three cardiac cycles on TTE, the diagnosis of an interatrial right-to-left shunt is established. Generally, administration of agitated saline in patients with suspected right-to-left shunts is considered safe, but there have been rare case reports of cerebral ischemic events from passage of bubbles into the systemic circulation.

TEE will likely be required in most adults for better visualization of the interatrial septum. TEE helps to differentiate between a PFO and a secundum ASD, both of which can have positive bubble studies. TEE also allows assessment of other potential sources of emboli, such as atheroma in the aortic arch, thrombus in the LA appendage, or cardiac tumors.

TABLE 29.2 Contraindications to Percutaneous Patent Foramen Ovale Closure

Presence of an alternative source of emboli
Severe pulmonary hypertension
Recent gastrointestinal bleeding
Presence of congenital heart defect that needs surgical repair
Documented hypercoaguable state
Hypersensitivity or contraindication to antiplatelet or anticoagulant therapy
Unexplained fever or infection

IV. TREATMENT. Unfortunately, there is no clear consensus on primary or secondary prevention measures for patients found to have a PFO or atrial septal aneurysm. In general, atrial septal abnormalities are not treated for primary prevention of stroke. Regarding secondary prevention, most patients with neurologic events are treated with antiplatelet agents (either aspirin or a thienopyridine, or both), anticoagulants (warfarin), and percutaneous or surgical closure, although no clear consensus exists and the only randomized controlled study reporting results to date failed to demonstrate a benefit of closure over medical therapy. The CLOSURE I trial (reported at AHA 2010) examined the role of PFO closure for first time stroke/TIA and found no difference in the composite primary end point of stroke or TIA at 2 years, all-cause 30-day mortality, and neurologic mortality between 31 days and 2 years, with closure compared with aspirin, warfarin, or both. There are several other ongoing trials that are comparing percutaneous PFO closure with medical therapy. These include the CLOSE trial, the PC-Trial, the RESPECT trial, and the REDUCE trial. In general, device closure should be mainly performed in patients with recurrent cryptogenic stroke despite aggressive medical therapy. The same devices utilized for ASD closure are generally used to percutaneously close PFO. Contraindications to percutaneous closure are noted in Table 29.2.

Primary surgical closure of PFO is generally not pursued, unless the patient needs concomitant surgery for other conditions. Indiscriminant repair of PFO incidentally found at surgery may actually increase short-term stroke risk and should therefore be avoided.

There is a dearth of data to support PFO closure in patients with migraine headaches. The MIST (Migraine Intervention with STARFlex Technology) trial randomized 147 participants with severe migraine headaches and right-to-left shunt consistent with PFO to either percutaneous closure or sham procedure. After 6 months, there was no statistically significant difference in the primary end point of complete cessation of migraine headache or in a host of secondary end points including change in severity, quality, and frequency of headache as well as quality of life. As such, device closure should only be performed in migraine patients who are part of a randomized clinical study.

Patients with platypnea–orthodeoxia syndrome (acute arterial desaturation with change in position from supine to upright) should be considered for closure, as oxygen saturation generally improves with successful elimination of the right-to-left shunt.

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CHAPTER 30

Christopher H. May

Ventricular Septal Defect

I. Introduction

A. Ventricular septal defect (VSD) is one of the most common congenital heart defects in both children and adults. The prevalence in neonates has been reported to be as high as 5% when screened with color Doppler echocardiography, although most of these are miniscule defects that close spontaneously within the first year. Thus the true prevalence is difficult to ascertain, given that many defects close spontaneously

and patients are frequently asymptomatic with smaller lesions. VSDs are frequently associated with other congenital defects, particularly infundibular stenosis or valvar pulmonary stenosis. Isolated VSDs account for about 20% to 25% of all congenital heart defects in childhood. Unlike many other congenital abnormalities, males and females appear to be affected equally.

B. Isolated VSDs are found in approximately 10% of adult patients with congenital heart disease. This reflects the natural tendency for spontaneous closure during infancy and an improved ability to confirm the diagnosis in childhood, which leads to surgical closure.

C. Natural history

1. **Spontaneous closure** occurs most commonly with smaller, restrictive VSDs, usually before the age of 2 years. In general, nearly 35% of perimembranous defects close spontaneously and 75% to 80% of all small VSDs close spontaneously by 10 years of age. These higher rates of spontaneous closure in more recent series are a reflection of the ability to diagnose much smaller defects with more contemporary echocardiographic modalities. Large and nonrestrictive defects have significantly lower spontaneous closure rates (approximately 10% to 15%); malalignment defects rarely close spontaneously. Defects close by two mechanisms: (1) by muscular septum growth and (2) by "aneurysmal tissue" from a septal leaflet of the tricuspid valve as in the case of perimembranous defects. For VSDs that persist, a restrictive nature can protect the patient from pulmonary vascular injury given the flow-limiting nature of these defects.
2. **Endocarditis** is a risk because of the presence of a high-velocity, turbulent jet into the right ventricle. Endocarditis most frequently involves the septal leaflet of the tricuspid valve apparatus at the point of jet impact. The risk of endocarditis is roughly 4% to 10% for the first 30 years of life. Muscular VSDs have a lower incidence of endocarditis, as the jet is attenuated prior to reaching the tricuspid valve.
3. A large VSD during childhood is typically associated with significant **left-to-right shunt** and eventual development of congestive heart failure. Children with very large defects usually present during infancy or early childhood with signs and symptoms of heart failure and pulmonary hypertension. Patients with moderate-sized VSDs can survive to adulthood before detection. Given the gradual development of symptoms in these patients, they may not present until late in the disease course. In these patients, the excess right-sided flow may lead to pulmonary vascular disease and Eisenmenger physiology if left untreated. As pulmonary vascular resistance increases, the left-to-right shunt changes to a right-to-left flow. The VSD murmur disappears during this transition and is often replaced by the murmur of tricuspid regurgitation. After Eisenmenger physiology has developed, patients rarely survive beyond the fourth decade. Complications in patients with Eisenmenger syndrome include pulmonary hemorrhage, endocarditis, cerebral abscess (from hypoxemia), ventricular arrhythmias, and the complications associated with erythrocytosis. Poor prognostic factors in this population include syncope, congestive failure, and hemoptysis.
4. Risk factors for decreased survival include cardiomegaly seen on the chest radiograph; elevated pulmonary artery systolic pressure (> 60 mm Hg and/or more than one-half of the systemic pressure); cardiovascular symptoms such as shortness of breath, fatigue, or dyspnea on exertion; and progressive aortic insufficiency. Good prognostic factors include normal left ventricular (LV) size and function, small left-to-right shunt, normal pulmonary pressures or resistance, an intact vasodilator response in the pulmonary vasculature, and a lack of symptoms.
5. Genetic factors play a significant role in this disease, as in other forms of congenital heart disease. Having an affected father increases the risk of VSD in

the offspring to 2%; moreover, an affected mother appears to confer an even higher risk of recurrence in offspring—as high as 6% to 10%. In general, VSDs arise due to a combination of polygenic, multifactorial abnormalities. However, several monogenetic abnormalities leading to VSDs such as mutations in the transcription factors TBX5 and GATA4 have recently been described.

II. ANATOMY

A. Embryology. Partitioning of the ventricular mass begins as a muscular ridge in the floor of the ventricle near the apex. This ridge later undergoes active growth, which forms the muscular ventricular septum. Concomitantly, the endocardial cushions fuse and the two regions meet, completing closure of the interventricular foramen. Figure 30.1 shows anatomic localization of VSDs.

B. Defect size. The consequences of a VSD depend on the size of the defect and the pulmonary and systemic vascular resistances. Smaller defects provide higher resistance to flow and will have little impact on right-sided flow. **The VSD is** described as **small** when the defect size is **less than one-third of the size of the aortic root, moderate** when the defect size is **less than one-half of the size of the aortic root,** and **large** when the defect size is equal to or **larger than the size of the aortic root.** However, other indirect measures, including clinical signs and symptoms and echocardiographic features, must be taken into consideration when determining the size and clinical significance of a VSD. VSD size is often classified on the basis of its hemodynamic consequences:

1. **Restrictive** VSDs result in a significant pressure gradient between the left and right ventricles (e.g., pulmonary/aortic systolic pressure ratio < 0.3) and are associated with a small shunt ($Q_p/Q_s \leq 1.4{:}1$).
2. **Moderately restrictive** VSDs produce an intermediate interventricular gradient and result in a moderate shunt ($Q_p/Q_s = 1.4$ to $2.2{:}1$).
3. **Nonrestrictive** VSDs are usually larger than 1 cm^2 and are associated with a large shunt ($Q_p/Q_s > 2.2{:}1$). The pressures in the left ventricle and right ventricle will eventually approach equalization, and the amount of flow across the defect will be determined by the ratio of pulmonary-to-systemic vascular resistance.

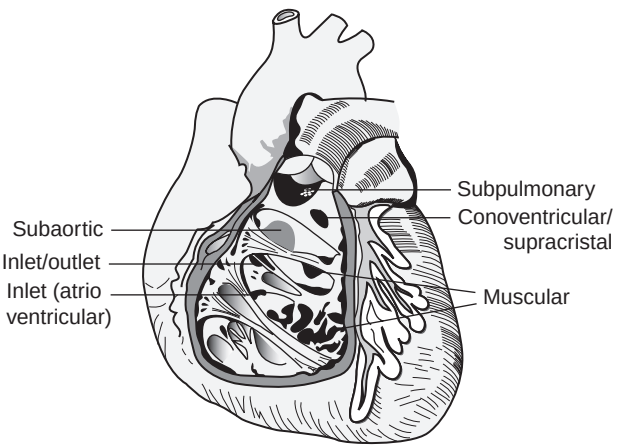

FIGURE 30.1 Anatomic localization of ventricular septal defects.

C. VSD types

1. **Membranous** defects are the most common type, accounting for approximately **70% to 80% of VSDs**. The membranous septum is the area under the aortic valve on the left side and next to the septal leaflet of the tricuspid valve on the right side. Most of these defects extend into the infundibular region and are then referred to as perimembranous. **Membranous defects** are less likely to be associated with additional intracardiac defects and **have a high rate of spontaneous closure**. However, when there is malalignment of the defect, spontaneous closure is unlikely.
2. **Muscular** defects account for approximately 5% to 20% of VSDs and can be single or multiple (i.e., Swiss cheese septum). These defects, when single, also have a high spontaneous closure rate.
3. **Inlet or atrioventricular (AV) canal–type** defects account for approximately 5% to 8% of cases. These defects rarely close spontaneously, are usually large, and are associated with abnormalities of the AV valves. These abnormalities range from cleft mitral and tricuspid valves to the common AV valve, as seen in complete AV canal defect. This type of defect in the inlet ventricular septum is commonly seen in patients with Down syndrome (Trisomy 21).
4. **Supracristal or subaortic** defects account for approximately 5% to 7% of cases and are located immediately beneath the pulmonary and aortic valves. These defects vary in size but are often small. Because of their **proximity to the aortic valve, aortic leaflet tissue can invaginate and result in their closure, with the unfortunate result of significant aortic regurgitation**.

D. Associated lesions. Approximately 20% of VSDs are associated with many other forms of congenital heart disease, including aortic coarctation, bicuspid aortic valve, and patent ductus arteriosus. Of patients who present with a VSD, 5% to 10% will develop aortic regurgitation because of poor support of the right coronary cusp and the Venturi effect caused by the VSD jet, resulting in prolapse of one of the aortic valve leaflets. Discrete, fibrous subaortic stenosis and right ventricular (RV) outflow tract obstruction are less common associations. Less than 10% develop subvalvular pulmonary stenosis or an obstructive muscle bundle referred to as a double-chamber right ventricle. VSD is also associated with transposition of the great arteries, tetralogy of Fallot, and Trisomies 13, 18, and 21.

III. CLINICAL PRESENTATION.

Adult presentation occurs most frequently in small, restrictive VSDs and occasionally occurs in patients with moderate lesions and associated pulmonary hypertension or with Eisenmenger syndrome in large, unoperated lesions.

A. Symptoms. The most common symptoms in adult patients with hemodynamically significant VSD are dyspnea on exertion and exercise intolerance. The symptoms are related to the degree and chronicity of left-to-right shunt and the resultant increase in pulmonary pressure and resistance.

B. Physical findings. The auscultatory findings classically include a holosystolic murmur of varying intensity. Smaller muscular defects may produce a high-frequency early systolic murmur that ends before the second heart sound (S_2) because of closure from muscular contraction of the septum. The pitch of the murmur can be a clue to the size and nature of the defect. Smaller and more restrictive defects produce higher pitched and louder murmurs that may be associated with a palpable thrill. Another important feature is the intensity of the pulmonary component of S_2, which if increased suggests increased pulmonary pressure. An RV heave may be appreciated in patients with RV volume overload. A diastolic flow rumble at the apex may be heard in large left-to-right shunts due to increased flow across an otherwise normal mitral valve. Depending on associated lesions, other findings may be present such as a diastolic murmur of aortic insufficiency that may occur with

subaortic defects. A prominent systolic ejection murmur at the left upper sternal border suggests subvalvular pulmonic stenosis or double-chamber right ventricle. As pulmonary hypertension and right-to-left shunting develop, other signs including cyanosis, elevated jugular venous pressure, enlarged and pulsatile liver, clubbing, and a decrease in murmur intensity may occur. A systolic murmur in this setting often reflects concomitant tricuspid insufficiency. Notably, the murmur of a large VSD is often less harsh and more blowing in nature than that of a small VSD because of the absence of a significant pressure gradient across the larger defect which results in less turbulent flow.

C. The **differential diagnosis** on examination includes tricuspid regurgitation, acyanotic tetralogy of Fallot with a pulmonary outflow murmur, isolated subvalvular pulmonic stenosis, and hypertrophic cardiomyopathy.

IV. LABORATORY TESTS

A. The **electrocardiogram (ECG)** may be unremarkable with small defects or reveal left atrial and LV enlargement in patients with larger defects. An inlet or AV canal defect can be diagnosed from the ECG based on the presence of marked left-axis deviation. Right-axis deviation suggests elevated RV and pulmonary artery pressure. After surgical repair, right bundle branch block may occur.

B. A **chest radiograph** is often helpful in determining the degree of left-to-right shunt. A small-sized or normal-sized heart with normal pulmonary vascular markings on the chest radiograph suggests a hemodynamically insignificant lesion, whereas cardiomegaly and left atrial and LV enlargement are seen with large left-to-right shunts. A large defect associated with a small heart and oligemic lung fields should raise the suspicion of pulmonary vascular disease.

V. DIAGNOSTIC TESTING

A. **Echocardiography** is the diagnostic modality of choice for VSDs and associated lesions. Transthoracic echocardiographic imaging is almost always sufficient in the child and young adult, but transesophageal echocardiographic imaging may be required in some older adult patients. Defect size and location should be defined using two-dimensional and color Doppler techniques. Complete scans of the ventricular septum should be made to rule out additional defects. Optimal images are usually obtained from the parasternal long-axis and short-axis views and the apical four-chamber view; other views may fail to visualize the VSD jet, owing to perpendicular alignment of the echocardiographic probe and the jet. In the younger patient, subcostal coronal and sagittal views may also be helpful. Measurements of left atrial and LV size are key to determining the amount of volume load and magnitude of the left-to-right shunt. Echocardiographic features of pulmonary hypertension are helpful in confirming the impending reversal of shunt. Quantification of shunt velocity provides an estimate of the restrictive nature of the defect. Higher velocities indicate a more restrictive defect, reducing the likelihood that the patient has experienced pulmonary vascular insult. Systemic blood pressure should be noted when the velocity across the VSD is measured. Assuming no LV outflow obstruction, RV pressure can then be estimated based on the gradient across the VSD. This pressure can also be estimated if tricuspid insufficiency exists. A **perimembranous VSD** can be associated with a **ventricular septal aneurysm formed by the septal leaflet of the tricuspid valve bowing into the defect**. Similarly, supracristal VSDs are associated with aortic insufficiency caused by prolapse of the right or left coronary cusps into the VSD. A complete evaluation is always indicated to exclude other associated findings such as aortic coarctation, atrial septal defect, patent ductus arteriosus, and RV or LV outflow tract obstruction.

B. Catheterization is seldom needed in the management of isolated VSD in the infant or child. Surgical correction, when indicated, proceeds in most cases based on echocardiographic evaluation. In the adult, catheterization should be considered if anatomic questions remain despite transthoracic and transesophageal echocardiography or if pulmonary hypertension is suspected based on these studies. Hemodynamic assessment should include quantification of cardiac index and careful oximetric definition of the shunt level and quantity. A step-up in saturation measured at the pulmonary artery level confirms persistent left-to-right shunt across the defect and should correlate with acceptable pulmonary artery pressures and resistance. Evidence of low pulmonary artery saturations is expected with elevations of pulmonary resistance. Simultaneous comparison of RV pressure with systemic pressure is mandatory in these cases, along with the documentation of changes in response to oxygen or nitric oxide administration. Left ventriculography performed with **left anterior–oblique and cranial angulation** demonstrates the defect in most cases. If an inlet-type defect is present, the hepatoclavicular view (about 40° left anterior–oblique and 40° cranial) is usually adequate. Right ventriculography does not adequately opacify the left ventricle unless there is suprasystemic RV pressure. Coronary angiography should be performed when patients are felt to be at risk for coronary artery disease and likely to require operative intervention. Aortography can be helpful in eliminating the possibility of an associated ductus arteriosus or coarctation of the aorta.

C. Cardiac **computed tomography** (CT) can be used to assess VSD anatomy in patients with suboptimal echocardiographic images, but unlike magnetic resonance imaging (MRI), CT does not provide added information about shunt fraction (see Chapter 52) and carries additional risk associated with radiation and intravenous contrast administration.

D. MRI, using spin–echo and velocity-encoded cine sequences, can also be used to delineate VSD location and shunt fraction. MRI is particularly helpful in patients with associated complex lesions and those with inadequate echocardiographic images (see Chapter 51).

VI. THERAPY. Factors supporting intervention include cardiomegaly on the chest radiograph, significant left-to-right shunt (pulmonary-to-systemic flow ratios > 1.5:1), elevated but responsive pulmonary vascular resistance, symptoms of congestive failure or associated lesions such as aortic insufficiency, RV or LV outflow tract obstruction, and recurrent endocarditis. Management of VSD after myocardial infarction is discussed separately in Chapter 3.

A. Medical management in symptomatic cases without Eisenmenger physiology involves anticongestive measures such as the use of diuretics and digoxin. Efforts should then be focused on addressing suitability for surgical closure. Endocarditis is a recognized complication of VSD. In the patient with culture-proven endocarditis, 4 to 6 weeks of antibiotics should be administered parenterally before consideration of intervention. This must be tailored to the individual patient's clinical status and the infective organism's identification and sensitivity as well as the presence of concomitant valvular lesions and prosthetic material. For patients who have developed elevated pulmonary vascular resistance, selective pulmonary vasodilators, including phosphodiesterase-5 inhibitors, prostacyclin analogs, and endothelin receptor antagonists, may improve hemodynamics and exercise tolerance (see Chapter 32).

B. Transcatheter device closure of VSDs is being performed on an investigational or compassionate-use basis in selected medical centers. The Amplatzer Muscular VSD Occluder is FDA approved and can technically close many muscular defects. Perimembranous defects, however, pose particular problems for transcatheter closure given their close proximity to the conduction system and the AV and semilunar valves, although recent data from the investigational Amplatzer Membraneous

VSD Occluder are promising. Although long-term data from these devices are lacking, recent studies show that the rate of complete closure for the Amplatzer membranous device at 6 months is 96% and is 100% for the muscular occluder at 3 to 96 months follow-up. Complications with these devices include early or late-onset complete heart block, arrhythmia, tricuspid valve damage resulting in stenosis or regurgitation, and mechanical device failure during deployment. Transcatheter closure of VSDs after ventricular septal rupture in the setting of myocardial infarction has also been performed in selected individuals who are considered high-risk surgical candidates. Surgery, however, is still the preferred treatment modality in this setting.

C. **Surgical closure** continues to be the primary means of defect repair. Outcomes after VSD closure are good in children, with low mortality rates of 2% to 3%. Repair of VSDs in patients with evidence of increased pulmonary artery pressure is generally performed before the age of 2 years and, in many centers, in the first year of life. Surgical closure in the symptomatic adult appears to be well tolerated, with acceptable mortality and improved functional status. Irreversible pulmonary vascular disease with Eisenmenger physiology, however, is a general contraindication for surgical closure because right heart failure will often develop thereafter. Pulmonary artery banding (performed to limit pulmonary blood flow) was more frequently done in the past and is now reserved for the few patients who are very small, have lung disease, or who have complex, multiple VSDs. Postoperative sequelae include residual patch leaks, as well as supraventricular and ventricular arrhythmias. More recent studies have shown the presence of a residual shunt following surgical closure in 5% to 31% of patients depending on the type of VSD that was repaired. Recent data suggest that postsurgical residual VSDs < 2 mm close spontaneously within 1 year in the majority (83%) of patients.

D. In children for whom transcatheter and surgical approaches are technically difficult or particularly high risk, a **hybrid approach** has been explored. In these patients, a sternotomy is performed, and the device is placed through the anterior wall of the right ventricle under fluoroscopic and echocardiographic guidance.

E. According to the American Heart Association (AHA) guidelines, **antibiotic prophylaxis** is recommended in three situations in relation to congenital heart disease: (1) unrepaired cyanotic defect (i.e., VSD with right-to-left shunt), (2) repaired defect (i.e., VSD) with prosthetic material/device for the first 6 months, and (3) repaired defect (i.e., VSD) with residual defect at the site of a prosthetic patch/device. In addition, excellent oral hygiene and regular dental examinations are an important component in reducing the risk of developing infective endocarditis.

F. **Eisenmenger syndrome** is usually referred to in the context of ***irreversible pulmonary hypertension from long-standing exposure of the pulmonary vasculature to left-to-right shunting*** across a VSD. However, this physiology can occur as a result of any left-to-right shunt, including patent ductus arteriosus and, less commonly, isolated atrial septal defect. As a result of the elevated pulmonary pressures, the direction of shunting is reversed across the defect, producing systemic cyanosis and its associated complications. As described above, newer agents aimed at decreasing resistance in the pulmonary vasculature may be beneficial in these patients. **Pregnancy is poorly tolerated and is contraindicated in the presence of Eisenmenger syndrome** (see Chapter 38).

G. Long-term follow-up is required in patients whose VSDs were repaired later in life, since the majority of patients already have some degree of pulmonary hypertension, LV dysfunction, or both. Patients with residual shunt after repair, arrhythmias, or conduction blocks also require continued follow-up.

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CHAPTER 31

Adam S. Goldberg
Richard A. Krasuski

Patent Ductus Arteriosus and Coarctation of the Aorta

I. PATENT DUCTUS ARTERIOSUS—INTRODUCTION

A. The ductus arteriosus is a fetal communication between the descending aorta just distal to the left subclavian artery and the main pulmonary artery near its bifurcation. A patent ductus arteriosus (PDA) occurs when the ductus arteriosus fails to close and regress after birth to form the ligamentum arteriosum. PDA occurs in approximately 1 of 2,000 live births, but it is relatively uncommon among the adult population. In infants, it accounts for 10% to 12% of all congenital heart disease.

B. Natural history. The natural history depends on the size of the PDA, the direction of the shunt, and the development of any associated complications. At birth, 95% of patients with isolated PDA have left-to-right shunts and normal, or near-normal, pulmonary pressures. Patients with normal pulmonary artery pressures and no evidence of chronic left ventricular volume overload have a better prognosis. If untreated, life expectancy of patients with PDA is shortened; one-third of patients with PDA die by the age of 40 and almost two-thirds die by the age of 60. With a PDA, **congestive heart failure (CHF) can occur** because of chronic left heart volume overload. In patients with death related to PDA, CHF is the most common cause. Development of right-to-left shunting is also an ominous sign because it reflects the development of advanced pulmonary vascular disease and associated elevation in right-sided cardiac pressures (see Chapter 32 for discussion on Eisenmenger's syndrome).

C. Risk factors. Factors that increase risk for PDA include maternal rubella infection, birth at high altitude, premature birth, female sex, and genetic factors. In infants born at < 28 weeks of gestation, there is a 60% incidence of PDA. PDAs are twice as common in female infants as in male infants and in some instances have a genetic component. In a family in which one child has a PDA, there is approximately a 3% risk of having a PDA in subsequent offspring.

II. ANATOMY AND PATHOPHYSIOLOGY

A. Embryology. The ductus arteriosus is a **normal and essential component** of cardiovascular development that originates from the distal sixth left aortic arch. A PDA is most commonly funnel shaped with the larger aortic end (ampulla) distal to the left subclavian artery, then narrowing toward the pulmonary end, with insertion at the junction of the main and left pulmonary arteries. The Krichenko classification system describes the angiographic appearance of PDA (Table 31.1). In right-sided aortic arch, the anatomy of PDA can vary significantly: the PDA can arise from the left innominate artery and insert into the proximal left pulmonary artery or arise distal to the right subclavian artery with insertion into the proximal right pulmonary artery. Bilateral PDAs can also occur.

B. Fetal circulation. The presence of the ductus arteriosus in the fetal circulation is essential to allow **right-to-left shunting of nutrient-rich, oxygenated blood**

TABLE 31.1 Krichenko Classification of Patent Ductus Arteriosus Appearance on Angiography

Type A	Conical	Well-defined aortic ampulla and constriction near pulmonary insertion
Type B	Window	Short, with narrowing near aortic insertion
Type C	Tubular	Tubular duct without constrictions
Type D	Complex	Multiple constrictions
Type E	Elongated	Long PDA with conical appearance and multiple constrictions

PDA, patent ductus arteriosus.

from the placenta to the fetal systemic circulation, thereby bypassing the fetal pulmonary circuit. In the normal fetal circulation, oxygenated blood travels from the mother through the placenta to the fetus. The oxygen-rich blood traverses the fetal inferior vena cava, right atrium, right ventricle, and main pulmonary artery. The fetal pulmonary arteries are constricted and have high pulmonary vascular resistance. Oxygenated blood bypasses the fetal pulmonary circulation and enters through the ductus arteriosus to the lower resistance systemic circulation. Oxygenated blood then enters the fetal aorta distal to the left subclavian artery, perfuses the fetal systemic circulation, becomes deoxygenated, and returns to the maternal circulation. **In the fetus, the ductus arteriosus is kept open by low arterial oxygen content and placental prostaglandin E2 (PGE2).**

C. Birth. Several **changes occur at birth** to initiate normal functional **closure of the ductus arteriosus within the first 15 to 18 hours of life.** Spontaneous respirations result in increased blood oxygen content. Prostaglandin levels decrease because of placental ligation and increased metabolism of prostaglandins within the pulmonary circulation by prostaglandin dehydrogenase. The combination of increased oxygen content and lowered circulating prostaglandin levels usually results in closure of the ductus arteriosus. Generally, the ductus arteriosus is hemodynamically insignificant within 15 hours and completely closed by 2 to 3 weeks. The **fibrotic remnant** of this structure persists in the adult as the **ligamentum arteriosum. Spontaneous closure of a PDA is unlikely in term infants after 3 months and in preterm infants after 12 months.**

III. CLINICAL PRESENTATION

A. Symptoms. Severity of symptoms depends on the degree of left-to-right shunting; and it is determined by the size of the PDA, ductal resistance, cardiac output, as well as the systemic and pulmonary vascular resistances. PDA size is categorized by the degree of left-to-right shunting determined by the pulmonary-to-systemic flow ratio: Q_p:Q_s (Table 31.2). Between 25% and 40% of patients with PDA are asymptomatic, especially those with a small PDA. They are often diagnosed by auscultation

TABLE 31.2 Patent Ductus Arteriosus Size by Q_p:Q_s

Q_p:Q_s	Size
< 1.5	Small
1.5–2.2	Moderate
> 2.2	Large

of a continuous murmur on examination or incidentally during diagnostic testing. With larger PDAs, symptoms may develop. The most common symptom is exercise intolerance followed by dyspnea, peripheral edema, and palpitations. As is often the case in adult congenital heart disease, a previously well-tolerated PDA may become manifest in the setting of acquired heart disease such as ischemia, essential hypertension, and valvular disease.

B. Physical examination. Patients with PDAs may present with a wide range of physical findings. Pulse pressure may be wide because of diastolic runoff into the PDA, and peripheral pulses may be bounding. The jugular venous pressure is often normal with a small PDA, whereas with a large PDA, prominent *a* and *v* waves may be present. Precordial palpation often reveals a normal precordial impulse with a small PDA and a prominent left ventricular impulse with a large PDA. A **harsh, continuous murmur may be heard at the left first or second intercostal space**. The murmur envelops the second heart sound (S_2) and decreases in intensity during diastole. A small PDA has a soft, high-frequency, continuous murmur, whereas a large PDA classically has a machinerylike, loud murmur. With a large PDA, a middiastolic apical murmur may occur because of increased diastolic flow across the mitral valve. If **pulmonary hypertension** is present, a right ventricular lift may be present and the pulmonic component of S_2 will have increased intensity. The duration of the diastolic murmur reflects pulmonary artery pressures; elevated pulmonary artery pressures lead to a decreased gradient for left-to-right flow through the PDA during diastole, which results in a shorter diastolic murmur. As pulmonary pressure increases, the systolic component of the murmur shortens. Right-to-left flow may not generate a systolic murmur. For patients with a right-to-left shunt, a pathognomonic physical finding is **differential cyanosis of the lower extremities and left hand**.

C. Complications. The most common complications of PDA include **CHF, infective endocarditis**, and **pulmonary hypertension**. CHF occurs through volume overload of the left side of the heart and may be accompanied by **atrial fibrillation**. Vegetations generally develop on the pulmonary side of the PDA, and septic lung emboli may occur. Untreated PDAs with audible murmurs have a risk of infective endocarditis of 0.45%/y after the second decade. Spontaneously occurring **aneurysms of the ductus arteriosus** have been reported, although they are typically seen in association with endarteritis or among very young or very old patients. Pulmonary hypertension develops as a result of increased pulmonary vascular flow from a large PDA with significant left-to-right flow. Elevation in right-sided pressures may eventually result in Eisenmenger's physiology, right-to-left flow, and isolated cyanosis and clubbing of lower extremities (occurring in 5% of unrepaired PDA patients) with signs of pulmonary hypertension.

D. Differential diagnosis. The differential diagnosis of PDA includes ventricular septal defect associated with aortic insufficiency, aortopulmonary window, pulmonary atresia with systemic collateral vessels, innocent venous hum, and arteriovenous communications such as pulmonary arteriovenous fistula, coronary artery fistula, systemic arteriovenous fistula, and ruptured sinus of Valsalva aneurysm.

IV. LABORATORY TESTING

A. Hematology. Blood laboratory results are generally unremarkable, although compensatory erythrocytosis may be present in the setting of long-standing cyanosis resulting from a right-to-left shunt.

B. Electrocardiogram (ECG). ECG is neither sensitive nor specific for PDA. The ECG for a patient with a small PDA is often normal. Depending on the duration and hemodynamic significance of the PDA, electrocardiographic criteria for left atrial enlargement or left ventricular hypertrophy may be present. If pulmonary hypertension exists, the ECG may demonstrate right ventricular hypertrophy or right atrial enlargement.

C. Chest radiography (CXR). CXR is neither sensitive nor specific for PDA. A normal chest radiograph implies a small, hemodynamically insignificant PDA. With a large PDA, left atrial and left ventricular enlargement may be present, as well as increased pulmonary vascularity. With right-to-left shunting from pulmonary hypertension, the main pulmonary artery is frequently enlarged. The PDA occasionally appears as a separate convexity between the aortic knob and the pulmonary trunk. Calcification of the PDA may be visualized in older individuals.

V. DIAGNOSTIC TESTING. Standard transthoracic echocardiography (TTE) is the preferred initial diagnostic modality because of its low cost and noninvasive nature. Transesophageal echocardiography (TEE) may be required in subjects with suboptimal echocardiographic windows. Cardiac catheterization is typically reserved for therapeutic intervention.

A. TTE has a 42% sensitivity and 100% specificity for the diagnosis of PDA. The suprasternal notch view is usually best for demonstrating the PDA, particularly its aortic origin. The complete course of a PDA may be difficult to follow in some patients because of its tortuosity. Color Doppler imaging can often reveal flow between the descending aorta distal to the left subclavian artery and the pulmonary trunk. It is imperative to demonstrate color Doppler flow within the pulmonary artery, typically on a high parasternal short-axis view. Color Doppler and continuous wave Doppler help determine the direction of flow in the PDA. The timing of flow (systolic or diastolic) depends on pressure gradients between the systemic and pulmonary circulation. Quantitative assessment of shunt velocity is valuable to estimate the degree of restriction across the PDA. This measurement becomes important when planning transcatheter intervention. Diastolic aortic flow reversal is seen in the descending aorta if the shunt is significant. Associated left atrial and left ventricular enlargement also suggest a hemodynamically significant lesion.

B. TEE may be required if TTE windows are suboptimal or nondiagnostic. TTE and TEE have nearly 100% specificity for the diagnosis of PDA, but TEE has a much higher sensitivity (97%) than TTE (42%).

C. Cardiac catheterization is rarely needed for diagnostic purposes. Rarely, PDAs undiagnosed by physical examination or noninvasive testing may be diagnosed during left heart or right heart cardiac catheterization by recognizing the unexpected course of the catheter as it crosses the PDA by measuring a step-up in the oxygen saturation at the level of the left pulmonary artery or by documenting pulmonary opacification by descending aortography.

1. A PDA is best demonstrated by a **descending aortogram** performed in the **lateral projection** with a standard angiographic catheter positioned just below the ductal ampulla. If biplanar imaging is used, the right anterior–oblique cranial projection is sometimes helpful.
2. A PDA can be crossed from the main pulmonary artery or from the descending aorta, with the latter being easier and best guided by the lateral projection. Oximetric sampling typically demonstrates an increase in saturation in the main pulmonary artery compared with the right ventricle. Pulmonary artery and right ventricular pressures may be slightly elevated but typically remain below systemic levels. The etiology is usually pulmonary arterial vascular disease, but it can also be due to pulmonary venous stenosis, mitral stenosis, or left ventricular failure. The presence of systemic pulmonary pressures generally indicates severe and advanced pulmonary vascular disease.

D. Magnetic resonance imaging (MRI) and computed tomography may be useful in defining the anatomy in patients with unusual PDA geometry and in patients with associated abnormalities of the aortic arch.

VI. THERAPY. ACC/AHA 2008 guidelines for adults with congenital heart disease recommend closure of PDA (catheter or surgical) if there is **left atrial or left ventricular**

enlargement or if pulmonary arterial hypertension (PAH) is present with net left-to-right shunt (class I); or of an **asymptomatic small PDA by catheter device** (class IIa). PDA closure is **contraindicated** in patients with **PAH and right-to-left shunt**. Successful closure of PDA generally results in a good prognosis and may prevent adverse left ventricular remodeling resulting from volume overload.

The shape and size of a PDA determine the mode of therapy. Small- or moderate-caliber PDAs are generally closed percutaneously with coils. Large PDAs may require the Amplatzer Duct Occluder (ADO) or surgery. Heavily calcified PDAs represent a relative contraindication to surgical closure because of an increased risk of bleeding and incomplete closure with surgery. Cardiopulmonary bypass may be required for heavily calcified PDAs. PDAs with significant right-to-left shunts and Eisenmenger's physiology should generally not be closed. In patients with pulmonary vascular resistance > 8 U/m^2, lung biopsy has been recommended to determine candidacy for closure. However, even histologically severe pulmonary vascular disease may resolve after closure of the PDA. Reactivity of the pulmonary vascular bed to pulmonary vasodilating agents or significant reduction in pulmonary artery pressure during test occlusion may signal reversibility of pulmonary hypertension, but the absence of these findings does not rule out the possibility of reversibility in the long-term and natural history may be significantly altered by treating with pulmonary vasoactive medications.

A. Since the early 1990s, **transcatheter techniques** have become the **first-line therapy for most PDAs**. Many centers use single or multiple stainless steel coils to achieve complete closure. Numerous devices have been adapted or are under clinical investigation to allow transcatheter closure of larger defects. These procedures can often be performed on an outpatient basis, and complete closure rates at follow-up generally exceed 90% to 95% in most studies. The mortality rate is typically < 1% at experienced centers. Success has been reported even when ductal calcification has been apparent, but large clinical series are lacking.

1. **Percutaneous coil occlusion.** Percutaneous coils were developed in 1992 and are the **preferred treatment for older children and adults with PDAs < 3.5 mm in diameter**. Embolization coils have thrombogenic strands spanning the coils and are placed across the PDA to occlude flow. Advantages include low cost, small-caliber venous access, and easy implantation. Advances include detachable coils and development of a snare-assisted technique, both of which allow assessment and fine-tuning to ensure correct coil position before actual release of the coil. The coils are loaded at the tip of a catheter, the catheter is placed in the PDA under fluoroscopic guidance, and the coils are then deployed. Selected coil sizes are 2 to 2.5 times the narrowest diameter of the PDA. With moderate-sized or large-sized PDAs, multiple coils may be used. However, as PDA size becomes larger (> 3.5 to 4.0 mm), percutaneous, 0.038" coils become a less desired closure option, and alternative therapies become preferred. Although complete closure is usually accomplished with a single coil in children, multiple coils are frequently needed for complete closure in the adult. Although coil embolization may occur, the snare-assisted technique is almost always successful at percutaneous removal of the coil.
2. The **ADO**, a cone-shaped plug occluder made of thrombogenic wire mesh delivered with a 5F to 7F venous system, is the **preferred device for percutaneous closure of moderate to large PDAs**. The ADO stents the PDA, and blood is forced to flow through the center of the device, which is lined with thrombogenic wire mesh. The PDA then essentially clots off. Advantages include simple implantation, ability to retract the ADO into the sheath and redeploy if needed, and high success rates. There is an 89% occlusion rate on postprocedure day 1 and 97% to 100% complete occlusion after 1 month.
3. **Complications** of transcatheter closure are rare. The most common complication is embolization of the coil or device. Embolized coils can usually be retrieved; but even when this is impossible, adverse consequences are rare. Other

potential complications include flow disturbance in the pulmonary artery or aorta from device protrusion, hemolysis from high-velocity residual shunting, vascular access complications, and infection.

B. Surgical closure. In 1938, the first successful closure of a PDA was performed, which, coincidentally, was the first repair of a congenital heart defect. Surgical closure is the most effective method for complete closure and is usually performed without cardiopulmonary bypass by double ligation and division of the PDA. Ligation may be performed without division, but there is a risk of recanalization of the PDA in up to 20% of cases. In neonates and premature infants, ligation without division is performed because of the small size of the structures. With continued advances in percutaneous closure devices, **surgery has become second-line therapy for most adults with PDAs**. If surgery is necessary, the procedure is > 95% successful and has a low complication rate. The operative mortality rate is < 1%. However, the thoracotomy approach can be painful for adults and necessitates inpatient recovery. Newer surgical techniques such as transaxillary thoracotomy and video-assisted thorascopic ligation have improved surgical morbidity.

C. Medical therapy. In adults, medical therapy is ineffective to close a PDA. Medical therapy is indicated to prevent and treat complications of PDA, including heart failure, atrial arrhythmias, and pulmonary hypertension. **The most recent guidelines from the American Heart Association (AHA)** recommend antibiotic prophylaxis for endarteritis only in the setting of transcutaneous closure of the PDA for 6 months after the procedure; and prophylaxis is not recommended for those with repaired PDA without residual shunt.

D. Follow-up. If immediate duct closure is demonstrated after the procedure, a 6-month follow-up with TTE should suffice to assess for residual flow through the PDA. If residual shunt exists after the procedure, TTE should be performed every 2 to 3 months and early repeat attempt of complete closure considered, depending on the size of the residual shunt or the presence of hemolysis. For long-term follow-up, annual transthoracic echocardiograms are adequate.

VII. COARCTATION OF THE AORTA.

Coarctation of the aorta (CoA) has been found at autopsy in approximately 1 in every 1,550 individuals. It accounts for 5% to 10% of congenital heart disease and occurs more frequently in whites (7:1) and males (2:1). The disorder is typically diagnosed in childhood but may go undetected well into adulthood. Most patients develop persistent systemic hypertension, often as children, and are at risk for premature coronary artery disease. Cases usually occur sporadically, but an autosomal-dominant inheritance pattern has been observed. It is frequently associated with bicuspid aortic valve, and coarctation should be excluded in patients with bicuspid aortic valve and hypertension. Coarctation also occurs in 15% to 35% of patients with Turner's syndrome. Potential catastrophic complications include aortic rupture or dissection and cerebral berry aneurysm rupture. The mean survival for unrepaired patients is 35 years, with a 25% survival rate beyond 50 years.

VIII. ANATOMY.

CoA usually consists of a **narrowing in the region of the ligamentum arteriosum**, the remnant of the ductus arteriosus, just distal to the origin of the left subclavian artery. Most coarctations, therefore, are juxtaductal. The exact anatomy, however, varies, and the coarctation may include a long segment, the transverse arch, or the abdominal aorta. Rarely, tortuosity of the arch is identified. The main anatomic substrate is a prominent posterior shelf of the aorta, composed predominantly of thickened media.

A. Embryology. The exact embryonic origin remains uncertain, but two main theories exist. The first suggests that the narrowing is caused by aberrant ductal tissue

that constricts the aorta at time of ductal closure. The second proposes that aortic hypoplasia develops as a consequence of reduced blood flow in utero.

B. Associated cardiac defects include **bicuspid aortic valve** in 50% to 85% of cases, valvular and subvalvular aortic stenoses, ventricular septal defects, PDA, and congenital malformations of the mitral valve (i.e., smaller orifice, supravalvular ring, and parachute mitral valve resulting from a single papillary muscle). Multiple left-sided heart lesions may be associated with CoA and are often referred to as the Shone complex.

C. Associated extracardiac defects include intracranial aneurysms, especially within the circle of Willis (3% to 5% of cases), hemangiomas, hypospadias, and ocular defects.

IX. CLINICAL PRESENTATION

A. Symptoms. For patients with CoA who survive to adulthood, symptoms are usually negligible and nonspecific. Patients may complain of headaches, nosebleeds, cool extremities, leg weakness, or claudication with exertion. More serious manifestations include angina and heart failure.

B. Physical examination

1. A thorough cardiovascular examination may identify a systolic ejection murmur at the left upper sternal border that radiates to the intrascapular area located immediately anterior or posterior to the CoA. The murmur may be longer in systole and even continue into diastole, depending on the degree of obstruction. Increased flow through the collateral intercostal arteries can produce a continuous murmur appreciated diffusely over the precordium.
2. Upper extremity hypertension is often present, usually in conjunction with **diminished and delayed femoral pulsations**. CoA should always be considered in the differential diagnosis of refractory hypertension, especially in younger patients.
3. Funduscopic examination may demonstrate a "corkscrew" tortuosity of the retinal arterioles.

X. DIAGNOSTIC TESTING

A. The **ECG** is frequently normal but may demonstrate manifestations of long-standing hypertension, such as left ventricular hypertrophy and left atrial enlargement.

B. Chest radiography. Cardiomegaly, dilated ascending aorta, and prominent pulmonary vasculature are common. **Rib notching** usually develops by 4 to 12 years of age and is caused by enlarged intercostal collaterals. The **classic "3" or inverted-E sign is pathognomonic** for CoA and is created by a dilated left subclavian artery above the CoA and poststenotic dilation of the aorta below the CoA.

C. Echocardiography is most useful in infants and children. In adults, the suprasternal notch view is most helpful; color Doppler can be used to localize the site of turbulence. Continuous wave Doppler can assess the pressure gradient. If severe narrowing is present, persistence of flow in diastole (widening of the flow profile from systole into diastole) is seen by continuous wave Doppler in the aorta below the coarctation, such as in the abdominal aorta. This is a useful method to ascertain the presence of significant coarctation, even if imaging the direct site of the obstruction is impossible. A complete study should measure left ventricular size and ascending aortic size, determine aortic valve anatomy and function, and identify any potential associated congenital anomalies. TEE can also better define the anatomy if TTE proves inadequate.

D. MRI provides excellent anatomic and hemodynamic information. MRI is increasingly utilized as a first-line investigation before catheterization, particularly in adults. This enables the precise anatomy to be delineated and helps in the decision making regarding surgery or catheterization as treatment options. Serial MRI scans may be

used to follow results of therapeutic procedures. It is also useful in evaluating the intracranial vessels for associated berry aneurysms.

E. Cardiac catheterization provides excellent image data and pressure information and is often more reliable than echocardiography in adults. An **aortic angiogram** in left anterior–oblique or caudal and direct lateral projections usually best defines the lesion. Pressures should be obtained in the left ventricle and the ascending aorta, and the gradient across the lesion should be measured. A **pullback pressure of > 20 mm Hg** signifies hemodynamic significance and usually warrants intervention if concomitant clinical factors allow. A **gradient of > 50 mm Hg** generally mandates intervention. The presence of collateral vessels may falsely diminish the gradient.

XI. THERAPY. Several factors need to be taken into account when deciding on optimal therapy for CoA, including the age of the patient, the anatomy of the coarctation, any prior CoA operations, and the local surgical expertise. Whatever mode of treatment is chosen, the presence of postprocedural upper extremity hypertension influences survival.

A. In general, **medical therapy** for CoA has very limited utility, but it may be useful in a supportive role along with mechanical treatment. Hypertension should be medically treated, with the goal of controlling blood pressure and preventing end-organ damage.

B. Percutaneous management

1. **Percutaneous balloon angioplasty** is generally less effective than surgery for treatment of primary coarctation. Neonates and infants treated with angioplasty experience high rates of recurrent CoA (about 50% to 60%) and aneurysm formations (5% to 20%); therefore, surgical repair is preferred in this patient population. Likewise, balloon angioplasty of the unoperated coarctation in adults is controversial, with data suggesting higher rates of restenosis and aneurysm formation compared with surgical repair. Procedural complications can include acute aortic rupture (rare), aortic dissection, femoral artery trauma, recurrent coarctation (8%), and aneurysm formation (8% to 35%). The suspected mechanism for late aneurysm formation is intimal tear at the site of cystic medial necrosis within the coarctation site. It should be noted that the clinical impact of aneurysm formation is unclear, as most defects are small and have a low risk of rupture. Percutaneous angioplasty, however, is the preferred therapy for recurrent postsurgical coarctation. The procedure is successful in reducing the gradient to < 20 mm Hg in approximately 80% of interventions, with only a 1.5% incidence of late aneurysm formation.
2. **Stent implantation.** Theoretically, stent implantation may mitigate the development of aneurysm or dissection for a few reasons. By apposing the torn intima to the media and through dispersion of force, stenting may limit vascular trauma. It can also oppose the vascular recoil of the coarcted segment and avoid overdilation. By allowing the use of smaller balloons and graded inflations in staged procedures, stents may also reduce rates of aneurysm formation. Early and intermediate outcomes are promising, with a good safety and efficacy profile as well as lower rates of restenosis and aneurysm formation compared with balloon angioplasty. Despite the lack of long-term outcome data, stenting has become the preferred treatment modality in adults and adult-sized adolescents with native CoA. For recoarctation, balloon angioplasty with or without stenting is preferred in adults as well, as long as the anatomy is suitable.

C. Surgery remains the therapy of choice in neonates and infants. Three types of surgical repair have been used for correction of CoA: resection of the stenosed segment with end-to-end anastomosis, use of a subclavian flap, and patch aortoplasty. The approach with the best long-term outcome and sustained resolution of obstruction has been resection of the stenosed segment with end-to-end anastomosis. This approach carries with it the lowest risk of recurrent CoA (3%) and late aneurysm

formation (rare). Paradoxical hypertension and bowel ischemia may occur in the postoperative period. Major surgical complications include paraplegia caused by perioperative spinal cord ischemia (0.4% to 1%), residual coarctation, aneurysm formation at the site of repair, and, rarely, death. Survival rates of > 90% at 10 years and 84% at 20 years have been reported. Late deaths after surgical repair are related primarily to coronary artery disease, CHF, and aneurysm rupture. Young age favorably influences outcomes after surgery.

XII. FOLLOW-UP. Lifelong follow-up is indicated after the diagnosis of CoA is established, especially after any type of mechanical repair. Key issues to be cognizant of include the progression of hypertension either at rest or with exercise, development of CoA recurrence, aneurysm formation, left ventricular dysfunction, and associated aortic valve dysfunction when bicuspid valve is present. In patients repaired at older ages, hypertension commonly persists despite treatment by percutaneous intervention or surgery. Serial echocardiography is an important component of follow-up. Advanced imaging modalities such as computed tomography or MRI are used increasingly post repair to screen for aortic wall complications, with a preference for MRI given the radiation and contrast issues. Therefore, these patients should be considered "treated" and not "cured" despite repair.

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CHAPTER 32

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Complex Congenital Heart Disease

I. TETRALOGY OF FALLOT (TOF). TOF is the most common form of cyanotic heart disease. It occurs in approximately 1 in 3,000 live births and accounts for 10% of congenital heart disease in infants. It is also the most common congenital heart disease requiring surgical correction in the first year of life. The earliest description of TOF dates back to the 17th century; however, Fallot is credited with describing the classic features of the disease in 1888. Surgical treatment for TOF did not become available until well into the 20th century, and it dramatically improved life expectancy. The **current reparative approach has shifted from palliative shunt procedures to primary surgical repair**, most recently with valve-sparing techniques and usually performed in infancy. Without surgical intervention, only about 10% of patients survive beyond the age of 20 years. Adults with TOF usually have undergone surgical repair or palliation. A wide and complex spectrum of TOF exists including association with pulmonary atresia, absent pulmonary valve, and atrioventricular (AV) canal defects. Classic "simple" TOF is discussed here.

A. Anatomy

1. **Anterocephalad deviation of the outlet septum** results in four defining features:
   - **(a)** Right ventricular (RV) outflow tract obstruction
   - **(b)** Nonrestrictive ventricular septal defect (VSD)
   - **(c)** Aortic override of the ventricular septum (> 50% over the right ventricle)
   - **(d)** Right ventricular hypertrophy (RVH)
2. **Associated defects.** Anomalous origin of the left anterior descending coronary artery from the right coronary artery (5%) or a prominent conal branch from the right coronary artery can occur. These vessels cross the RV outflow tract. This anatomic feature is important to surgeons because infundibular resection or future conduit placement may be needed in this location and can lead to inadvertent arterial damage. Right aortic arch occurs in 25% of cases. A secundum atrial septal defect (ASD) occurs in 15% of cases, completing the pentalogy of Fallot. Persistent left superior vena cava is found in 5% of patients. Among adult patients, aortic insufficiency can occur naturally from long-term dilation of the aortic root, after endocarditis or as a postoperative sequela. Rare complications include pulmonary hypertension, supravalvular mitral stenosis, and subaortic stenosis. There is an association with deletion in the chromosome 22q11 region, which is also present in DiGeorge syndrome and/or velocardiofacial syndrome.

B. Clinical presentation

1. **Patients who have not undergone surgical repair** have variable clinical features depending on the amount of RV outflow tract obstruction, degree of aortic override, and, to a lesser extent, systemic vascular resistance, all of which dictate the amount and direction of shunting across the VSD.
   - **a.** With severe RV outflow tract obstruction, patients have central cyanosis and clubbing by 6 months of age. Hypoxic "spells" may be seen and are characterized by tachypnea, dyspnea, cyanosis, or even loss of consciousness or

death. If the obstruction is mild, however, the shunt through the VSD may be left-to-right, resulting in "pink tet" with minimal symptoms.

b. On physical examination, the patient is usually cyanotic and clubbed. A prominent RV impulse may be appreciated because of equalization of right and left ventricular pressures. A lift may be palpated under the right sternoclavicular junction in patients with a right-sided arch. The first heart sound (S_1) is usually normal, but the second heart sound (S_2) is often single because of an inaudible P_2. Auscultation is notable for a prominent systolic ejection murmur at the left upper sternal border, possibly with an associated thrill. The shorter the murmur, the more severe the infundibular pulmonary stenosis. The murmur of aortic insufficiency may be audible along with an aortic click resulting from a dilated overriding aorta. Continuous murmurs may be heard due to aortopulmonary collateral vessels. The presence of these vessels is more likely in the setting of pulmonary atresia, but they can also be acquired if RV outflow tract stenosis develops gradually.

2. Most adult congenital patients will have undergone surgical repair with or without a prior palliative procedure. The term "**palliation**" (as opposed to "repair") in these patients refers to a surgical procedure that consists of a **systemic-to-pulmonary artery shunt** (modified Blalock-Taussig shunt, classic Blalock-Taussig shunt, Potts shunt, or Waterston shunt; Table 32.1). These procedures are initially performed to supplement the deficiency of antegrade pulmonary

TABLE 32.1 Index of Postoperative Anatomy among Adult Patients with Congenital Heart Disease

Underlying pathology	Procedure	Notes
Single ventricle Hypoplastic left heart Tricuspid atresia	**1. Norwood**	Incorporation of native aorta and pulmonary artery (one of which may be hypoplastic or atretic) to produce a "**neo-aorta**" for the single ventricle
Pulmonary atresia with intact ventricular septum Unbalanced complete AV canal defect		Main pulmonary artery is transected from the heart Pulmonary flow is maintained with placement of a **Blalock-Taussig shunt** **Atrial septectomy** is often performed to allow complete mixing at the atrial level
	2. Bidirectional Glenn	Usually performed at 4–6 mo if pulmonary arterial anatomy, pressures, and resistances are adequate Anastomosis of the **superior vena cava to the pulmonary artery**, usually with takedown of a previously placed systemic-to-pulmonary artery shunt and repair of pulmonary arterial branch stenosis if necessary Term *bidirectional* is used in descriptions of this procedure because both right and left pulmonary arteries usually remain in continuity

TABLE 32.1 Index of Postoperative Anatomy among Adult Patients with Congenital Heart Disease (*Continued*)

Underlying pathology	Procedure	Notes
	3. Fontan	Usually performed at 1–5 y depending on growth of vasculature and cyanosis Anastomosis of **inferior vena cava to the pulmonary artery** by intra-atrial lateral tunnel or extracardiac conduit Pulmonary blood flow is achieved passively, without the assistance of a ventricular pumping chamber
dTGA (ventriculoarterial discordance)	**Rashkind**	**Atrial balloon septostomy** to create mixing of systemic and pulmonary circulation
	Blalock-Hanlon	Surgical atrial septectomy
	Mustard or Senning (atrial switch)	Baffle material (Mustard) or native atrial tissue (Senning) used to direct pulmonary venous blood → right ventricle → aorta; systemic venous blood → left ventricle → pulmonary artery
	Jatene (arterial switch)	Great arteries are transected and reanastomosed to the appropriate ventricle
		Coronary arteries are removed with a button of surrounding tissue and reimplanted to the appropriate sinuses
	Rastelli	For dTGA with VSD and pulmonary outflow tract obstruction
		VSD patch closure that directs left ventricular blood across the VSD to the aorta
		Pulmonary valve is oversewn
		Valved conduit from the right ventricle to the pulmonary artery to create RV outflow
Deficient pulmonary artery or RV outflow tract Pulmonary atresia Tetralogy of Fallot with hypoplastic pulmonary arteries	**Classic Blalock-Taussig** **Modified Blalock-Taussig** **Waterston shunt** **Potts shunt**	Native subclavian artery anastomosed to the right or left pulmonary artery Expanded polytetrafluoroethylene (Gore-Tex) material connecting the subclavian or innominate artery to the pulmonary artery Anastomosis between the ascending aorta and right pulmonary artery Anastomosis between the descending aorta and left pulmonary artery

AV, atrioventricular; RV, right ventricular; TGA, transposition of the great arteries; VSD, ventricular septal defect.

blood flow and are taken down at the time of complete repair. The latter two procedures have been abandoned owing to associated uncontrolled pulmonary blood flow and the subsequent development of pulmonary hypertension.

a. Patients who have undergone palliative repair alone have variable clinical findings depending on the type of palliation performed. In those who have undergone a classic Blalock-Taussig shunt, the brachial pulse on that side may be diminished or absent. If patent, shunts can produce a continuous murmur. Continuous murmurs can also result from aortopulmonary collaterals. Branch pulmonary artery stenosis at prior shunt insertion sites can produce unilateral systolic or continuous murmurs. Systolic ejection murmurs may be audible depending on the degree of antegrade flow across the outflow tract.

3. **Complete (or total) repair** consists of patch closure of the VSD and variable degrees of RV outflow tract resection and reconstruction. It may involve pulmonary valvotomy, RV outflow tract patch augmentation, transannular patch enlargement, or placement of a right ventricle–to–pulmonary artery conduit (i.e., bioprosthetic or homograft). Distal branch pulmonary artery stenosis may have been repaired, or residual lesions may be present. These patients typically have first undergone a palliative shunt procedure, but the current surgical approach has shifted to primary complete repair in infancy.

a. Patients are often asymptomatic. They may present with late symptoms such as dyspnea, exercise intolerance, palpitations, signs of right heart failure, or syncope.

b. The jugular venous pressure is usually normal unless there is RV dysfunction, in which case elevated jugular venous pressure with a prominent *a* wave is seen. The brisk pulse of aortic insufficiency may also be appreciated. On palpation, there may be an RV lift or a lift under the right sternoclavicular junction when the arch is right-sided. Some degree of turbulence almost always remains across the RV outflow tract and produces a variable systolic ejection murmur at the left upper sternal border, with radiation to the back and peripheral lung fields. Of importance is the presence of associated pulmonary insufficiency. This, even if severe, may occasionally be inaudible due to low-pressure hemodynamics. It is generally appreciated at the left upper sternal border, sometimes producing a to-and-fro murmur together with the outflow tract murmur. A high-frequency systolic murmur at the left lower sternal border suggests the presence of a residual VSD (often due to a small leak in the VSD patch). Continuous murmurs from collateral formation or prior shunts may be appreciated. The diastolic murmur of aortic insufficiency may also be heard.

C. Laboratory examination

1. **Chest radiographic** findings depend on the surgical history. The presence of a right aortic arch may be confirmed. A concave deficiency of the left heart border reflects various degrees of pulmonary arterial hypoplasia. Upturning of the apex from RVH causes the classic finding of a "boot-shaped" heart. Pulmonary vascular markings may vary throughout the lung fields, depending on associated branch pulmonary artery stenosis and relative blood flow. Calcification or aneurysmal dilation of surgical conduits or RV outflow tract repair may be visible on plain radiographs.

2. An **electrocardiogram** usually demonstrates sinus rhythm with RVH. Both atrial and ventricular rhythm disturbances can be present. The QRS axis is usually normal or rightward. If left axis deviation is present, an associated AV canal defect should be suspected. A patient who has undergone surgical repair typically has right bundle branch block. **A QRS duration of > 180 milliseconds is a predictor of sustained ventricular tachycardia and sudden cardiac death**.

D. Diagnostic testing

1. Echocardiography

a. For a child or young adult, transthoracic echocardiography may be the only modality necessary for diagnosis. For adults or patients who have undergone surgical intervention, catheterization or magnetic resonance imaging (MRI) may be necessary in order to identify the presence and location of residual lesions.

(1) Adequate views are obtained of the right heart, RV outflow tract, and proximal pulmonary arteries. Helpful views to identify a residual VSD or the presence of aortic insufficiency include the parasternal long-axis, parasternal short-axis, and apical four-chamber views. Further definition of residual lesions in the branch pulmonary arteries may be possible with a high parasternal short-axis view.

(2) Palliative shunts are often best visualized in the suprasternal notch view where the subclavian arteries course distally.

(3) Continuous flow is typically demonstrated with color Doppler techniques. Less common shunts may be difficult to image in adult patients. Aortopulmonary collateral vessels are extremely difficult to visualize, but may be seen in suprasternal notch views of the descending aorta.

b. Transesophageal echocardiography may allow improved imaging of the intracardiac anatomic structures in adults, but limitations often remain with regard to the distal pulmonary arteries, and additional testing is frequently necessary.

2. Cardiac magnetic resonance (CMR) imaging is considered the gold standard for evaluating the right ventricle and quantitating pulmonary insufficiency in these patients. It can demonstrate the presence of scar, distal pulmonary arterial anatomy, and RV aneurysms, as well as other associated defects. It can also provide hemodynamic information about residual lesions. Previously placed shunts and possibly aortopulmonary collateral vessels can be identified as well. The anatomic information may be sufficient to proceed with surgical treatment or to guide the interventional cardiologist in planning a transcatheter procedure.

3. Cardiopulmonary testing should be performed as a baseline study and with progression of symptoms. It is useful in determining the timing for reintervention in the setting of RV volume overload secondary to free pulmonary insufficiency.

4. Quantitative pulmonary flow scans are useful to determine discrepancies in pulmonary flow that may be caused by branch pulmonary artery stenosis. These scans also provide objective baseline clinical information when obtained after surgical or transcatheter intervention.

5. The role of **cardiac catheterization** is decreasing with the advent of other imaging modalities, but can be helpful in assessing residual shunts and pulmonary hypertension.

a. Right heart catheterization. Residual shunts are actively sought at the atrial and ventricular levels. The pulmonary arteries and branches are evaluated extensively in search of peripheral pulmonary stenosis. Findings at right heart catheterization and their clinical significance are as follows:

(1) RV pressure is generally systemic in a patient who has not undergone surgical repair.

(2) After surgical repair, elevated RV pressure suggests the presence of residual obstructive lesions, the levels of which are to be documented.

(3) Careful pullback recordings are performed from the branch pulmonary arteries to the right ventricle because stenosis at each level is possible.

(4) The presence of stenosis at a prior shunt site is expected.

(5) RV end-diastolic pressures may be elevated in the setting of pulmonary insufficiency.

b. Left heart catheterization is performed if noninvasive studies suggest residual VSD.

(1) Angiography includes a cranialized right ventriculography and possibly selective pulmonary arterial injections if hemodynamic findings suggest stenosis.

(2) Left ventriculography better demonstrates residual VSD in the presence of subsystemic RV pressures.

(3) Aortic root injection demonstrates the presence of aortic insufficiency, confirms the presence of grossly abnormal coronary artery origins or branching patterns, and reveals prior surgical shunts or aortopulmonary collateral vessels. If present, shunts and collateral vessels are best visualized in the posteroanterior and lateral projections after selective injection by hand.

(4) Selective coronary angiography is recommended in the care of adult patients to exclude acquired coronary artery disease and to identify the path of any anomalous coronaries before surgical intervention. **The anomaly that is not to be missed is the left anterior descending artery originating from the right coronary artery**—it crosses the RV outflow tract anteriorly and can be damaged during surgery.

E. Therapy and follow-up care

1. Medical treatment

a. If an adult has **not been surgically treated or has undergone palliative treatment**, a relatively well-balanced situation must exist. However, the following problems are to be expected.

(1) Long-term effects of RV outflow obstruction
(2) Progressive infundibular pulmonary stenosis
(3) Exposure of the pulmonary circulation to systemic shunt flow
(4) Development of distal pulmonary arterial stenosis, typically at shunt sites
(5) Erythrocytosis
(6) Chronic hypoxemia
(7) Pulmonary hypertension
(8) Paradoxical emboli
(9) Atrial and ventricular arrhythmias
(10) Increased risk of aortic insufficiency over time
(11) Endocarditis

b. Follow-up care increasingly involves **patients who have undergone surgical repair** and management of residual postoperative lesions.

(1) These patients are at increased risk for **sudden cardiac death**. Atrial and ventricular rhythm disturbances are common in the postoperative patient. Frequent Holter monitoring is warranted for this reason. Atrial tachyarrhythmias are found in up to one-third of patients and are predictive of morbidity and mortality. If patients are found to have nonsustained ventricular tachycardia, an electrophysiologic study and possibly an implantable cardioverter–defibrillator implantation can be considered. Atrial and ventricular arrhythmias may be the presenting problem for post-repair patients when a component of the repair is failing. There are no data to support prophylactic antiarrhythmic therapy to lower risk of sudden death in this patient population. An increased incidence of ventricular rhythm abnormalities has been associated with RV volume overload from pulmonary insufficiency and with QRS prolongation > 180 milliseconds (QRS duration correlates with degree of RV dilation).

(2) Pulmonary insufficiency can be tolerated for years, even decades, but chronic volume loading of the right ventricle can lead to diminished exercise tolerance, dysrhythmias, and **right heart failure**. Pulmonary

insufficiency is the most common indication for redo surgery after an initial repair.
(3) Residual VSD
(4) Progressive dilation of the ascending aorta
(5) Residual RV outflow tract gradient
(6) RV outflow tract aneurysm at previous patch site

c. Recent **infective endocarditis guidelines** have departed considerably from prior iterations such that antibiotic prophylaxis is recommended only for those who are at highest risk for adverse outcomes from endocarditis. Specifically, prophylaxis is still appropriate for patients with TOF who are unrepaired, including those who have undergone a palliative procedure. For patients with TOF who have undergone total repair, antibiotic prophylaxis is now recommended only for 6 months following the placement of prosthetic material or device or if there is a residual defect at, or adjacent to, the site of prosthetic material (VSD patch leak, for example). If the pulmonary valve has been replaced or repaired with prosthetic material, antibiotic prophylaxis is appropriate as well.

2. The primary therapeutic consideration for patients with TOF is **surgical intervention**—either repair or reintervention.
   a. The goal of **total repair** is to relieve the outflow tract obstruction while maintaining competency of a preferably native pulmonary valve with closure of the VSD. Some younger patients need extensive reconstruction of the RV outflow tract with early placement of a bioprosthetic valved conduit or homograft. In time, these usually become restrictive to flow and/or are insufficient. The result is progressive right heart hypertrophy, fibrosis, and failure if revision is not performed.
   b. A common indication for **reintervention** is pulmonary valve replacement (PVR) for severe pulmonary valve insufficiency. The ideal timing for PVR, however, remains controversial. Cardiac MRI may be helpful in determining optimal timing, and there is evidence to support pursuing pulmonic valve replacement before the RV end-diastolic volume index reaches 160 mL/m^2.
   c. Other indications for **reintervention** include the replacement or revision of conduits/homografts in the presence of symptoms, residual VSD with reasonable shunt (approximately 1.5:1), RV pressures greater than two-thirds of systemic pressures because of residual obstructive lesions, progressive aneurysmal dilation of RV outflow tract patch, residual systemic–pulmonary shunts with left ventricular volume overload, clinically significant arrhythmias, symptomatic or progressive aortic insufficiency, and dilated aortic root > 5.0 cm.
3. Although the mainstay of therapy has been surgical, **transcatheter techniques** are increasingly used to treat patients in certain situations. For the most part, transcatheter therapies for adults with TOF are limited to patients who have undergone prior surgical treatment, with attention to residual obstructive lesions in the main pulmonary artery, right ventricle–to–pulmonary artery conduit, or distal pulmonary arteries. Prior shunt sites may become stenotic with time and necessitate balloon angioplasty and possibly stent placement. Residual VSD and ASD may be closed percutaneously in select situations. Percutaneous pulmonic valve replacement has been approved for use both in Europe and the United States. The Melody valve (Medtronic; Minneapolis, MN) is a therapeutic option available for selected patients with stenotic or regurgitant conduits 23 mm or less in size.

II. COMPLETE TRANSPOSITION OF THE GREAT ARTERIES (D-TGA). This is a relatively common congenital anomaly that occurs with a prevalence of 20 to 30 in 100,000 live births and is found more often in males (2:1). It is not associated with other syndromes and does not tend to cluster in families. Although it represents **5% to 8% of**

all congenital heart disease, it accounts for **25% of deaths in the first year of life**. Adult patients almost invariably have undergone prior surgery and carry with them important morbidities that require ongoing surveillance and care.

A. Anatomy

1. The defining feature of this anomaly is **ventriculoarterial discordance**, in which there is an abnormal alignment between the ventricles and great arteries. Hence the aorta arises from the right ventricle and the pulmonary artery arises from the left ventricle, creating two parallel circuits instead of one in series. Deoxygenated blood flows from the right atrium across a tricuspid valve → right ventricle → aorta, whereas oxygenated blood flows from the left atrium across the mitral valve → left ventricle → pulmonary artery. Unless there is bidirectional shunting at the atrial (ASD), ventricular (VSD), or great artery level (patent ductus arteriosus) to allow mixing of blood, this anatomy is incompatible with life (Fig. 32.1).
2. There is an abnormal spatial relationship between the great arteries such that instead of the normal spiral configuration, they run parallel to one another. The **aorta is rightward and anteriorly displaced**, whereas **the pulmonary artery occupies a position more leftward and posterior**. This is the most common pattern, but other configurations can also be seen such as side-by-side great arteries with the aorta to the right or an aorta directly anterior to the pulmonary artery.
3. Associated cardiac anomalies include **VSD in 40%** to 45% of cases (usually perimembranous but can involve any portion of the interventricular septum), **left ventricular (or subpulmonary) outflow tract obstruction in 25%**, aortic coarctation in 5%, patent foramen ovale (PFO), and patent ductus arteriosus. Patients with these associated cardiac anomalies are considered to have **complex** transposition, whereas patients without these associated anomalies are considered to have simple transposition.
4. This lesion is also referred to as "dTGA," in which the "d" refers to the dextroposition of the bulboventricular loop, which is characterized by a right-sided right ventricle.
5. The coronary anatomy in dTGA is variable. The aortic sinuses are described according to their relationship to the pulmonary artery, such that the "facing

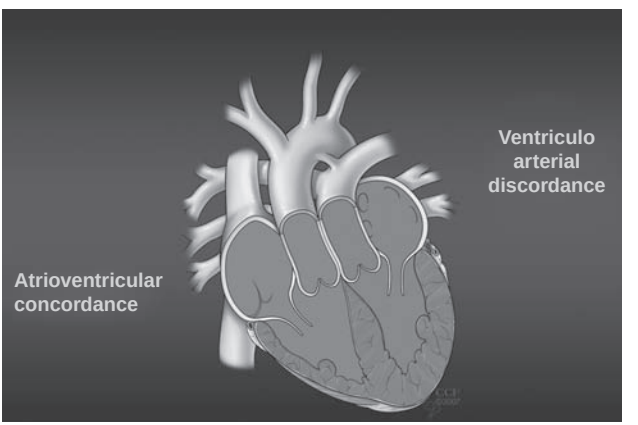

FIGURE 32.1 Complete (d) transposition of the great arteries.

sinuses" are closest to the pulmonary artery. The most frequent coronary arrangement is when the "left-facing" sinus gives rise to the left main coronary artery, whereas the "right-facing" sinus gives rise to the right coronary artery.

B. Natural history and surgical repair

1. Without surgical intervention, survival beyond infancy is dismal, with 89% mortality by the first year of life and worse outcomes for those without an associated lesion to allow for adequate mixing of blood. At birth, infants are treated with intravenous prostaglandin E to keep the ductus arteriosus open and some may undergo a **Rashkind procedure** (refer Table 32.1) to improve oxygenation until definitive surgery can be performed.
2. Adults invariably have undergone some type of cardiac surgery, although in rare cases they may present with Eisenmenger physiology (see subsequent text) if a "balanced" situation exists with a concomitant large VSD and pulmonary vascular disease. Surgical repairs include the atrial switch procedure **(Senning or Mustard operation)**, the **arterial switch** procedure (Fig. 32.2), or the **Rastelli operation** (Table 32.1).

C. Clinical presentation

1. The clinical presentation of the surgically repaired patient with dTGA depends on the type of previous surgery. Although no longer cyanotic, these patients have a host of mid- to late-term morbidities that require lifelong surveillance. Patients who have undergone an arterial switch procedure are approaching adulthood only now and presenting in adult congenital cardiology clinics.
2. **Atrial switch**
   a. Patients who have undergone an atrial switch operation often report New York Heart Association (NYHA) functional class I–II symptoms, but on exercise testing may have significant exercise intolerance. They have a systemic right ventricle, which, over time, can develop systolic dysfunction and progressive tricuspid regurgitation. These patients may present with signs and symptoms of congestive heart failure—the most common cause of death. Arrhythmias are common and patients may present with palpitations,

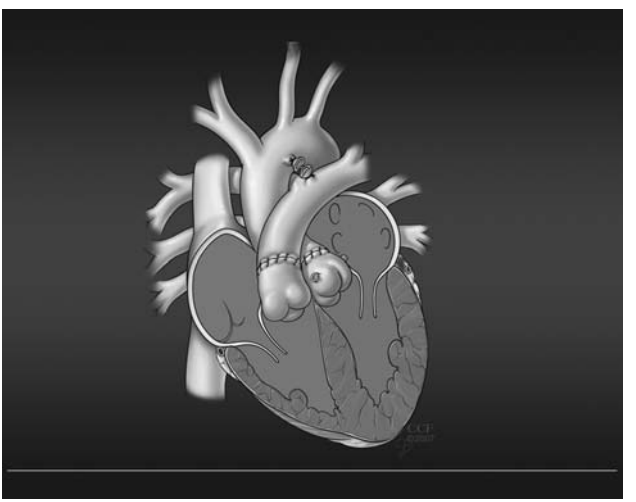

FIGURE 32.2 Arterial switch operation.

presyncope, or syncope. Venous baffle obstruction can lead to peripheral edema, hepatomegaly, ascites, and fatigue due to low cardiac output. The obstruction of the superior limb can produce a superior vena cava syndrome. Pulmonary venous baffle obstruction can lead to fatigue, exertional dyspnea, and chronic cough. Baffle leaks are often asymptomatic, but large leaks can lead to intracardiac shunting and cyanosis.

b. On physical examination, focus should be on signs of AV regurgitation and heart failure. There may be an RV heave at the left sternal border on palpation. S_2 is loud at the second left intercostal space from an anterior aorta. Audible splitting of the S_2 may indicate the development of pulmonary hypertension.

3. Arterial switch

a. The majority of these patients are asymptomatic with NYHA functional class I symptoms. Arrhythmias are not a significant problem with this subset. Few will present with chest pain, and in these patients ischemia must be ruled out.

b. The physical examination is sometimes notable for turbulence across the RV outflow tract, which may be palpated as a thrill. The diastolic murmur of aortic insufficiency should also be sought.

4. Rastelli operation

a. Both atrial and ventricular arrhythmias are mid- to late-term complications, and these patients may present with palpitations or syncope. Conduit obstruction may manifest as insidious exercise intolerance, dyspnea, or new-onset arrhythmias. On physical examination, the character of the pulmonic ejection murmur should be carefully noted to evaluate for conduit obstruction.

D. Laboratory examination

1. The **chest radiograph** of patients with dTGA displays a narrow mediastinum due to the parallel orientation of the great arteries. The cardiothoracic silhouette is normal. The pulmonary vasculature is normal in patients without pulmonary hypertension. The right ventricle–to–pulmonary artery conduit in patients who have undergone a Rastelli procedure may be visualized on plain radiograph due to calcification.

2. In patients who have undergone an atrial switch operation, the **electrocardiogram** may display an ectopic atrial or junctional rhythm due to loss of sinus node function. There is usually right-axis deviation and RVH as a result of the systemic position of the right ventricle. In patients who have undergone arterial switch, RVH is distinctly abnormal and suggests pulmonary outflow tract obstruction. After a Rastelli operation, the electrocardiogram is notable for a right bundle branch block and patients may develop complete heart block.

E. Diagnostic testing

1. Transthoracic echocardiography in atrial switch patients can assess the degree of tricuspid regurgitation and estimate RV function. Color Doppler is helpful in detecting baffle leaks or obstruction, although more detailed analysis may require transesophageal echocardiography. For those who have undergone arterial switch, transthoracic echocardiography can assess left ventricular function and help exclude supravalvular and pulmonary artery stenosis. Two-dimensional Doppler can be used to look for conduit stenosis after the Rastelli operation and estimate RV systolic pressures. It can also exclude any residual VSDs in these patients.

2. As in the TOF population, **CMR** imaging has emerged as an invaluable imaging modality for patients with repaired dTGA. For postatrial switch patients, CMR imaging is used to quantify the size and function of the right ventricle, assess tricuspid regurgitation, and evaluate the systemic and pulmonary venous limbs of the atrial baffle for potential obstruction or leaks. In patients who have undergone

arterial repair, right and left ventricular function can be quantitated and both the right and left outflow tracts examined. Focus is placed on the great arteries to look for the presence of supravalvular and branch pulmonary artery stenosis as well as dilation of the neo-aorta. Conduit stenosis and gradients as well as RV size and function can be determined in those who have had a Rastelli operation.

3. **Cardiopulmonary testing** is very useful in detecting subtle clinical changes and decrease in functional capacity. As mentioned previously, there is often a discrepancy between self-reported symptoms and performance on metabolic exercise testing. Patients who have undergone atrial switch often have chronotropic incompetence and may benefit from pacemaker implantation. Stress testing may be useful in patients after arterial switch to detect coronary artery stenosis and resultant ischemia.
4. **Quantitative pulmonary flow scans** are an important part of the diagnostic work-up for suspected pulmonary artery or branch pulmonary artery stenosis in those who have undergone arterial switch repair. It is useful to obtain these scans before and after potential intervention to assess for functional improvement.
5. **Cardiac catheterization** does not have a role in the routine management of these adult patients. It does have a role, however, in the diagnosis and treatment of baffle obstruction and leaks, pulmonary hypertension, pulmonary artery stenosis, coronary artery stenosis, conduit obstruction, and residual VSD.

F. Therapy and follow-up

1. Follow-up should focus on potential late complications after repair and depends on the type of surgery the patient has undergone.
   - **a.** Atrial switch
     - **(1)** Arrhythmias including sinus node dysfunction and intra-atrial reentry tachycardia (frequent Holter monitoring is recommended)
     - **(2)** RV dysfunction
     - **(3)** Tricuspid regurgitation
     - **(4)** Sudden cardiac death
     - **(5)** Baffle obstruction or leak
     - **(6)** Pulmonary hypertension
     - **(7)** Endocarditis
   - **b.** Arterial switch
     - **(1)** Supravalvular or peripheral pulmonary artery stenosis
     - **(2)** Pulmonary outflow tract obstruction
     - **(3)** Neo-aortic regurgitation and aortic root dilation
     - **(4)** Coronary artery stenosis leading to ischemia and sudden death
     - **(5)** Left ventricular dysfunction
     - **(6)** Endocarditis
   - **c. Rastelli operation**
     - **(1)** Atrial and ventricular arrhythmias
     - **(2)** Complete heart block
     - **(3)** Sudden cardiac death
     - **(4)** Left ventricular dysfunction
     - **(5)** Conduit stenosis
     - **(6)** Endocarditis
2. **Medical management**
   - **a.** In the treatment of systemic RV dysfunction, there are limited data to suggest any long-term benefits from applying the evidence-based drugs utilized for left ventricular dysfunction. Despite this, angiotensin-converting enzyme (ACE) inhibitors are often utilized for afterload reduction. β-Blockers should be used with caution in patients after atrial switch repairs, as this could precipitate heart block (due to sinus node and AV conduction abnormalities).
   - **b.** As mentioned previously, the latest **infective endocarditis** guidelines have changed such that in the absence of valve replacement or prosthetic material

used to repair a valve, implantation of prosthetic material within the last 6 months, or prosthetic material accompanied by residual leaks, it is no longer officially recommended that dTGA patients post-repair receive antibiotic prophylaxis.

3. Late intervention options include both surgical and transcatheter procedures and, again, depend on the type of repair. Systemic ventricular failure may ultimately require work-up for orthotopic heart transplantation.
   a. **Atrial switch**
      (1) The procedure of choice in patients with baffle obstruction is transcatheter stent implantation, with best results in the systemic venous baffle. Although technically more challenging, transcatheter dilation of the pulmonary venous baffle can be performed but may require surgical revision. Clinically significant baffle leaks can be treated with catheter-based techniques as well as with septal occluder devices.
      (2) Due to the high prevalence of atrial arrhythmias and sinus node dysfunction, these patients are referred for radiofrequency ablation procedures and pacemaker implantation.
      (3) Conversion to an arterial switch for systemic RV dysfunction or left ventricular "training" by pulmonary artery banding has not been reliably successful in the adult population and has been largely supplanted by cardiac transplantation in many centers.
   b. **Arterial switch**
      (1) Percutaneous balloon angioplasty with or without stent placement is an excellent option for those with pulmonary artery and supravalvular or branch pulmonary artery stenosis with suitable anatomy. Balloon angioplasty being a safe procedure, there is an approximately 15% restenosis rate, with lower risk after stent implantation. The greatest success lies with branch pulmonary artery stenosis.
      (2) Coronary artery stenosis can be treated with both stenting and coronary bypass surgery.
      (3) Severe neo-aortic regurgitation is treated surgically with either valve repair or replacement.
   c. **Rastelli operation**
      (1) All right ventricle to pulmonary artery conduits inevitably fail and require replacement. There is a role for percutaneous stenting of conduit obstruction in some patients, as this can delay the need for surgery. These transcatheter procedures have a risk of stent fracture as well as potential for coronary artery compression, which can lead to catastrophic outcomes in the catheterization laboratory.
      (2) Residual VSD leaks may be amenable to closure by percutaneous means, but often require surgical revision. Clinically significant residual left ventricular outflow tract obstruction is also managed surgically.

III. CONGENITALLY CORRECTED TRANSPOSITION OF THE GREAT ARTERIES (ccTGA).

Ventricular inversion or ccTGA is a rare congenital anomaly that occurs in < 1% of children with congenital cardiovascular defects. Among these patients, it is equally rare to have no other associated structural abnormalities. The natural history of ccTGA is gradual congestive failure caused by systemic AV valve insufficiency and systemic ventricular dysfunction, even in the absence of other associated malformations. The presence of associated defects and conduction abnormalities contributes to a further decrease in life expectancy without intervention. Life expectancy is generally good but does not reach normal.

A. Anatomy

1. The defining feature of this congenital abnormality of cardiac looping is **AV and ventriculoarterial discordance**. Blood flows from the right atrium across

a mitral valve → right-sided, morphologic left ventricle → pulmonary artery → lungs → left atrium across a tricuspid valve → left-sided, morphologic right ventricle → aorta (Fig. 32.3).

2. The great arteries are not in their normal configuration and often run parallel to one another instead of crossing. The pulmonary artery is more posterior and rightward than usual and the aorta is more anterior and leftward.
3. The anatomic coronary arteries, like the AV valves, follow their respective ventricles. The left-sided coronary artery resembles the anatomic right coronary artery as it courses in the AV groove and gives rise to infundibular and marginal branches. The right-sided coronary artery resembles the morphologic left coronary artery, which branches into the anterior descending and circumflex arteries (Fig. 32.4).
4. The conduction system likewise follows the respective ventricle, as the right-sided, morphologic left ventricle depolarizes first. Accessory AV nodal tissue is located anteriorly with respect to normal, and the His bundle must traverse

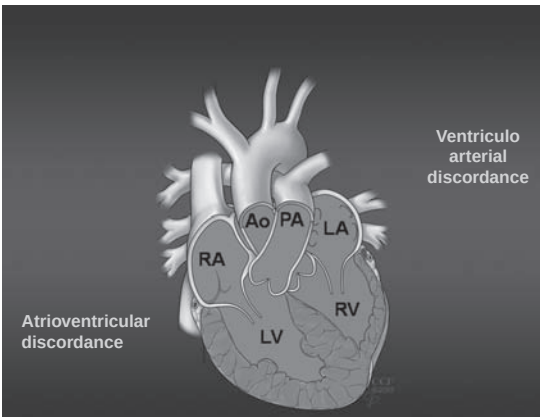

FIGURE 32.3 Congenitally corrected (l) transposition of the great arteries. Ao, aorta; LA, left atrium; LV, left ventricle; PA, pulmonary artery; RA, right atrium; RV, right ventricle.

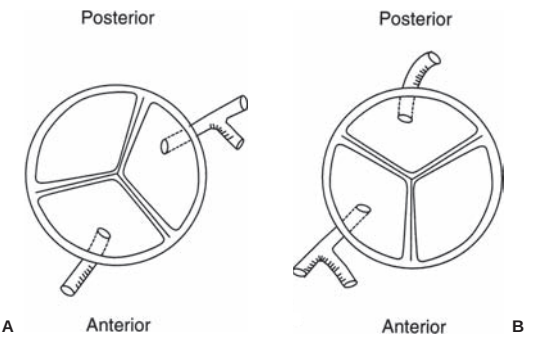

FIGURE 32.4 Schematic representation of coronary artery origins and branching in the normal heart (**A**) and in a congenitally corrected transposition (**B**).

anterior to the pulmonary artery and along the superior margin of a VSD if present. There is increased risk of acquired **complete heart block** in this lesion because of the abnormally placed AV node and its extended course. Approximately 30% of adolescents and adults develop complete heart block, the incidence of which is 2% per year without surgical intervention, with the site of block being within or above the His bundle. Accessory pathways have been described and are typically left-sided in the presence of an Ebstein anomaly–like malformation of the left-sided (tricuspid) AV valve.

5. Isolated ccTGA is the exception. **Associated lesions** are common and are considered in the diagnostic evaluation. They include VSD (70%), pulmonary outflow obstruction (~40% and usually subvalvular), or abnormalities of the left-sided, systemic tricuspid valve. Up to 90% of patients have an abnormality of the tricuspid valve in some form (i.e., dysplastic or Ebstein-like tricuspid valves).

B. Clinical presentation

1. Because physiologic blood flow is preserved, patients may have no symptoms through adulthood in the absence of other structural lesions or associated complications. This scenario is rare, however, because associated lesions commonly dictate the clinical features.
2. Without associated structural abnormalities, **failure of the systemic morphologic right ventricle** with various degrees of systemic AV valve (tricuspid) insufficiency is the norm. In this setting, the patient has nonspecific descriptions of fatigue, shortness of breath, and exercise intolerance or congestive failure. Patients may have **syncope or presyncope** caused by conduction abnormalities or complete heart block.
3. On physical examination, there is a loud A_2 due to an anterior and leftward aorta. The murmurs of a VSD or pulmonary stenosis may also be appreciated. Tricuspid insufficiency can be heard with systemic ventricular failure.

C. Laboratory examination

1. In the usual anatomic configuration of ccTGA, the aorta is anterior and to the left, which produces a **chest radiograph** with a straight left heart border. The left pulmonary artery is not well defined and the ascending aorta is not visible on the right. The chest radiograph may appear normal or reflect the presence of associated lesions, such as increased pulmonary flow from a VSD or decreased pulmonary flow in the setting of pulmonary stenosis. Dextrocardia occurs in approximately 20% of these patients and the diagnosis should be suspected if seen with abdominal situs solitus.
2. The typical **electrocardiogram** shows a left axis deviation. Among pediatric patients, there is loss of the usual Q waves in the precordial leads, with deep Q waves in leads II and aVF reflecting reverse septal activation. A variety of AV node conduction abnormalities may manifest with time and progress to complete heart block.

D. Diagnostic evaluation

1. In most instances, the diagnosis can be made with **echocardiography**. The essential findings of AV and ventriculoarterial discordance must be demonstrated. Imaging may be difficult in the presence of dextrocardia or mesocardia. Close attention must be paid to the morphologic details of each chamber.
   a. The morphologic **right ventricle** is identified on the basis of its **triangular** shape, the presence of **trabeculations and moderator band**, an inferiorly positioned AV valve, and the absence of AV valve attachments to the interventricular septum.
   b. The morphologic **left ventricle** is identified on the basis of its bullet shape, smooth wall, and more superiorly positioned AV valve and presence of AV valve attachments to the interventricular septum. In the case of ccTGA, these relationships are preserved but reversed.

c. There is lack of anatomic continuity between the **left-sided (tricuspid) AV valve and aorta**, but continuity is present between the **right-sided (anatomic mitral) valve and pulmonary artery**. The left-sided AV valve is displaced inferiorly relative to the right-sided (mitral) valve and may appear malformed or have the characteristics of Ebstein anomaly.

d. Apical four-chamber and subcostal images are particularly helpful. The suprasternal notch view is essential in evaluating the great vessels that lie parallel to each other.

e. The **aortic arch** typically lies to the left of midline in the sagittal plane and can often be visualized from the high left parasternal position. Because variations in great vessel position occur, the spatial orientation must be clarified.

f. **Associated defects** (e.g., systemic AV valve insufficiency, VSD, and outflow tract obstruction) with ccTGA must be excluded or defined.

2. **Catheterization is unnecessary** for the diagnosis of ccTGA, but may be helpful in preoperative planning with regard to the hemodynamic significance of associated lesions. In rare instances, ccTGA is diagnosed by catheterization and was not recognized during routine echocardiography. An unusual arterial catheter course is caused by the anterior and leftward position of the aorta in most instances. The left-sided coronary artery typically arises from the posterior sinus and assumes a right coronary branching distribution, whereas the right-sided coronary artery arises from the anterior and rightward sinus and assumes a typical left coronary branching distribution (Fig. 32.4). Because the ventricular septum often lies in the sagittal plane, ventriculography is usually best performed in the straight posteroanterior and lateral projections.

E. Therapy

1. **Medical management** is dictated primarily by the associated malformations.

a. In the rare case of isolated ccTGA, the risk of development of conduction abnormalities is cumulative over time; therefore, periodic Holter monitoring is warranted. Permanent pacemaker placement is often needed.

b. The systemic AV valve and ventricle may show signs of failure that necessitate initiation of heart failure measures in the form of diuretics and afterload reduction, although data are lacking for the use of agents such as ACE inhibitors or β-blockers in systemic right ventricles.

c. Associated lesions such as pulmonary stenosis or atresia, severe systemic AV valve regurgitation, or VSD may likewise contribute to the medical treatment of these patients, but often also necessitate surgical intervention.

d. The recent American Heart Association (AHA) guidelines do not recommend routine antibiotic prophylaxis for these patients unless they have had recent placement of prosthetic material within the preceding 6 months or have a leak at, or adjacent to, the site of a previous prosthesis.

2. **Surgery**

a. Infants and children who are brought to medical attention early often need surgical intervention in the form of relief of pulmonary outflow tract obstruction or placement of palliative shunts, depending on the associated lesions.

b. For selected children, a **double switch** procedure may be performed. An **atrial switch** corrects the AV discordance by baffling atrial blood to the appropriate ventricle (i.e., oxygenated blood diverted from the left atrium rightward to the right-sided left ventricle and vice versa by the Mustard or Senning procedure). **Arterial switch** is performed in the same operation to restore anatomic ventriculoarterial concordance. The double switch operation may necessitate a period of "training" of the left ventricle by means of pulmonary artery banding. The results of this operation are generally less favorable in older patients in whom the right ventricle has been the systemic ventricle for a more prolonged period. The intermediate-term results of this procedure are encouraging, but data for long-term results are limited. Those

with a large VSD may undergo atrial baffling with a **Rastelli operation** (see Table 32.1).

c. Adult patients with symptoms of progressive systemic AV valvular insufficiency may need valve repair or replacement. Most centers that have reported results with this procedure have found improved functional status after surgical treatment and acceptable risks. The timing of surgical intervention among patients with less severe symptoms is a topic of debate, but it is agreed that referral should be considered early before irreversible changes in ventricular function occur.

IV. EBSTEIN ANOMALY. This anomaly of the tricuspid valve represents 0.5% of congenital heart defects. The natural history of this lesion varies from early death to nearly normal expected survival, depending on the degree of tricuspid valve involvement and the presence and type of arrhythmias. An increased risk of **sudden death** irrespective of functional class, presumably caused by arrhythmia, has been observed. **Predictors of poor outcome** include earlier **age** at presentation, **cardiomegaly**, severe **RV outflow abnormalities**, and **disproportionate dilation of the right atrium** relative to the other chambers. There is an association with maternal lithium administration, but most cases are sporadic.

A. Anatomy

1. The **tricuspid valve** is morphologically and functionally abnormal. The basic features include adherence of the septal and posterior leaflet to the myocardium, which lowers the functional annulus toward the RV apex. This results in the classic **atrialization** of the right ventricle (Fig. 32.5) and dilation of the true tricuspid annulus. The anterior leaflet usually is not displaced, but is redundant and may be fenestrated and tethered.
2. **Associated structural anomalies** include **a PFO or ASD** (found in ≥ 80%), **VSD, mitral valve prolapse, and pulmonary stenosis**. ccTGA is associated with Ebstein-like anomaly of the tricuspid (systemic) valve.

B. Clinical presentation

1. **Signs and symptoms** are variable.
   a. The presence of a severely insufficient valve can be apparent at birth because of right-to-left shunting across a stretched PFO or ASD, resulting in cyanosis. Pulmonary vascular resistance is high in the neonate and worsens cyanosis,

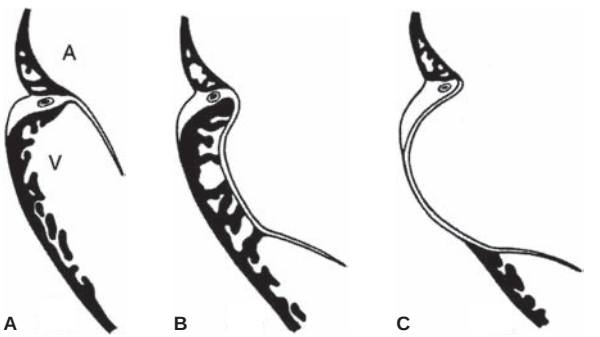

FIGURE 32.5 Section through the right atrioventricular junction. **A:** Normal heart, showing the right atrium (A) and right ventricle (V). **B:** Mild degree of Ebstein anomaly. **C:** Severe Ebstein anomaly. In (**B**) and (**C**), there is apparent displacement of the tricuspid valve. (From Adams FH, Emmanouilides GC, Riemenschneider TA, eds. *Moss' Heart Disease in Infants, Children, and Adolescents.* 4th ed. Baltimore, MD: Williams & Wilkins, 1989, with permission.)

but as pulmonary vascular resistance falls, cyanosis may resolve. In adulthood, as tricuspid regurgitation becomes longstanding with associated decreased RV compliance, cyanosis can reappear. In subtle cases, the anomaly may not be evident until adulthood and then results in nonspecific fatigue, shortness of breath, palpitations, near-syncope, or syncope. In the presence of an interatrial communication, patients may present with paradoxical embolization or brain abscess. Because the spectrum of involvement varies greatly, a high index of suspicion must be maintained.

b. The downward displaced septal leaflet creates a substrate for **accessory pathways**, and clinical Wolff-Parkinson-White syndrome is found in 10% to 25% of patients. Arrhythmias include supraventricular tachycardia mediated by an accessory pathway or caused by atrial arrhythmias from progressive atrial dilation. The combination of atrial fibrillation or flutter conducted rapidly across an accessory pathway is often poorly tolerated.

2. Physical examination

a. General inspection usually reveals normal jugular venous pulsations despite severe tricuspid regurgitation, which is masked by a large compliant atrium. Cyanosis may be present as a result of right-to-left shunting at the atrial level. Digital clubbing will vary depending on the amount of cyanosis.

b. The most common auscultatory findings are the regurgitant murmur of tricuspid insufficiency, gallop rhythms, multiple systolic ejection sounds, and a widely split S_2.

C. Laboratory examination

1. Chest radiography may reveal cardiomegaly, caused by right atrial enlargement from tricuspid insufficiency. Typically, it is described as a globe-shaped heart with a narrow waist.

2. The **electrocardiogram** can demonstrate PR prolongation, right atrial enlargement ("Himalayan" P waves), and superior axis with or without right bundle branch block (Fig. 32.6). The QRS amplitude is characteristically low over the right precordial leads due to a diminutive right ventricle. The preexcitation pattern, if present, is almost always type B (i.e., left bundle branch pattern). Deep Q waves may be seen in leads II, III, and aVF from fibrotic thinning of the RV free wall and/or septal fibrosis.

D. Diagnostic evaluation

1. The diagnosis can be confirmed with transthoracic or transesophageal **echocardiography**, with the tricuspid valve readily visualized in the parasternal short-axis, apical four-chamber, and subcostal views.

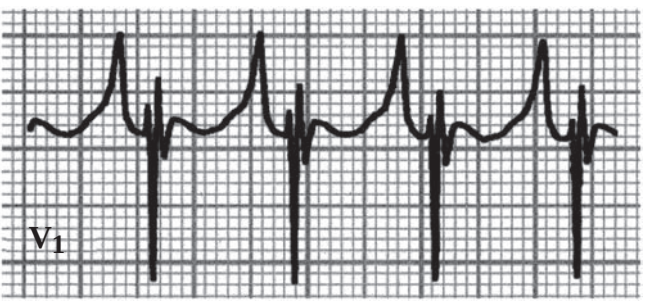

FIGURE 32.6 Lead V_1 of an electrocardiogram from a newborn infant with Ebstein anomaly demonstrates marked right atrial enlargement and an rSR′ pattern.

a. **Apical displacement of the septal leaflet** from the insertion of the anterior mitral valve leaflet by at least 8 mm/m^2 body surface area is considered diagnostic. In less obvious cases, only tethering of the septal leaflet may be found, defined as at least three accessory attachments of the leaflet to the ventricular wall causing restricted motion. An imperforate valve may rarely occur.
b. The **anterior leaflet** may produce functional obstruction of the pulmonary outflow tract. The leaflet in this circumstance is often called "sail-like." The pulmonary outflow is carefully studied to discern functional obstruction from such a leaflet rather than true anatomic atresia of pulmonary outflow.
c. Views of the **atrial septum** are included in all studies to assess the size of the ASD and degree of shunting, if present.
d. The size of the **right ventricle** and true tricuspid annulus is assessed because size guides the feasibility of surgical intervention.
e. The size and function of the **left ventricle** are assessed. The shape of the left ventricle may be unusual because of extreme leftward bowing of the ventricular septum. Left ventricular function can be affected, and abnormalities may affect long-term outcome.
f. **Associated lesions** must be excluded, such as ASD, RV outflow tract obstruction, patent ductus arteriosus, and, in rare instances, mitral valve abnormalities with associated insufficiency.

2. **Cardiac catheterization is unnecessary** for the diagnostic evaluation of Ebstein anomaly, except to exclude coronary artery disease in adult patients with risk factors for whom surgical intervention is planned. Increased risk of cardiac arrest during catheterization has been reported. A diagnostic right heart study may be indicated in the presence of associated hemodynamic abnormalities as part of preoperative planning.
3. Formal **electrophysiologic study** may be considered for patients with arrhythmias or for those being considered for surgical treatment. Radiofrequency ablation of accessory pathways is performed.

E. Therapy

1. A large number of adult patients may undergo **medical treatment**, which includes standard heart failure medications such as diuretics and digoxin. There are no good data to support ACE inhibitors in right heart failure due to Ebstein anomaly. Particular attention must be focused on the management of atrial dysrhythmias, which become more common with age. Permanent pacemaker therapy is required in 3.7% of patients, mostly for AV block and rarely for sinus node dysfunction. Endocarditis prophylaxis is no longer recommended for these patients unless they are cyanotic and unrepaired, have undergone placement of prosthetic material within the preceding 6 months (i.e., ASD occluder device), have a leak adjacent to or at the site of prosthetic material, or have had tricuspid valve replacement.
2. **Surgical correction** usually is recommended for patients with NYHA functional class III–IV symptoms despite medical therapy. The tricuspid valve may be repaired primarily or complete replacement may be necessary, and an interatrial communication, if present, is closed. Patients with symptomatic cardiomegaly, cyanosis, or arrhythmias are considered for surgical intervention. Favorable results have been achieved at centers experienced in the care of adult patients, and functional class has improved after therapy.
3. **Transcatheter closure** of an interatrial shunt can be considered in select patients with cyanosis at rest (oxygen saturation < 90%). Patient selection must be carefully evaluated, as closure of an ASD or PFO may lead to worsening RV dysfunction due to increased right-sided heart pressures. In the case of paradoxical embolic events (i.e., stroke), ASD/PFO closure is considered.

V. EISENMENGER SYNDROME. Eisenmenger syndrome is the clinical phenotype of an **extreme form of pulmonary arterial hypertension associated with congenital heart disease**. Over the last few decades, rapid advances in the modalities of diagnosis and treatment of congenital heart disease have resulted in the ability to repair defects at a much younger age. Pulmonary vascular injury is prevented in many of these children. However, Eisenmenger syndrome is still seen in older patients and occasionally in younger patients, particularly in those from developing countries where access to care may be limited. The natural history of Eisenmenger syndrome is variable; and although a cause of significant morbidity, many Eisenmenger patients survive 30 years or more after the onset of the syndrome.

A. Physiology. Patients with a systemic-to-pulmonary circulation connection will initially have left-to-right shunting of blood due to the lower pulmonary vascular resistance compared with systemic vascular resistance. Over time, because of excessive flow to the pulmonary vasculature resulting in increased shear and circumferential stress, pulmonary vascular resistance increases. Eventually, the shunt reverses, creating right-to-left flow. Although the classic form of the disease was initially used to describe the long-term consequences of a VSD, it can occur with any congenital defect with an initial left-to-right shunt including ASD, AV canal defect, patent ductus arteriosus, aortopulmonary window, and surgically created systemic-to-pulmonary artery shunts. It is important to note, however, that the **physiology and clinical presentation differ depending on the *level* of shunt**. In contrast to patients with nonrestrictive shunts at the ventricular or arterial level, most patients with ASDs do not develop Eisenmenger syndrome, and if they do, they present much later in life. In this case, atrial-level shunting is determined by the compliance of the ventricles and not due to systemic or supra-systemic pulmonary artery pressures.

B. Clinical presentation of Eisenmenger syndrome has multi-organ involvement

1. **Symptoms.** Pulmonary congestion (from the left-to-right shunt) in early childhood may be evident from the history, but improves as the shunt reverses with ensuing cyanosis. Exercise intolerance is very common. Hypoxemia can lead to erythrocytosis and symptoms of hyperviscosity (e.g., headache, dizziness, fatigue, and cerebrovascular accidents). These patients can have a bleeding diathesis due to thrombocytopenia and inadequate clotting factors. This can complicate the management of intrapulmonary thrombosis, which occurs in up to one-third of patients. Hemoptysis is a common symptom—alone or due to pulmonary infarction. Infectious complications include bacterial endocarditis and septic cerebral emboli. Atrial arrhythmias and symptoms of congestive heart failure are usually a late sign and are associated with an increased risk of sudden cardiac death.
2. **Physical examination.** The initial murmur of the associated lesion goes away with reversal of the shunt. Cyanosis and digital clubbing are present, and arterial pulses may be diminished. The cardiac examination reveals signs of elevated right heart pressure, such as jugular venous distention with a prominent *v* wave, a right parasternal heave, a loud pulmonary component of S_2 (sometimes palpable), a right-sided S_4, a holosystolic murmur of tricuspid regurgitation, and a diastolic decrescendo murmur of pulmonary regurgitation. Signs of congestive heart failure such as peripheral edema, ascites, and hepatosplenomegaly are seen later in the disease course.

C. Laboratory examination

1. **Chest radiography** is variable. It may show dilated, even calcified, central pulmonary arteries. Reduced peripheral lung markings are not commonly seen. Patients with ASDs tend to have cardiomegaly due to RV enlargement.
2. The **electrocardiogram** shows evidence of right atrial enlargement and RV hypertrophy. The presence of atrial arrhythmias should be investigated, particularly in the presence of palpitations.

D. Diagnostic evaluation

1. **Echocardiography.** Two-dimensional echocardiography helps in the detailed assessment of the level of the defect, associated lesions, and ventricular function. Doppler measurements can demonstrate and assess the size of the shunt as well as RV pressure and volume overload.
2. **Cardiac catheterization.** Cardiac catheterization is often necessary in these patients to assess the pulmonary vascular resistance. Demonstration of pulmonary vasoreactivity to oxygen, nitric oxide, or other pulmonary vasodilators is prognostic for these patients and can help identify which patients will most benefit from advanced therapies for pulmonary arterial hypertension.

E. Therapy

1. **Medical management**
   a. Chronic nocturnal oxygen therapy has not been shown to be beneficial, although it may improve symptoms in some patients. Anticoagulation is controversial because it can also predispose to hemorrhage or hemoptysis, but it is helpful in preventing thromboembolic events. Hyperviscosity can be managed in ***symptomatic*** patients by performing phlebotomy with isovolumic replenishment, but **routine phlebotomy is contraindicated** due to its effect on iron stores, oxygen-carrying capacity, and increased risk of stroke. Monitoring of iron levels and iron replacement, therefore, is paramount. The management of right-sided heart failure is problematic and the use of digoxin in these patients is controversial. Diuretics should be used cautiously because aggressive diuresis predisposes to hyperviscosity and decreases preload. Endocarditis prophylaxis is warranted.
   b. Over the last few years, there has been a paradigm shift regarding the treatment of pulmonary hypertension in Eisenmenger syndrome. While traditional therapy focused on preventive and palliative measures, there is accruing evidence to suggest that the **disease is in fact modifiable and that selective pulmonary vasodilators are not only safe but likely beneficial** in this population. These agents include endothelin antagonists, prostacyclin analogs, and phosphodiesterase-5 inhibitors. The only randomized, placebo-controlled trial performed to date in Eisenmenger patients, BREATHE-5, showed reduction in pulmonary vascular resistance and improvement in exercise capacity (with no detriment to oxygen saturation) using bosentan (an endothelin antagonist). In general, intravenous treatments are avoided in this population due to the risk of paradoxical embolism and increased infectious risk with indwelling lines.
2. **Surgical management.** Selected patients may be candidates for combined heart–lung transplantation or lung transplantation with concomitant repair of the intracardiac defect, if feasible. Timing of these interventions may be difficult because of the relatively long-term survival of these patients after the onset of the disease process and the recent availability of selective pulmonary vasoactive therapy.

F. Eisenmenger syndrome in special situations

1. **Travel** to areas of high altitude should be avoided because it may result in acute right heart failure. Air travel, however, is not contraindicated, as cabin pressures during commercial flights are generally well-tolerated.
2. **Pregnancy** in these patients is high risk to the fetus and the mother (> 50% maternal mortality) and is generally contraindicated. Given the high risk of maternal and fetal mortality, contraceptive methods (preferably without the use of estrogen) are critical. Elective termination should be discussed with pregnant Eisenmenger patients.
3. **Noncardiac surgery** is also associated with high risk and should be performed under the supervision of anesthesiologists familiar with Eisenmenger syndrome.

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