Review Article

Medical Progress

Congenital Heart Disease in Adults

Second of Two Parts

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CYANOTIC CONDITIONS

Patients with cyanotic congenital heart disease have arterial oxygen desaturation resulting from the shunting of systemic venous blood to the arterial circulation. The magnitude of shunting determines the severity of desaturation. Most children with cyanotic heart disease do not survive to adulthood without surgical intervention. In adults, the most common causes of cyanotic congenital heart disease are tetralogy of Fallot[61] and Eisenmenger's syndrome.

Tetralogy of Fallot

Tetralogy of Fallot, the most common cyanotic congenital heart defect after infancy, is characterized by a large ventricular septal defect, an aorta that overrides the left and right ventricles, obstruction of the right ventricular outflow tract (obstruction may be subvalvular, valvular, supravalvular, or in the pulmonary arterial branches), and right ventricular hypertrophy (Fig. 5). Several abnormalities may occur in association with tetralogy of Fallot, including right aortic arch in 25 percent of patients,[62,63] atrial septal defect in 10 percent (so-called pentalogy of Fallot),[62] and coronary arterial anomalies in 10 percent.[64]

Most patients with tetralogy of Fallot have substantial right-to-left shunting and therefore have cyanosis. Because of the large ventricular septal defect, the right and left ventricular pressures are equal. Right-to-left shunting of venous blood occurs because of increased resistance to flow in the right ventricular outflow tract, the severity of which determines the magnitude of shunting. Since the resistance to flow across the right ventricular outflow tract is relatively fixed, changes in systemic vascular resistance affect the magnitude of right-to-left shunting. A decrease in systemic vascular resistance increases right-to-left shunting, whereas an increase in systemic resistance decreases right-to-left shunting.

Most patients with tetralogy of Fallot have cyanosis from birth or beginning in the first year of life. In childhood, such patients may have sudden hypoxic "spells," characterized by tachypnea and hyperpnea, followed by worsening cyanosis and, in some cases, loss of consciousness, seizures, cerebrovascular accidents, and even death.[65] Such spells do not occur in adolescents or adults. Adults with tetralogy of Fallot have dyspnea and limited tolerance of exercise. They may have complications of chronic cyanosis, including erythrocytosis, hyperviscosity, abnormalities of hemostasis, cerebral abscesses or stroke, and endocarditis.[66,67] Without surgical intervention, most patients die in childhood: the rate of survival is 66 percent at 1 year of age, 40 percent at 3 years, 11 percent at 20 years, 6 percent at 30 years, and 3 percent at 40 years.[68]

Patients with tetralogy of Fallot have cyanosis and digital clubbing, the severity of which is determined by the degree of obstruction of the right ventricular outflow tract. The peripheral pulses are normal. A right ventricular lift or tap is palpable. In some patients, a systolic thrill (caused by turbulent flow across the right ventricular outflow tract) is palpable. The first heart sound is normal, but the second heart sound is single, since its pulmonary component is inaudible. An aortic ejection click (due to a dilated, overriding aorta) may be heard. A systolic ejection murmur, audible along the left sternal border, is caused by the obstruction of right ventricular outflow. The intensity and duration of the murmur are inversely related to the severity of the obstruction of right ventricular outflow; a soft, short murmur suggests that severe obstruction is present.

The electrocardiogram shows right-axis deviation and right ventricular hypertrophy. On radiography, the size of the heart is normal or small, and lung markings are diminished. The heart is classically "boot-shaped," with an upturned right ventricular apex and a concave main pulmonary arterial segment. A right-sided aortic arch may be present. Arterial oxygen desaturation is evident, as is compensatory erythrocytosis, the magnitude of which is proportional to the severity of the desaturation.

Echocardiography can be used to establish the diagnosis,[69] as well as to assess the presence of associated abnormalities, the level and severity of the ob-

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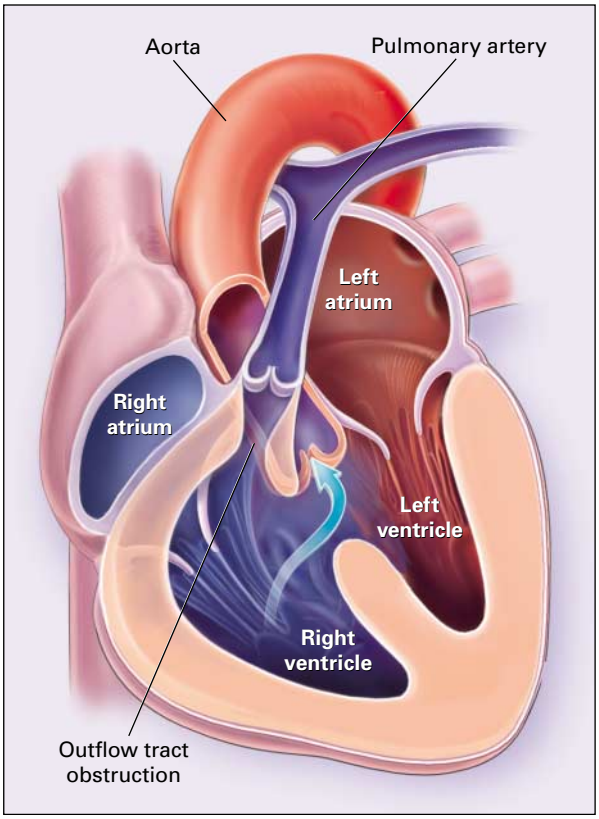


Figure 5. Tetralogy of Fallot.

Tetralogy of Fallot is characterized by a large ventricular septal defect, an aorta that overrides the left and right ventricles, obstruction of the right ventricular outflow tract, and right ventricular hypertrophy. With substantial obstruction of the right ventricular outflow tract, blood is shunted through the ventricular septal defect from right to left (arrow).

struction of the right ventricular outflow tract, the size of the main pulmonary artery and its branches, and the number and location of ventricular septal defects.[70] Right-to-left shunting through the ventricular septal defect can be visualized by color Doppler imaging, and the severity of right ventricular outflow tract obstruction can be determined by spectral Doppler measurement. With catheterization, it is possible to confirm the diagnosis and obtain additional anatomical and hemodynamic data, including the location and magnitude of right-to-left shunting, the level and severity of right ventricular outflow obstruction, the anatomical features of the right ventricular outflow tract and the main pulmonary artery and its branches, and the origin and course of the coronary arteries.[71] Magnetic resonance imaging can also provide much of this information.[72-74]

Surgical repair is recommended to relieve symptoms and to improve survival. Previously, infants underwent one of three palliative procedures to increase pulmonary blood flow (all three involve anastomosis of a systemic artery to a pulmonary artery), thereby reducing the severity of cyanosis and improving exercise tolerance. These procedures are the Waterston operation (a side-to-side anastomosis of the ascending aorta and the right pulmonary artery), the Potts operation (a side-to-side anastomosis of the descending aorta to the left pulmonary artery), and the Blalock–Taussig operation (end-to-side anastomosis of the subclavian artery to the pulmonary artery). Often, however, these procedures were associated with long-term complications, such as pulmonary hypertension, left ventricular volume overload, and distortion of the pulmonary arterial branches.[75]

Currently, complete surgical correction (closure of the ventricular septal defect and relief of right ventricular outflow obstruction) is performed when patients are very young.[76,77] The mortality associated with surgery is less than 3.0 percent in children[76,78] and 2.5 to 8.5 percent in adults.[79,80] At present, palliative shunting or balloon pulmonary valvuloplasty is performed only in severely ill infants for whom complete repair is unsuitable (e.g., those with underdeveloped pulmonary arteries).[81] These procedures increase pulmonary blood flow and allow the pulmonary arteries to enlarge so that corrective surgery may be undertaken at a later time. Patients with tetralogy of Fallot (either repaired or unrepaired) are at risk for endocarditis and should therefore receive prophylaxis with antibiotics before dental or elective surgical procedures.

Although patients with repaired tetralogy of Fallot are usually asymptomatic, their survival is somewhat poorer than that of an age-matched control population, because of an increased risk of sudden death (presumably from cardiac causes).[82,83] In one series,[82] the rate of survival 32 years after surgery was 86 percent among patients with repaired tetralogy and 96 percent in an age-matched control population. Ventricular arrhythmias can be detected with Holter monitoring in 40 to 50 percent of patients with repaired tetralogy of Fallot[84] and are most likely to occur in patients who are older at the time of surgical repair[85] and those with moderate or severe pulmonary regurgitation,[86] systolic and diastolic ventricular dysfunction,[87] prolonged cardiopulmonary bypass,[84] or prolongation of the QRS interval (to >180 msec).[88] Patients with repaired tetralogy of Fallot often have atrial fibrillation or flutter, which may cause considerable morbidity.[89]

Patients with repaired tetralogy of Fallot are at risk for other chronic complications. Pulmonary regurgitation may develop as a consequence of surgical repair of the right ventricular outflow tract.[86,90] Although even substantial regurgitation can be tolerated for long periods, enlargement of the right ventricle eventually occurs, with resultant right ventricular dysfunction, and repair or replacement of the pulmo-

nary valve may be required.[91] An aneurysm may form at the site where the right ventricular outflow tract was repaired. Although such aneurysms are usually identified incidentally, rupture has been reported in rare cases.[92]

Alternatively, patients may have residual or recurrent obstruction of the right ventricular outflow tract, requiring repeated surgery. Approximately 10 to 20 percent of patients with repaired tetralogy of Fallot have residual ventricular septal defects, and such patients may require repeated surgery if the defects are of sufficient size. Right bundle-branch block is common after repair of tetralogy of Fallot, but complete heart block is rare. Finally, aortic regurgitation may occur but is usually mild.

Ebstein's Anomaly

Ebstein's anomaly is an abnormality of the tricuspid valve in which the septal leaflets and often the posterior leaflets are displaced into the right ventricle and the anterior leaflet is usually malformed, excessively large, and abnormally attached or adherent to the right ventricular free wall.[93] Thus, a portion of the right ventricle is "atrialized" in that it is located on the atrial side of the tricuspid valve, and the remaining functional right ventricle is small (Fig. 6). The tricuspid valve is usually regurgitant but may be stenotic. Eighty percent of patients with Ebstein's anomaly have an interatrial communication (atrial septal defect or patent foramen ovale) through which right-to-left shunting of blood may occur.

The severity of the hemodynamic derangements in patients with Ebstein's anomaly depends on the degree of displacement and the functional status of the tricuspid-valve leaflets. Patients with mild apical displacement of the tricuspid leaflets have normal valvular function, whereas those with severe tricuspid-leaflet displacement or abnormal anterior leaflet attachment, with valvular dysfunction, have elevated right atrial pressure and right-to-left interatrial shunting. Similarly, the clinical presentation of Ebstein's anomaly varies from severe heart failure in a fetus or neonate to the absence of symptoms in an adult in whom it is discovered incidentally.[94]

When Ebstein's anomaly is discovered during fetal life, the rate of intrauterine mortality is high.[95] Neonates with severe disease have cyanosis, with heart failure and a murmur noted in the first days of life. Transient improvement may occur as pulmonary vascular resistance falls, but the condition worsens after the ductus arteriosus closes, thereby decreasing pulmonary blood flow. Older children with Ebstein's anomaly often come to medical attention because of an incidental murmur, whereas adolescents and adults present with a supraventricular arrhythmia.[94] In adults with Ebstein's anomaly, the most important predictors of outcome are the New York Heart Association (NYHA) functional class, the heart size, the presence or absence of cyanosis, and the presence or absence of paroxysmal atrial tachycardias. Such tachycardias may lead to cardiac failure, worsening cyanosis, and even syncope. Patients with Ebstein's anomaly and an interatrial communication are at risk for paradoxical embolization, brain abscess, and sudden death.[94]

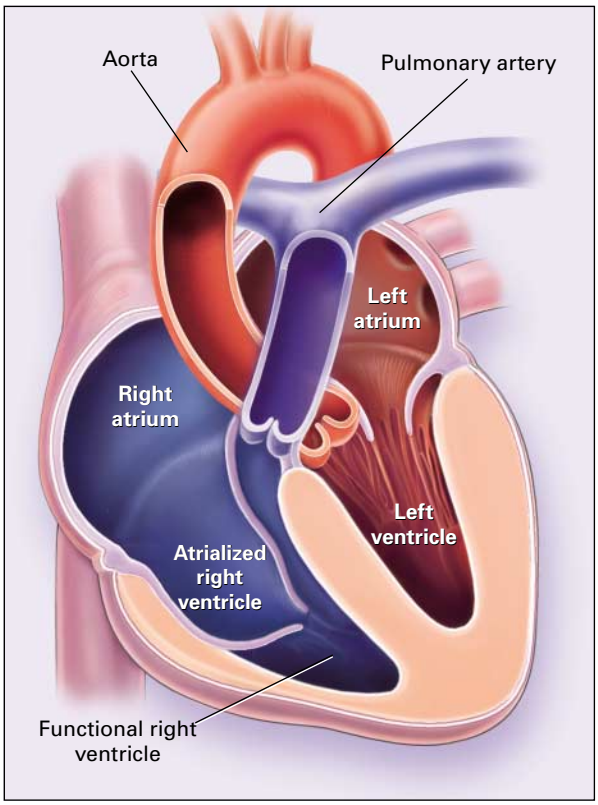


Figure 6. Ebstein's Anomaly.
In patients with Ebstein's anomaly, a portion of the right ventricle is atrialized (i.e., located on the atrial side of the tricuspid valve), and as a result, the functional right ventricle is small. In addition, most patients have an interatrial communication (atrial septal defect or patent foramen ovale), through which right-to-left shunting may occur.

On physical examination, the severity of cyanosis depends on the magnitude of right-to-left shunting.[96] The first and second heart sounds are widely split, and a third or fourth heart sound is often present, resulting in a "triple" or "quadruple" rhythm. A systolic murmur caused by tricuspid regurgitation is usually present at the left lower sternal border. Hepatomegaly (resulting from passive hepatic congestion due to elevated right atrial pressure) may be present.

Tall and broad P waves are common on the electrocardiogram, as is right bundle-branch block. First-degree atrioventricular block occurs frequently. Since about 20 percent of patients with Ebstein's anomaly have ventricular preexcitation by way of an accessory electrical pathway between the atrium and ventricle

(Wolff–Parkinson–White syndrome), a delta wave may be present.[97] The radiographic findings depend on the severity of the anatomical abnormality.[97] In mild cases, the heart size and pulmonary vasculature are normal. In more severe cases, marked cardiomegaly, which is largely due to right atrial enlargement, is present. In severe cases (with little functional right ventricle and marked right-to-left shunting), pulmonary vascular markings are decreased. Echocardiography is used to assess right atrial dilatation, anatomical displacement and distortion of the tricuspid-valve leaflets, and the severity of tricuspid regurgitation or stenosis; in addition, the presence and magnitude of interatrial shunting can be determined (by color Doppler imaging or bubble study), as can the presence of associated cardiac abnormalities.[98,99] Electrophysiologic evaluation is warranted in patients with atrial tachyarrhythmias.

The management of Ebstein's anomaly centers on the prevention and treatment of complications. Prophylaxis against infective endocarditis is recommended. Patients with symptomatic heart failure are given diuretic agents and digoxin. Those with atrial arrhythmias may be treated pharmacologically or with catheter ablation (if an accessory pathway is present). Ablation of accessory pathways has a lower rate of success in patients with Ebstein's anomaly than in those with structurally normal hearts, and the risk of recurrence of arrhythmia is higher.[100,101] In severely ill infants with Ebstein's anomaly, an arterial shunt from the systemic circulation to the pulmonary circulation is created to increase pulmonary blood flow, thereby decreasing cyanosis. Further surgery to create a univentricular heart (i.e., by the Fontan procedure) may also be considered in neonates.[102]

Repair or replacement of the tricuspid valve in conjunction with closure of the interatrial communication is recommended for older patients who have severe symptoms despite medical therapy. In addition, repair or replacement should be considered for patients with less severe symptoms who have cardiac enlargement, since this condition has a poor prognosis.[103] When possible, valve repair is preferable to valve replacement, because it is associated with lower mortality and has fewer long-term complications.[104,105] However, when valve replacement is required, a bioprosthesis is preferable to a mechanical prosthesis.[106] The complications of surgery to correct Ebstein's anomaly include complete heart block, persistence of supraventricular arrhythmias, residual tricuspid regurgitation after valve repair, and prosthetic-valve dysfunction.

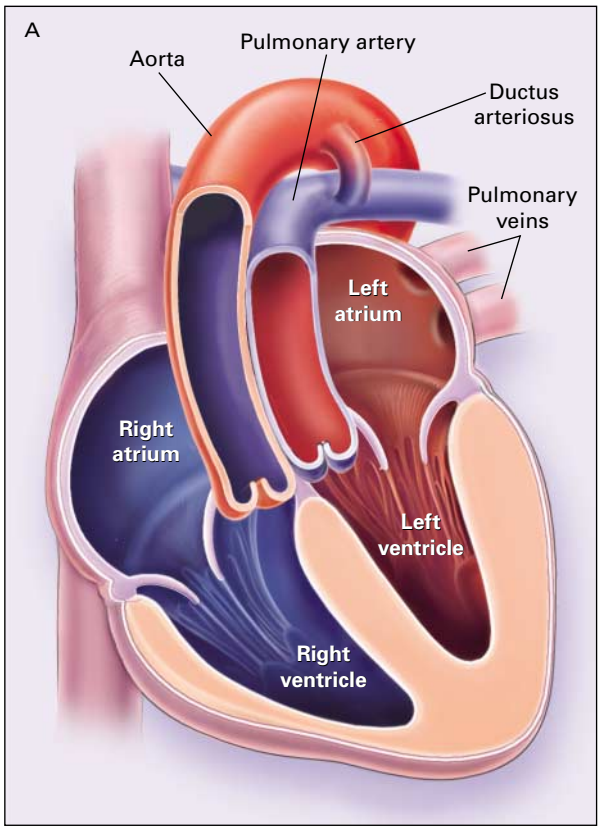
Transposition of the Great Arteries

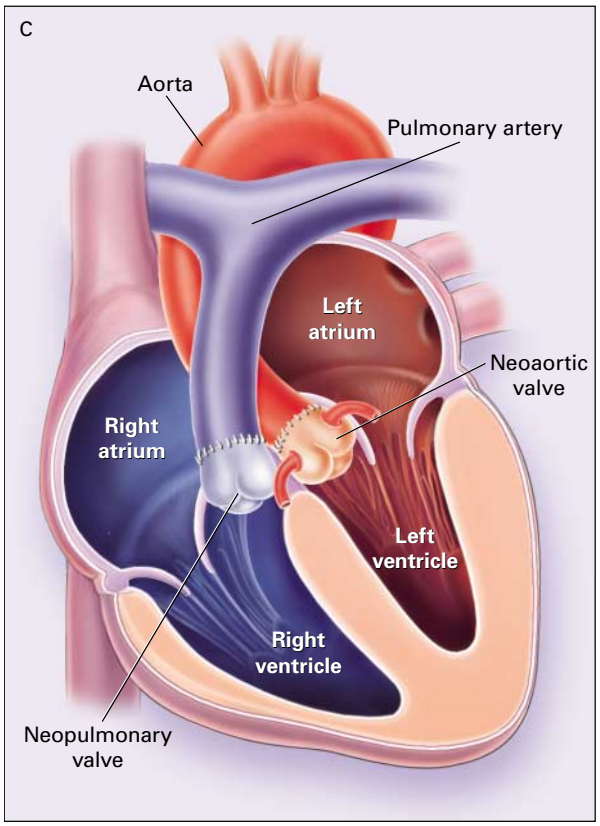
With D-transposition of the great arteries (also known as complete transposition), the aorta arises in an anterior position from the right ventricle and the pulmonary artery arises from the left ventricle (Fig. 7A). Therefore, there is complete separation of the pulmonary and systemic circulations: systemic venous blood traverses the right atrium, right ventricle, aorta, and systemic circulation, whereas pulmonary venous blood traverses the left atrium, left ventricle, pulmonary artery, and pulmonary circulation. In order for an infant with this condition to survive, there must be a communication between the two circuits. In about two thirds of patients, no other associated cardiac defect is present, so that the ductus arteriosus and foramen ovale allow communication between the two circuits.[107,108] Infants with this condition have severe cyanosis. The one third of patients with other associated defects that permit intracardiac mixing (e.g., atrial septal defect, ventricular septal defect, or patent ductus arteriosus) are less critically ill, since they have less severe cyanosis. However, they are at risk for left ventricular failure due to volume overload caused by left-to-right shunting.

Patients with complete transposition have cyanosis from birth and often have heart failure in the newborn period. The findings on physical examination are nonspecific. Infants have cyanosis and tachypnea. The second heart sound is single and loud (due to the anterior position of the aorta). In patients with mild cyanosis, a holosystolic murmur caused by a ventricular septal defect may be heard. Likewise, a soft systolic ejection murmur (due to pulmonary stenosis, ejection into the anteriorly located aorta, or both) may be audible. The electrocardiogram shows right-axis deviation and right ventricular hypertrophy (since the right ventricle is the systemic ventricle). Patients with a large ventricular septal defect or patent ductus arteriosus, as well as those with pulmonary stenosis, have left ventricular hypertrophy. The chest radiograph shows cardiomegaly with increased pulmonary vascularity. Classically, the cardiac silhouette is described as being egg-shaped, with a narrow "stalk."

Without intervention, patients with complete transposition have a poor prognosis. Unless intracardiac mixing is improved, progressive hypoxemia and acidosis develop; the mortality rate is 90 percent by six months of age.[109] Infants who have less severe cyanosis (because of a sizable ventricular septal defect or patent ductus arteriosus) fare better in the neonatal period, but pulmonary vascular obstructive disease (due to increased pulmonary blood flow) is more likely to develop than in infants with more severe cyanosis; infants with less severe cyanosis are also more likely to have higher operative mortality and are less likely to have complete repair of their defect.

The immediate management of complete transposition involves creating intracardiac mixing or increasing its extent. This can be accomplished with an infusion of prostaglandin E (to maintain or restore patency of the ductus arteriosus),[110] the creation of an atrial septal defect by means of balloon atrial septostomy (the Rashkind procedure), or both.[111] In addi-





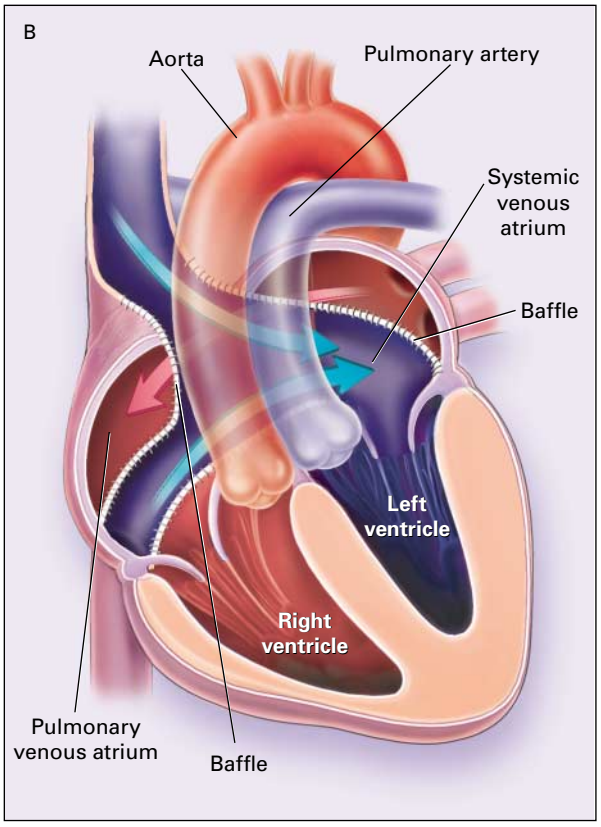


Figure 7. Transposition and Switching of the Great Arteries.

In D-transposition of the great arteries (complete transposition) (Panel A), systemic venous blood returns to the right atrium, from which it goes to the right ventricle and then to the aorta. Pulmonary venous blood returns to the left atrium, from which it goes to the left ventricle and then to the pulmonary artery. Survival is possible only if there is a communication between the two circuits, such as a patent ductus arteriosus. With the "atrial switch" operation (Panel B), a pericardial baffle is created in the atria, so that blood returning from the systemic venous circulation is directed into the left ventricle and then the pulmonary artery (blue arrows), whereas blood returning from the pulmonary venous circulation is directed into the right ventricle and then the aorta (red arrow). With the "arterial switch" operation (Panel C), the pulmonary artery and ascending aorta are transected above the semilunar valves and coronary arteries, then switched (neoaortic and neopulmonary valves).

tion, oxygen is given to most patients (to decrease pulmonary vascular resistance and to increase pulmonary blood flow), as are digoxin and diuretic drugs (to treat heart failure).

Two surgical procedures have been used in patients with complete transposition of the great arteries. With the initial approach, known as the "atrial switch" operation (the Mustard or Senning operation),[112] the atrial septum was excised, then a "baffle" within the atria was constructed to direct systemic venous blood across the mitral valve into the left ventricle and pulmonary venous blood across the tricuspid valve into the right ventricle (Fig. 7B). Thus, physiologic circulation was restored; however, after this procedure was performed, the right ventricle continued to function as the "systemic ventricle." This operation corrected cyanosis and improved survival. The complications associated with it were leakage of the atrial baffle (often clinically inconsequential)[113,114]; obstruction of the baffle (often insidious and frequently asymptomatic)[115-117]; sinus-node dysfunction and atrial arrhythmias, particularly atrial flutter[118-120]; right (systemic) ventricular dysfunction[121]; and an increased risk of sudden death.[120,121]

The atrial-switch operation has been replaced by the arterial-switch operation, in which the pulmonary artery and ascending aorta are transected above the semilunar valves and coronary arteries and then switched, so that the aorta is connected to the neoaortic valve (formerly the pulmonary valve) arising from the left ventricle, and the pulmonary artery is connected to the neopulmonary valve (formerly the aortic valve) arising from the right ventricle (Fig. 7C). The coronary arteries are relocated to the neoaorta to restore normal coronary circulation. This operation can be performed in neonates and is associated with a low operative mortality[122,123] and an excellent long-term outcome.[124]

Eisenmenger's Syndrome

A patient with Eisenmenger's syndrome has a large left-to-right shunt that causes severe pulmonary vascular disease and pulmonary hypertension, with resultant reversal of the direction of shunting (Fig. 8). With substantial left-to-right shunting, the exposure of the pulmonary vasculature to increased blood flow as well as increased pressure often results in pulmonary vascular obstructive disease. The initial morphologic alterations (medial hypertrophy of the pulmonary arterioles, intimal proliferation and fibrosis, and occlusion of capillaries and small arterioles) are potentially reversible. However, as the disease progresses, the more advanced morphologic changes (plexiform lesions and necrotizing arteritis) are irreversible. The result is obliteration of much of the pulmonary vascular bed, leading to increased pulmonary vascular resistance.[125] As the pulmonary vascular resistance approaches or exceeds systemic resistance, the shunt is reversed.

The morphologic changes in the pulmonary vasculature that occur with Eisenmenger's syndrome usually begin in childhood, but symptoms may not appear until late childhood or early adulthood. In many patients, pulmonary congestion in early infancy (a result of the large left-to-right shunt) resolves in later infancy or early childhood as pulmonary vascular resistance increases and the magnitude of shunting decreases. Likewise, the patient may have a murmur in early childhood that disappears (as the pulmonary disease progresses and the magnitude of shunting decreases), leading to the mistaken assumption that the intracardiac communication has closed. Occasionally, patients have no history of pulmonary congestion or a murmur in childhood.

As right-to-left shunting develops, cyanosis appears. Most patients will have impaired exercise tolerance and exertional dyspnea, but these symptoms may be well compensated for years.[126] Palpitations are common and are most often due to atrial fibrillation or flutter. As erythrocytosis due to arterial desaturation develops in patients with Eisenmenger's syndrome, symptoms of hyperviscosity (visual disturbances, fatigue, headache, dizziness, and paresthesias) may appear. Hemoptysis may occur, as a result of pulmonary infarction or rupture of dilated pulmonary arteries, arterioles, or aorticopulmonary collateral vessels. Since patients with arterial desaturation have abnormal hemostasis, they are at risk for both bleeding and thrombosis.[66,127-129] Cerebrovascular accidents may occur as a result of paradoxical embolization, venous thrombosis of cerebral vessels, or intracranial hemorrhage. In addition, patients with this condition are at risk for brain abscess. Patients with Eisenmenger's syndrome may have syncope owing to inadequate cardiac output or, less commonly, an arrhythmia. Symptoms of heart failure, which are uncommon until the disease is far advanced, portend a poor prognosis. Finally, these patients are at risk for sudden death.[130]

On physical examination, patients have digital clubbing and cyanosis, the severity of which depends on the magnitude of right-to-left shunting. The jugular venous pressure may be normal or elevated, and prominent V waves are seen if tricuspid regurgitation is present. Arterial pulses are small in volume. A right parasternal heave (due to right ventricular hypertrophy) is present, and the pulmonary component of the second heart sound is loud (and often palpable). The murmur caused by a ventricular septal defect, patent ductus arteriosus, or atrial septal defect disappears when Eisenmenger's syndrome develops. Many patients have a decrescendo diastolic murmur caused by pulmonary regurgitation or a holosystolic murmur caused by tricuspid regurgitation. A right-sided fourth heart sound is usually present. The lungs are clear. Peripheral edema and hepatic congestion are absent unless there is substantial right ventricular dysfunction.

The electrocardiogram shows right ventricular hy-

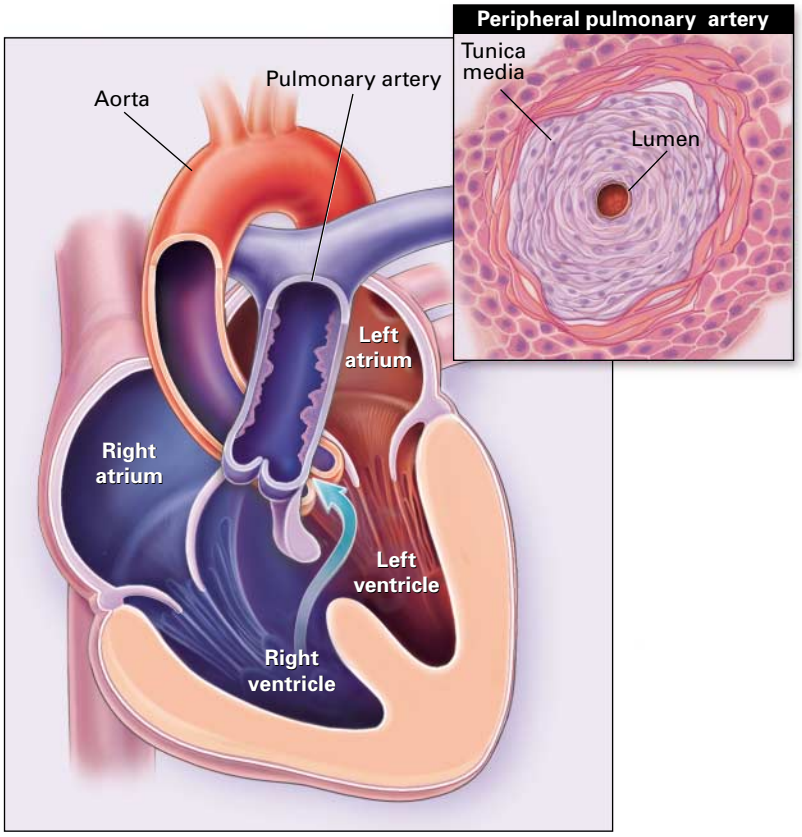


Figure 8. Eisenmenger's Syndrome.

In patients with Eisenmenger's syndrome, in response to substantial left-to-right shunting, morphologic alterations occur in the small pulmonary arteries and arterioles (inset), leading to pulmonary hypertension and the resultant reversal of the intracardiac shunt (arrow). In the small pulmonary arteries and arterioles, medial hypertrophy, intimal cellular proliferation, and fibrosis lead to narrowing or closure of the vessel lumen. With sustained pulmonary hypertension, extensive atherosclerosis and calcification often develop in the large pulmonary arteries. Eisenmenger's syndrome may occur in association with a ventricular septal defect (as shown), but it also may occur in association with an atrial septal defect or patent ductus arteriosus.

pertrophy. Atrial arrhythmias may be present, particularly in patients with atrial septal defect. The chest film reveals prominent central pulmonary arteries and decreased vascular markings ("pruning") of the peripheral vessels. The size of the heart is normal in patients with a ventricular septal defect or patent ductus arteriosus, but cardiomegaly (due to right ventricular enlargement) is usually seen in those with atrial septal defect. On transthoracic echocardiography, there is evidence of right ventricular pressure overload and pulmonary hypertension.[70] The underlying cardiac defect can usually be visualized, although shunting across the defect may be difficult to demonstrate by color Doppler imaging because of the low velocity of the jet. Contrast echocardiography permits the location of the shunt to be determined. Catheterization should be performed in any patient with suspected Eisenmenger's syndrome in order to assess the severity of pulmonary vascular disease and to quantify the magnitude of intracardiac shunting. Pulmonary vasodilators — such as oxygen, inhaled nitrous oxide, or intravenous adenosine or epoprostenol — should be administered to permit assessment of the reversibility of pulmonary hypertension.

The rate of survival among patients with Eisenmenger's syndrome is 80 percent 10 years after diagnosis, 77 percent at 15 years, and 42 percent at 25 years.[30,126] Death is usually sudden, presumably caused by arrhythmias, but some patients die of heart failure, hemoptysis, brain abscess, or stroke.[130,131] A history of syncope, clinically evident right ventricular systolic dysfunction, low cardiac output, and severe hypoxemia portend a poor outcome.

Patients with Eisenmenger's syndrome should avoid intravascular volume depletion, heavy exertion, high altitude, and the use of vasodilators. Because of high

maternal and fetal morbidity and mortality, pregnancy should be avoided.[130,132] Although no therapy has been proved to reduce pulmonary vascular resistance, intravenous epoprostenol may be beneficial.[132,133] Phlebotomy with isovolumic replacement should be performed in patients with moderate or severe symptoms of hyperviscosity; it should not be performed in asymptomatic or mildly symptomatic patients (regardless of the hematocrit).[127] Repeated phlebotomy may result in iron deficiency, which may worsen symptoms of hyperviscosity, since iron-deficient erythrocytes are less deformable than iron-replete erythrocytes.[67,134]

Patients with Eisenmenger's syndrome who are undergoing noncardiac surgery require meticulous management of anesthesia, with attention to the maintenance of systemic vascular resistance, the minimization of blood loss and intravascular volume depletion, and the prevention of iatrogenic paradoxical embolization.[135,136] In preparation for noncardiac surgery, prophylactic phlebotomy (usually of 1 to 2 units of blood, with isovolumic replacement) is recommended for patients with a hematocrit above 65 percent in order to reduce the likelihood of perioperative hemorrhagic and thrombotic complications. In general, anticoagulants and antiplatelet agents should be avoided, since they exacerbate the hemorrhagic diathesis.

Lung transplantation with repair of the cardiac defect or combined heart–lung transplantation is an option for patients with Eisenmenger's syndrome who have markers of a poor prognosis (syncope, refractory right-sided heart failure, a high NYHA functional class, or severe hypoxemia).[126,137] Because of the somewhat limited success of transplantation[137] and the reasonably good survival among patients treated medically, careful selection of patients for transplantation is imperative.

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