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# Congenital Heart Disease in the Newborn Period

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## INTRODUCTION

Children with congenital heart disease (CHD) have structural defects of the heart and/or great vessels that are present before birth. Defects range from relatively simple lesions, which neither induce symptoms nor need therapy, to complex life-threatening lesions, which require surgery in the neonatal period.

CHD is the most common birth defect. Recent prevalence estimates for CHD range from 6 to 10 per 1000 live births. Approximately 40,000 infants are born with a congenital heart defect each year in the United States.

One of every four infants with CHD has *critical CHD* (i.e., a defect that requires either a surgical or a transcatheter procedure within the first year of life for survival). Ductal-dependent heart defects, which require the ductus arteriosus to remain patent after birth to ensure survival, are examples of critical lesions.

## FETAL CIRCULATION

Before birth, the fetus is dependent on the utero-placental unit for survival. The relatively oxygen-rich blood from the placenta enters the inferior vena cava via the umbilical vein and ductus venosus. Preferential streaming of blood occurs in the right atrium between the blood returning via the superior vena cava (relatively oxygen poor) and that returning from the inferior vena cava (Rudolph, 2009). The more highly saturated blood from the inferior vena cava crosses the foramen ovale to the left side of the heart, facilitating delivery of blood with relatively high oxygen content to the fetal myocardium and brain (Edelstone and Rudolph, 1979). Deoxygenated fetal blood returning from the superior vena cava travels through the right ventricle, across the ductus arteriosus, and down the descending aorta to the placenta, where oxygen and carbon dioxide transfer occurs via simple diffusion. Both the fetal right and left ventricles are responsible for blood flow to the systemic circuit and placenta. Because the resistance in the fetal pulmonary vasculature is high, less than 15% of right ventricular output is delivered to the lungs (Rudolph, 2009). Thus the parallel fetal circulatory system promotes efficient oxygen delivery in a relatively hypoxic environment (Fig. 16.1A).

The fetal circulation is forgiving to neonates with even the most severe forms of CHD. Intra- and extracardiac shunts allow fetal circulatory adaptations to abnormal heart anatomy. For example, in neonates with severe obstruction to either ventricular outflow tract, diversion of flow into the other ventricle and great vessel occurs across the foramen ovale and the ductus arteriosus.

## CASE STUDY 1

A 3.2 kg infant is born via cesarean section (due to nonprogression of labor) at 39 weeks' gestation to a primigravida woman with an unremarkable medical and obstetric history. The infant is breathing comfortably and appears pink. There are no risk factors for infection. At 5 minutes of life, the preductal saturation value in room air is 90% and the postductal value is 82%.

### Exercise 1

#### Question

What is the best course of action for this infant?

A. Continued observation
B. Consultation with pediatric cardiology
C. Stat echocardiogram
D. Four extremity blood pressures
E. Arterial blood gas determination from the left radial artery.

#### Answer

A

### Transitional Circulation

Most of the circulatory changes that happen in the transition from intra- to extrauterine life occur in the first few moments after birth, with additional circulatory adjustments occurring over a period of several weeks. The primary events that trigger the alteration in blood flow patterns are removal of the low resistance placental circuit and the establishment of alveolar ventilation (Rudolph, 2009). With establishment of alveolar gas volume, there is a substantial decline in pulmonary vascular resistance and a several-fold increase in pulmonary blood flow. A rise in left atrial pressure results from an increase in pulmonary venous return and allows closure of the foramen

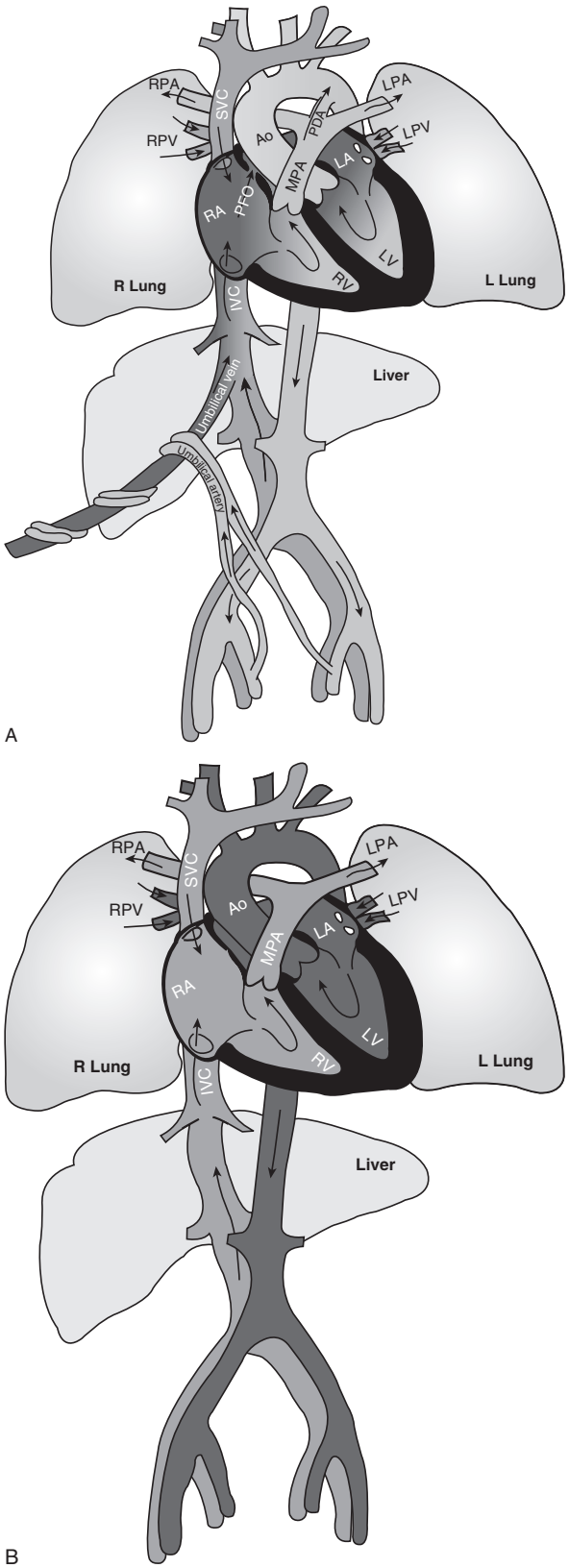


**Fig. 16.1** (A) Fetal circulation. (B) Adult circulation. Arrows depict direction of blood flow. *Ao,* Aorta; *IVC,* inferior vena cava; *LA,* left atrium; *L Lung,* left lung; *LPA,* left pulmonary artery; *LPV,* left pulmonary veins; *LV,* left ventricle; *MPA,* main pulmonary artery; *PDA,* patent ductus arteriosus; *PFO,* patent foramen ovale; *RA,* right atrium; *R Lung,* right lung; *RPA,* right pulmonary artery; *RPV,* right pulmonary veins; *RV,* right ventricle; *SVC,* superior vena cava.

ovale, abolishing the atrial level shunt. The higher oxygen tension in the blood initiates postnatal closure of the ductus arteriosus, establishes complete separation of pulmonary and systemic blood flows, and leads to a circulation in series (Fig. 16.1B). In full-term infants, functional closure of the ductus arteriosus is initiated within the first hours and days following birth, and anatomic closure follows.

The switch from a parallel fetal circulation to a transitional circulation in series results in a slow rise in hemoglobin oxygen saturation in the first few minutes after birth. The median preductal oxygen saturation in healthy term newborn babies is around 90% at 5 minutes of life and increases to 98% by 15 minutes. Postductal oxygen saturation is significantly lower than the preductal oxygen saturation in the first 15 minutes of life, with oxygen saturation gradient narrowing over time. Babies born by cesarean section have lower pre- and postductal oxygen saturations in the first 15 minutes of life compared with those born vaginally. The neonate described in Case Study 1 is exhibiting a normal postnatal transition and therefore warrants only continued observation.

Postnatal closure of fetal shunts can be life threatening in babies with ductal-dependent CHD. Closure of the ductus arteriosus can lead to hypoxemia and cyanosis when there is severe anatomic obstruction to pulmonary blood flow and decreased perfusion to vital organs when there is severe anatomic obstruction to systemic blood flow. The ductus arteriosus with rare exceptions is patent at birth and hence these signs will rarely be noted in the delivery room during transition.

The transitional period can be life threatening in babies with d-transposition of the great arteries with an intact ventricular septum (d-TGA/IVS). Postnatal closure of the foramen ovale can cause severe hypoxemia in babies with this condition. In this lesion, the aorta arises from the right ventricle and the pulmonary artery arises from the left ventricle. After birth, the circulation remains in parallel and severe hypoxemia may result if the shunt at the atrial level is abolished. Only adequate mixing at the atrial level will permit a stable transition. Transition to extrauterine life may also be difficult in babies with hypoplastic left heart syndrome (HLHS) with mitral atresia and an intact or restrictive atrial septum. Because of restricted egress of pulmonary venous return, pulmonary edema quickly ensues, and hence these babies are severely hypoxemic from birth with signs of inadequate cardiac output. However, with the few exceptions described earlier, most babies with CHD should transition normally.

## SCREENING METHODS FOR CONGENITAL HEART DISEASE

Although antenatal diagnosis of CHD is increasing, a significant proportion of babies with CHD are not diagnosed before birth. Postnatal diagnosis of CHD in the delivery room or the newborn nursery is possible only if signs of CHD manifest during the hospital stay or if there is a universal screening protocol utilizing pulse oximetry. In a review of 20-year trends in the diagnosis of life-threatening cardiovascular malformations, 62% of babies with such

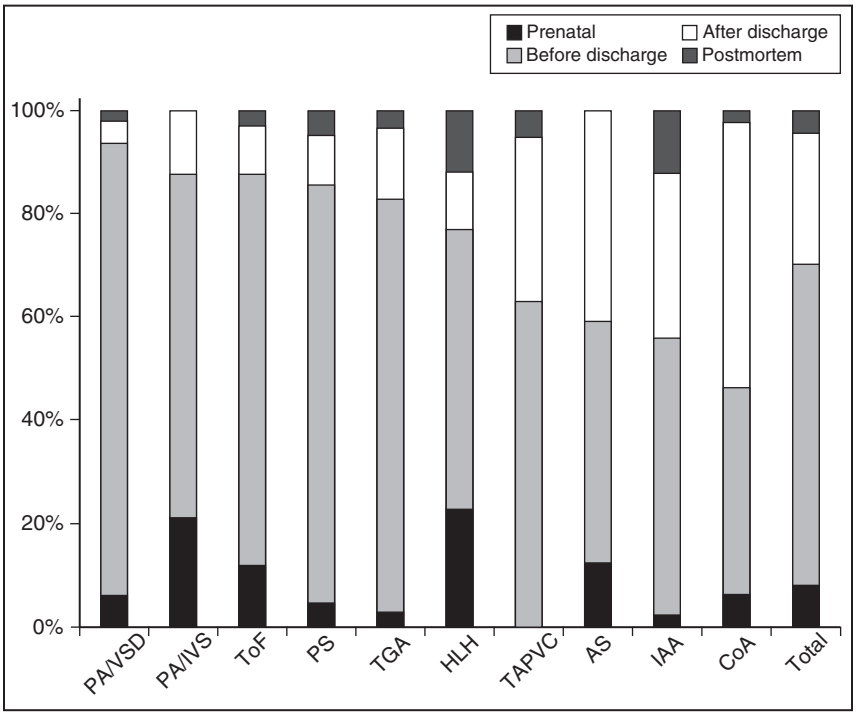


**Fig. 16.2** Congenital heart disease and timing of diagnosis. *AS,* Aortic stenosis; *CoA,* coarctation of the aorta; *HLH,* hypoplastic left heart syndrome; *IAA,* interrupted aortic arch; *PA/IVS,* pulmonary atresia, intact ventricular septum; *PA/VSD,* pulmonary atresia, ventricular septal defect; *PS,* pulmonary stenosis; *TAPVC,* totally anomalous pulmonary venous connection; *TGA,* transposition of the great arteries; *ToF,* tetralogy of Fallot. (Adapted from Wren C, et al: Twenty-year trends in diagnosis of life-threatening neonatal cardiovascular malformations, *Arch Dis Child Fetal Neonatal Ed* 93[1]:F33–F35, 2008, with permission from BMJ Publishing Group Ltd.)

lesions presented before discharge from the hospital, 25% of babies with critical CHD were diagnosed after discharge from the nursery, and 5% were diagnosed at autopsy (Fig. 16.2) (Wren et al, 2008). Babies with left sided obstructive lesions such as coarctation of the aorta were more likely to be diagnosed after discharge from the nursery (Fig. 16.2), whereas those who had cyanotic CHD were more likely to be identified while still in the nursery.

Critical CHD is difficult to uncover in asymptomatic newborn infants because several congenital heart defects do not produce visible central cyanosis despite severe hypoxemia. Screening by pulse oximetry provides an opportunity to detect clinically silent hypoxemia in critical CHD. In September 2011, the U.S. Department of Health and Human Services recommended that all newborns be screened for critical CHD before discharge from the newborn nursery using pulse oximetry. This recommendation has been endorsed by several national organizations, including the American Academy of Pediatrics. Pulse oximetry has now been included in the Recommended Uniform Screening Panel for newborns across several states. The proposed newborn screening strategy is described in Fig. 16.3.

Screening by pulse oximetry is highly specific for detection of critical CHD (99.9%) and has moderate sensitivity (70%). The false positive rate is very low (0.035%) when screening occurs after 24 hours of age (Mahle et al, 2009, 2012). It is important to note that although pulse oximetry is generally a reliable screening tool, it can miss lesions, particularly those that involve obstruction to systemic blood flow.

Neonates with critical CHD may escape detection at all three stages of screening (i.e., antenatal ultrasound, routine neonatal examination in the nursery, and pulse oximetry). A high index of suspicion, along with prompt and timely recognition of babies with critical CHD, improves prognosis.

## EVALUATION OF NEONATES FOR CHD

### History

Most babies with critical CHD follow an ordinary transition to extrauterine life, and perinatal history is often unremarkable. The *absence* of important clinical information that would foster the consideration of an alternative diagnosis is a notable feature of CHD. For example, babies with severely obstructed totally anomalous pulmonary venous connection commonly present with respiratory distress and cyanosis within the first 24 hours of life. However, respiratory distress is a common symptom in neonates and has several etiologies. Fortunately, in most of these other disorders, the etiology is apparent from the history. Respiratory distress caused by surfactant deficiency is seen in preterm or late-preterm infants and is rarely encountered in infants born at term. Respiratory distress caused by an invasive bacterial infection is likely if there is a maternal history of prolonged rupture of membranes, a history of chorioamnionitis or maternal vaginal

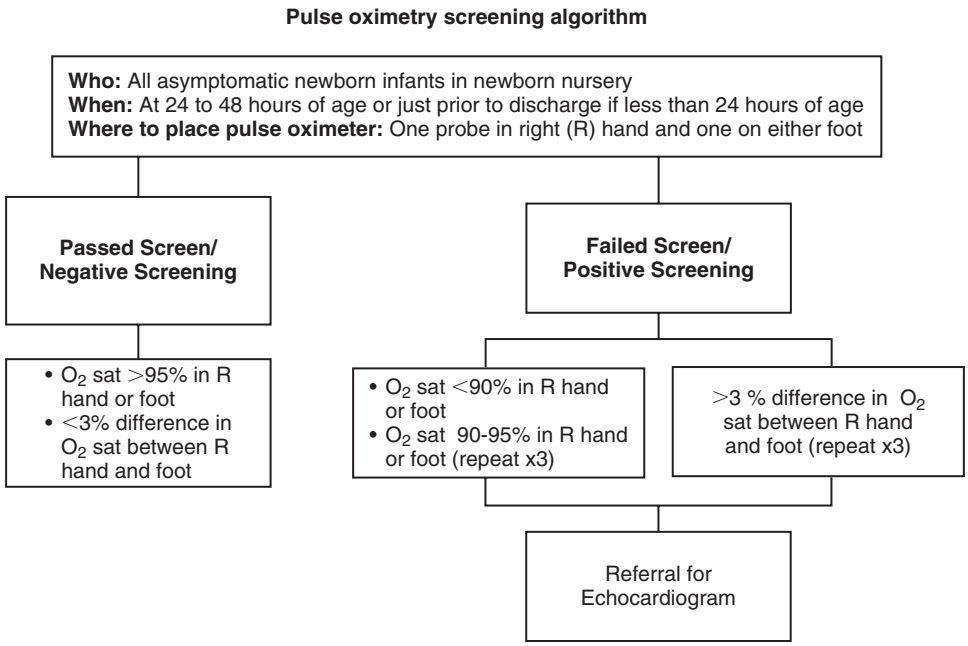


**Fig. 16.3** Algorithm for pulse oximetry screening for congenital heart disease.

carriage of group B *Streptococcus*. In the presence of such historical data, a diagnosis of the usual etiologies of respiratory distress (e.g., sepsis or surfactant deficiency) is easily made. It is the *absence* of such relevant historical information that makes a diagnosis of CHD more likely.

Babies with cyanotic CHD usually present with cyanosis or cyanotic "spells." Lesions that cause obstruction to pulmonary blood flow or poor mixing often present during the initial hospital stay in the nursery. In these patients, cyanosis may not be noticed at birth because the ductus arteriosus is still patent. Parents or medical caretakers may initially note transient cyanosis during crying or feeding. As the ductus arteriosus begins to close, cyanosis becomes more apparent and persistent. Most importantly, despite the cyanosis, a history of respiratory distress with dyspnea is usually not elicited.

Parents of babies with left sided obstructive lesions may report an increase in the rate of breathing, irritability, and progressive difficulty in feeding. These symptoms emerge as systemic blood flow becomes compromised with closure of the ductus arteriosus. Infants usually present after nursery discharge, typically within the first 2 weeks of life. As circulatory failure ensues, patients may present to the emergency room in extremis.

Babies with large left-to-right shunts manifest symptoms of heart failure (e.g., rapid respirations, diaphoresis, feeding difficulties). These symptoms are subtle at first, usually appear by 4 to 6 weeks of age, and worsen over time.

## PHYSICAL EXAMINATION

### General Physical Examination

**Anthropometric measurements:** Weight, height, and head circumference should be measured. A small head circumference is noted in some babies with CHD, such as hypoplastic left heart syndrome. In babies with congestive cardiac failure who are several weeks old, comparison of current weight to birth weight may uncover inadequate interim growth.

**Vital signs:** Tachycardia (normal heart rate 120–160 beats/minute) in babies with CHD may be reflective of depressed ventricular function. An increased respiratory rate (normal 40–60 breaths/minute) may be caused by pulmonary edema, excessive pulmonary blood flow, or metabolic acidosis. Blood pressure should be measured in all four extremities. Normally, the measured blood pressure in the lower extremities is a little higher than that measured in the upper extremities. A blood pressure gradient of greater than 10 to 20 mm Hg between the right arm and lower extremities may indicate juxta-ductal coarctation of the aorta or interruption of the aortic arch. Systemic hemoglobin oxygen saturation should be measured using pulse oximetry. Ideally, both preductal (right hand) and postductal (any foot) hemoglobin oxygen saturation values should be recorded simultaneously. Normally, both preductal and postductal saturations are above 95% with minimal difference in measurements. Low (<95%) preductal or postductal saturation may be suggestive of cyanotic CHD especially in the absence of respiratory symptoms.

**General examination:** CHD often has an underlying genetic etiology with recognizable patterns indicative of a chromosomal abnormality or syndrome. Underlying hypoxemia with central cyanosis is best recognized in the buccal mucosa, lips, and tongue. Cool extremities, feeble pulses, mottled skin, and prolonged capillary refill time indicate poor cardiac output and systemic perfusion. Peripheral pulses are globally diminished when ventricular function is depressed. Disparity in both pulses and blood pressure between the upper and lower extremities suggests juxtaductal coarctation of the aorta or interruption of the aortic arch distal to the origin of the left subclavian artery.

**Cardiovascular examination:** The site of precordial activity should be noted. Dextrocardia should be suspected if the precordial impulse or activity is noted over the right hemithorax rather than the left. Parasternal impulse rather than an apical impulse is normal in neonates and signifies right ventricular dominance. A prominent parasternal impulse is noted with right ventricular pressure overload (right ventricular outflow tract obstructive lesions, pulmonary hypertension, and d-TGA). A diminished parasternal impulse is noted in right ventricular inflow obstruction (e.g., tricuspid atresia or tricuspid stenosis with hypoplasia of the right ventricle). Left ventricular volume overload in infants with left-to-right shunts (large ventricular septal defect, large patent ductus arteriosus) causes a prominent and hyperdynamic apical impulse.

Abnormalities of the first heart sound are rarely appreciated in newborns. Split $S_1$ may be seen in infants with Ebstein's anomaly. Soon after birth, when the pulmonary vascular resistance is still elevated, closure of both aortic and pulmonary valves occurs almost simultaneously. Hence, a single $S_2$ is commonly heard. As the pulmonary vascular resistance falls, the pulmonary valve closes after the aortic valve and a split $S_2$ becomes apparent. A rapid heart rate makes it difficult to appreciate physiologic splitting of the second heart sound in newborn infants. Fixed splitting of the second heart sound in newborns is heard when pulmonary blood flow is excessive, as in unobstructed total or partial anomalous pulmonary venous connection. Wide, fixed splitting of the second heart sound occurs in atrial septal defects but is not typically heard in the newborn period. A split second heart sound is also appreciated when there is right ventricular obstruction or conduction delay. A single second heart sound is appreciated when there is only one semilunar valve, as in pulmonary or aortic atresia or truncus arteriosus. A loud pulmonic component is heard in pulmonary hypertension, whereas a soft $P_2$ may suggest pulmonary stenosis. Stenosis of semilunar valves, a bicuspid aortic valve, or a dysplastic truncal valve (truncus arteriosus) may produce additional sounds or ejection clicks. A midsystolic click is sometimes appreciated in Ebstein's anomaly or with mitral valve prolapse.

Murmurs are often associated with structural abnormalities of the heart. Quite often, the murmurs are innocent and bear little clinical significance. It may be difficult for the inexperienced practitioner to distinguish innocent from pathologic murmurs. A systematic approach to evaluation may assist in identifying an underlying anatomic malformation causing the cardiac murmur. The intensity, quality, location, radiation, duration, and timing of the murmur should be assessed. Murmurs can occur during systole, diastole, or continuously during the entire cardiac cycle. Timing and duration of murmurs during the different phases of systole or diastole should be noted. A harsh murmur of at least grade 3 intensity—best heard in the left lower sternal border and occupying the whole duration of systole—is likely to be secondary to a ventricular septal defect. A harsh 3- to 4-grade intensity murmur with a crescendo–decrescendo configuration, best heard in the upper right sternal border and radiating to the carotids, may suggest stenosis of the aortic valve. A murmur heard continuously across systole and diastole and best appreciated in the left upper sternal border is probably due to a widely patent ductus arteriosus. Innocent murmurs are common in the newborn period. Innocent murmurs are softer, occur in systole, and do not have accompanying symptoms. It is extremely important to note that the absence of murmur does *not* rule out CHD.

**Pulmonary examination:** Respiratory rate, effort, quality of breath sounds, and the presence of adventitious sounds should be assessed. Babies with significant left-to-right shunts and increased pulmonary blood flow are tachypneic and show an increased respiratory effort. Most babies with cyanotic CHD exhibit normal respiratory activity despite low oxygen saturation. A *normal* respiratory examination in the presence of cyanosis *strongly* suggests CHD.

**Abdominal examination:** Location and size of the liver should be assessed. A left sided liver is present in situs inversus and a midline liver is often noted in heterotaxy syndromes. Hepatomegaly suggests hepatic congestion and right ventricular dysfunction or volume overload. Neonates with hepatic arteriovenous malformation and high output cardiac failure may have a bruit over the liver.

## Diagnostic Tests

**Chest radiograph:** Characteristic chest radiographs may be useful in the diagnosis of some CHD. However, in most cases of CHD, chest radiographs are rarely diagnostic.

**Electrocardiogram:** A 12-lead electrocardiogram (ECG) often reveals typical ECG findings in some types of CHD. However, a normal ECG should *not* rule out the presence of a serious underlying CHD.

**Hyperoxia test:** Hyperoxia test is helpful in differentiating hypoxemia caused by structural heart disease from that caused by lung disease. Arterial blood gas is obtained at baseline and after exposure to 100% oxygen under an oxyhood for at least 15 minutes. Babies with structural heart disease do not show a significant increase in $Pao_2$ (remains less than 150 mm Hg) after exposure to 100% oxygen.

**Echocardiogram:** An immediate cardiology consultation should be requested when CHD is suspected. Echocardiogram is often the only definitive procedure required to confirm a diagnosis of structural heart disease.

**Blood tests:** Baseline blood work includes complete blood count to help rule out infection, serum chemistry to assess for electrolyte and renal function abnormalities, and an arterial blood gas with lactate level to assess gas exchange and the presence or absence of lactic acidosis.

## Early Management and Stabilization

Airway, breathing, and circulation must be assessed in patients with signs consistent with pulmonary or cardiac disease. In patients presenting with severe hypoxia and increased respiratory effort, intubation and mechanical ventilation may assist in improving gas exchange. Circulation cannot be reestablished without a patent ductus

arteriosus in ductal-dependent lesions. Prostaglandin E1 (PGE-1) infusion can reopen a closing ductus arteriosus and must be initiated as soon as ductal-dependent CHD is suspected. It is not necessary to wait for an echocardiogram for confirmatory evidence before initiating a PGE-1 infusion except in cases of totally anomalous pulmonary venous connection where an infusion of PGE-1 has the potential to increase pulmonary edema, thereby worsening oxygenation. Reopening the ductus arteriosus will improve oxygen saturation in patients with ductal-dependent pulmonary circulation, and systemic perfusion will improve in patients with ductal-dependent systemic circulation after initiation of a PGE-1 infusion. Correction of hypovolemia and initiation of cardiotonic drugs to enhance inotropy may be required in patients presenting in cardiogenic shock. Metabolic derangements including hypoglycemia and hypocalcemia should be corrected. Early transfer to a cardiac center is important.

The three **major** presenting features of CHD in the newborn period are *central cyanosis, decreased perfusion to the body,* and *tachypnea.* The predominant clinical manifestation depends on the type of CHD. The following case studies provide examples of typical presentations of CHD.

## EVALUATION OF THE CYANOTIC NEWBORN

## CASE 2

A 32-year old gravida 2, para 1 woman delivers a male infant at 39 weeks by elective cesarean section. Routine prenatal laboratory tests are unremarkable. Normal fetal anatomy was noted on an 18-week screening ultrasound.

A term male infant with a vigorous cry is handed to you. Apgar scores of 8 and 8 at 1 and 5 minutes respectively are assigned. You provide free flow oxygen at 10 minutes of life for central cyanosis. There is minimal improvement in skin color. At 20 minutes of life, you note that the baby's face, oral mucosa, and tongue continue to have a bluish hue but the abdomen and both legs appear pinker. The baby is breathing comfortably (respiratory rate is 50 breaths/minute) with neither grunting nor subcostal retractions, that is, without dyspnea. The lungs are clear to auscultation with equal air entry. The precordium is quiet, the heart rate and rhythm are normal, and there are no murmurs heard. The second heart sound is loud. Peripheral pulses are normal. There is no hepatomegaly. A chest radiograph shows well-aerated lung fields with no focal pathology, a normal heart size, and a left aortic arch.

### Exercise 2

#### Questions

1. Indicate whether the following statements are true (T) or false (F):
   A. Peripheral cyanosis signals underlying arterial hypoxemia.
   B. Clinical recognition of central cyanosis is easier in neonates with polycythemia than in those with a normal hemoglobin concentration.
   C. This infant's cyanosis is most likely related to lung disease.
2. What is the differential diagnosis of central cyanosis in a newborn infant?

#### Answers

1. **A:** F; **B:** T; **C:** F
2. See Fig. 16.4.

Because the normal systemic arterial oxygen saturation in fetal life is around 60% to 65%, generalized cyanosis at birth is a normal finding but is transient. In most babies who are born at term, skin color improves rapidly as alveolar ventilation is established. Persistent cyanosis is abnormal. Cyanosis signals the presence of elevated levels of deoxyhemoglobin in the underlying capillaries. At least 3 to 5 g/dL of deoxyhemoglobin should be present in the microcirculation for cyanosis to be apparent. Cyanosis may not be recognized if deoxyhemoglobin levels are less than this critical amount. For example, let us assume that this infant has a total hemoglobin concentration of 18 g/dL and an oxygen saturation of 83%. The calculated oxyhemoglobin concentration for this infant would be 15 g/dL ($0.83 \times 18$ g/dL) and the calculated deoxyhemoglobin level would be 3 g/dL. At this absolute concentration of deoxyhemoglobin, cyanosis is likely to be apparent. In the same example, if the absolute concentration of deoxyhemoglobin were 2 g/dL, this infant would *not* appear cyanotic despite an abnormal hemoglobin oxygen saturation of 89% (oxyhemoglobin concentration = 16/18 g/dL or 89%).

It is important to note that hemoglobin concentration determines the saturation level at which cyanosis is visible and detected (Fig. 16.5). Cyanosis may not be appreciated in newborn infants with normal hemoglobin levels unless oxygen saturation falls below 85%. Cyanosis is identified at a higher level of hemoglobin saturation in newborns with polycythemia. For example, if the hemoglobin concentration were 22 grams/dL, cyanosis would be detected at a saturation of 86% (22 − 3 grams/dL = 19 grams/dL, 19/22 = 86%). Cyanosis is more difficult to detect in patients with anemia. In anemic infants, the hemoglobin saturation has to fall profoundly before cyanosis is visible. For example, with a hemoglobin concentration of 6 grams/dL, cyanosis would be noticeable only if the hemoglobin saturation fell below 50% (6 − 3 grams/dL = 3 grams/dL, 3/6 = 50%).

Other factors that affect detection of cyanosis include skin pigmentation, fetal hemoglobin concentration, and conditions that influence the position of the hemoglobin-oxygen dissociation curve.

In peripheral cyanosis, cyanosis is restricted to the periphery (e.g., nail beds, hands, and feet). Sluggish peripheral circulation associated with hypothermia, vasomotor instability, or polycythemia causes increased oxygen extraction by the tissues and elevated levels of deoxyhemoglobin in the microcirculation. However, in peripheral cyanosis, oxygen tension and saturation of hemoglobin in the systemic circulation are normal. Peripheral cyanosis is a common finding in newborn infants. It is usually innocuous unless it is associated with low cardiac output states.

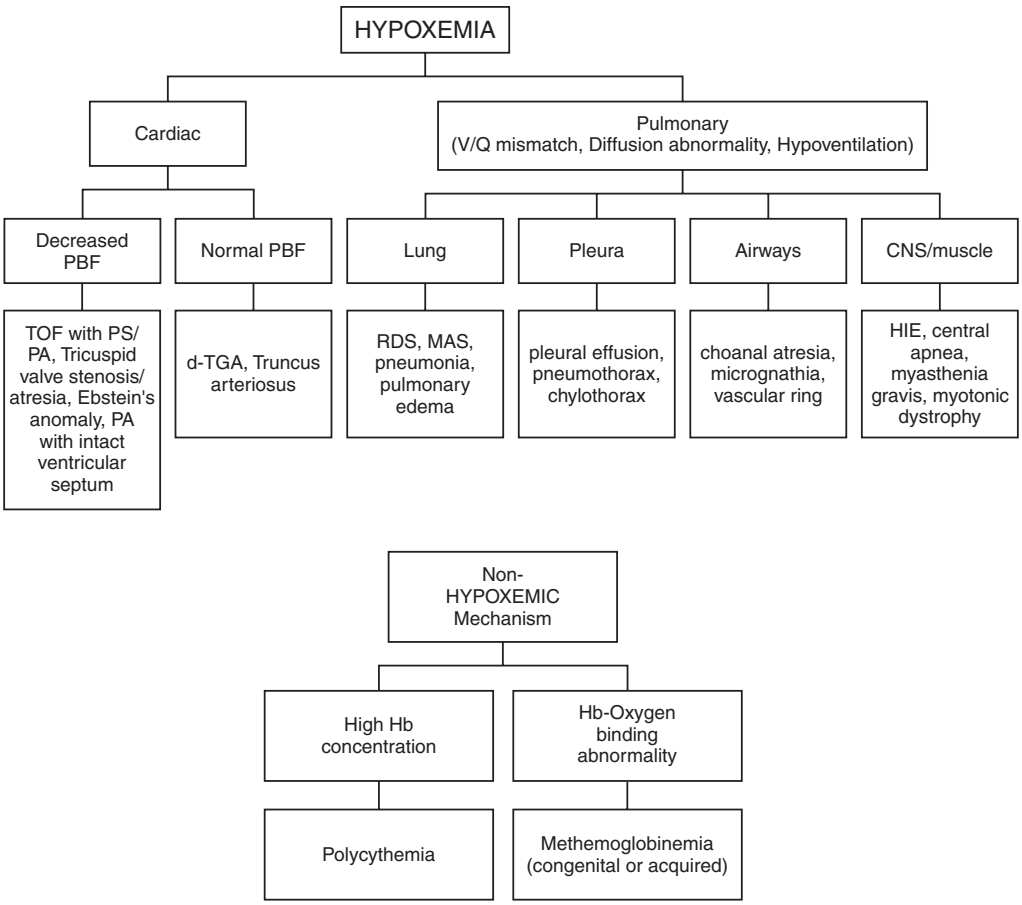


**Fig. 16.4** Pathophysiologic mechanisms of and examples of conditions that can cause central cyanosis. *CNS,* Central nervous system; *d-TGA,* d-transposition of the great arteries; *Hb,* hemoglobin; *HIE,* hypoxic ischemic encephalopathy; *MAS,* meconium aspiration syndrome; *PA,* pulmonary atresia; *PBF,* pulmonary blood flow; *PS,* pulmonary stenosis; *RDS,* respiratory distress syndrome; *TOF,* tetralogy of Fallot.

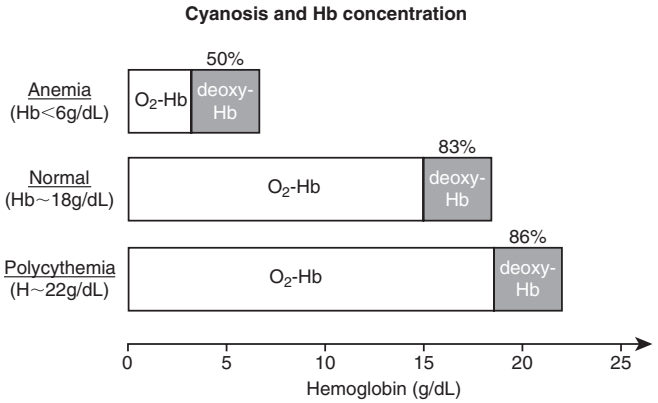


**Fig. 16.5** Effect of hemoglobin concentration and cyanosis. *Hb,* Hemoglobin; *$O_2$*-Hb, oxyhemoglobin.

Central cyanosis is more ominous and *never* a normal finding. It is caused by elevated levels of deoxyhemoglobin and reduced levels of oxyhemoglobin in the *circulation.* Unlike peripheral cyanosis, central cyanosis is most often indicative of underlying *hypoxemia.* Hypoxemia results from two underlying pathophysiologic mechanisms: (1) reduced oxygen tension in pulmonary venous blood (and thereby in the aorta) or (2) extrapulmonary right-to-left shunting of systemic venous blood with low $Pao_2$ into the systemic arterial circuit.

Conditions that lead to ventilation/perfusion mismatch and intrapulmonary right-to-left shunting or those that result in impairment of oxygen diffusion across the alveolar epithelium lead to decreased oxygen tension in pulmonary venous blood. Etiologies for low oxygen tension in pulmonary veins include pulmonary (respiratory distress syndrome, meconium aspiration, pneumonia), airway abnormalities (choanal atresia), neurologic, neuromuscular or muscular (myotonic dystrophy), and skeletal anomalies (severe scoliosis, thoracic dystrophies). Extrapulmonary right-to-left shunting occurs in the setting of cyanotic CHD or persistent pulmonary hypertension. Other pathophysiologic mechanisms that may cause central cyanosis but that are not associated with hypoxemia include polycythemia (excessive hemoglobin concentration and high levels of circulating deoxyhemoglobin) and abnormalities of hemoglobin-oxygen binding (congenital or acquired methemoglobinemia). Fig. 16.4 lists conditions that cause central cyanosis in newborn infants.

It is possible to distinguish cyanosis caused by CHD from other conditions that cause hypoxemia and systemic arterial hemoglobin oxygen desaturation. Diseases involving the lung parenchyma (e.g., pneumonia, meconium aspiration) or involving the pleural space (e.g., effusion or pneumothorax) commonly affect gas exchange and oxygenation (Fig. 16.4). In these conditions, other clinical features suggestive of respiratory disease (e.g., nasal flaring, grunting, dyspnea) accompany cyanosis, as does hypercarbia. Infants born with congenital neurologic, muscular, or neuromuscular conditions may present with cyanosis and hypercarbia caused by decreased respiratory effort from hypotonia. In neonates with cyanotic CHD, cyanosis is often the *sole* clinical feature. The *absence* of respiratory distress and hypercarbia in a cyanotic infant should raise a strong suspicion of CHD.

Hypoxemia caused by extrapulmonary right-to-left shunting in CHD can be distinguished from that caused by pulmonary venous desaturation by employing the hyperoxia test.

The primary determinant of hemoglobin-oxygen association is the partial pressure of oxygen in the blood (Fig. 16.6). Oxygen binds readily to hemoglobin in the lungs where the partial pressure of oxygen is high and dissociates from hemoglobin in tissues where the partial pressure is much lower. Because of the sigmoidal properties of the hemoglobin-oxygen dissociation curve, increasing partial pressure of oxygen beyond 100 mm Hg does not produce significantly greater binding of oxygen to hemoglobin; hence, there is negligible increase in hemoglobin oxygen saturation and oxygen content when alveolar partial pressure of oxygen is increased beyond 100 mm Hg. The hyperoxia test uses the sigmoidal properties of the hemoglobin-oxygen dissociation curve to differentiate hypoxemia caused by intrinsic lung disease from that caused by cyanotic CHD. The $Pao_2$ from an arterial blood gas is measured at baseline and after administering 100% oxygen for at least 10 to 15 minutes. The partial pressure of oxygen in the alveolus, pulmonary vein, and aorta is reduced in babies with parenchymal lung disease. An increase in inspired oxygen concentration

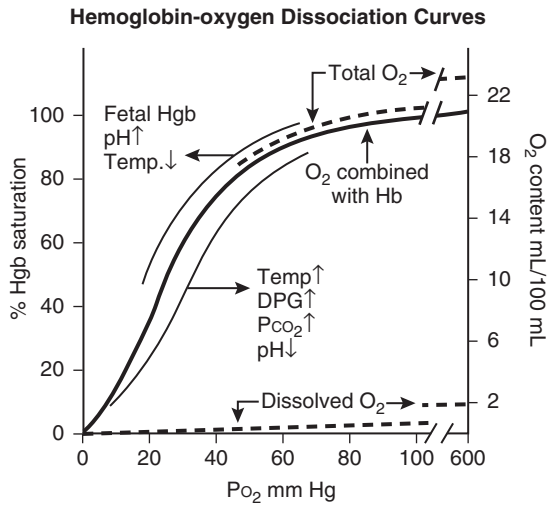


**Fig. 16.6** Oxyhemoglobin-dissociation curve demonstrating the sigmoid relationship between $Pao_2$ of the blood and hemoglobin saturation and the linear relationship between dissolved oxygen and $Pao_2$.

to 100% increases alveolar partial pressure of oxygen, which in turn results in a higher pulmonary vein oxygen tension and a higher oxygen tension and saturation in the aorta. Typically, in babies with intrinsic lung disease, the $Pao_2$ increases to greater than 150 mm Hg after exposure to 100% oxygen for 10 to 15 minutes.

Babies with cyanotic CHD are hypoxemic primarily due to right-to-left shunting of systemic venous blood into the systemic arterial circuit. The systemic arterial circuit therefore has an admixture of pulmonary venous blood (with $Pao_2$ of 100 mm Hg and oxygen saturation of 100%) and systemic venous blood (with $Pao_2$ of approximately 40 mm Hg and oxygen saturation of approximately 70%). Administering 100% oxygen to patients with cyanotic CHD and no lung disease will increase alveolar and pulmonary venous partial pressure of oxygen (to above 600 mm Hg) but will not increase the oxygen saturation of pulmonary venous blood. As mentioned previously, due to the sigmoidal properties of the hemoglobin-oxygen dissociation curve, increasing alveolar partial pressure of oxygen beyond 100 mm Hg does not cause a significantly greater binding of oxygen to hemoglobin. As noted in Fig. 16.6, neither oxygen saturation nor the oxygen content at $Pao_2$ of 100 mm Hg and at 600 mm Hg is remarkably different. Hence, as administering 100% oxygen does not significantly alter the oxygen saturation and content of the pulmonary venous blood, the net oxygen saturation and $Pao_2$ in the arterial circuit in babies with cyanotic CHD is not changed significantly. Typically, the $Pao_2$ in babies with cyanotic CHD remains below 100 mm Hg despite exposure to 100% oxygen. The one exception to the rule is persistent fetal circulation where $Pao_2$ may remain below 100 mm Hg despite a normal intracardiac anatomy.

Examples of congenital heart lesions likely to present with central cyanosis include those that involve restriction of blood flow to the lungs, e.g., severe pulmonary valve stenosis or atresia, and tetralogy of Fallot with severe valvar and/or subvalvar pulmonary stenosis. In these lesions, a combination of right-to-left shunting of desaturated blood across a patent foramen ovale into the left side of the heart and into the aorta and decreased blood flow into the lungs cause arterial hypoxemia and central cyanosis. Typically, these defects are diagnosed when constriction of the ductus arteriosus causes further decrease in pulmonary blood flow. Defects without restriction to pulmonary blood flow but characterized by the admixture of desaturated blood in the aorta may also present with central cyanosis. These include d-TGA and truncus arteriosus, where there is a single arterial trunk. Table 16.1 lists congenital heart lesions likely to present with central cyanosis.

## Exercise 3

### Question

Indicate whether the following statement is true (T) or false (F):

Pulse oximetry sensor on the left hand is the ideal location to measure preductal hemoglobin oxygen saturation in infants with a left aortic arch and normal head vessel branching.

**TABLE 16.1 Congenital Heart Lesions Likely to Present With Central Cyanosis**

| A. Right Ventricular Inflow/Outflow Abnormality | Defect |
|---|---|
| Tricuspid valve stenosis/atresia | Stenosis/atresia of tricuspid valve |
| Ebstein's anomaly | Inferior displacement of tricuspid valve |
| Pulmonary atresia with intact ventricular septum | Atresia of pulmonary valve |
| Pulmonary stenosis | Subvalvar, valvar, or supravalvar obstruction to pulmonary blood flow |
| Tetralogy of Fallot with pulmonary stenosis or atresia | Anterior malalignment of the conal septum leading to variable degree of obstruction to pulmonary blood flow, overriding aorta, ventricular septal defect, and right ventricular hypertrophy |
| **B. Without Right Ventricular Inflow/Outflow Abnormality** | **Defect** |
| Transposition of the great arteries | Ventriculoarterial discordance: aorta arises from the right ventricle, pulmonary artery arises from the left ventricle |
| Truncus arteriosus | Single arterial trunk arises from the ventricles with variable origins of the pulmonary arteries from the trunk |
| Totally anomalous pulmonary venous connection with obstruction | Abnormal connection of all the pulmonary veins to the systemic venous system |

### Answer

False. Preductal and postductal hemoglobin oxygen saturation measurements are critical in the evaluation of a neonate for CHD. A pulse oximetry sensor placed on the right hand in an infant with a presumed left aortic arch and a normal branching pattern of the head vessels measures preductal hemoglobin oxygen saturation; a sensor on either leg measures postductal hemoglobin oxygen saturation. A pulse oximetry sensor on the left hand is not an accurate reflection of preductal oxygen saturation because the origin of the left subclavian artery is close to the region where the ductus arteriosus connects to the aorta.

## Exercise 4

### Question

In which conditions would you expect the preductal hemoglobin oxygen saturation to be higher than the postductal hemoglobin oxygen saturation value, and in which congenital heart lesion would you expect the reverse to be true?

### Answer

Preductal saturation is higher than postductal saturation with persistent pulmonary hypertension of the newborn and left heart obstructive lesions such as critical coarctation or interrupted aortic arch. Postductal saturation is higher than preductal saturation with d-TGA with pulmonary hypertension or with coarctation of the aorta.

## CASE 2 (CONTINUED)

Pulse oximetry readings from the right hand and left foot are 60% and 80% respectively. The baby continues to breathe comfortably with unchanged skin color despite oxygen administration by nasal cannula at 1.5 L/minute and $Fio_2$ of 1.0. Peripheral pulses are normal. A baseline arterial blood gas obtained from the right radial artery shows pH of 7.32, $Pco_2$ of 40 mm Hg, $Pao_2$ of 34 mm Hg, base deficit of −2, and bicarbonate of 21 mEq/L. The $Pao_2$ after a hyperoxia test was 40 mm Hg.

## Exercise 5

### Question

What is the most likely diagnosis in Case Study 2?

### Answer

d-TGA. A centrally cyanotic infant without respiratory distress and a positive hyperoxia test suggests an underlying cyanotic CHD. Reverse differential cyanosis, absent murmur but loud $S_2$ (anterior aortic valve in d-TGA), and a normal sized heart without oligemic lung fields, make the diagnosis of d-TGA most likely.

## CASE 2 (CONTINUED)

The pediatric cardiologist confirms the diagnosis of d-TGA. The interventricular septum is intact, and concern about a restrictive foramen ovale is confirmed. The pediatric cardiologist suggests starting a PGE-1 infusion at 0.01 micrograms/kg/minute and to make arrangements for an urgent transfer to a cardiac care center where a balloon atrial septostomy may be performed to improve mixing.

In babies with d-TGA, the aorta arises from the right ventricle and the pulmonary artery arises from the left ventricle (Fig. 16.7; Video 16.1). After birth, the circulation remains in parallel and deoxygenated blood returning to the right atrium recirculates into the aorta. For survival to occur, adequately oxygenated blood from the left side of the heart must enter the systemic circulation through septal defects at the atrial or ventricular level or at the level of the ductus arteriosus. If the ventricular septum is intact and the foramen ovale becomes restrictive after birth, there are no other major venues for adequate mixing of oxygenated and deoxygenated blood.

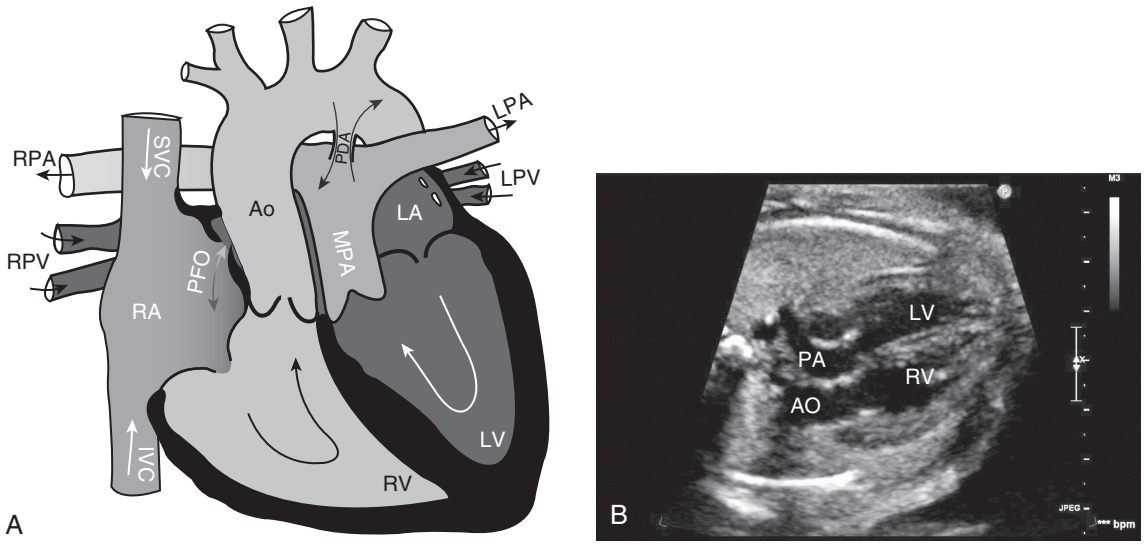


**Fig. 16.7** (A) Cartoon of d-transposition of the great arteries. Arrows depict direction of blood flow. (B) Outflow tract view on echocardiogram in fetus with d-transposition of the great arteries showing the transposed relationship (LV-PA and RV-AO) of the ventricles and great vessels. *Ao,* Aorta; *IVC,* inferior vena cava; *LA,* left atrium; *LPA,* left pulmonary artery; *LPV,* left pulmonary veins; *LV,* left ventricle; *MPA,* main pulmonary artery; *PDA,* patent ductus arteriosus; *PFO,* patent foramen ovale; *RA,* right atrium; *RPA,* right pulmonary artery; *RPV,* right pulmonary veins; *RV,* right ventricle; *SVC,* superior vena cava.

Babies are consequently profoundly hypoxemic and cyanotic in the first minutes to hours after birth. Survival depends on the rapid creation of an atrial level communication through a transcatheter route. Only interventional cardiologists at cardiac centers can perform these procedures, and urgent transfer to such centers is critical.

A simple d-TGA without critical outflow tract obstruction is not a ductal-dependent lesion because there is neither restriction to pulmonary nor systemic blood flow. However, the majority of blood flow into the lungs and into the aorta is *ineffective.* Oxygenated blood in the left ventricle is pumped back into the lungs and deoxygenated blood in the right ventricle is pumped into the aorta. PGE-1 is instituted to increase effective pulmonary and systemic blood flows (Fig. 16.8). Maintaining patency of the ductus arteriosus promotes aorta-to-pulmonary-artery shunting, thereby increasing effective pulmonary blood flow (deoxygenated blood from aorta to pulmonary artery through the ductus arteriosus). The increased pulmonary blood flow will in turn increase left atrial pressure and increase effective systemic oxygenated blood flow (oxygenated blood shunts from left atrium to right atrium across the foramen ovale). Sometimes, the anticipated improvement in oxygenation does not occur after initiating PGE-1 because the foramen ovale is restrictive. An urgent balloon atrial septostomy (a bedside procedure that enlarges the foramen ovale) is required to improve mixing (Video 16.2). Once the balloon atrial septostomy is performed, systemic oxygenation usually improves dramatically. *After a few days of observation, an elective arterial switch procedure is performed.* This procedure involves switching the great vessels so that they connect to the appropriate ventricles. In addition, the coronary arteries are transferred to their new location in the neoaorta. In the current era, operative survival and long-term outcomes after the arterial switch procedure are excellent.

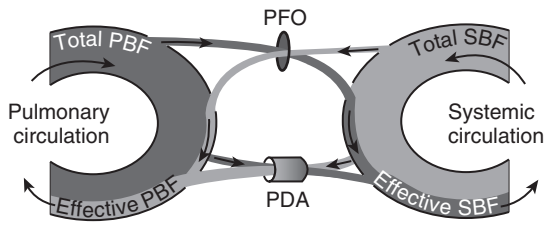


**Fig. 16.8** Cartoon depicting the relative contributions of oxygenated and desaturated blood in pulmonary and systemic circulations and areas of mixing in d-transposition of the great arteries and intact ventricular septum. Effective pulmonary blood flow (PBF) denotes desaturated blood directed toward the pulmonary circulation. Effective systemic blood flow (SBF) denotes oxygenated blood directed toward the systemic circulation. *PDA,* Patent ductus arteriosus; *PFO,* patent foramen ovale.

## CYANOTIC NEWBORN IN THE NEWBORN NURSERY

## CASE STUDY 3

You are called to evaluate a 4-hour-old female infant in the well-baby nursery. The nurse is concerned that the baby appears cyanotic. This infant was born at 39 weeks' gestation to a 24- year-old gravida 2, para 1 woman. The mother's pregnancy was unremarkable and delivery was by elective cesarean section. Apgar scores were 8 and 9 at 1 and 5 minutes respectively. This infant's vital signs are as follows: temperature: 36.8°C, heart rate 160 beats/minute, respiratory rate 65 breaths/minute, blood pressure 73/45, pre- and postductal

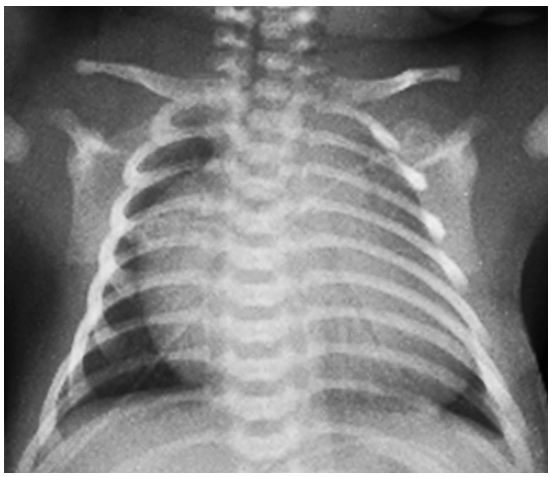

**Fig. 16.9** Chest radiograph of patient described in Case Study 3.

**BOX 16.1 List of Conditions That May Cause Cyanotic Spells in the Newborn Period**

1. Sepsis/pneumonia
2. Hypoglycemia
3. Hypothermia
4. Gastroesophageal reflux
5. Airway obstruction
6. Congenital heart disease
7. Persistent pulmonary hypertension
8. Intracranial hemorrhage related to birth trauma
9. Apnea, seizures
10. Effects of maternal sedation
11. Hypermagnesemia
12. Inborn errors of metabolism

saturations are 60% and 62% respectively. The infant appears nondysmorphic, active, and vigorous but with central cyanosis. She is breathing comfortably. Both lung fields receive equal air entry and are clear to auscultation. Her precordium is active, multiple heart sounds are heard, and a 3/6-pansystolic murmur is heard in the lower left parasternal region. The liver is palpable 2 cm below the right costal margin. Peripheral pulses and perfusion are normal. A chest radiograph is shown in Fig. 16.9.

An ECG reveals tall P waves and right ventricular conduction delay. Arterial blood gas: pH of 7.35, $Pco_2$ of 32 mm Hg, $Pao_2$ of 36 mm Hg, $HCO_3$ of 22 mEq/L. Complete blood count: white blood cell (WBC) 18 $\times$ $10^9$/L, hemoglobin 17 grams/dL, hematocrit 49%, platelet count 224 $\times$ $10^9$/L. WBC differential includes 55% neutrophils, 35% lymphocytes, and no bands. Pediatric cardiology consult has been requested.

## Exercise 6

### Questions

1. Under what conditions should cyanosis be considered a normal finding in a newborn infant?
2. What is the most likely diagnosis in Case Study 3?

### Answers

1. Cyanotic or "blue" spells can be seen in otherwise well babies. By definition, benign cyanotic spells are transitory and brief. These spells typically occur during crying and resolve rapidly when the baby is calm and quiet. The hemoglobin oxygen saturation measurement by pulse oximetry is normal after resolution of the cyanotic episode. There are no other symptoms or signs, and these babies are well appearing and have a normal examination (Box 16.1).
2. In this case the most likely cause of the cyanosis in this infant is incompetence of the tricuspid valve. The early auscultation of a parasternal pansystolic murmur is most likely to be related to a tricuspid regurgitant murmur. Regurgitation across the tricuspid valve can be seen in structurally normal as well as abnormal hearts. The most common cause of tricuspid regurgitation in structurally normal hearts occurs with pulmonary hypertension for a short time after birth and is generally transient. A flail tricuspid valve caused by necrosis or rupture of papillary muscle in the setting of perinatal asphyxia may result in severe tricuspid valve regurgitation. Congenital cardiac anomalies causing tricuspid regurgitation include Ebstein's anomaly and pulmonary atresia with intact ventricular septum. Other congenital abnormalities of the tricuspid valve—such as dysplasia of the tricuspid valve, abnormal chordal attachments of the tricuspid valve, unguarded tricuspid valve (where there is no valvar apparatus), or cleft tricuspid valve leaflet—are quite rare. The identification of several heart sounds, including split first and second heart sounds and third and fourth heart sounds, makes the diagnosis of a primary abnormality of the tricuspid valve—especially Ebstein's anomaly—more likely.

   Watch changes in margins. In Ebstein's anomaly, the tricuspid valve is abnormal (Fig. 16.10A,B; Video 16.3). The septal and posterior leaflets are displaced inferiorly and are usually tethered to the right ventricular wall. Mobility of the tricuspid valve is further limited by abnormal chordal attachments. Varying degrees of tricuspid regurgitation occurs, resulting in right atrial enlargement. A high right atrial pressure promotes right-to-left shunting across a patent foramen ovale or an atrial septal defect. The region of the right ventricle between the tricuspid valve annulus and the inferiorly displaced valve leaflets is called the atrialized portion of the right ventricle and has no role in right ventricular output. During systole, blood from the right ventricle regurgitates into the right atrium, especially in the setting of elevated pulmonary vascular resistance as seen in the newborn period. Pulmonary blood flow across the pulmonary valve may be minimal under these conditions. Therefore pulmonary blood flow may be dependent on the patency of the ductus arteriosus while pulmonary vascular resistance is still elevated. Hence Ebstein's anomaly is often diagnosed when the ductus arteriosus begins to constrict, further decreasing blood flow into the lungs. As a result, values of hemoglobin oxygen saturation fall, and cyanosis becomes apparent.

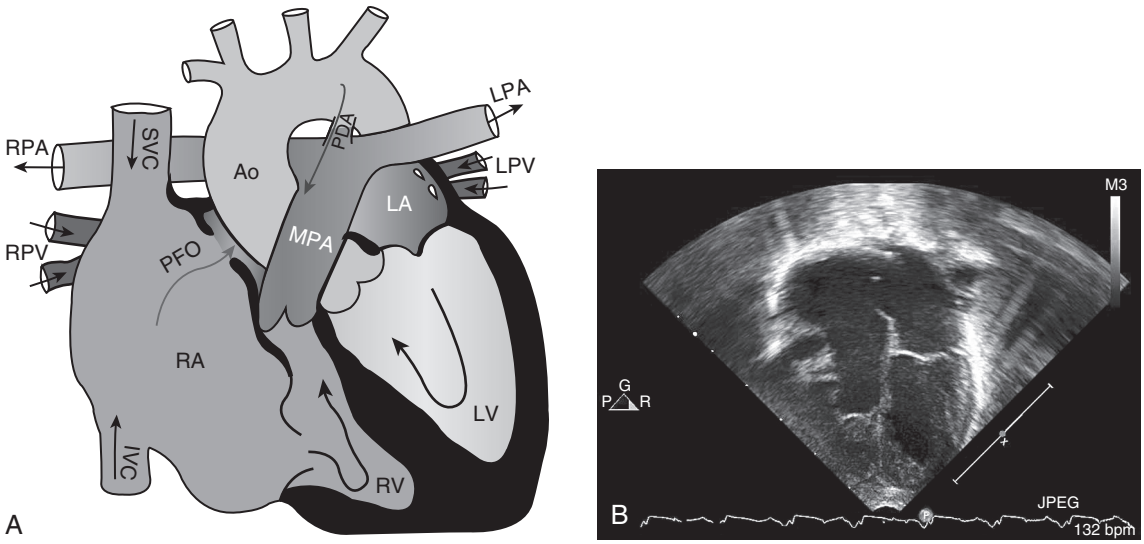


**Fig. 16.10** (A) Cartoon of Ebstein's anomaly. Arrows depict direction of blood flow. (B) Four chamber view on echocardiogram of patient with Ebstein's anomaly. The displaced tricuspid valve and atrialized portion of right ventricle are clearly seen. *Ao,* Aorta; *IVC,* inferior vena cava; *LA,* left atrium; *LPA,* left pulmonary artery; *LPV,* left pulmonary veins; *LV,* left ventricle; *MPA,* main pulmonary artery; *PDA,* patent ductus arteriosus; *PFO,* patent foramen ovale; *RA,* right atrium; *RPA,* right pulmonary artery; *RPV,* right pulmonary veins; *RV,* right ventricle; *SVC,* superior vena cava.

Babies with Ebstein's anomaly and moderate to severe tricuspid valve regurgitation may have a hyperdynamic precordium due to volume overload of the right ventricle. The tricuspid regurgitant murmur is best heard along the lower left sternal border. $S_1$ is split due to increased flow across the tricuspid valve. $S_2$ is often split due to right ventricular conduction delay. Third and fourth heart sounds are often appreciated and may be related to vibrations of the abnormal tricuspid valve. Multiple heart sounds and a parasternal pansystolic murmur in a cyanotic newborn are suggestive of Ebstein's anomaly.

## Exercise 7

### Question

What are the causes of a large cardiothymic silhouette in the newborn period?

### Answer

Chest radiograph and ECG are useful diagnostic tools in the evaluation of babies with CHD. The position and contour of the cardiovascular silhouette on chest radiographs is informative. Dextrocardia and presence of a right sided stomach bubble or a midline liver may indicate complex CHD, including heterotaxy syndromes. The presence or absence of a thymic shadow and sidedness of the aortic arch should be assessed. An absent thymic shadow (first day of life) may suggest 22q11.2 deletion syndrome and raises the possibility of a conotruncal malformation (congenital abnormalities of cardiac outflow tracts). Characteristic radiographic features are noted in some types of CHD (e.g., Coeur en Sabot or boot-shaped heart in tetralogy of Fallot, "egg on string" appearance in d-TGA). Prominence of pulmonary vasculature indicates excessive pulmonary blood flow; relatively oligemic lung fields suggest paucity of blood flow to the lungs. Pulmonary venous congestion and pulmonary edema are noted in totally anomalous pulmonary venous connection with obstruction.

Very few cardiac conditions cause a massive cardiothymic silhouette as seen on chest radiographs. Most neonatal cases of enlarged cardiac shadow on x-rays are due to an enlarged right atrium (Ebstein's anomaly, pulmonary atresia with intact ventricular septum). Other causes include cardiomegaly due to increase in myocardial mass or length (hypertrophic or dilated cardiomyopathy), enormous increase in right ventricular volume and pressure overload (large arteriovenous malformations), cardiac or mediastinal tumors, and pericardial effusions. The most common cause of massive cardiomegaly in a *cyanotic* newborn is Ebstein's anomaly, where massive right atrial enlargement results from tricuspid regurgitation.

## Exercise 8

### Question

What intervention(s) may improve the hemoglobin oxygen saturation in this patient?

### Answer

Increase the inspired oxygen concentration and consider starting inhaled nitric oxide.

As mentioned previously, the atrialized portion of the right ventricle contributes minimally toward right ventricular output. In the neonatal period, when the pulmonary vascular resistance is elevated, the right ventricle may not be able to generate adequate systolic pressure to open the pulmonary valve. The pulmonary valve is hence "functionally" atretic, as blood does not flow across it (Fig. 16.11). During this time,

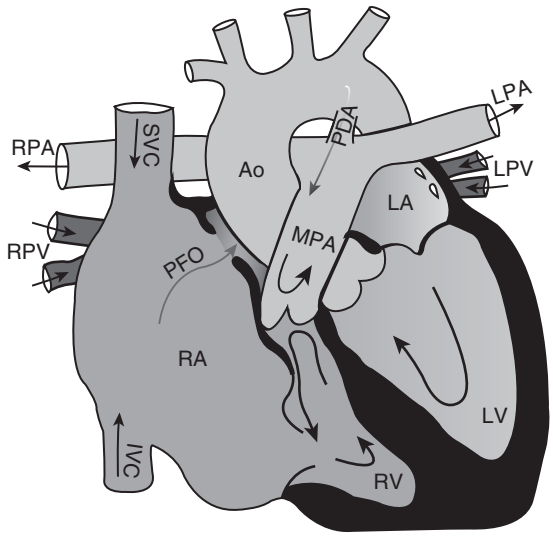


**Fig. 16.11** Cartoon depicting functional pulmonary atresia in Ebstein's anomaly. Arrows depict direction of blood flow. *Ao,* Aorta; *IVC,* inferior vena cava; *LA,* left atrium; *LPA,* left pulmonary artery; *LPV,* left pulmonary veins; *LV,* left ventricle; *MPA,* main pulmonary artery; *PDA,* patent ductus arteriosus; *PFO,* patent foramen ovale; *RA,* right atrium; *RPA,* right pulmonary artery; *RPV,* right pulmonary veins; *RV,* right ventricle; *SVC,* superior vena cava.

pulmonary blood flow is dependent on the patency of the ductus arteriosus. Hypoxemia and cyanosis may worsen if the ductus arteriosus constricts or closes. Antegrade flow across the pulmonary valve in the setting of functional pulmonary atresia may be promoted by decreasing the pulmonary vascular resistance, which may be accomplished by increasing the concentration of inspired oxygen or by providing inhaled nitric oxide and by awaiting spontaneous ductal closure. Oxygen and/or inhaled nitric oxide may be weaned over the course of several days as the pulmonary vascular resistance declines, antegrade flow across the pulmonary valve increases, and right-to-left flow across the foramen ovale or atrial septal defect diminishes. In the case of anatomic obstruction, ductal patency is of course critical until an intervention to open the pulmonary outflow tract can be performed. The differentiation of functional versus true pulmonary outflow obstruction can be difficult and requires consultation with pediatric cardiology and investigation with echocardiography. The institution of PGE-1 should be delayed, if possible, until the exact physiology—anatomic versus functional pulmonary atresia is determined.

## CASE 3 (CONTINUED)

The pediatric cardiologist confirms the diagnosis of Ebstein's anomaly with moderate to severe tricuspid regurgitation and functional pulmonary atresia. Inspired oxygen is increased to 50% by nasal cannula. Oxygen saturation improves steadily to above 90%. After 3 to 4 days, oxygen is weaned back to 21% and the patient is discharged home on the seventh day of life with a hemoglobin saturation of 85%.

Severity of Ebstein's anomaly varies. Patients with mild abnormalities of the tricuspid valve and minimal regurgitation may remain asymptomatic and require no intervention. Some may present with cyanosis in the newborn period as the patient described in this case study. More severe cases can present with cardiac failure and/or cyanosis in infancy and may require surgical intervention.

# MURMUR IN NEONATE

## CASE STUDY 4

You receive a call from a pediatrician in the well-baby nursery who wishes to transfer a 12-hour-old male infant to the neonatal intensive care unit (NICU) after a murmur was discovered in the admission physical examination. The mother is a 26-year-old primigravida. The pregnancy was uneventful. This infant was born at 39 weeks' gestation by normal spontaneous vaginal delivery. Apgar scores were 9 and 9 at 1 and 5 minutes, respectively. On examination, the infant appears comfortable, pink, and not in any apparent cardiorespiratory distress. The birth weight is 3.56 kg. Vital signs are as follows: heart rate is 150 beats/minute, respiratory rate is 50 breaths/minute, blood pressure is 68/45 mm Hg (right arm), preductal and postductal hemoglobin saturations are 86%. The baby is breathing comfortably, with neither tachypnea nor chest retractions. Precordial examination is significant for a prominent parasternal impulse. A harsh 3/6 ejection systolic murmur is best heard over the left upper sternal border. Peripheral pulses and blood pressure are normal.

Chest radiograph reveals mild cardiomegaly, left aortic arch, and mildly oligemic lung fields with no focal lung pathology. ECG reveals a normal sinus rhythm, rightward QRS axis, and right ventricular hypertrophy. Pediatric cardiology consultation is awaited.

### Exercise 9

#### Questions

1. On a physical examination, what features are used to differentiate an innocent murmur from a pathologic murmur?
2. Which of the following statements about murmurs is true?
   A. The most common innocent murmur in the newborn period is peripheral pulmonary artery stenosis.
   B. Absence of murmur in the newborn period rules out CHD.

#### Answers

1. Routine newborn physical examination within 24 hours of birth and again before discharge offers a critical window during which presymptomatic infants with CHD may be detected. Reported prevalence of murmurs in term newborns is highly variable. In most large series, the prevalence of murmurs in the newborn period is less than 1%.

   Cardiac murmurs may be innocent and of no consequence or may be associated with structural abnormalities of the heart. In one large series, more than 54% of babies in whom a murmur

was noted in the newborn period had CHD (Ainsworth, et al, 1999). Certain qualities may differentiate pathologic from innocent murmurs. High grade (grade 3 intensity or higher), harsh quality, murmurs extending through systole and best noted in the left upper sternal border, and those associated with an abnormal $S_2$ are most likely pathologic and indicative of an underlying structural heart disease.

2. A.

The most common lesions recognized from murmurs are those with left-to-right shunts, particularly ventricular septal defects. The remaining 46% in the same series (mentioned previously) (Ainsworth et al, 1999) had either a structurally normal heart or physiologic findings that accounted for the murmur, e.g., physiologic branch pulmonary artery stenosis. Common "innocent" murmurs heard in the newborn period include peripheral pulmonary artery stenosis (PPS), a closing ductus arteriosus, or Still murmur. The typical murmur of PPS is described as a low grade, 1 to 2/6 midsystolic ejection murmur best heard in the left upper sternal area and radiating to the axilla and back. PPS murmurs generally resolve in most patients by 6 months of age. This murmur is caused by turbulence created by the relative size discrepancy between the main and branch pulmonary arteries. Still murmur is generally heard in young, school-aged children but occasionally can be heard in newborn infants. Still murmur is a low-grade systolic murmur with a musical quality and is best heard in the lower left parasternal regions.

The *absence* of a murmur *does not* rule out CHD. Many serious congenital heart lesions do not present with a murmur at all. Some may have not yet developed the physiologic changes for the murmur to be detected in the newborn nursery. In the same large series described previously, 47% of infants who were eventually diagnosed with CHD later in infancy had no murmur in the neonatal period (Ainsworth et al, 1999).

The infant in our case study has a prominent precordial impulse suggestive of right ventricular pressure overload. An ejection systolic murmur, best appreciated in the left upper sternal border, is likely related to an obstruction of the right ventricular outflow tract at the supravalvar valvar or subvalvar levels. A low hemoglobin saturation of 86% suggests right to left shunting at the atrial level. Oligemic lung fields on chest radiograph indicate reduced blood flow to the lungs.

## CASE 4 (CONTINUED)

A diagnosis of critical valvar pulmonary stenosis is confirmed on echocardiogram by the pediatric cardiologist. The ductus arteriosus is restrictive. The cardiologist requests that a PGE-1 infusion be started immediately at 0.01 mcg/kg/min. The hemoglobin saturation increases to 94%. The next day, the infant undergoes a successful transcatheter balloon valvuloplasty.

One of the most common causes of obstruction to the right ventricular outflow tract is pulmonary valve stenosis

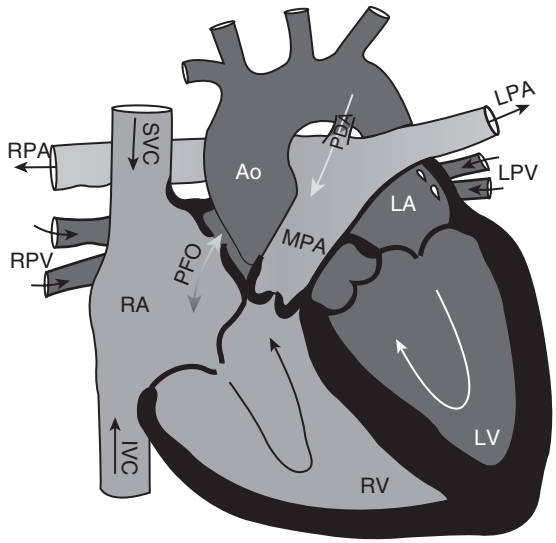


**Fig. 16.12** Cartoon depicting valvar pulmonary stenosis. Arrows depict direction of blood flow. *Ao,* Aorta; *IVC,* inferior vena cava; *LA,* left atrium; *LPA,* left pulmonary artery; *LPV,* left pulmonary veins; *LV,* left ventricle; *MPA,* main pulmonary artery; *PDA,* patent ductus arteriosus; *PFO,* patent foramen ovale; *RA,* right atrium; *RPA,* right pulmonary artery; *RPV,* right pulmonary veins; *RV,* right ventricle; *SVC,* superior vena cava.

(Fig. 16.12; Video 16.4). The pulmonary valve may be domed without distinct separation into leaflets or the leaflets may be fused at the commissures. Sometimes, especially in patients with Noonan syndrome, the valve leaflets are thickened and dysplastic. Obstruction at the pulmonary valve causes right ventricular hypertrophy, particularly of the infundibulum, which may contribute to the right ventricular outflow tract obstruction.

There are varying degrees of valvar pulmonary stenosis. Mild pulmonary valve stenosis rarely progresses and usually requires no treatment. Moderate or severe obstruction to the pulmonary valve is progressive and therapy is required. Severe obstruction to the right ventricular outflow tract (critical pulmonary stenosis) can cause compromise of pulmonary blood flow and requires ductal patency to provide an alternate source of pulmonary blood flow.

Transcatheter balloon valvuloplasty is curative when obstruction is restricted to the valvar level (Video 16.5). Neonatal transcatheter balloon valvuloplasty is very successful; surgical or transcatheter reinterventions are rarely required.

After balloon valvuloplasty, PGE-1 infusion is usually discontinued. Over the course of the next 48 hours, a decline in oxygen saturations is expected as the ductus arteriosus closes. Decline in oxygen saturation is due to continued right-to-left atrial shunting in the setting of diminished right ventricular compliance caused by right ventricular hypertrophy. As right ventricular hypertrophy regresses over several weeks to months, right ventricular compliance will improve, right-to-left shunting across the foramen ovale will diminish, and the hemoglobin oxygen saturation will improve.

# CYANOTIC NEWBORN WITH RESPIRATORY DISTRESS

## CASE 5

A full-term male neonate is born to a 23-year-old primigravida whose prenatal laboratory tests are unremarkable, including a negative cervical culture group B *Streptococcus.* Membranes ruptured 4 hours before delivery; the amniotic fluid was clear. There is no history of maternal fever during labor. Labor was spontaneous and uncomplicated; vaginal delivery occurred at 39 weeks of gestation. Apgar scores of 9 and 9 are assigned. You are called to evaluate this infant at 12 hours of life in the newborn nursery for grunting respirations. On physical examination, you find a 3 kg nondysmorphic, centrally cyanotic male infant of term gestation with significant respiratory distress manifest by nasal flaring and subcostal and intercostal chest retractions. Air entry is equal bilaterally; diffuse rales are appreciated. On precordial examination, the second heart sound appears loud. A 2/6 systolic murmur is appreciated over the upper left sternal border. His abdomen is not distended; however, the liver is palpable 1 to 2 cm below the right costal margin. The extremities are warm and distal pulses appear fairly strong. You bring him to the NICU for further management. Vital signs: respiratory rate 85 to 90 breaths/minute, heart rate 168 beats/minute, blood pressure 76/46, hemoglobin saturation is 60% breathing room air. He is placed on nasal prong continuous positive airway pressure (CPAP), but is intubated shortly thereafter for a persistently low saturation value of 65% and continuing respiratory distress. On conventional mechanical support and inspired oxygen of 1.0, his saturation measured by pulse oximetry is 68%. Arterial blood gas: pH of 7.32, $Pco_2$ of 42 mm Hg, $Pao_2$ of 35 mm Hg, $HCO_3$ of 20 meq/L, base deficit of −2/$Sao_2$ 65%.

A chest radiograph obtained on admission is shown in Fig. 16.13. Complete blood count: WBC 15 × $10^9$/L, hemoglobin 18 grams/dL, platelet count 245 × $10^9$/L. Differential: 54% neutrophils, no bands, and 35% lymphocytes.

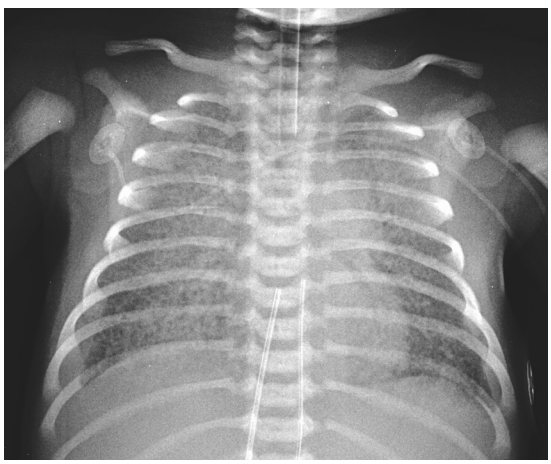

**Fig. 16.13** Chest radiograph of patient described in Case Study 5.

## Exercise 10

### Question

Which of the following diagnoses is most consistent with this infant's clinical course and chest radiograph?

A. Transient tachypnea of the newborn
B. Respiratory distress syndrome
C. Totally anomalous pulmonary venous connection with obstruction
D. Large ventricular septal defect

### Answer

C

It is not uncommon for newborn infants to have respiratory distress.

The timing of onset of symptoms, contributory information from prenatal and delivery history, and a thorough physical examination help in establishing the correct diagnosis. Respiratory distress in the term infant may have several etiologies, including transient tachypnea of the newborn (TTN), pneumonia, aspiration, or air-leak syndromes, pleural effusions, or CHD.

Excessive pulmonary blood flow occurs in lesions with an abnormal communication between the pulmonary and systemic circuit at the level of the atria, ventricles, or the great vessels. Examples of such lesions include large atrial or ventricular septal defects, atrioventricular septal defects, large patent ductus arteriosus, aortopulmonary window, truncus arteriosus, or totally abnormal pulmonary venous connection without obstruction. Typically, symptoms of increased respiratory effort manifest when there is a substantial decline in pulmonary vascular resistance and left-to-right shunt volume increases. As the pulmonary vascular resistance is still elevated after birth; the above lesions rarely exhibit symptoms of pulmonary over circulation at birth or in the first few days of life.

Some or all four pulmonary veins may not return normally to the left atrium. Instead, the pulmonary veins may establish an abnormal communication with a systemic venous channel (Fig. 16.14). If there is significant resistance to flow in the anomalous pulmonary venous pathway, pulmonary venous hypertension ensues. When the hydrostatic pressure within the pulmonary veins exceeds oncotic pressure, pulmonary edema follows. The decrease in lung compliance results in respiratory distress and the alveolar diffusion abnormality from edema results in hypoxemia and reduced hemoglobin oxygen saturation. Timing of symptoms depends on the number and degree of obstructed pulmonary veins. In isolated totally anomalous pulmonary venous connection with obstruction, symptoms of respiratory distress and cyanosis are seen within the first 24 hours after birth but are rarely noted at birth.

Finally, increased left atrial pressure may secondarily cause pulmonary venous hypertension and pulmonary edema and hence respiratory distress. Examples of lesions causing an increased left atrial pressure include hypoplastic left heart

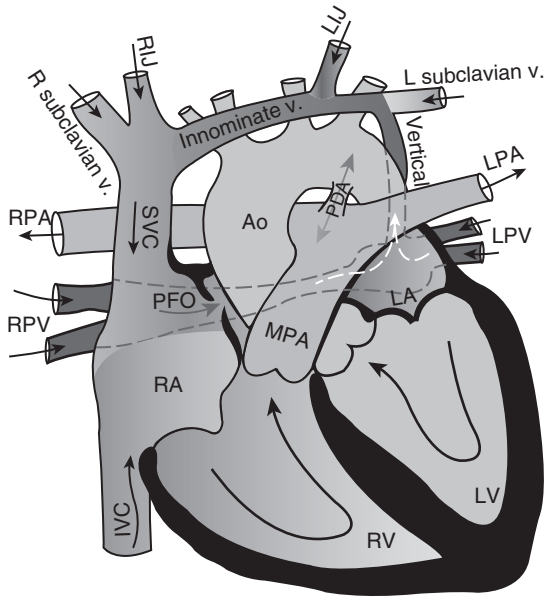


**Fig. 16.14** Cartoon depicting supradiaphragmatic totally anomalous pulmonary vein connection. Arrows depict direction of blood flow. *Ao,* Aorta; *IVC,* inferior vena cava; *LA,* left atrium; *LPA,* left pulmonary artery; *LPV,* left pulmonary veins; *LV,* left ventricle; *MPA,* main pulmonary artery; ; *PDA,* patent ductus arteriosus; *PFO,* patent foramen ovale *RA,* right atrium; *RIJ, LIJ,* right and left jugular vein; *r, l subclavian v,* right, left subclavian vein; *vertical v,* vertical vein; *RPA,* right pulmonary artery; *RPV,* right pulmonary veins; *RV,* right ventricle; *SVC,* superior vena cava.

syndrome with mitral atresia and a restrictive or intact atrial septum, severe mitral or aortic valve stenosis or regurgitation, decreased left ventricular systolic or diastolic function secondary to cardiomyopathy, or obstruction to the left ventricular outflow tract. Infants with these lesions typically show signs of decreased perfusion in addition to respiratory distress.

Totally anomalous pulmonary venous connection must be excluded in term infants presenting with respiratory distress, especially when there are chest radiographic findings of pulmonary edema and a normal heart size (Fig. 16.13). Totally anomalous pulmonary venous connection may be classified into different types based on the location of drainage of the pulmonary veins. Supracardiac, cardiac, and infracardiac types reflect the areas of connection of the pulmonary veins. Totally anomalous pulmonary venous connection may be also classified based on whether they are obstructed or not. The degree of obstruction often varies, and the clinical presentation depends on the severity of obstruction. Patients with *unobstructed* total anomalous pulmonary venous connection generally present with symptoms of pulmonary over circulation and cardiac failure by 4 to 6 weeks of age.

## CASE 5 (CONTINUED)

On an echocardiogram, the pediatric cardiologist makes the diagnosis of infracardiac totally anomalous pulmonary venous connection with obstruction. The four pulmonary veins join to form a confluence, which drains via a long vertical vein into the portal vein. Pulmonary artery pressure is elevated, right ventricular systolic function is mildly depressed, and the foramen ovale is not restrictive. Flow through the patent ductus arteriosus is right-to-left in systole. He recommends urgent transfer to a cardiac surgical center.

The hemoglobin oxygen saturation as measured by pulse oximetry is no higher than 70%, and he is placed on conventional mechanical ventilation with a peak inspiratory pressure of 22 mm Hg, positive end expiratory pressure of 5 mm Hg, and $Fio_2$ of 1.0.

## Exercise 11

### Question

While awaiting transport, a medical student suggests adding inhaled nitric oxide to improve oxygenation. This intervention will most likely:

A. Improve oxygenation by increasing pulmonary blood flow
B. Worsen oxygenation by increasing pulmonary blood flow

### Answer

B

Totally anomalous pulmonary venous connection with obstruction is a surgical emergency. Urgent transfer to a cardiac center where surgery can be performed is critical for survival. Infants with obstructed totally anomalous pulmonary venous connection exhibit hypoxemia, the severity of which varies with the degree of obstruction. Several factors contribute to the hypoxemia: (1) pulmonary edema and the secondary diffusion abnormality lead to low oxygen tension and saturation in the pulmonary veins; (2) mixing of oxygenated and deoxygenated blood—pulmonary venous return mixes with systemic venous return; and (3) hypoxic reflex pulmonary artery vasoconstriction leads to pulmonary artery hypertension, right-to-left shunting across the ductus arteriosus, and decreased pulmonary blood flow. Pulmonary artery vasoconstriction in the setting of pulmonary venous obstruction and hypertension restricts blood flow into the lungs and protects the pulmonary bed from worsening alveolar edema. Maneuvers that decrease pulmonary vascular resistance (e.g., inhaled nitric oxide) are expected to lead to an increase in pulmonary blood flow. In the setting of fixed downstream obstruction, pulmonary edema is likely to worsen if blood flow into the pulmonary circuit is greater than that drained from it. Therefore the use of pulmonary vasodilators in an effort to improve oxygenation may be counterproductive and may be ill advised.

## Exercise 12

### Question

The same medical student asks if PGE-1 may be used in this patient. The most appropriate answer to this question is:

A. PGE-1 is absolutely contraindicated in *all* cases of obstructed totally anomalous pulmonary venous connection.

B. PGE-1 may be used in *some* cases of obstructed totally anomalous pulmonary venous connection.

### Answer

B

The use of PGE-1 in obstructed total anomalous pulmonary venous connection is controversial. There may be a role for its use in select cases, but PGE-1 must always be used with caution. In obstructed total anomalous pulmonary venous connection, PGE-1 may be employed to off-load the failing right ventricle or when left ventricular inflow or outflow is inadequate. The latter can occur when the foramen ovale is restrictive. In total anomalous pulmonary venous connection, left ventricular preload and hence output is dependent on right-to-left shunting across the foramen ovale. If the foramen is small and restrictive, left ventricular preload or filling is reduced and hence left ventricular stroke volume is reduced. A posteriorly deviated interventricular septum (in the setting of severe pulmonary hypertension and right ventricular dilatation) can lead to encroachment of left ventricular cavity and impede left ventricular filling and output.

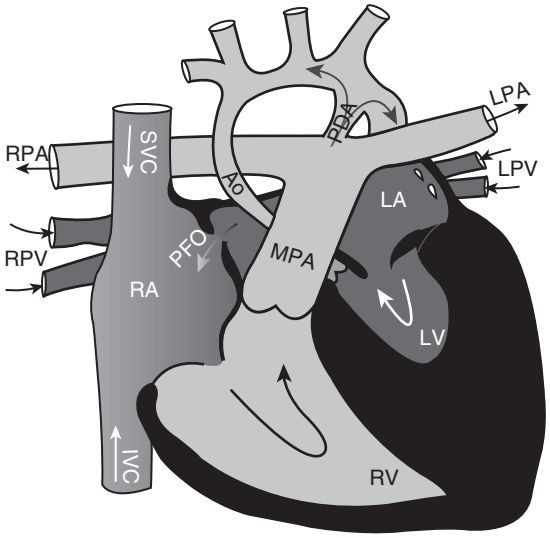


**Fig. 16.15** Cartoon depicting hypoplastic left heart syndrome. Arrows depict direction of blood flow. *Ao,* Aorta; *IVC,* inferior vena cava; *LA,* left atrium; *LPA,* left pulmonary artery; *LPV,* left pulmonary veins; *LV,* left ventricle; *MPA,* main pulmonary artery; *PDA,* patent ductus arteriosus; *PFO,* patent foramen ovale; *RA,* right atrium; *RPA,* right pulmonary artery; *RPV,* right pulmonary veins; *RV,* right ventricle; *SVC,* superior vena cava.

## NEONATE WITH DECREASED PERFUSION

## CASE 6

A 10-day-old female infant born at 39 weeks of gestation arrives at the emergency room of the community hospital where you are covering. She was born by normal spontaneous vaginal delivery at the same hospital and was discharged home within 48 hours. The mother's pregnancy, labor, and delivery were unremarkable. A normal neonatal admission and discharge physical examinations were documented in the hospital records. This infant was feeding and voiding appropriately while in the hospital. By parental account, their infant became progressively "fussy." She breathed faster and required a longer time for each bottle feeding. On the day of presentation, she fed no more than 1 ounce of formula and hadn't voided since the night before.

Vital signs: temperature 36.8, heart rate 190 beats/minute, noninvasive blood pressure from the right arm 78/50 mm Hg, respiratory rate 78 breaths/minute, $Sao_2$ from the right hand is 98%. Weight is 3.3 kg (birth weight and discharge weight are 3.5 and 3.4 kg). The infant appears alert but irritable. She is in moderate respiratory distress with nasal flaring and has subcostal and intercostal retractions. Equal breath sounds are heard bilaterally, and fine rales are heard at both lung bases. The precordium is hyperdynamic, pulmonary component of the second heart sound is loud, and no murmurs are appreciated on auscultation. The liver is palpable 4 cm below the right costal margin. Lower extremity pulses are difficult to palpate. Her feet are cool to touch. There are no skin lesions; the capillary refill is 5 seconds. CBC: WBC 15 $\times$ $10^9$/L, Hct 40%, platelet count 23 $\times$ $10^9$/L. Differential count 50% neutrophils, 35% lymphocytes, and no bands. Serum chemistry panel: sodium 145 mEq/L, potassium 5 mEq/L, chloride 110 mEq/L, bicarbonate 14 mEq/L, blood urea nitrogen 40 mg/dL, creatinine 1.0 mg/dL. Chest radiograph shows pulmonary edema and cardiomegaly and a left aortic arch. Blood culture is pending. Intravenous antibiotics have been administered.

### Exercise 13

#### Question

This infant's clinical presentation is most consistent with a:

A. Left heart obstructive lesion
B. Right heart obstructive lesion
C. Adrenal insufficiency
D. Sepsis

#### Answer

A.

Newborn infants with obstruction to left ventricular output may be difficult to distinguish from those with sepsis. The clinical presentation is often similar, but careful and thorough physical examination and historical evaluation may help in establishing an accurate clinical diagnosis. Obstruction to left ventricular outflow may occur at different levels. Examples include coarctation of the aorta, interrupted aortic arch, hypoplasia of the aortic arch, and valvar or subvalvar aortic stenosis. In extreme cases, the entire left sided structures may be exceedingly small (hypoplastic left heart syndrome). Severity of obstruction to flow from the left ventricle is variable and can range from mild (coarctation with minimal obstruction) to severe (hypoplastic left heart syndrome where the minute left ventricle is ill equipped to support the systemic circulation) (Fig. 16.15).

Coarctation of the aorta refers to narrowing of the aorta, usually discrete, and in the juxtaductal region (Fig. 16.16).

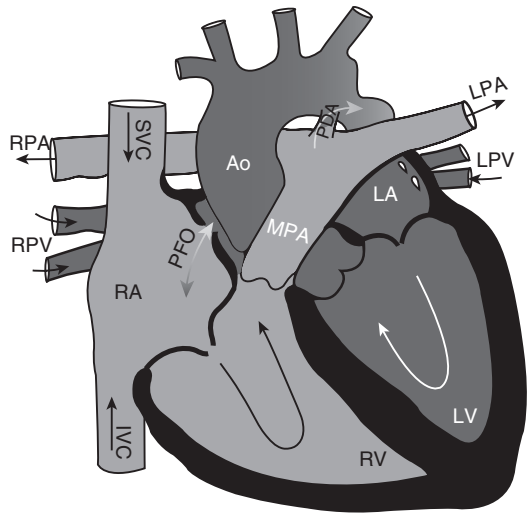


**Fig. 16.16** Cartoon depicting juxtaductal coarctation of the aorta. Arrows depict direction of blood flow. *Ao,* Aorta; *IVC,* inferior vena cava; *LA,* left atrium; *LPA,* left pulmonary artery; *LPV,* left pulmonary veins; *LV,* left ventricle; *MPA,* main pulmonary artery; *PDA,* patent ductus arteriosus; *PFO,* patent foramen ovale; *RA,* right atrium; *RPA,* right pulmonary artery; *RPV,* right pulmonary veins; *RV,* right ventricle; *SVC,* superior vena cava.

## CASE 6 (CONTINUED)

Femoral artery pulses are difficult to appreciate, whereas both brachial artery pulses are felt easily. You ask that noninvasive blood pressure be measured in all four extremities: right arm 78/50 mm Hg, left arm 66/40 mm Hg. After several failed attempts, blood pressure on the lower extremities is obtained: right leg 30/22 mm Hg, left leg 34/22 mm Hg. Pulse oximetry reading from sensor on the right hand is 98%; a similar sensor on the foot shows a poor tracing.

### Exercise 14

#### Question

Of the following, the most likely diagnosis is:

A. Juxtaductal coarctation of the aorta
B. Hypoplastic left heart syndrome
C. Aortic valve stenosis
D. None of the above

#### Answer

A.

As described previously, obstruction to left ventricular outflow can occur at different levels. When such an obstruction is suspected, clinical evaluation and vital sign measurements may offer clues to the level of obstruction (Table 16.2). A good starting point is to palpate femoral pulses. It is generally difficult to feel femoral pulses easily in newborn infants unless hips are abducted. In this optimal position, one should be able to easily palpate femoral artery pulses. If there is difficulty in feeling both femoral pulses, comparison should be made with brachial artery pulses. If brachial artery pulses are very strong and femoral pulses are poor, the level of aortic obstruction is below the level of the left subclavian artery (if the arch is leftward) or below the level of the right subclavian artery (if the arch is rightward). If the right brachial pulse is easily felt, but the left brachial and both femoral pulses are equally diminished, the arch is likely to be interrupted proximal to the origin of the left subclavian artery. Sometimes, in severe coarctation of the aorta, the adjacent subclavian artery also may be narrowed; hence the pulse on that arm may be difficult to appreciate or may be of lower amplitude than that of the contralateral arm. When both brachial and femoral pulses are diminished and the perfusion is poor, significant depression in cardiac performance is likely. The other possibility is the presence of an aberrant right subclavian artery arising distal to the obstruction. Feeling the carotid pulses may differentiate the two. When cardiac output is severely compromised, carotid pulses are also difficult to palpate. However, in coarctation of the aorta with an aberrant right subclavian artery, the carotid pulse amplitude will be very strong. Blood pressure measurement in the four extremities should show the same differences as that revealed by pulse strength. When obstruction is more proximal, e.g., aortic stenosis or hypoplastic left heart syndrome, there is no difference in pulse amplitude or blood pressure between the four extremities.

**TABLE 16.2 Level of Obstruction of Aortic Arch**

| Femoral Pulses | Right Brachial Pulse | Left Brachial Pulse | Possible Site of Obstruction |
|---|---|---|---|
| ++ | ++ | ++ | No obstruction |
| +/− | ++ | + | Juxtaductal coarctation of the aorta (left brachial pulse may be diminished due to narrowing extending into the left subclavian artery) |
| +/− | ++ | +/− | Interruption of the aortic arch proximal to the left subclavian artery (left brachial and femoral pulses are similar) |
| +/− | +/− | +/− | • Diminished left ventricular performance<br>• Aortic stenosis<br>• Hypoplastic left heart syndrome<br>• Aberrant origin of the right subclavian artery distal to the level of obstruction |

++, Normal pulse; +, palpable pulse but diminished; −, absent pulse.

### Exercise 15

#### Question

A pediatric cardiologist is not readily available. The emergency room physician requests your assistance in the management of this infant. The best option is to:

A. Start PGE-1 infusion right away before echocardiogram and arrival of pediatric cardiologist

B. Wait for pediatric cardiologist and echocardiogram to start PGE-1 infusion

### Answer

A.

PGE-1 must be started right away if critical left heart obstruction is suspected. It is not necessary to wait for a confirmatory echocardiogram if one cannot be obtained readily. Other therapeutic interventions such as volume resuscitation and inotropic therapy are rarely effective unless the ductus arteriosus is reopened and systemic blood flow is reestablished. PGE-1 is administered as a continuous infusion owing to its rapid metabolism. Low doses of PGE-1 (0.01 mcg/kg/min to 0.05 mcg/kg/min) are usually adequate to maintain patency of an open ductus arteriosus. A higher dose of PGE-1 (0.1–0.2 mcg/kg/min) may be effective in reopening a functionally closed ductus arteriosus. Once the ductus arteriosus is reopened, the dose of PGE-1 may be titrated to the lowest effective dose. PGE-1 induces several side effects, including apnea, hyperthermia, hypotension, and thrombocytopenia. These side effects are dose dependent and are usually encountered with higher doses of PGE-1.

## CONCLUSION

Congenital heart disease is the most common birth malformation. Despite the numerous forms, neonates with CHD present in limited ways: cyanosis, shock, and tachypnea. A careful history and physical examination guided by a systematic approach will help formulate a clinical diagnosis without much difficulty.

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