Evaluation and initial management of cyanotic heart disease in the newborn

INTRODUCTION — Cyanotic lesions comprise approximately one-third of potentially fatal forms of congenital heart disease (CHD) [1,2]. Early recognition, emergent stabilization, and transport to an appropriate cardiac care center are critically important in the outcome of newborns with these lesions.

Hypoxemia leading to cyanosis results from mechanisms including cardiac disorders, pulmonary abnormalities, and hemoglobinopathies (table 1) [3]. The usual presentations of the common forms of cyanotic CHD can be distinguished based upon the physical examination, chest radiography, and electrocardiography (table 2). Precise determination of cardiac anatomy and function is provided by echocardiography.

An approach to the evaluation and initial management of the newborn with suspected cyanotic heart disease is presented here. Cardiac causes of cyanosis in the newborn are discussed separately. (See "Cardiac causes of cyanosis in the newborn").

HISTORY — A thorough history may identify maternal medical conditions or prenatal disorders that increase the risk of CHD.

Family history — The risk for CHD increases if a parent or sibling has CHD, and triples if two close relatives are affected [4]. In a review of 393 children of women with CHD, the parental defect recurred in 4 percent of offspring [5]. If nonconcordant lesions are included, the risk of having a child with a cardiac anomaly may be as high as 10 percent [6]. In another report, the prevalence of CHD was greater in offspring of parents with than without CHD (3.1 versus 1.3 percent, adjusted OR 1.73) [7]. The risk to the offspring was greater if the mother rather than the father had congenital heart disease. Genetic testing is available for some forms of CHD and may identify families with recurrence risks up to 50 percent.
Prenatal testing — The results of any fetal ultrasounds performed during pregnancy are useful. Prenatal sonograms often identify structural malformations including CHD, diaphragmatic hernia, and congenital cystic adenomatoid malformation.

Perinatal history — Maternal history of premature rupture of membranes, fever, or the use of sedatives or anesthetics raises concern about sepsis or decreased respiratory effort. Gestational age, APGAR scores [calculator 1], or a history of meconium aspiration are useful to determine the likelihood of respiratory distress syndrome, perinatal asphyxia, persistent pulmonary hypertension of the newborn, or pneumonia.

Maternal diabetes is associated with transposition of the great arteries (TGA), ventricular septal defect, and hypertrophic cardiomyopathy [1]. Drugs taken in pregnancy may lead to cardiac defects. Examples include pulmonary or aortic stenosis in fetal hydantoin syndrome and Ebstein's anomaly and other cardiac defects with maternal lithium treatment [8,9]. (See "Infant of a diabetic mother").

PHYSICAL EXAMINATION — A thorough physical examination should be performed with particular attention to the cardiovascular and pulmonary systems, and the presence of any dysmorphic features. It should be noted whether cyanosis is peripheral or central. (See "Cardiac causes of cyanosis in the newborn", section on 'Definition'.)

Vital signs — The pulse, respiratory rate, oxygen saturation, and blood pressure (measured in the right arm and either leg) yield important information in a cyanotic infant.

- A blood pressure gradient between the arms and legs or weakened or absent femoral pulses suggests left ventricular dysfunction associated with severe coarctation of the aorta or interrupted aortic arch. However, if the ductus arteriosus is widely patent, no gradient may be detected between the arms and legs in this disorder.
- Severe respiratory distress manifested by tachypnea, retractions, and grunting usually indicates a respiratory problem. However, some structural heart diseases can present with similar symptoms. Examples of the latter include obstructed total anomalous pulmonary venous connection and left-sided obstructive disease (hypoplastic left heart, critical valvar aortic stenosis, severe coarctation of the aorta). Infants with cyanotic CHD commonly present with cyanosis with mild or absent tachypnea.
- Vital signs can be normal in some cyanotic infants with structural heart disease. They may also be normal in polycythemia, pulmonary arteriovenous malformation, or methemoglobinemia.
Peripheral cyanosis associated with tachycardia, tachypnea, and hypotension often suggests sepsis. However, it is also important to consider left-heart obstructive lesions such as hypoplastic left heart syndrome (HLHS), critical aortic stenosis, and severe coarctation of the aorta in the differential diagnosis.

**Second heart sound** — The second heard sound (S2) is normally split (aortic component before pulmonary component). Splitting is usually audible in 66 percent of infants at 16 hours of age and in 80 percent by 48 hours [1]. S2 is single on auscultation for many forms of cyanotic heart disease (table 2).

- In TGA, the pulmonary artery is located posterior and directly behind the aorta. Thus, the aortic component of S2 is loud because of its anterior location and the softer pulmonary component is often inaudible.
- Pulmonary atresia, truncus arteriosus, or hypoplastic left heart syndrome with aortic atresia have only a single semilunar valve so S2 has only one component.
- In tetralogy of Fallot (TOF), the diminished pulmonary valve excursion associated with pulmonary stenosis makes the pulmonary component of S2 soft and difficult to detect, especially with late peaking of the right ventricular outflow tract systolic murmur. (See "Pathophysiology; clinical features; and diagnosis of tetralogy of Fallot").

S2 is split in some patients with cyanotic CHD, such as total anomalous pulmonary venous connection or Ebstein's anomaly of the tricuspid valve.

**Murmur** — A murmur is audible in most common forms of cyanotic CHD (table 2). However, the most common form of transposition of the great arteries (TGA), d-transposition with intact ventricular septum and no pulmonary stenosis, typically has no murmur.

- Typical TOF has a murmur caused by pulmonary stenosis. TOF associated with pulmonary atresia often has a murmur associated with a patent ductus arteriosus or aortopulmonary collaterals that can be detected as pulmonary vascular resistance falls.
- In pulmonary atresia with intact ventricular septum, hypoplastic left heart syndrome, or truncus arteriosus, all the cardiac output crosses a single semilunar valve. This volume of blood flow is usually associated with a soft outflow systolic murmur. Some patients with truncus arteriosus also have a diastolic murmur of truncal valve regurgitation.
- Pulmonary atresia is often associated with tricuspid regurgitation. This produces a systolic murmur at the left lower sternal border.
Tricuspid atresia is usually associated with a ventricular septal defect and pulmonary stenosis, which create a systolic murmur.

The tricuspid valve in Ebstein’s anomaly is nearly always regurgitant and produces a systolic murmur at the left lower sternal border.

**Hepatomegaly** — Patients with heart failure due to left-sided obstructive lesions (eg, hypoplastic left heart, coarctation, critical aortic stenosis, cardiomyopathy) or infradiaphragmatic total anomalous pulmonary venous return often have hepatomegaly. A palpable liver in the midline suggests complex congenital heart disease (heterotaxy syndromes) associated with asplenia or polysplenia.

Some infants with pulmonary disease can appear to have hepatomegaly. This results from hyperinflation and inferior displacement of the liver produced by a flattened diaphragm.

**LABORATORY STUDIES** — Laboratory investigations should be performed to assist in the diagnosis of CHD and identify other causes of cyanosis.

**Complete blood count** — Newborns with cyanosis should have a complete blood count and differential analysis. An elevated hematocrit or hemoglobin concentration identifies patients with polycythemia. (See "Neonatal polycythemia"). An elevated or decreased white blood cell count or thrombocytopenia suggests possible sepsis.

**Sepsis evaluation** — A blood culture should be obtained to evaluate possible sepsis. Depending upon the level of clinical suspicion, a lumbar puncture should be performed, with analysis and culture of the cerebrospinal fluid. A urinalysis and urine culture are usually obtained.

**Chest radiograph** — A chest radiograph is essential to the diagnosis of cardiac and pulmonary disorders. Examination of the lung fields identifies major pulmonary causes of cyanosis including pneumothorax, pulmonary hypoplasia, diaphragmatic hernia, pulmonary edema, pleural effusion, or airway disease.

Three features of the chest radiograph are important in the evaluation of CHD: heart size or shape, pulmonary vascular markings, and situs of the aortic arch.

**Heart size or shape** — Patients with left-sided obstructive lesions may have cardiomegaly due to heart failure. Extreme cardiomegaly suggests lesions associated with a dilated right atrium since this chamber is very compliant. These include pulmonary atresia with intact ventricular septum or Ebstein’s anomaly.

Characteristic abnormalities of heart shape are associated with specific lesions. Examples are the boot-shaped (coeur en sabot) contour of TOF and the egg-on-a-string pattern of d-TGA. The latter is caused by a narrow mediastinal shadow
produced by the anterior-posterior rather than right-left relationship of the great arteries.

**Pulmonary vascular markings** — The pattern of pulmonary blood flow depends upon the specific cardiac lesion. Pulmonary vascular markings are decreased in most cyanotic CHD. However, they are increased in patients with truncus arteriosus or mixing lesions such as common atrioventricular canal (CAVC) as pulmonary vascular resistance falls.

The pattern of vascular markings in d-transposition of the great arteries can vary. In this condition, the right pulmonary artery branches from the main pulmonary artery along the long-axis of the left ventricle while the left pulmonary artery branches acutely. This anatomy often promotes preferential flow to the right lung. This asymmetric blood flow results in reduced markings in the left lung.

Pulmonary venous congestion due to heart failure is characterized by indistinct vascular markings spreading in a butterfly distribution from the central region of the chest. This is often seen in obstructed total anomalous pulmonary venous connection or left-sided obstructive lesions (hypoplastic left heart syndrome, coarctation, cardiomyopathy).

**Situs of aortic arch** — The situs of the aortic arch is defined by which of the mainstem bronchi the arch crosses. This is best determined by noting which side of the trachea is indented on the anteroposterior image; the indentation indicates on which side the aortic arch is coursing (picture 1). The normal anatomy is a left-sided aortic arch with indentation of the left side of the trachea as the arch crosses over the left mainstem bronchus.

A right aortic arch results in an indentation on the right side of the trachea. Approximately 20 percent of patients with TOF [10] and 30 percent with truncus arteriosus [11] have a right aortic arch. However, because TOF is much more common than truncus arteriosus, a right aortic arch in a cyanotic infant usually suggests TOF. A right aortic arch may also be associated with other lesions, such as TGA.

**Electrocardiogram** — In the fetus, the right ventricle has a larger volume load than the left ventricle since there is limited pulmonary flow and thus reduced blood volume in the left heart. As a result, the normal neonatal electrocardiogram (ECG) has right axis deviation (QRS axis +90 to +180 degrees) and a precordial pattern of right ventricular hypertrophy. In many cyanotic heart lesions, the ECG is normal in the neonatal period. However, some patterns are associated with specific diagnoses (table 2). The most common patterns include the following conditions.
Lesions associated with a small right ventricle have left axis deviation for age (for pulmonary atresia intact ventricular septum typically +30 to +90, and for tricuspid atresia typically −30 to −90 degrees), right atrial enlargement (tall peaked P wave usually most easily identified in lead II), and left ventricular hypertrophy.

- Hypoplastic left heart syndrome often has marked right ventricular hypertrophy and decreased left ventricular forces in the lateral precordial leads.
- Ebstein's anomaly has right atrial enlargement and occasionally a delta wave of Wolff-Parkinson-White syndrome.

**Oxygen saturation** — Transcutaneous oxygen saturation should be measured from preductal (right hand) and postductal sites (right or left foot). Oxygen saturation values are reduced with central cyanosis and usually normal with peripheral cyanosis. A difference in values at the two sites identifies patients with differential cyanosis. In patients with a right aortic arch, the preductal saturation should be measured in the left hand.

**Arterial blood gas** — A blood gas measurement on an arterial sample should be obtained in any newborn with cyanosis.

- An arterial PO2 value provides more specific data than oxygen saturation. Because of the increased affinity of fetal hemoglobin for oxygen, PO2 values at a given level of oxygen saturation are often lower in newborns than adults.
- An elevated arterial PCO2 value often indicates the presence of pulmonary disease. PCO2 may also be increased in heart failure.
- A reduced pH level raises concern about poor cardiac output. The combination of severe hypoxemia, metabolic acidosis, and marked hypercarbia may occur in patients with d-transposition of the great arteries when there is inadequate mixing at the levels of the atria, ventricles, and great vessels.
- Patients with methemoglobinemia typically have low oxygen saturation and normal oxygen tension. In this uncommon condition, the blood has a chocolate-brown color and does not become red when exposed to air (picture 2).

**Hyperoxia test** — The hyperoxia test is useful in distinguishing cardiac from pulmonary causes of cyanosis. In CHD associated with intracardiac right-to-left shunting, blood in the pulmonary veins is fully saturated with oxygen in ambient air. Administering higher concentrations of inspired oxygen increases the amount of dissolved oxygen but has minimal effect on oxygen tension levels. In contrast, patients with pulmonary disease have pulmonary venous desaturation. Supplemental oxygen administration in pulmonary disease typically increases pulmonary venous oxygen levels and improves systemic oxygenation.
In the hyperoxia test, arterial oxygen tension is measured in the right radial artery (preductal) while the patient breathes 100 percent oxygen concentration for 10 minutes. Oxygen can be administered via an oxyhood or an endotracheal tube if the patient is already intubated.

A transcutaneous oxygen monitor can be used to assess whether arterial oxygen tension rises in response to the increased inspired oxygen concentration, thereby avoiding arterial puncture for blood sampling. However, an abnormal or equivocal response must be verified by measurement of an arterial blood gas. (See "Oxygen monitoring and therapy in the newborn".)

**Interpretation** — The preductal oxygen tension while breathing 100 percent oxygen concentration rarely exceeds 150 mmHg in cyanotic heart disease, and usually exceeds this value in pulmonary disease ([table 3](#)) [12]. However, some patients with severe lung disease may have only minimal improvement with supplemental oxygen. In these cases, the chest radiograph or arterial PCO2 aid in establishing the underlying disorder ([table 3](#)).

The level of PaO2 in 100 percent oxygen helps to distinguish among the types of cyanotic heart disease ([table 4](#)). Patients with lesions such as TGA or severe pulmonary outflow obstruction typically have PaO2 <50 to 60 mmHg during hyperoxia.

It is important to recognize that systemic oxygen tension can sometimes increase with supplemental oxygen in patients with cyanotic heart disease. One situation in which this occurs is with mixing lesions that involve both right-to-left and left-to-right shunting, such as truncus arteriosus or single ventricle with patent ductus arteriosus. In this case, supplemental oxygen may decrease pulmonary vascular resistance, thereby increasing pulmonary flow. The increased flow mixed with a fixed amount of systemic venous return results in increased aortic oxygenation, typically to PaO2 values of 75 to 150 mmHg, but rarely higher [12]. In these patients, the chest radiograph typically demonstrates cardiomegaly and prominent pulmonary vascularity.

Increased oxygenation with supplemental oxygen is also seen when pulmonary disease, such as pulmonary edema or pneumonia, is associated with cyanotic CHD. However, the PO2 rarely exceeds 150 mmHg.

A pulse oximeter should not be used for the hyperoxia test because it may not detect an inadequate increase in oxygen tension. Because of the characteristics of the oxygen dissociation curve, normal hemoglobin is fully saturated with oxygen when the arterial PO2 exceeds 70 mmHg ([figure 1](#)). Therefore, a patient receiving 100 percent inspired oxygen concentration could have an oxygen saturation of nearly 100 percent associated with an arterial PO2 of 75, a value that is abnormal. Thus, discrimination between cardiac mixing lesions and pulmonary
disease may be limited. However, pulse oximetry may be helpful if saturation remains less than 93 to 95 percent.

**Echocardiography** — Echocardiography should be performed in any newborn with central cyanosis who has failed a hyperoxia text or has an equivocal result. Other indications for echocardiography include blood pressure or pulse differential between upper and lower extremities, cardiomegaly with murmur or cyanosis, or severe cardiomegaly. Echocardiography, including imaging and pulsed and color Doppler interrogation of flow patterns, provides a definitive determination of cardiac anatomy and function.

**INITIAL MANAGEMENT** — Newborns with cyanosis require immediate assessment and specific therapy for an underlying cause if known. However, until a specific diagnosis is made, empiric treatment is begun.

**General approach** — The initial approach includes cardiorespiratory support and monitoring. If there is respiratory compromise, an adequate airway should be established immediately and supportive therapy (e.g., oxygen, mechanical ventilation) instituted as needed. Patients with hypotension or poor perfusion require cardiopulmonary resuscitation.

Vital signs should be monitored and vascular access established for sampling of blood and administration of medications. Placement of secure intravenous and intraarterial catheters is most easily accomplished via the umbilical vessels. This will enable efficient correction and monitoring of acid-base balance, metabolic derangements (e.g., hypoglycemia, hypocalcemia), and blood pressure. Inotropic agents such as dopamine or dobutamine may be necessary to correct hypotension.

In infants with severe polycythemia (>70 percent), an isovolumetric partial exchange transfusion should be performed with saline to reduce the hematocrit. (See "Neonatal polycythemia"). If cyanosis is due to acquired methemoglobinemia, the offending agent is removed. In severe cases, methylene blue, 1 percent solution, in a dose of 1 to 2 mg/kg (0.1-0.2 mL/kg of a 1 percent solution) is infused intravenously over five to 10 minutes. The dose can be repeated in one hour if needed. Congenital methemoglobinemia does not respond to methylene blue.

**Antibiotics** — Sepsis can lead to cyanosis and left ventricular dysfunction or pulmonary disease. As a result, unless another specific etiology is promptly identified, broad spectrum antibiotics should be initiated (ampicillin and gentamicin) after obtaining a complete blood count, urinalysis, and blood and urine cultures.
**Prostaglandin E1** — An infant who fails the hyperoxia test and does not have persistent pulmonary hypertension of the newborn or a chest radiograph consistent with lung disease is likely to have a congenital heart defect that is dependent upon the ductus arteriosus for pulmonary or systemic blood flow. If metabolic acidosis is present or if timely echocardiography is not available, prostaglandin E1 should be administered until a definitive diagnosis is established. This is usually started as an intravenous infusion in a dose of 0.05 µg/kg per minute.

Complications of prostaglandin E1 infusion include hypotension, tachycardia, and apnea [13]. As a result, a separate reliable intravenous catheter must be in place to provide fluids for resuscitation. Intubation equipment should be immediately available because apnea can occur at any time during infusion.

If transfer to another medical facility is needed, intubation and ventilation are usually initiated prior to transport [14]. Although an Australian report suggested that transported infants with suspected CHD who receive low-dose of prostaglandin E1 (less than 0.015 µg/kg/min) may not require mechanical ventilation, significant limitations of the study (ie, retrospective nature of the study and the non-systematic use of mechanical ventilation and prostaglandin E1) dictate caution in general application of these results [15]. Until controlled trials are performed, we continue to intubate and ventilate all infants prior to transport if they are receiving prostaglandin E1.

Deterioration of the clinical status after starting prostaglandin E1 usually indicates the presence of rare congenital cardiac defects associated with pulmonary venous or left atrial obstruction. These include obstructive (usually infradiaphragmatic) total anomalous pulmonary venous connection or various conditions associated with a restrictive atrial septum (eg, hypoplastic left heart syndrome, cor triatriatum, severe mitral stenosis or mitral atresia, or TGA). These patients require urgent echocardiography followed by interventional cardiac catheterization or surgery [14].

**Cardiac catheterization** — Some conditions can be corrected by interventional cardiac catheterization. Balloon atrial septostomy can relieve marked cyanosis in patients with TGA associated with restrictive atrial shunting. This procedure is also effective in patients with a restrictive atrial septum associated with left-sided obstructive disease.

Balloon valvuloplasty can be effective in patients with critical pulmonary stenosis or aortic stenosis. Selected patients with pulmonary atresia are also candidates for balloon valvuloplasty if the obstruction is membranous, if tricuspid annulus and right ventricular sizes are adequate to support a two ventricle repair, and if the coronary circulation does not depend upon the right ventricle [16].
Transcatheter occlusion of pulmonary arteriovenous malformations can also be accomplished [17].

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