The Critically Ill Infant with Congenital Heart Disease

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KEYWORDS

- Congenital heart disease • Cyanotic cardiac disease • Pediatric cardiology
- Critically ill neonate • Decompensated neonate

KEY POINTS

- Neonates presenting with acute and profound systemic hypoperfusion or cyanosis have a ductal-dependent cardiac lesion until proven otherwise.
- Ductal-dependent lesions typically present within the first 2 weeks of life, whereas shunting lesions with heart failure present within 1 to 6 months of life.
- Prostaglandin E1 is a life-saving medication. Be wary of its adverse effects of apnea and hypotension.
- Essential elements in the evaluation of a critically ill infant with congenital cardiac disease include (1) right upper and lower extremity blood pressure, (2) pulse oximetry, (3) brachial–femoral pulse differential, (4) electrocardiography, (5) chest radiography, (6) brain natriuretic peptide, and (7) bedside echocardiogram.

INTRODUCTION

Critically ill infants presenting to the emergency department (ED) inherently produce anxiety for emergency physicians (EPs). They often have nonspecific or subtle findings, making timely accurate diagnosis and implementation of life-saving interventions fraught with difficulty. The differential diagnosis for an ill neonate is best remembered by the mnemonic THE MISFITS (Box 1).[1] Children with congenital cardiac disease are especially challenging to diagnose and manage because of their complex physiology

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Box 1
THE MISFITS

- *T*rauma (accidental and nonaccidental)
- *H*eart disease and hypovolemia
- *E*ndocrine (congenital adrenal hyperplasia and thyrotoxicosis)
- *M*etabolic (hypocalcemia, hypoglycemia, etc)
- *I*nborn errors of metabolism
- *S*epsis
- *F*ormula dilution
- *I*ntestinal catastrophes (necrotizing enterocolitis, volvulus, intussusception)
- *T*oxins
- *S*eizures

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and age-dependent variability. This article discusses the tools necessary for the identification and initial ED management of the infant with undifferentiated decompensated congenital heart disease (CHD).

Critical congenital cardiac lesions can be classified into 3 broad categories based on physiology: left-sided obstructive ductal dependent, right-sided obstructive ductal dependent, and shunting or mixing lesions. As with all pediatric cases, physiology is age dependent, so the child's age at presentation is among the most important variables to consider. Infants who present early—in the first month of life—most likely have a ductal-dependent lesion. They might be cyanotic from an obstructive right heart lesion or, more commonly, profoundly hypoperfused from an obstructive left heart lesion. After 1 month of age, infants most likely present in respiratory distress or congestive heart failure caused by a left-to-right shunt.[2] A rapid compilation of data obtained from the history and physical examination, focusing on essential elements (**Box 2**), can provide clues to the presence and physiology of the cardiac lesion. Subsequent interventions, such as use of supplemental oxygen, initiation of prostaglandin E1 (PGE1), or administration of fluid boluses can then be tailored to fit the patient's unique physiology.

Box 2
Toolkit for identification of a congenital cardiac disease

- Hyperoxia test
- Weight gain, murmur, hepatomegaly, brachial–femoral pulse differential
- Right upper and lower extremity blood pressure differential of greater than 10 mm Hg
- Pulse oximetry differential of greater than 3%, or less than 94% in lower extremity, or less than 90% in any extremity
- Electrocardiography (ECG)
- Chest radiography (CXR)
- Brain natriuretic peptide (BNP)
- Bedside limited echocardiography by the emergency physician (BLEEP)

Epidemiology

The true incidence of CHD is difficult to determine because of the variability in its definition. Some studies have broadly included physiologically trivial atrial septal defects (ASDs) and ventricular septal defects (VSDs); others have specifically defined critical CHD (CCHD). A CCHD lesion is defined as one that requires surgical repair or intervention to prevent significant morbidity and mortality within the first year of life. In the United States and the United Kingdom, it is estimated that 6 in 1000 live-born infants have a serious congenital heart defect.[3–6] A more recent review, with clear definition of CCHD, by The Tennessee Task Force on Screening Newborn Infants for Critical Congenital Heart Disease, estimated the incidence of CCHD to be approximately 1.7 in 1000 live births.[7] Among those, nearly 1 infant in 1000 was discharged home from the nursery with a missed critical left heart obstructive lesion.[7]

Screening

Overreliance on the newborn screening examination to rule out CCHD is commonplace. At 1 pediatric cardiology referral center, 8% of all neonates admitted for CHD were diagnosed after discharge from the hospital.[8] The most common lesions presenting after discharge are left obstructive lesions, which include coarctation of the aorta, interruption of the aortic arch, aortic valve stenosis, total anomalous pulmonary venous return (TAPVR), and hypoplastic left heart syndrome (HLHS).[6,8] A study of missed congenital cardiac lesions found that more than one-half of infants with a missed diagnosis of CCHD died at home or in the ED. Their median age at death was 13.5 days, and the most common delayed diagnoses were HLHS and coarctation of the aorta.[9]

The use of fetal echocardiography to detect cardiac lesions in the prenatal period has certainly lowered morbidity and mortality rates, but fetal ultrasonography still has limitations. Chew and colleagues[10] found that CCHD was diagnosed before birth in only about one-fourth of their study population.

Unfortunately, the screening physical examination in the newborn nursery is inadequate to detect many critical congenital heart defects. There are even fewer opportunities to diagnose CCHD in the newborn nursery, because infants are being discharged earlier than in the past. It is estimated that 8% to 44% of infants with CCHD are being discharged undiagnosed.[2,4,5,8,11–14] In the patient series studied by Wren and colleagues,[6] only 50% of infants with CHD had an abnormal nursery examination finding (usually a murmur) and 65% had abnormal findings during the 6-week examination. Left obstructive lesions are even less likely to be detected during the nursery physical examination. Fewer than one-third of 108 neonatal examinations of children with left-obstructive lesions were abnormal over a 4-year period.[5] Undiagnosed children with CCHD frequently present to nontertiary EDs for initial management before transfer for subspecialist care.[15] It is therefore critical for all EPs to be prepared to recognize and manage undiagnosed congenital cardiac lesions in the critically ill infant.

In 2009, the American Heart Association and the American Academy of Pediatrics published a joint statement noting the potential for pulse oximetry to improve clinicians' ability to identify CCHD before discharge from the nursery.[16,17] Since 2011, many states have adopted legislation calling for mandatory pulse oximetry screening of all newborns before discharge. Screening entails obtaining a pulse oximetry measurement (saturation of peripheral oxygen [SpO_2]) from the preductal right upper extremity (RUE) and either postductal lower extremity (LE; **Box 3**). Normal newborns have a median SpO_2 of 98% after 24 hours of life. A positive screen is indicated by

> **Box 3**
> **CCHD screening pulse oximetry**
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> - SpO_2 of less than 90% RUE or either LE → echocardiography
> - SpO_2 of 94% or less RUE and either LE → echocardiography
> - SpO_2 difference of greater than 3% between RUE and LE → echocardiography
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> *Abbreviations:* LE, lower extremity; RUE, right upper extremity; SpO_2, saturation of peripheral oxygen.

a RUE or LE SpO_2 of less than 90%, both preductal and postductal SpO_2 of 94% or less, or a difference of greater than 3% between the preductal and postductal SpO_2 (see **Box 3**). Any patient with a positive screen is either referred for echocardiogram before discharge or scheduled for a diagnostic follow-up with the local pediatric cardiology referral center. The ability of this CCHD pulse oximetry screening protocol to lower the false-positive rate was demonstrated by Granelli and colleagues,[18] who documented a rate of 0.17% compared with 1.9% achieved with physical examination alone. The CCHDs targeted in the pulse oximetry screening are HLHS, pulmonary atresia, tetralogy of Fallot, TAPVR, transposition of the great arteries (TGA), tricuspid atresia, and truncus arteriosus. The timing of the screen allows assessment for HLHS, but not for other left-obstructive lesions such as coarctation of the aorta. Interestingly, many patients with false-positive pulse oximetry screens have an urgent disease process, such as persistent pulmonary hypertension.[19]

Cyanosis

Cyanosis becomes apparent when the oxygen saturation drops below 80% or the concentration of deoxygenated hemoglobin is 5 g/dL or greater. Central cyanosis involves the lips, tongue, and mucous membranes, as opposed to acrocyanosis, which affects the hands, feet, and circumoral region. Acrocyanosis is caused typically by cool ambient temperatures, gastroesophageal reflux, sepsis, and tracheoesophageal fistula. It is important to examine infants in a well-lit room to assess for appearance and cyanosis.

The presentation of cyanotic CHD can be very similar to that of persistent pulmonary hypertension. Supplemental oxygenation with the "hyperoxia test" (discussed elsewhere in this article) fails to improve cyanosis in either condition. It is often difficult to recognize mild to moderate cyanosis, especially in infants with dark skin; therefore, a "pink" infant should not be reassuring. Pulse oximetry is an important vital sign for every neonate, because color change might not be evident on examination. Confounding the picture, the nadir of physiologic anemia of infancy typically occurs at 3 months of age in a term infant and sooner, at 4 to 6 weeks, for a preterm infant.[20] The timing of physiologic nadir coincides with the transition of shunting from right to left at birth, which progresses to left to right by 3 months of age as right ventricular compliance increases and pulmonary vascular resistance (PVR) decreases.[21] Differential cyanosis (ie, cyanosis of the lower extremities without accompanying cyanosis of the upper body) raises concern for persistent pulmonary hypertension of the newborn with right-to-left shunt, interrupted aortic arch, and coarctation of the aorta. In patients with these conditions, desaturated blood from the patent ductus arteriosus (PDA) supplies the postductal descending aorta and lower extremities and oxygenated blood from the preductal aortic arch supplies the upper extremities, creating a differential cyanosis. Reverse differential cyanosis is unique and requires a

dextro-TGA (d-TGA) in combination with a PDA and severe coarctation of the aorta or interrupted aortic arch.[21] The upper extremities are supplied by deoxygenated blood from the transposed aortic arch. The lower extremities are supplied by oxygenated blood from the pulmonary artery shunting left to right distal to the coarctation through the PDA.

Cyanosis is part of the presentation of the following imminent emergencies: shock, cyanotic CHD, persistent pulmonary hypertension, and methemoglobinemia. Cyanotic CHD can be divided into right-sided obstructive ductal-dependent lesions, right outflow tract obstruction that diminishes blood flow to the pulmonary arteries, and mixing lesions (Fig. 1). Many children present to the ED without a known diagnosis of congenital cardiac disease, so management should be guided by considering the underlying physiology, as described elsewhere in this article.

Presentation

The diagnosis of CCHD might be missed during the birth hospitalization; therefore, clinicians should be aware of its clinical manifestations during the first week of life. Although there is no single test or historical feature that serves to differentiate CHD from other conditions in the differential for the ill-appearing infant, a compilation of red flags should alert the EP to the possibility of its presence. Few studies have examined the signs and symptoms that prompt parents to bring their children to the ED. Symptoms classically associated with CHD include irritability, sweating, and crying with feeding.[22] Other parental concerns include poor weight gain, cyanosis, respiratory difficulties, and decreased activity. The history alone is usually inadequate to differentiate between an inborn error of metabolism, sepsis, and a congenital cardiac lesion. The most sensitive and specific findings for serious congestive heart failure in infants is a history of less than 3 ounces of formula per feed or more than 40 minutes per breast feed, respiratory rate higher than 60 breaths per minute or irregular breathing, and the liver edge located more than 2.5 cm below the right costal margin.[23] Older children have symptoms similar to those of adults with congestive heart failure: dyspnea on exertion, exercise intolerance, syncope, facial or abdominal swelling, and abdominal pain. In addition to a thorough history of the chief complaint, a thorough family history must be obtained, because 20% of critical congenital cardiac defects have a genetic component.

In various studies, the common presenting signs documented as leading to the diagnosis of CHD are the presence of a murmur, cyanosis, respiratory distress, heart failure, and shock.[2,8,15] Two studies retrospectively examined pediatric ED presentations leading to a diagnosis of CHD.[2,8,15] A study from a US pediatric cardiology referral center found 8 new diagnoses of CHD among children admitted with decompensated CHD over a 5-year period.[2] Five children presented to the ED with pulmonary edema and 2 with cyanosis and circulatory collapse. Left obstructive lesions have the highest postdischarge mortality rate, and almost all infants with these lesions present by 3 weeks of age, the majority of them (68%) presenting with heart failure.[5]

DIAGNOSIS

The challenge for the EP is early identification of children with the potential for rapid decompensation. First and foremost, a neonate in distress should be presumed septic. Empiric antibiotics for sepsis should be initiated as soon as possible for every critically ill infant. Cefotaxime and ampicillin are recommended in neonates. For infants more than 1 month old, ceftriaxone and vancomycin can be used to cover for meningitis.[24] However, in the setting of cyanosis or hypotension, CCHD should also be

Pink Baby	Blue Baby	Blue Baby	Grey Baby
1-6 months	1-6 months	<2 weeks	<2 weeks
Too much pulmonary blood flow Qp>Qs	Obstruction of pulmonary blood return	Too little pulmonary blood flow Qp<Qs	Poor perfusion and oxygenation
Heart failure	Cyanosis + heart failure	Cyanosis	Circulatory collapse
Left-to-right shunt	Mixing right-to-left shunt	Right obstructive lesion	Left obstructive lesion
Toolkit clues: • CXR white lungs • Hepatomegaly • Murmur • BNP > 100 pg/mL • BLEEP: possible interventricular defect • ECG possible extreme superior axis or AV block	Toolkit clues: • Fail hyperoxia test • CXR white lungs • BNP >40-100 pg/mL • SpO$_2$ <80% • Hepatomegaly	Toolkit Clues: • Fail hyperoxia test • CXR black lungs • SpO$_2$ < 80% • ECG RVH	Toolkit clues: • CXR white lungs • Differential SpO$_2$ > 3%, BP > 10 mm Hg, pulse RUE vs RLE • Delayed capillary refill time • ECG LVH in >7 days of life, RVH in newborn • BLEEP possible single ventricle
Treatment goals: • Increase PVR (decrease oxygen) • Decrease SVR • Increase Qs • Increase inotropy • Diuretics	Treatment goals: • Diuretics • Do not increase pulmonary blood flow • Restrict IV fluids • Increase right-to-left shunting and inotropy (milrinone)	Treatment goals: • Shunt left-to-right across ductus arteriosus (PGE) • Decrease PVR (add oxygen or iNO) • Increase Qp	Treatment goals: • Shunt right-to-left across ductus arteriosus (PGE) • Afterload reduction • Volume support • Minimize oxygen consumption • Initiate early antibiotics • May need pressors
Lesions: • PDA • VSD • AVM • AV canal defect	Lesions: • TAPVR • Truncus arteriosus • Double outlet right ventricle • d-TGA with a VSD (or PDA)	Lesions: • Tricuspid atresia • Pulmonary atresia • Pulmonary stenosis • Ebstein anomaly	Lesions: • Hypoplastic left heart syndrome • Coarctation of the aorta • Interrupted aortic arch • Aortic stenosis or atresia
		Exception: • d-TGA without a VSD • Tetralogy of Fallot	Exception: • Anomalous Left Coronary Artery from the Pulmonary Artery

Fig. 1. Diagnosis and management of the infant with undifferentiated critical congenital heart disease. [a] Goal oxygen saturations of greater than 80% are adequate for initial resuscitation, however Qp:Qs balance is obtained at different oxygen saturations for each critical congenital heart disease. Monitor resuscitation based on both the perfusion and respiratory examination. AV, atrioventricular; AVM, arteriovenous malformation; BLEEP, bedside limited echocardiography by the emergency physician; BNP, brain natriuretic peptide; CXR, chest x-ray; d-TGA, dextrotransposition of the great arteries; ECG, electrocardiograph; iNO, inhaled nitric oxide; PDA, patent ductus arteriosus; PGE, prostaglandin E; Qp, pulmonary blood flow; Qs, systemic blood flow; RLE, right lower extremity; RUE, right upper extremity; RVH, right ventricular hypertrophy; SVR, systemic vascular resistance; TAPVR, total anomalous pulmonary venous return; VSD, ventricular septal defect.

considered. Infants presenting at a younger age most likely have a ductal-dependent lesion; shunting lesions are more common during later infancy.[5,22] Several essential tests can aid in narrowing the differential diagnosis.

Hyperoxia Test

When a critically ill infant presents with cyanosis or respiratory distress, the "hyperoxia test" can be attempted to determine whether the symptoms are a result of a problem with the pulmonary or systemic circulation. The test is performed by measuring the infant's arterial blood gas while breathing room air, then remeasuring the arterial blood gas after providing 100% oxygen for 10 minutes. If the cause of the cyanosis is a primary pulmonary deficiency, then administration of 100% oxygen will augment the lungs' ability to saturate the blood with oxygen, and the partial pressure of oxygen in the arterial blood should increase to above 150 mm Hg. However, if the lungs are oxygenating fully, supplemental oxygen will have no significant effect, and the partial pressure of oxygen will usually remain below 100 mm Hg. In this circumstance, the cyanosis is most likely owing to a shunting lesion that bypasses the lung, such as a congenital heart lesion. Because of the difficulty in obtaining 1 arterial blood gas measurement, let alone 2, in a critically ill neonate, pulse oximetry can be used instead.[18] One should be wary of the pitfall that pulse oximetry is less accurate for saturations of less than 80%. Caution should be emphasized, because 100% oxygen is a pulmonary vasodilator and could worsen respiratory distress in a patient with ductal-dependent lesions by decreasing PVR and increasing pulmonary blood flow, leading to pulmonary overcirculation.

Physical Examination

Although the physical examination alone does not rule out cardiac disease, it can be helpful in the diagnosis or management of CHD. The routine examination should assess for cardiac murmur, tachypnea, adequate weight gain, presence and quality of LE pulses, capillary refill time, hepatomegaly, and lack of fever.

Vital signs should include preductal and postductal blood pressure and pulse oximetry measurements, respiratory rate, temperature, and weight. Tachypnea is commonly observed in infants with CCHD. An afebrile infant with respiratory distress should raise suspicion for CHD rather than infectious or primary pulmonary pathology. Poor weight gain (<30 g/d) or failure to regain birth weight by 2 weeks might be indicative of a progressively worsening process rather than an acute respiratory illness. Abnormally diminished or absent femoral pulses compared with brachial pulses could be indicative of aortic narrowing. Poor perfusion, evidenced by prolonged capillary refill time or peripheral pulses deficits, signifies profound hemodynamic collapse consistent with a left obstructive ductal-dependent lesion. In 1 study that involved almost 40,000 patients, the addition of pulse oximetry screening to the physical examination detected all cases of ductal-dependent lesions.[18] The term *preductal* refers to the RUE, because most ductus arteriosus attachments are distal to the subclavian artery. The term *postductal* refers to the right or the left LE. Any value less than 90% requires further investigation in a healthy neonate. A pulse oximetry differential of greater than 3% should raise concern because it might indicate a left obstructive lesion (see **Box 3**).[16–18] Ing and colleagues[25] observed that a murmur combined with a systolic blood pressure gradient of greater than 10 mm Hg between the arms and legs was the most consistent clinical finding in 50 patients with known coarctation of the aorta.

It is challenging to distinguish between pathologic murmurs caused by cardiac lesions and "innocent" physiologic murmurs. Six cardinal signs make a murmur more likely to be pathologic: pansystolic murmur, murmur intensity of 3/6 or greater grade

intensity, point of maximal intensity at the upper left sternal border, harsh quality of the murmur, early midsystolic click, and abnormal second heart sound[26] (**Box 4**). In a series of 201 neonates without dysmorphic features or previous cardiology evaluation, the pediatric cardiologists to whom they were referred found murmur characteristic (harsh quality, location, and cardiac cycle timing) to be the most significant indication of a pathologic condition. Fifty-six percent of the study group had CHD. The pediatric cardiologists had a sensitivity of 81% and specificity of 91% for determining if the murmur was pathologic; those percentages were not changed by the addition of an electrocardiogram (ECG).[27] Farrer and Rennie[28] asked pediatric house officers to differentiate innocent from clinically significant murmurs in 112 neonates. They were accurate 76% of the time. Six percent of the murmurs they deemed innocent had echocardiographic evidence of structural heart disease.

In the ED, the lack of an audible murmur should not exclude CCHD. Similarly, the presence of a murmur does not mean a congenital cardiac lesion is present. Echocardiographic screening should be reserved for patients with a murmur. In a study of murmurs detected in newborns, which excluded children requiring neonatal intensive care or with risk factors for CHD, Lardhi[29] found that 43% had a structural defect, with ASD being the most common. When in doubt about a murmur, refer the patient to a cardiologist and prevent diagnostic delay.

Electrocardiography

An ECG can give valuable information regarding anatomy.[30–32] Similar to physiology, the ECG is also age dependent. Specific electrocardiographic abnormalities can be used to identify structural abnormalities, with special attention to axis deviation, atrioventricular (AV) prolongation, and atrial or ventricular enlargement. Intervals, axis, and criteria for ventricular hypertrophy are age dependent.[33,34] Although CHD physiology often results in electrical abnormalities, it is important to understand that a normal ECG does not rule out structural heart disease.

As the neonate transitions into infancy, the axis shifts from rightward to the normal adult leftward axis during the first 6 months of life. An extreme superior axis $-90°$ to $-180°$ suggests an AV canal defect or ostium primum ASD.[30] Right axis deviation suggests strong rightward forces, as noted in single ventricle physiology lacking leftward forces (eg, HLHS) and right outflow tract obstructive lesions causing right ventricular hypertrophy (RVH; eg, tricuspid atresia, pulmonary atresia, pulmonary stenosis, tetralogy of Fallot, and Ebstein's anomaly). Similarly, an AV block suggests either an AV canal defect or postoperative repair.

Box 4
Murmur characteristics that warrant echocardiography

- Pansystolic, continuous, diastolic

- Grade of 3/6 or greater murmur

- Point of maximal intensity at left upper sternal border

- Harsh quality

- Early midsystolic click

- Abnormal second heart sound

Data from McCrindle BW, Shaffer KM, Kan JS, et al. Cardinal clinical signs in the differentiation of heart murmurs in children. Arch Pediatr Adolesc Med 1996;150:169–74.

Voltage criteria for hypertrophy

The voltage criteria for both right and left ventricular hypertrophy (LVH) on ECG also vary with age, so close attention must be paid to age and relevant physiology to avoid confusion. Whereas right axis deviation is normal at birth, RVH is abnormal. Newborns have upright T waves in V1, which invert after the first week of life until adolescence, when they typically become upright again. Therefore, some important criteria for diagnosing RVH include a positive T wave in V1 after day of life 5 to 7, R in V1 of greater than the 98th percentile for age, or S in V6 of greater than the 98th percentile for age. The criteria for diagnosing LVH include the S wave in V1 of greater than the 98th percentile or the R wave in V6 of greater than the 98th percentile for age.

RVH in a newborn is likely a ductal-dependent left obstructive lesion, such as coarctation. LVH in a newborn, in combination with small right-sided forces, suggests an atretic right ventricle lesion, such as tricuspid or pulmonary atresia. In contrast, RVH in an infant suggests a ductal-dependent right obstructive lesion or right-to-left shunt. These infants typically present with cyanosis. LVH in an infant is typically a ductal-dependent left obstructive lesion, such as coarctation or a large hemodynamically significant left-to-right mixing lesion.

Laboratory analysis

Several laboratory studies can be helpful when considering causes in the differential diagnosis for the critically ill infant. Initial analysis should include a complete blood count for anemia, a complete metabolic panel for electrolyte derangements, methemoglobin level, lactic acid, pH, ammonia, blood culture, urine culture, urine organic acids, cortisol, thyroid-stimulating hormone, and free thyroxine.

Brain natriuretic peptide (BNP)/N-terminal pro-BNP (NT-proBNP) can be used as an adjunctive biomarker to differentiate a pulmonary process as a cause for respiratory distress from a cardiac disease in children. In contrast with the robust literature in the adult populations, there are fewer studies of BNP/NT-proBNP in the pediatric population.[35] Maher and associates[22] compared the results of laboratory tests for respiratory disease in children without a significant past medical history and with a new diagnosis of CCHD. The average BNP values were as follows: 3624 ± 1512 pg/mL among patients with congenital cardiac disease, 2837 ± 1681 pg/mL among those with acquired heart disease, and 17.4 pg/mL for those with respiratory illness. A cutoff BNP of less than 100 pg/mL for the identification of heart disease has a sensitivity of 100% and specificity of 98%.[22] In an evaluation of preterm infants with signs of CHD, Davlouros and associates[36] found that a BNP greater than 132.5 pg/mL had 93% sensitivity and 100% specificity for detecting hemodynamically significant left-to-right shunts. Koulouri and colleagues[37] calculated that a BNP concentration of greater than 40 pg/mL had 84% accuracy in differentiating cardiac from pulmonary causes of respiratory distress. In their series, the BNP value was observed to be significantly higher in patients with left ventricular systolic dysfunction than in those with left-to-right shunting lesions. Law and associates[38] studied the use of BNP as a diagnostic tool to differentiate hemodynamically significant cardiovascular disease from other disease processes with a similar presentation and found a cutoff of 170 pg/mL produced a sensitivity of 94% and specificity of 73% for neonates 0 to 7 days of age (n = 42). For the older age group (n = 58), a cutoff of 41 pg/mL produced a sensitivity of 87% and specificity of 70%.

Imaging

Chest radiography can reveal the causes of respiratory distress or shock as well as aid in the diagnosis of CCHD. Cardiomegaly, in which more than one-half of the chest

cavity is consumed by the heart, can be an indicator of congenital cardiac disease. Some cardiac malformations are associated with classic appearances on radiographs. TGA has an "egg on a string" appearance owing to malrotation of the great vessels. TAPVR has a "snowman" or "Fig. 1" appearance owing to the input of pulmonary veins into the right atrium. Tetralogy of Fallot causes a "boot-shaped" heart on a chest radiograph. Radiography can also be used to evaluate other congenital causes of respiratory distress such as a diaphragmatic hernia or congenital cystic adenomatoid malformation.

The appearance of the radiograph can also guide management. A "white out" appearance suggests pulmonary vascular edema consistent with heart failure as seen in left-obstructive lesions and shunting lesions with left-to-right flow. These interstitial markings might be confused for infiltrates indicative of pneumonia. In contrast, right-obstructive lesions, right-to-left shunt lesions, and persistent pulmonary hypertension have a paucity of pulmonary vascular markings. This "black out" appearance is more suggestive of decreased pulmonary blood flow and cyanotic collapse as seen in right-obstructive lesions.

Echocardiography

Significant advances in the rapid diagnosis of life-threatening diseases have been made with the advent of bedside limited echocardiography by the emergency physician (BLEEP). The use of ultrasonography is becoming more prevalent in pediatric EDs owing to its ease of use, accessibility, and low radiation. With limited training, physicians can use this technology to obtain valuable information and provide evidence of CHD. Although no study has yet assessed the effectiveness of BLEEP for diagnosing CCHD in the ED, information about contractility and confirmation of the presence of 4 heart chambers has been obtained by using this modality to facilitate early diagnosis.[39–41]

EMERGENCY DEPARTMENT EVALUATION

Although congenital cardiac lesions can be differentiated broadly in 3 groups—left-sided obstructive ductal dependent, right-sided obstructive ductal dependent, and mixing—there is an even more simplified approach to categorize these disorders. Patients present in one of 3 ways: heart failure ("pink"), circulatory collapse ("gray"), or cyanotic ("blue"). The EP can identify which disorder is present by incorporating the age, history, physical examination, laboratory data, ECG, chest x-ray, and BLEEP (see Fig. 1).

Heart failure is a presentation of mixing lesions, typically in a "pink" well-perfused and oxygenated infant 1 to 6 months of age. The infant presents with tachypnea, poor feeding, inadequate weight gain, hepatomegaly, murmur, and "white out" on a chest radiograph. The ECG may show AV block or ventricular voltage criteria for hypertrophy, and BNP might be increased. BLEEP may show a septal defect.

Circulatory collapse is a presentation of a left-obstructive ductal-dependent lesion in a "gray" poorly perfused infant within the first few weeks of life. The neonate presents with hypotension, tachypnea, brachial–femoral pulse differential, systolic blood pressure differential greater than 10 mm Hg, and a pulse oximetry RUE and LE differential of greater than 3%. Poor perfusion evidenced by prolonged capillary refill time and peripheral pulse deficits signifies profound hemodynamic collapse consistent with a left obstructive ductal-dependent lesion. A chest radiograph shows "white out," the ECG varies based on age at presentation, and BNP is most likely increased. BLEEP may show a hypoplastic left ventricle or narrowing of the aorta.

Cyanosis, the "blue" baby, is a presentation of a right obstructive ductal-dependent or mixing lesion. An infant with a ductal-dependent lesion presents in the first weeks of

life, "blue" with respiratory distress. After 1 month of age, the cyanotic mixing lesion presents with a combination of cyanosis and signs of heart failure. Examination reveals central cyanosis, murmur, and a "black" chest radiograph (unlike findings from a purely respiratory cause). The ECG might show either early dominant right forces or, after 1 week of life, dominant left forces. The BNP will not be increased. BLEEP may show hypoplastic right ventricular valves or septal defect. Once an infant with potential CHD has been identified and categorized by physiology, it is important to determine whether he or she would benefit from PGE1 and cardiology consultation.

It can be helpful to envision critical cardiac lesions in terms of a circuit in series with 2 systems: PVR and systemic vascular resistance (SVR). Managing the hemodynamics in these infants requires balancing the circulations like a teeter–totter. Pediatric cardiologists refer to the Qp:Qs ratio, in which Qp is the pulmonary blood flow and Qs is the systemic blood flow. Because each congenital cardiac disease has multiple variations, with each change altering the physiology, it might be simpler to consider the underlying physiology and balance the SVR and PVR instead of memorizing each defect. If PVR is decreased or SVR is increased, blood will flow to the lungs and become oxygenated. If SVR is decreased or PVR is increased, blood flows to the systemic vasculature but receives inadequate oxygenation in the lungs. The equation to guide the clinician is based on Fick's principle:

$$Qp:Qs = (SaO_2 - SvO_2):(SpvO_2 - SpaO_2),$$

where SaO_2 is the oxygen saturation, SvO_2 is the mixed venous oxygen saturation, $SpvO_2$ is the Pulmonary venous desaturation, and $SpaO_2$ is the pulmonary arterial oxygen saturation. The PVR and SVR must be manipulated to attain the goal Qp:Qs ratio of 1:1. If the child has had a surgical correction, the EP should ask the parents for the baseline oxygen saturation and target that goal. Increasing the oxygen saturation from 80% (Qp:Qs 25:20) to 100% for the hyperoxia test (Qp:Qs 25:0) increases the pulmonary vascular flow by 25 times. Oxygen is both a potent pulmonary vasodilator and vasoconstrictor of the ductus arteriosus. In fact, hypoxemia attained by blending nitrogen with oxygen can help to maintain the patency of the ductus arteriosus if prostaglandin is not available.[42] When considering an alteration of SVR, the goal mean arterial blood pressure is 40 mm Hg in neonates, which should be adjusted according to the normal mean arterial blood pressure for the child's age.

PVR can be manipulated by adding supplemental oxygen to vasodilate the pulmonary vasculature, thereby increasing pulmonary blood flow to assist with oxygenation in cyanosis. Alternatively, PVR can be increased to shunt blood toward the systemic circulation and decrease pulmonary edema or overload by mild hypoventilation, positive-pressure ventilation, and decreasing supplemental oxygen. SVR can be increased with medications such as phenylephrine, a purely α1-receptor agonist, and dopamine, a β1-agonist at low doses and β1-agonist with α1-agonist at higher doses. In a patient with a ductal-dependent right-obstructive lesion or a left-to-right shunting lesion, increased SVR will shunt blood from the systemic circulation to the pulmonary circulation, increasing oxygenation or pulmonary edema, respectively. In contrast, SVR can be decreased with medications such as milrinone, a phosphodiesterase III inhibitor, or nitroprusside. These vasodilators decrease SVR, promote right-to-left shunt, and increase systemic blood flow, decreasing pulmonary edema and oxygenation. Additionally, diuretics can be given for pulmonary edema.

As stated, infants with a hemodynamically significant cardiac lesion can be categorized by their appearance: pink, blue, or gray (see **Fig. 1**). A "pink" baby has too much pulmonary blood flow and too little systemic blood flow. A "pink" infant's oxygen saturation is greater than 85% to 90%; therefore, the Qp:Qs is 25:15 oxygen. To achieve a

balanced Qp:Qs, the use of positive-pressure ventilation, hypoventilation, and vasodilators will increase the PVR, decrease the SVR, and increase systemic perfusion. Thus, the balance shifts from pulmonary overcirculation to balanced hemodynamics. A "blue" or cyanotic infant has too little pulmonary blood flow and too much systemic blood flow. The oxygen saturation for a "blue" infant is less than 75%, so the Qp:Qs is 25:25. Although this might seem to be balanced, recall that pulse oximetry is less reliable at oxygen saturations below 80%, so this would only be the best case scenario. Because the baby is "blue," the goal is to increase pulmonary blood flow. PGE1 can be initiated to increase flow to the lungs through the PDA, which typically improves oxygenation quickly. Furthermore, PVR can be decreased or SVR can be increased to increase pulmonary blood flow (Qp). PVR can be decreased with addition of supplemental oxygen, inhaled nitric oxide, and hyperventilation. SVR can be increased with intravenous fluids, phenylephrine, or knee-to-chest positioning. A "gray" baby is decompensated in circulatory collapse with hypoxemia and hypotension. The goal is to increase cardiac output globally and minimize oxygen consumption. It is critical to initiate PGE1 therapy to maintain patency of the ductus arteriosus. The addition of dopamine or epinephrine will augment systemic perfusion and improve inotropy. Intubation will increase oxygen saturation and provide positive-pressure ventilation to increase PVR. An exception is mixing "blue" lesions rather than right obstructive "blue" lesions, which have an obligatory shunt between the pulmonary and systemic circulations. The shunt is obligatory because, otherwise, the circulatory system would be a circuit in parallel, recycling blood within the same system instead of in series between the pulmonary and systemic circulation. Deoxygenated blood mixes with oxygenated blood. Eventually, this scenario creates pulmonary overcirculation and mixing of the deoxygenated and oxygenated blood, producing cyanosis and heart failure. Supplemental oxygen will decrease PVR and temporarily improve the clinical condition as less deoxygenated blood shunts to the systemic circulation. However, ultimately, the Qp:Qs balance needs to be obtained surgically.

Medical Management

After initiating the steps described to optimize the balance of pulmonary and systemic blood flow, consultation with a pediatric cardiologist is recommended to obtain diagnostic echocardiography and initiate transfer to the appropriate facility. As with any critically ill patient, the ABCs of resuscitation should be addressed sequentially. For intubation of children in respiratory distress or hypotension, ketamine is often chosen as an induction agent. However, caution is advised for its use the critically ill neonate, because it will increase SVR, further worsening left-to-right shunt. Hemodynamically neutral agents, such as etomidate, an α-agonist and a γ-aminobutyric acid receptor agonist, should be considered instead. Although sepsis is always on the differential diagnosis of a critically ill infant, the risks of adrenal suppression from etomidate are outweighed by the benefits of optimizing the hemodynamics of a decompensated cardiac lesion.[43–46] Rapid-sequence intubation should be induced with neuromuscular blockade using either rocuronium or vecuronium. After intubation, attention should be paid to hemodynamics, because positive-pressure ventilation increases PVR and decreases SVR and preload. This can affect shunting and the Qp:Qs flow, especially in a cyanotic baby. Children in respiratory distress should be intubated, especially those requiring PGE1 infusion. Prostaglandin has adverse effects, the most significant being apnea and hypotension. Thus, infants should be intubated empirically for transfer and given judicious use of intravenous fluids.

Vascular access and titrating hemodynamic medications is crucial to rapid-sequence intubation. In a neonate with circulatory collapse, rapid vascular access

can be obtained by placement of a peripheral intravenous catheter, intraosseous catheter, or umbilical vein catheter. The umbilical stump is usually a viable vascular access option for up to 1 week after birth. The stump contains only 1 umbilical vein, which is larger and has less muscular walls than the arteries. An umbilical vein catheter has the advantage of providing central access and multiple ports for infusing medications. The emergent umbilical vein ("low lying") catheter should be advanced just beyond the point of initial blood flow within the catheter. Many umbilical lines are misplaced into the hepatic vein during cannulation, so low lying umbilical lines provide central vascular access without the risk of hepatic vein cannulation. The ideal depth of insertion of a nonemergent umbilical venous catheter can be estimated based on the infant's weight with the equation (weight in kilograms/2) + 9, and is confirmed radiographically by the location of the distal tip above the diaphragm between the seventh and ninth thoracic vertebrae. Alternatively, if peripheral intravenous access is not rapidly successful, intraosseous access should be established.[47–49]

PGE1 is a life-saving medication that stimulates ductal endothelium and maintains patency of the ductus arteriosus while awaiting definitive surgical management. PGE1 therapy should be implemented for any neonate with hemodynamic collapse or cyanosis in the first month of life.[50,51] The ductus arteriosus typically closes by 72 hours of life, but if flow depends on the ductus, it could take longer for the muscular walled conduit to become fibrotic. PGE1 is especially beneficial in neonates with coarctation of the aorta, hypoplastic left heart, critical aortic stenosis, interrupted aortic arch, transposition of the great vessels, tricuspid atresia/stenosis, pulmonary atresia/stenosis, and Ebstein's anomaly.[52] Because the diagnosis of CCHD is often unknown in the ED, infusion of PGE1 is critical for both "blue" babies with right-obstructive ductal-dependent physiology and "gray" babies with left-obstructive ductal-dependent physiology (see Fig. 1).

Further management is guided by the unique physiology of the type of CCHD. "Gray" shocklike infants with circulatory collapse require PGE1 to support systemic circulation. It may take hours for shock to resolve after PGE1 infusion and the patient will most likely remain undifferentiated until further diagnostic testing can be obtained in a tertiary pediatric intensive care unit. In addition to initiating a PGE1 infusion, additional therapeutic interventions include intubation to minimize oxygen consumption, inhaled nitric oxide, inotropic support, afterload reduction with milrinone, and hemodynamic support with dopamine or epinephrine. Oxygen administration should be adjusted to maintain the target Qp:Qs. Intravenous fluids boluses should be given to improve preload.

Neonates with cyanotic lesions causing circulatory collapse also require PGE1 to increase the pulmonary blood flow across the PDA. This should produce a prompt improvement. However, if the neonate is still cyanotic, consider the diagnosis of d-TGA without a VSD. Circulation in d-TGA flows in parallel, not in series like a normal heart, and would be immediately lethal without an intracardiac systemic to pulmonary connection. A PDA defect allows mixing until its closure, and a VSD or ASD could allow more permanent mixing by creating a circuit in series. d-TGA is a special scenario; it might require an emergent atrial septostomy to create a circuit in series.

Persistent pulmonary hypertension can also present in neonates as cyanosis with circulatory collapse. Persistent pulmonary hypertension can be differentiated from cyanotic CCHD after stabilization, and its initial management is similar to that of cyanotic CCHD with circulatory collapse. Patients with persistent pulmonary hypertension are difficult to ventilate after they are intubated, and their oxygen saturation will decrease episodically owing to vasospasm and ventilation/perfusion mismatch. Inhaled nitric oxide is beneficial for these patients and is usually instituted after

echocardiography reveals the pulmonary hypertension and lack of cardiac defect at the tertiary care pediatric intensive care unit.

The "blue" infant with congestive heart failure is typically older than 1 month of age. These children do not need PGE1 and, in fact, might do worse if it is administered, because blood will be shunted left to right across the ductus, increasing the pulmonary blood flow. PGE1 will not alter the mixing of oxygenated and deoxygenated blood, which is the underlying cause of cyanotic congestive heart failure.

The "pink" infant with congestive heart failure is usually 1 to 6 months of age. The therapeutic goal is to increase PVR with low oxygen, positive-pressure ventilation, or intubation and to decrease SVR with a vasodilator such as milrinone. PGE1 is not necessary in these infants. Achieving an appropriate fluid balance is challenging in these infants because, although they have reduced preload, which may benefit from slow 10-mL/kg IV increments, they often need diuretics to prevent worsening of respiratory distress from volume overload.

Medications commonly used for the acutely decompensated infant with CCHD are listed in **Box 5**.[53]

SPECIAL CONSIDERATIONS

A child with anomalous left coronary artery from the pulmonary artery behaves similarly to the "pink" infant with heart failure or the "gray" neonate in shock. These babies typically present at 2 to 3 months of age. As the PVR decreases, decreased retrograde deoxygenated flow from the pulmonary artery to the left coronary artery causes myocardial ischemia in the left coronary distribution (anterolateral) and eventually heart failure. These babies typically have "white out" on chest radiography, caused by pulmonary edema, and a characteristic ECG, with Q waves laterally or ST elevation anterolaterally, from myocardial ischemia owing to persistent deoxygenated coronary perfusion. The ECG differentiates these infants from the "pink" CHF infant or the "gray" neonate in shock. Echocardiography or angiography should be obtained to diagnose the origin of the coronary arteries.

TAPVR is a problem of pulmonary overload returning to the right atrium. An infant with infradiaphragmatic or infracardiac obstructed TAPVR presents similarly to a cyanotic

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Box 5
Emergency cardiac medications

Medication	Dose
Dopamine	5–20 μg/kg/min
Epinephrine	0.01–0.1 μg/kg/min
Esmolol	500 μg/kg bolus, 50–300 μg/kg/min
Etomidate	0.3 mg/kg/dose
Fentanyl	1–3 μg/kg/min
Furosemide	0.5–2 mg/kg IV q6–12 h
IV fluid bolus	10 mL/kg/dose
Ketamine	1–2 mg/kg/dose
Milrinone	0.5 μg/kg load, 25–75 μg/kg/min
Morphine	0.1 mg/kg/dose
Nitroprusside	0.5–4 μg/kg/min
Phenylephrine	10–20 μg/kg bolus, 2–5 μg/kg/min
Prostaglandin E1	0.05–0.1 μg/kg/min titrating up q15–20 min

Data from Costello JM, Almodovar MC. Emergency care for infants and children with acute cardiac disease. Clin Pediatr Emerg Med 2007;8:145–55.

infant with congestive heart failure.[54] Infants with obstructed TAPVR typically present earlier than those with unobstructed forms of TAPVR. This is a unique scenario, in which prostaglandin can be detrimental. Opening the ductus arteriosus will increase left-to-right shunt and increase pulmonary blood flow, worsening heart failure.

Another scenario in which an infant with cyanosis might fail to improve or could worsen with prostaglandin infusion is a d-TGA with an intact ventricular septum or restrictive atrial or ventricular communication. Mixing in the heart via left-to-right shunt to oxygenate the systemic blood is required; thus, these infants need emergent atrial septostomy by a cardiologist.

Last, tetralogy of Fallot behaves differently with less ductal-dependent physiology. Its episodic presentation can occur earlier or later than the classic "blue" neonate. It can behave as a "blue tet" with right-obstructive ductal-dependent lesion early in life when PVR is still suprasystemic, owing to severe right ventricular outflow tract obstruction. The severe right ventricular outflow tract obstruction decreases pulmonary blood flow and will present as a cyanotic "blue" baby who is responsive to PGE1. If the obstruction is severe, left-to-right shunt at the ductus arteriosus might provide the much-needed pulmonary blood flow. In contrast, "pink tets" have enough mixing of blood at the VSD level that the preload can typically overcome a less severe obstruction. A classic "tet spell" can be seen in these babies awaiting surgical repair at 3 to 6 months of age. Decompensation, known as a "cyanotic tet spell," is caused by an acute decrease in pulmonary blood flow owing to either increased PVR (eg, from crying) or decreased preload from hypovolemia.[55] The agitation increases the heart rate and causes decreased diastolic filling time; therefore, the infundibulum does not fully relax, so the right ventricular outflow tract obstruction is worsened. The ductus arteriosus would subsequently shunt less blood left to right as the PVR nears the SVR. Tetralogy of Fallot spells are managed uniquely. The goal is to decrease PVR and increase SVR. If the first episode is presenting undiagnosed, PGE1 would not be detrimental and the infant can be treated like any other infant with a right-obstructive ductal-dependent lesion who is "blue." The chest radiograph will be black owing to decreased pulmonary blood flow. The ECG will show RVH. Hypercyanotic "tet spells" should be managed with calming. Child Life specialists and parents can be recruited for this endeavor. Morphine can be another adjunct. Bringing the child's knees to his or her chest will increase SVR, shunting more blood from left to right across a PDA or the VSD, and thus increasing preload in the right ventricle. A fluid bolus will also increase preload. Supplemental oxygen benefits by vasodilating the pulmonary vasculature, thereby decreasing PVR. Different modalities can be attempted to increase SVR and left-to-right shunt: manual external compression of the aorta, phenylephrine infusion, and ketamine.[55] Propranolol or esmolol can decrease the heart rate, thereby decreasing the infundibular overriding of the pulmonary artery and increasing time for diastolic filling.[56] If the child is still cyanotic after medical optimization and the Qp:Qs is balanced, then surgery may be the next best option.

SUMMARY

Any neonate with cyanosis or shock should be considered to have a ductal-dependent critical congenital cardiac disease until proven otherwise. Circulatory collapse and cyanosis caused by ductal-dependent lesions typically present within the first 2 weeks of life. Shunting lesions and those associated with heart failure present later during infancy. The crashing neonate certainly produces anxiety among ED providers, but following a clear and decisive algorithm can mitigate this stress. The essential elements discussed throughout this article provide a framework for the diagnosis of

congenital cardiac disease. Cornerstones of this diagnosis include assessment of the neonate for cyanosis, hepatomegaly, murmur, and measurement of the proximal versus distal pulses and the blood pressure. Other vital tools include an ECG, chest x-ray, BNP, and BLEEP. Circulatory balance should be maintained with a Qp:Qs ratio of 1:1. Cyanotic infants require oxygen and most require PGE1 infusion. Infants with profound hemodynamic collapse can be harmed with oxygen and need circulatory support and PGE1 infusion. Owing to the complexity of CHD, in addition to age-dependent physiologic variability, a rapid compilation of data obtained from the history and physical (see **Box 2**) will guide the EP toward identifying and managing these infant. By using a simplified approach that categorizes the critically ill infant as "pink" (excessive pulmonary blood flow), "blue" (insufficient pulmonary blood flow), or "gray" (circulatory collapse; see **Fig. 1**), the EP will be able to provide life-saving stabilization until specialized care can be obtained.

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