Interpretation of Oxygen Saturation in Congenital Heart Disease: Fact and Fallacy

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EDUCATION GAP

Oxygen saturation as measured by pulse oximetry is a key component of the physical examination of any child with congenital heart disease, starting with newborn pulse oximetry screening. The oxygen saturation of a patient with congenital heart disease depends on the anatomical lesion, surgical palliation, and any additional pulmonary or cardiac pathology that may derange oxygen saturation. Pediatric providers seeing these patients in the newborn nursery, the primary care clinic, and the emergency department should be knowledgeable about the principles and implications of pulse oximetry and oxygen saturations.

OBJECTIVES *After completing this article, readers should be able to:*

1. Describe the principles of oxygen saturation and its measurement by pulse oximetry (including limitations).

2. Describe the nonrespiratory causes of hypoxemia that are unique to patients with congenital heart disease.

3. Understand the rationale for and pitfalls of pulse oximetry screening for critical congenital heart disease.

4. Anticipate the expected saturation range for a given cardiac diagnosis and identify scenarios in which supplemental oxygen may be contraindicated.

5. Interpret and respond to visible cyanosis in patients with congenital heart disease.

ABBREVIATIONS

CCHD	critical congenital heart disease
CHD	congenital heart disease
Hb	hemoglobin
HbF	fetal hemoglobin
PDA	patent ductus arteriosus
Sao₂	arterial oxygen saturation
Spo₂	pulse oximetry oxygen saturation
VSD	ventricular septal defect

ABSTRACT

Oxygen saturation is the percentage of hemoglobin that is saturated with oxygen, converting it to oxyhemoglobin. Oxygen saturation is a critical part of the physical examination of children with congenital heart disease (CHD). The expected oxygen saturation of a patient with CHD depends on their anatomical lesion, their previous surgeries, and any additional pulmonary

or systemic pathology that may derange their saturation. Oxygen saturation can be noninvasively measured using pulse oximetry. Pulse oximetry is based on the differential absorption of infrared and red light by oxyhemoglobin and deoxyhemoglobin, with the former absorbing more infrared than the latter. Pulse oximetry readings may be inaccurate in settings of low cardiac output, peripheral vasoconstriction, arrhythmia, hypothermia, and venous pulsations. The use of pulse oximetry in the care of a child with CHD begins with the newborn critical CHD screen. A failed screen indicates a need for further investigation, such as repeated pulse oximetry or echocardiography. The oxyhemoglobin dissociation curve may be used to estimate the partial pressure of oxygen in the blood at various oxygen saturations. It is also a marker of the affinity of hemoglobin for oxygen, with a right-shifted curve indicating a higher oxygen tension needed to saturate hemoglobin. This is a helpful adaptation of the body to situations of stress such as fever, acidosis, and hypercapnia. An understanding of these concepts is paramount for providers caring for patients with known or potential CHD in any setting to appropriately interpret and respond to abnormal saturations for each child.

INTRODUCTION

Oxygen saturation is a key vital sign that conveys information about clinical status, stability, and need for intervention. However, although abnormal oxygen saturation is easy to identify and respond to in children with structurally normal hearts wherein expected oxygen saturations are 95% to 100% in room air, interpretation of oxygen saturation in a child with congenital heart disease (CHD) requires knowledge of the anatomy, the expected saturation range based on diagnosis and previous interventions, and the pathophysiology of lower or higher saturation for that congenital heart lesion. Underlying these details are the principles of oxygen content and saturation, and their role in oxygen delivery. We review pulse oximetry and its limitations, the pathophysiology of oxygen saturation and desaturation in children with CHD, common clinical scenarios and pitfalls while interpreting oxygen saturation in children with CHD, and the newborn screen for critical CHD (CCHD).

PRINCIPLES OF PULSE OXIMETRY

Oxygen is carried in the blood primarily attached to the 4 binding sites on each hemoglobin (Hb) molecule, with a small additional quantity of oxygen dissolved in the plasma. (1) Systemic oxygen saturation is the percentage of Hb molecules that are bound to oxygen, called oxyhemoglobin. The gold standard for measurement of oxygen saturation in the arterial blood (Sao_2) is a blood gas sample, which can be used to measure the oxyhemoglobin content as well as the partial pressure of dissolved oxygen. Since the 1970s, pulse oximetry has become a widely used correlate for Sao_2, favored for both its noninvasiveness and continuous data acquisition.

Pulse Oximetry Technology

Measurement of oxygen saturation by pulse oximetry (Spo_2) is based on the difference in light absorption properties of oxyhemoglobin and deoxyhemoglobin. Specifically, oxyhemoglobin absorbs more infrared light (wavelength, 940 nm) and less red light (wavelength, 660 nm) than does deoxyhemoglobin. Most pulse oximetry probes comprise 1 portion that contains 2 light-emitting diodes, 1 for each wavelength of light. The photodetector on the other portion of the probe is positioned on the opposite side of a finger, toe, or earlobe and measures the relative amounts of red and infrared light that are absorbed by the structures between the light source and the detector. (2)

Most soft tissues, such as skin, nails, fat, muscle, and bone, have relatively constant light absorption over the short term. On the other hand, with each pulse there is an increase in arterial blood flow, and thus an increase in the quantity of Hb—saturated or not—available for light absorption. The algorithm used by pulse oximeters discounts the constant absorption by venous flow, measuring only the variable absorption caused by changing arterial blood flow.

Limitations of Pulse Oximetry

Given the ubiquitous nature of pulse oximetry within pediatrics, it is imperative for every pediatrician to understand the tool's significant limitations, several of which are particularly pertinent to patients with CHD.

Low Cardiac Output, Poor Perfusion, Arrhythmia. The oximeter relies on detection of the periodic fluctuation in the absorption of light that occurs with each pulse. Thus, decreased pulsatility can result in an inability to sense and calculate a reliable signal. Intermittent dropout of the pulse oximetry reading may occur with poor cardiac output, arrhythmia, vasoconstriction, or occlusion of arterial blood flow in the setting of a blood pressure cuff or thrombus.

Pulsatile Veins. Venous pulsatility, as seen in severe tricuspid regurgitation or a tightly placed probe, can

result in a falsely low SpO_2 reading. The pulse oximeter algorithm subtracts the constant level of red and infrared light absorption, interpreting only the variable absorption caused by each pulse. When the veins are also measurably pulsatile, the relative light absorption of the venous Hb will be factored into the overall pulse oximetry reading. Because venous blood contains significantly less oxyhemoglobin than arterial blood, the reading will be falsely low.

Low Oxygen Saturation. Calibration of pulse oximeters is based on studies of healthy volunteers. Because patients are rarely permitted to maintain saturations less than 70%, there are no available data to validate pulse oximetry readings in severely hypoxemic patients, and calibration below this level is based on extrapolation. Some studies have demonstrated decreased accuracy at lower saturations. (3) This is especially important to consider in children with CHD, many of whom have baseline saturations near the level of reliable pulse oximetry readings. (4)(5) Hypoxemia should be confirmed with measurement of SaO_2 on blood gas analysis.

Skin Color. Another consequence of the pulse oximeter algorithm's basis on healthy volunteers, most of whom had light skin, is the potential for less accurate readings in patients with more skin pigmentation. Several studies have demonstrated falsely elevated pulse oximetry readings among patients with dark skin, and research about the accuracy of oximetry across skin colors is ongoing. (6)(7)(8)(9)(10) Theoretically, light absorption by the skin should remain constant over the cardiac cycle and thus be discounted by the pulse oximeter's algorithm. However, particularly at low oxygen saturations, pulse oximeters can overestimate the saturation measured by blood gas analysis in patients with darker skin. This introduces the potential for racial bias in the instance of missed hypoxemia, especially because many patients with CHD are expected to have oxygen saturation less than 80%, where this inaccuracy is most prominent.

Hb Variants. Carbon monoxide binds Hb molecules with a markedly greater affinity than oxygen, displacing the oxygen and reducing the proportion of Hb saturated with oxygen. Because Hb molecules carrying carbon monoxide have similar light absorption properties as oxyhemoglobin, the pulse oximeter cannot distinguish between the two. Even with profoundly desaturated blood, the pulse oximeter will report normal saturation.

Methemoglobin is formed when the iron in Hb is oxidized, either due to a rare hereditary disorder (deficiency of nicotinamide adenine dinucleotide–cytochrome b5 reductase or glucose-6-phosphate dehydrogenase deficiency)

or from exposure to oxidizing substances (such as nitrates in well water or topical anesthetics such as benzocaine). This decreases the Hb's affinity for oxygen. Methemoglobin absorbs red and infrared light at relatively equal levels, and a 1:1 ratio of absorption correlates with oxygen saturation of 80% to 85%. As such, in patients with significant concentrations of methemoglobin, pulse oximetry will read falsely high in patients with SaO_2 less than 80% and falsely low in patients with normal oxygen levels. (11)

Fetal Hb (HbF), another natural Hb variant with high oxygen affinity, does not significantly impact the accuracy of pulse oximetry. (12)

ROLE OF OXYGEN SATURATION IN DETERMINING OXYGEN DELIVERY IN CHD

End-organ function is dependent on overall oxygen delivery to the tissues. Oxygen delivery is determined by 1) cardiac output, 2) the relative distribution of blood flow to each capillary bed, 3) total oxygen content in the blood, and 4) the Hb molecule's affinity for oxygen (Fig 1). It is important to note that pulse oximetry provides bedside information about only the saturation aspect of the total oxygen content of the blood and, hence, is just part of the interpretation of oxygen delivery. In the following sections, we discuss the latter 2 components of oxygen delivery, with an emphasis on where these concepts differ for patients with CHD.

Determinants of Systemic Oxygen Content and Desaturation in CHD

The amount of oxygen dissolved in plasma is relatively small compared with that bound to Hb, so the systemic arterial oxygen content depends primarily on the Hb concentration and percentage saturation. This is also evident from the mathematical equation describing oxygen content:

$$\text{Oxygen Content (mL/dL of blood)} = [\text{Oxygen Saturation} \times 1.34 \ (\text{mL/g}) \times \text{Hb} \ (\text{g/dL})] + [0.003 \ (\text{mL of oxygen/dL/mm Hg}) \times \text{PaO}_2 \ (\text{mm Hg})],$$

wherein 1.34 is the amount of oxygen bound per gram of Hb (this factor may vary from 1.3 to 1.39 depending on the reference) and 0.003 represents the solubility of oxygen. (13)

As can be deduced from this equation, a lower Hb level reduces oxygen content of the blood, and, hence, patients with anemia have reduced oxygen-carrying capacity. This is particularly clinically important in patients with intracardiac mixing, as discussed later herein. In addition, in patients with anemia or those receiving high amounts of inspired oxygen (eg, in a hyperbaric chamber or on 100%
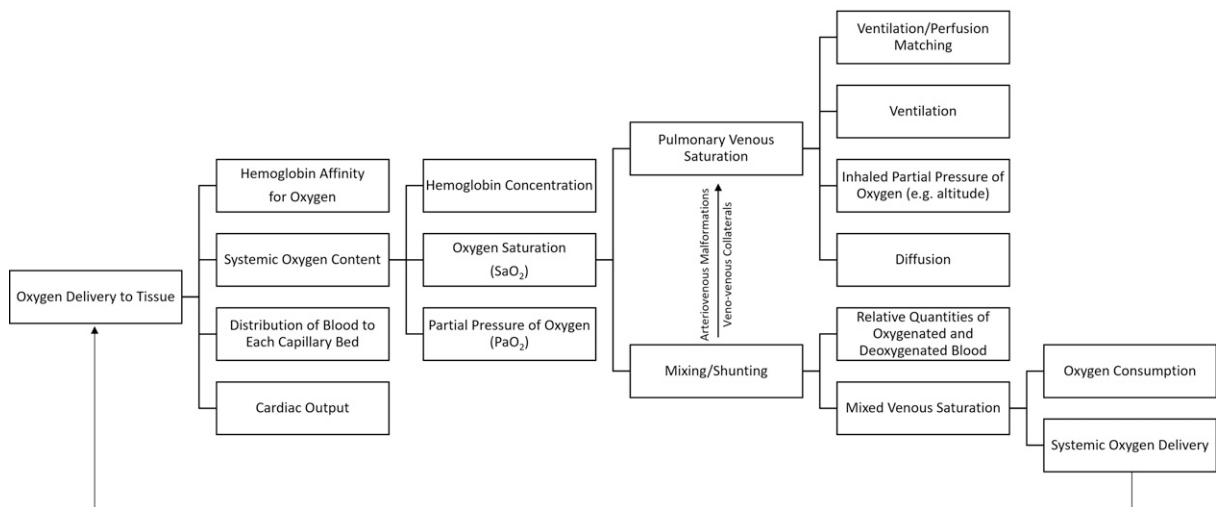
Figure 1. Determinants of oxygen delivery.

oxygen through a ventilator), the dissolved oxygen component becomes more significant.

The more intuitive determinant of oxygen delivery is saturation. Traditional teaching identifies 5 main etiologies of desaturation: 1) hypoventilation, 2) impaired diffusion across alveolar membranes as in parenchymal lung disease, 3) decreased partial pressure of oxygen as at high altitude, 4) ventilation-perfusion mismatch (eg, ineffective perfusion due to regions of atelectasis receiving pulmonary blood flow), and 5) shunting. For the sake of simplicity with reference to CHD, these can be summarized as either respiratory etiologies or shunting/admixture lesions.

Shunting and mixing permit desaturated systemic venous blood to enter the systemic circulation without first getting oxygenated in the lungs. This can occur in an enormous variety of anatomical diagnoses, including but not limited to septal defects, patent ductus arteriosus (PDA), transposition of the great arteries, double outlet right ventricle, tetralogy of Fallot, truncus arteriosus, total anomalous pulmonary venous return, and single-ventricle variants such as tricuspid atresia and hypoplastic left heart syndrome. Extracardiac shunts such as arteriovenous malformations and collateral vessels that form in some patients with CHD between the systemic veins and pulmonary veins or left atrium also fall into this category.

Importantly, a shunt will result in desaturation only when the systemic venous blood enters the systemic circulation (a so-called right-to-left shunt), not the other way around. For example, in a patient with total anomalous pulmonary venous return, all of the oxygenated blood returning from the lungs is directed into the right atrium, where it mixes with the deoxygenated blood returning from the vena cavae; it is this mixed somewhat desaturated blood that passes into the left atrium and out to the body. On the other hand, in an infant with healthy lungs and an isolated ventricular septal defect (VSD), blood will typically flow across the defect from the left to right ventricle—from oxygenated to deoxygenated. The systemic arterial saturation in this case is expected to be normal. A low Sp_{O_2} would imply either a respiratory etiology of the desaturation or elevated pulmonary artery pressures (elevated pulmonary vascular resistance or pulmonary hypertension). Because blood flows down the path of least resistance, if pulmonary arterial pressures are higher than systemic pressures, the direction of shunting will be reversed to right to left (instead of left to right in typical situations when systemic blood pressures are higher than pulmonary arterial pressures). This reversal of the shunt leads to hypoxemia.

Relative Quantities of Deoxygenated and Oxygenated Blood

In patients with healthy lungs and no shunting, the blood returning to the heart from the pulmonary veins, and thus circulating to the body, should be fully saturated. In patients with right-to-left shunts or intracardiac mixing, the saturation of blood circulated to the body depends on the relative quantities of deoxygenated and oxygenated blood that compose the systemic arterial blood and on the saturation of deoxygenated blood. Hence, the Sa_{O_2} for these patients is essentially a weighted average of systemic venous saturation and pulmonary venous saturation. (14)

Consider a newborn patient with pulmonary atresia whose only source of pulmonary blood flow is from a PDA. If the circulation is well-balanced, blood leaving the heart and entering the ascending aorta will go in equal parts to the lungs (via the PDA) and to the body (via the descending aorta). This means that there are equal quantities of pulmonary venous return (>95% saturated if the lungs are normal) and systemic venous return (typically 70%–75% saturated), so when the 2 sources of blood mix in the heart, the saturation is their average, or approximately 85%. This is the blood that leaves the heart and reaches the body. The saturation of blood going to this patient's pulmonary bed is also 85%.

If, on the other hand, this patient's pulmonary vascular resistance drops with increasing age, blood will prefer to flow down the path of least resistance to the lungs (instead of the higher blood pressure in the systemic circulation). The ratio of pulmonary to systemic blood flow may be 2:1 or more. In this situation, the blood entering the aorta is composed of 2 parts fully saturated pulmonary venous blood and 1 part desaturated systemic venous blood. The weighted average, and thus the systemic arterial saturation, is higher: $[(2 \times 100\%) + (1 \times 70\%)]/3 = 90\%$. It is also important to note that this scenario of robust oxygen saturations is also indicative of pulmonary overcirculation (and hence risk of systemic undercirculation) and that higher saturations are not always indicative of better hemodynamics.

Broadly speaking, then, patients with intracardiac mixing and proportionally more pulmonary blood flow will have higher systemic arterial saturation. Conversely, decreased pulmonary blood flow must be considered in a patient with cyanotic CHD who is more desaturated than usual, as in the case of a closing PDA, narrowed aorta-to-pulmonary artery shunt (such as a Blalock-Taussig-Thomas shunt), or worsening right ventricular outflow tract obstruction.

Saturation of Deoxygenated Blood. In patients with mixing lesions, the saturation of blood that reaches the body depends on both the amount of desaturated blood, as discussed previously herein, and the degree of desaturation. If the patient with well-balanced circulation described previously herein had vena cava saturation of 60% instead of 70%, then the average, and the resulting systemic arterial saturation, would decrease from 85% to 80%.

The saturation of systemic venous blood is determined, similar to arterial saturation, by the quantity of oxygen in the blood. The amount of oxygen in venous blood, in turn, depends on how much oxygen is carried to the tissues in arterial blood and how much is released from the blood to the tissues, dictating how much is left over in the venous blood that leaves the tissue capillary bed. The former is dependent on the factors discussed previously herein (cardiac output, Hb concentration, arterial saturation, and quantity of dissolved oxygen), and the latter is a result of metabolic demand and Hb affinity for oxygen. Hence, the systemic venous oxygen content and saturation will be lower if the cardiac output is low (such as in patients with depressed systolic function), Hb level is low (such as in chronic anemia or blood loss), or metabolic demand and oxygen consumption are high (such as in fever or agitation). So, in patients with a right-to-left shunt or mixing, conditions of low cardiac output, anemia, and high metabolic demand can manifest as systemic desaturation. This physiologic principle guides the differential diagnosis and management of a patient with cyanotic CHD who has worsening desaturation; in addition to providing more respiratory support with oxygen, reducing oxygen demand with sedation, improving the Hb concentration with red blood cell transfusion, and increasing cardiac output using inotropes are strategies that can lead to improved systemic saturations and clinical stabilization of the child.

However, this is not the case for patients with structurally normal hearts or those with left-to-right shunting. Although systemic venous saturation would also be lower in states of low cardiac output, anemia, or high metabolic demand, this blood does not mix with the fully saturated pulmonary venous blood and so does not impact the oxygen saturation of pink blood leaving the heart. Hence, low cardiac output, anemia, and high metabolic demand will not cause systemic desaturation but may cause tissue hypoxia as a result of oxygen delivery inadequate to meet the tissue needs. In contrast, in a patient with mixing or right-to-left shunting, these conditions can cause both systemic desaturation and tissue hypoxia.

Determinants of Hb Oxygen Affinity

For oxygen to be delivered to the tissues, it must be released from its temporary binding sites on Hb. How tightly Hb holds onto oxygen, potentially limiting tissue oxygenation, is described by the oxyhemoglobin dissociation curve (Fig 2). For a given partial pressure of oxygen dissolved in the plasma, the curve gives the expected percentage saturation of Hb. It is important to recognize both the sigmoid shape of this curve and the factors that may shift it to the right or left.

The shape of the curve portrays a more rapid decline in saturation once the partial pressure of oxygen falls below approximately 60 mm Hg, reflecting the tendency of Hb to give up oxygen to the tissues more readily in an oxygen-poor
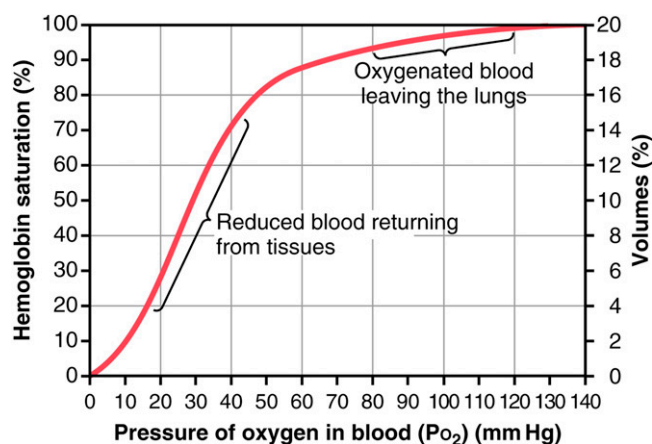
Figure 2. Oxyhemoglobin dissociation curve. Effect of blood P_{O_2} on the quantity of oxygen bound with hemoglobin in each 100 mL of blood. (Reprinted with permission from Hall JE, Hall ME. Transport of oxygen and carbon dioxide in blood and tissue fluids. In: Hall JE, Hall ME, eds. *Guyton and Hall Textbook of Medical Physiology*. 14th ed. Philadelphia, PA: Elsevier; 2021:521–530.)

state. This describes the natural condition of many patients with CHD, who live at a low baseline oxygen saturation, both preserving tissue oxygenation and putting them at risk for a precipitous drop in saturation with small decreases in the partial pressure of oxygen. Conversely, this means that a small increase in Pa_{O_2}, as with the administration of supplemental oxygen, can rapidly increase saturation. (15)

Several conditions in the tissue and blood impact the position of the curve itself. Intuitively, the conditions that cause a rightward shift and lower affinity of Hb for oxygen, allowing for easier release of oxygen to the tissues, are those that reflect greater metabolic activity: increased carbon dioxide, lower pH, higher temperature, and higher 2,3-bisphosphoglyceric acid (an isomer of a metabolic intermediate in the glycolytic pathway). The opposite conditions lead to a leftward shift, higher affinity of Hb for oxygen, and less release of oxygen to the tissues.

One additional factor that can affect the position of the oxyhemoglobin dissociation curve is the presence of Hb subtypes with affinity for oxygen that differs from that of adult Hb. HbF has a greater affinity for oxygen, shifting the curve leftward. (16) Normally, HbF is the primary form of Hb for most of fetal life, gradually decreasing to less than 10% of Hb by approximately 2 weeks of age (11) and less than 1% by 1 year of age. Newborns with cyanotic CHD demonstrate the same decline in HbF level as normal infants.

ASSESSMENT OF OXYGEN SATURATION IN PATIENTS WITH KNOWN OR SUSPECTED CHD

CCHD Screening

Screening for CCHD as a part of the Recommended Uniform Screening Panel was first recommended by the Secretary of Health and Human Services in 2011 and was subsequently endorsed by the American Academy of Pediatrics. (17) It is currently adopted in 48 states and the District of Columbia.

Testing is performed at 24 hours of age or shortly before hospital discharge. Traditionally, 3 scenarios constituted a failed test: 1) oxygen saturation less than 90% on initial screening, 2) Sp_{O_2} of 90% to 95% on 3 successive tests 1 hour apart, or 3) a difference of at least 3 percentage points between preductal saturation (measured in the right hand) and postductal saturation (measured on either lower extremity) on 3 successive tests 1 hour apart. Various studies have explored the nuances of the tool, such as saturation cutoff values, the number of repeated tests required in cases of borderline saturations, the position of the pulse oximeter, and timing of the screen. (18) Based on these investigations, an expert panel convened in 2018 and recommended 2 modifications to the current algorithm: a passing test should require saturation of at least 95% in both the upper and lower extremities, not just 1, and only 1 repeated screen rather than 2 should be performed for an initially borderline test (Fig 3). (19) Any newborn not cleared by screening is recommended to undergo echocardiography. It is important to note that this screening is directed at the detection of 7 CCHD lesions: tetralogy of Fallot, hypoplastic left heart syndrome, transposition of the great arteries, total anomalous pulmonary venous return, tricuspid atresia, pulmonary atresia, and truncus arteriosus. (20)

A 2018 Cochrane review that included more than 400,000 neonates identified overall sensitivity of 76.3% and specificity of 99.9% for the detection of CCHD. (21) Of course, the screen is designed for use in community
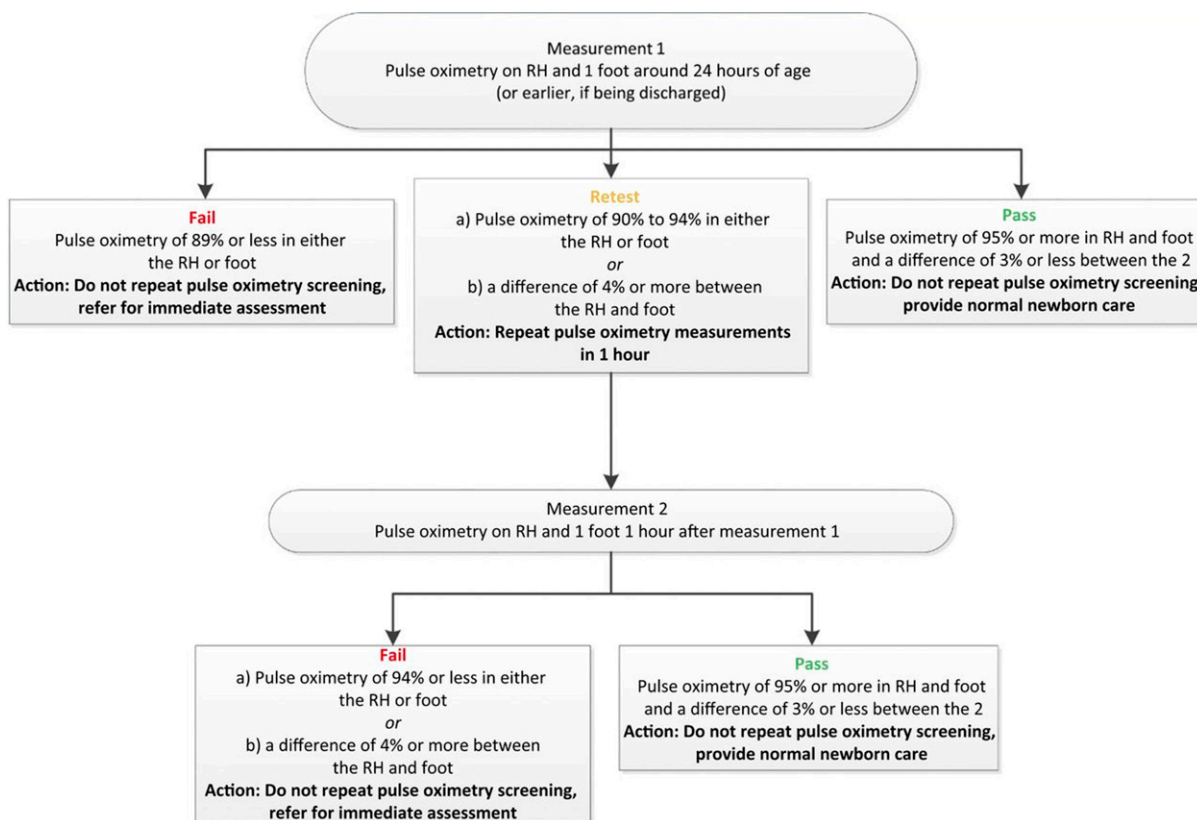
Figure 3. Revised algorithm for critical congenital heart disease screening with pulse oximetry. RH=right hand. (Reprinted with permission from Martin GR, Ewer AK, Gaviglio A, et al. Updated strategies for pulse oximetry screening for critical congenital heart disease. *Pediatrics*. 2020;146[1]:e20191650.)

settings, hence its applicability in referral centers and NICUs may be limited. (22) In addition, at high altitudes it has been found to have more false-positives, with the rate increasing with higher altitude. (23)

Expected Saturations in Palliated and Unpalliated CHD: Clinical Scenarios

Patients with CHD in various stages of palliation may have a range of saturations, with different clinical implications. It is helpful to review the medical record or history provided by family to assess whether the patient is within their usual saturation range. Although each patient is unique and there are exceptions to every rule, there are some broad categories of physiologies that may allow clinicians to identify patients who deviate from the expected. The Table summarizes the expected saturations as well as physiologic considerations for various common types of CHD.

Left-to-Right Shunts. A child with an unrepaired or repaired VSD, atrial septal defect, PDA, aortopulmonary window, complete balanced atrioventricular septal defect, or partial anomalous pulmonary venous return will generally saturate normally because the direction of abnormal blood flow in each of these lesions is typically from oxygenated to deoxygenated blood. Systemic saturation less than 90% in this scenario would imply either a respiratory etiology of desaturation or reversal of the shunt requiring further investigation for right ventricular outflow tract obstruction, pulmonary hypertension, or misdiagnosis (eg, total anomalous pulmonary venous return rather than partial).

Right-to-Left Shunts. Patients who have 1 of the shunts listed previously herein (eg, an unrepaired VSD, atrial septal defect, or PDA) combined with obstruction to right ventricular outflow, whether from tricuspid stenosis, tetralogy of Fallot, pulmonary valve or artery stenosis, or elevated pulmonary vascular resistance, will have varying degrees of desaturation due to shunting of deoxygenated blood into the systemic circulation. Placement of a pulmonary artery band to prevent pulmonary overcirculation results in the same physiology by increasing resistance to pulmonary flow and, thus, the volume of the right-to-left shunt. Generally, saturation in the 80s would reflect a well-balanced circulation, in which there is enough restriction to pulmonary blood flow to protect the lungs from excessive flow but not enough to severely limit pulmonary

Table. Oxygen Saturation Values in Children with Various Types of Congenital Heart Disease

LESION	PALLIATION	RANGE OF SATURATION %	SPECIAL CONSIDERATIONS
VSD	Unrepaired	Normal saturation	May be desaturated into the 80s if the patient has pulmonary hypertension and, hence, right-to-left shunting through the VSD
	Repaired	Normal saturation	
ASD	Unrepaired	Normal saturation	May be desaturated into the 80s if the patient has pulmonary hypertension and, hence, right-to-left shunting through the ASD
	Repaired	Normal saturation	
Coarctation of aorta	Unrepaired	90–100	Postductal saturation may be lower than preductal saturation if PDA open (differential cyanosis)
	Repaired	Normal saturation	
Interrupted aortic arch	Unrepaired	70–100	Postductal saturation lower than preductal saturation (differential cyanosis); often seen with a large VSD, which can result in higher saturation from left-to-right shunting
	Repaired	Normal saturation	
Tetralogy of Fallot	Unrepaired	80–100	Desaturation depends on degree of pulmonary obstruction
	Repaired	Normal saturation	
Transposition of the great arteries	Unrepaired	75–95	If good mixing at the atrial septum or VSD (especially if the PDA is also open), may saturate higher If additional coarctation or interrupted aortic arch, PDA shunting from pink pulmonary artery to blue aorta will lead to higher postductal saturation than preductal saturation (reverse differential cyanosis)
	Repaired	Normal saturation	
Hypoplastic left heart syndrome	Unpalliated	75–95	Mixing lesions; hence, higher saturation indicates more pulmonary venous component than systemic venous component in the blood mixing in the heart (hence, more pulmonary overcirculation)
	Norwood or hybrid (stage 1 palliation)	75–95	Mixing lesions; hence, higher saturation indicates more pulmonary venous component than systemic venous component in the blood mixing in the heart (hence, more pulmonary overcirculation)
	Glenn (stage 2 palliation)	75–90	Saturation tends to decrease over time as the child becomes older and more systemic venous return from lower extremities mixing into the pink blood in the heart[&]
	Fontan (stage 3 palliation)	90–100	85%–95% if fenestrated Fontan (hence, shunting from blue venous blood in Fontan circuit to the atrium where it mixes with pink blood from pulmonary veins)
Partial anomalous pulmonary venous return	Unrepaired	90–100	If pulmonary hypertension develops, then right-to-left shunting through the ASD may reduce saturation
	Repaired	Normal saturation	
Total anomalous pulmonary venous return	Unrepaired	75–90	All the oxygenated pulmonary venous return mixes with systemic venous return in the right atrium, and shunts right to left across the ASD to then be pumped by the left heart to the body
	Repaired	Normal saturation	
Tricuspid atresia/ pulmonary atresia/ Ebstein anomaly with insufficient prograde flow through the pulmonary valve (functional pulmonary atresia)	Unpalliated	75–95	Pulmonary blood flow depends on PDA shunting from the aorta to the pulmonary artery; higher saturation indicates more pulmonary overcirculation
	PDA stent or BTT shunt (stage 1 palliation)	75–95	Mixing lesions; hence, higher saturation indicates more pulmonary venous component than systemic venous component in the blood mixing in the heart (hence, more pulmonary overcirculation)
	Glenn (stage 2 palliation)	75–90	

Continued

Table. Oxygen Saturation Values in Children with Various Types of Congenital Heart Disease (Continued)

LESION	PALLIATION	RANGE OF SATURATION %	SPECIAL CONSIDERATIONS
			Saturation tends to decrease over time as the child becomes older and more systemic venous return from lower extremities mixing into the pink blood in the heart[&]
	Fontan (stage 3 palliation)	90–100	85%–95% if fenestrated Fontan (hence, shunting from blue venous blood in Fontan circuit to the atrium where it mixes with pink blood from pulmonary veins)
Truncus arteriosus	Unrepaired	85–95	Higher saturation indicates more pulmonary overcirculation
	Repaired	Normal saturation	
Ebstein anomaly with sufficient prograde pulmonary blood flow	Biventricular circulation/ repair	Normal saturation	Patients with Ebstein anomaly may have significant pulmonary disease due to cardiomegaly and poor lung development in utero and, hence, may have desaturations of respiratory etiology
Pulmonary AVMs	Unrepaired	70–100	Pulmonary AVMs bypass the normal gas exchange at the alveoli, leading to desaturation; they may occur with or without other CHD
Heart transplant		Normal saturation	

ASD=atrial septal defect, AVM=arteriovenous malformation, BTT=Blalock-Taussig-Thomas, CHD=congenital heart disease, PDA=patent ductus arteriosus, VSD=ventricular septal defect.

blood flow. Complete obstruction to right ventricular outflow, as in tricuspid or pulmonary atresia, is discussed in the next section.

If the right-to-left shunting occurs at the level of the PDA, as in severe pulmonary hypertension or peripheral pulmonary artery stenosis, the patient's right hand may be normally saturated while the lower body is desaturated. An interrupted aortic arch or severe aortic coarctation produces the same differential cyanosis, as the blood supply beyond the interruption or the coarctation is provided by the blue blood from the PDA. Any of these diagnoses combined with transposition of the great arteries, such that blood flows from the more saturated pulmonary artery to the less saturated aortic arch, results in "reverse differential cyanosis," with lower saturation in the right hand than in the feet. These anatomies are the rationale for inclusion of a saturation percentage point difference in the CCHD screening algorithm.

Single Ventricles/Complete Intracardiac Mixing. Patients who have complete mixing of desaturated and saturated blood leading to equal saturations in the pulmonary arteries and aorta can generally be expected to have systemic saturation of 75% to 85% when there is equal blood flow to the lungs and the body. When more blood goes to the lungs, these children may saturate higher. This category of patients encompasses the unpalliated forms of a variety of diagnoses, including hypoplastic left heart syndrome, tricuspid atresia, pulmonary atresia, truncus arteriosus, and unobstructed total anomalous pulmonary venous return. Patients who have undergone the first stage of single-

ventricle palliation with a shunt or stented PDA are also included here.

Critically, this is the group of patients in whom supplemental oxygen can be harmful and in whom "normal" saturations in the high 90s may portend hemodynamic instability if the fine balance between pulmonary and systemic blood flow is disrupted. As a potent pulmonary vasodilator, oxygen can encourage more pulmonary flow and less systemic flow, decreasing systemic perfusion. That said, if a patient in this group is hypoxemic, with saturation below 75%, oxygen should not be withheld.

Palliated Single-Ventricle CHD (Glenn and Fontan). The second stage of single-ventricle palliation consists of taking down the previous source of pulmonary blood flow (typically a shunt or PDA stent) and connecting the superior vena cava to the pulmonary arteries—a bidirectional cavopulmonary or Glenn anastomosis. Patients with a single ventricle tend to saturate slightly higher after a Glenn procedure than they did before, around 80% to 90%. This is because the systemic output consists of a proportionally higher amount of cerebral blood flow, which goes to the lungs and returns to the heart oxygenated, compared with flow to the body, which returns to the heart desaturated. As these patients grow, the amount of systemic output to the lower extremities increases, hence increasing the proportion of desaturated blood returning from the inferior vena cava and mixing with pink blood from the lungs in the heart. Hence, older patients in Glenn physiology may start to saturate in the 75% to 80% range. After the total cavopulmonary anastomosis or the Fontan operation, the final

stage of palliation, the inferior vena cava is also connected directly to the pulmonary arteries, so the cardiac output consists of only fully saturated pulmonary venous return. In the absence of a fenestration between the Fontan conduit and the atrium, significant collateral vessels, or lung disease, patients who undergo the Fontan operation should have normal oxygen saturation of greater than 90%.

Complex Lesions. Several diagnoses, including unrepaired double outlet right ventricle, double inlet left ventricle, transposition of the great arteries, and Ebstein anomaly, can result in widely varying systemic saturations from severe cyanosis to normal saturation. The expected saturation will depend on anatomical details such as the relationship of the great arteries, the size and position of a VSD, valvar stenosis or regurgitation, and the degree of atrial-level shunting and mixing. The same can be said for repaired states of each of these lesions because the specific intervention and the resulting saturation can differ depending on the anatomical variant.

In general, saturation less than 70% for any congenital heart lesion may require urgent intervention, such as prostaglandin, balloon atrial septostomy, or surgical relief of obstruction. If a patient with known CHD has this degree of desaturation "at baseline," it may be from something not amenable to intervention, such as pulmonary arteriovenous malformations, in the setting of care directed toward palliative/noninterventional goals or in a patient for whom intervention is contraindicated for other reasons.

Visible Cyanosis

Visual assessment of cyanosis is an unreliable measure of the degree of desaturation and should always be confirmed by pulse oximetry or blood gas. However, since blue or purple discoloration may be the first sign of desaturation in a patient with undiagnosed CHD or a presenting complaint in the clinic and emergency department, it is helpful for every pediatrician to have a basic understanding of cyanosis.

Anemia and Polycythemia. Blood becomes visibly blue when there is a total deoxyhemoglobin concentration of at least 5 g/dL. (24) This is an absolute value, not a percentage, so the degree of desaturation that will be visibly detectable depends on the total amount of Hb. An anemic patient with only 7 g/dL (70 g/L) of total Hb would have to be severely desaturated to have 5 g/dL of deoxyhemoglobin (because 2 g/dL would be oxyhemoglobin, hence an oxygen saturation of ~29%). Chronic hypoxemia stimulates production of erythropoietin, causing a secondary erythrocytosis and increasing red blood cell mass. It is not

uncommon, then, for children with cyanotic CHD to be polycythemic. With a total Hb level of 17 g/dL (170 g/L), a patient with only mild desaturation may appear cyanotic, reaching the threshold of visibility much sooner than someone with less total Hb. This should not, of course, be used as reassurance when faced with a cyanotic patient, and the degree of desaturation should be confirmed with objective measures.

Central and Peripheral Cyanosis. Deoxyhemoglobin will be visible in areas where the skin is thinnest and where there is a high concentration of capillaries, such as hands, feet, earlobes, and mucous membranes. Systemic arterial desaturation causes central cyanosis visible in the lips, mucous membranes, and tongue, in addition to peripheral cyanosis visible in the hands, feet, nail beds, and perioral region. Patients who have normal Sao_2 will not have central cyanosis, but they may demonstrate peripheral cyanosis if there is significant tissue extraction of oxygen from the capillaries or if passage of blood through the capillaries is slow enough to allow for higher-than-normal oxygen extraction. The latter can occur when there is poor cardiac output or another reason for limited flow to the region (eg, arterial thrombus), vasoconstriction from cold exposure, venous congestion, or polycythemia. One should always consider alternative causes of discoloration as well, such as birthmarks, vascular malformations, and ecchymosis. As with the interpretation of pulse oximetry, skin pigmentation can also impact one's ability to perceive cyanosis.

SUMMARY

- Based on research evidence, pulse oximetry is less reliable when the pattern of blood flow sensed by the oximeter probe is altered, such as with low cardiac output, hypothermia, peripheral vasoconstriction, arrhythmia, and venous pulsations due to tricuspid regurgitation. Because the pulse oximeter algorithms were developed in healthy and predominantly light-skinned volunteers, pulse oximetry may be inaccurate in severely hypoxemic patients and those with greater skin pigmentation. In cases in which pulse oximetry may be unreliable, hypoxemia should be confirmed by blood gas analysis.

- Based on consensus, in children with congenital heart disease (CHD), oxygen saturation is determined by gas exchange in the lungs (respiratory), shunting mechanisms that permit deoxygenated blood leaving the heart to avoid the pulmonary circulation (intracardiac as well as extracardiac), and the

saturation of venous blood returning from the systemic circulation. Pediatricians should understand the factors that affect each of these to safely evaluate and treat hypoxemia in patients with CHD.

- Based on research evidence, the presence of a shunt does not equate to systemic desaturation. Patients with isolated, uncomplicated left-to-right shunts, such as those seen in a ventricular septal defect, atrial septal defect, partial anomalous pulmonary venous return, and patent ductus arteriosus, are expected to saturate normally outside the immediate newborn period. Desaturation in these patients deserves evaluation for respiratory causes or reasons for shunt reversal.

- Based on research evidence, low cardiac output, anemia, and high metabolic demand may cause tissue hypoxia in structurally normal hearts and can additionally cause systemic desaturation in patient with mixing or shunting.

- Based on research evidence, the oxyhemoglobin dissociation curve describes the relationship between partial pressure of oxygen in the blood and pulse oxygen saturation. A right-shifted curve suggests that greater partial pressure of oxygen is needed to fully bind and saturate hemoglobin, indicating that oxygen is more easily released to the tissues. A left-shifted curve suggests the opposite. Clinicians should remain cognizant of factors impacting a patient's ability to deliver oxygen to the tissues.

- Based on strong recommendation, newborns should be screened for critical CHD using pulse oximetry, and failed screenings should be evaluated further with echocardiography.

- Based on research evidence, hypoxemia generally results in visible cyanosis only when there is at least 5 g/dL of deoxyhemoglobin. Anemia and polycythemia can thus impact the degree of desaturation that is visible. Although many factors may contribute to peripheral cyanosis, central cyanosis is caused by systemic desaturation and should be explored further with pulse oximetry or blood gas analysis.

References and teaching slides for this article can be found at
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1. An 8-month-old girl with a complete balanced atrioventricular canal defect is being seen in follow-up after a recent respiratory syncytial virus infection. She previously had been scheduled for surgical closure of her defect due to concerns of increasing pulmonary vascular resistance. However, the surgery was postponed due to the recent illness. As her primary care provider, you are assisting her cardiologist in closely monitoring her oxygen saturations. Which of the following best describes the characteristic features of pulse oximetry?

    A. Does not need to be followed in this congenital heart lesion.
    B. Is a reliable surrogate for arterial oxygen saturation even with low cardiac output.
    C. Is not impacted by the presence of a dysrhythmia.
    D. Is not reliable below a reading of approximately 70%, and hypoxemia below that level should be confirmed by blood gas analysis.
    E. May underestimate the true oxygen saturation in patients with darker skin pigment.

2. You are seeing a female infant with pulmonary atresia and an intact ventricular septum and an atrial-level shunt. She is in the NICU and is receiving a prostaglandin E1 infusion to ensure that the ductus arteriosus remains patent, allowing pulmonary blood flow. She is awaiting surgical palliation. When you saw her in the first 24 hours after birth, her pulse oxygen saturation (Sp_{O_2}) measurements were approximately 80%. Five days later, her Sp_{O_2} is reading 92%. Clinical examination is largely unchanged, except for increasing mild to moderate tachypnea. Her nurse reports that the patient's skin feels slightly cooler. The increase in Sp_{O_2} in this patient is most likely related to which of the following pathophysiologic factors?

    A. Decreased hemoglobin level.
    B. Increased blood flow across the atrial septal defect.
    C. Increased pulmonary blood flow.
    D. Increasing metabolic demand.
    E. Worsening myocardial function.

3. You are screening a 1-day-old infant for critical congenital heart disease before discharge from the hospital. Which of the following findings is consistent with the infant passing the screening?

    A. An Sp_{O_2} of 98% in the right hand and 95% in the left foot.
    B. An Sp_{O_2} of 95% in the right hand and 94% in the left foot.
    C. An Sp_{O_2} of 98% in the right hand and 94% in the right foot.
    D. An Sp_{O_2} of 89% in the right foot, but improved to 95% on subsequent check.
    E. An Sp_{O_2} of 98% in the right hand and 97% in the left hand.

4. An 8-month-old infant is brought to the emergency department with respiratory distress and low-grade fever. The baby has hypoplastic left heart syndrome. After initial Norwood palliation, she underwent a Glenn procedure 2 months ago. Mom reports that her saturations have been typically around 85% to 88% since surgery, including at her cardiology appointment last week. She currently has a heart rate of 130 beats/min, respiratory rate of 40 breaths/min, Spo_2 of 78%, and blood pressure of 86/49 mm Hg. Mom states that before her Glenn procedure, saturations were frequently in the 70s. Which of the following is the most appropriate next step in the management of this patient?

    A. Agree that her current saturations are appropriate for Glenn physiology and do not require further evaluation.

    B. Avoid starting fraction of inspired oxygen but continue evaluation for respiratory infection.

    C. Measure hemoglobin/hematocrit because a change in saturations most likely reflects anemia.

    D. Order echocardiography because saturations most likely reflect change in cardiac output.

    E. Start oxygen by nasal cannula to support a likely respiratory illness, and reassure the mother that oxygen is not harmful with Glenn physiology.

5. A 1-year-old patient is brought to your clinic as a new patient. He was delivered at home and has received minimal health care. His mother reports concerns that the infant has been more tired, is not gaining weight, and at times appears "blue." Which of the following is the most accurate statement about cyanosis?

    A. Blood becomes visibly blue when 30% of hemoglobin is deoxygenated.

    B. Clinicians should be concerned only about central cyanosis because peripheral cyanosis is likely only environmental.

    C. Cyanosis will be visible only when there is systemic arterial desaturation.

    D. In patients with cyanotic heart disease, it requires more severe desaturation to appreciate cyanosis.

    E. Peripheral cyanosis may appear with low cardiac output and high tissue oxygen extraction.