

# Problems in Family Practice

## Evaluation of Cyanosis in the Newborn

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The appearance of cyanosis in the newborn may be an indication of pathology in the cardiovascular, pulmonary, central nervous, or hematologic systems. Peripheral cyanosis (pink tongue, blue extremities) encountered in the newborn with vasomotor instability is usually a "physiologic" or normal variant of no significance. When central cyanosis (blue mucous membranes and tongue, blue extremities) is evident, a pathologic cause of cyanosis is present. Characteristic patterns of respiratory effort, response to crying, breathing oxygen, and inhalation of 100 percent oxygen by face mask with positive pressure may help to differentiate the organ system involved. An approach, founded on basic physiologic principles, is presented to aid in determining the type of cyanosis present. By means of a series of simple bedside observations, the clinician can make a rapid, accurate assessment of the cause of the cyanosis in a particular infant, as well as decisions regarding further diagnostic evaluation and treatment.

Cyanosis is a common finding in the newborn nursery. Frequently the bluish color in an infant is first noted by an observant nurse. The causes of this discoloration range from benign peripheral vasoconstriction related to vasomotor instability, to the potentially fatal "true right-to-left shunt" associated with cyanotic forms of congenital heart disease.

In some infants, the physical findings, chest x-ray, or electrocardiogram will suggest a specific disease entity or organ system involvement. Frequently, however, a specific diagnosis will not be obvious. The physician is then faced with the choice of "watchful waiting" and frequent reevaluation, or of assuming immediately that the cyanosis may indicate a severe pathologic process and alarming the parents, perhaps needlessly, by arranging for additional diagnostic studies to obtain a definitive diagnosis. It is a clinical axiom that newborns with persistent cyanosis always get worse. Therefore, by choosing to wait for additional

findings on serial examinations the physician risks deterioration of the infant with an organic cause for his cyanosis.

It would be extremely valuable to have a practical system which permitted rapid, reliable assessment of the cause of the cyanosis, based on a few easily and rapidly performed clinical and laboratory observations. Decisions could then be made with confidence regarding the need for further evaluation and/or referral. The purpose of this paper is to describe such a system of evaluation, based upon an understanding of basic physiologic principles related to the causes of cyanosis. These principles will be discussed individually and then will be synthesized into a scheme for evaluation of the newborn with cyanosis.

### Definition

Cyanosis may be defined as a bluish discoloration of the skin, nail beds, or mucous membranes resulting from the presence of an absolute amount of reduced hemoglobin in the blood. Slightly more than 3 gm% of reduced hemoglobin must be present in the central arterial blood, or 4 to 6 gm% in a sample of "capillary" blood obtained from a finger or heel stick.<sup>1,2</sup> The presence of clinically detectable cya-

nosis is dependent upon both the arterial oxygen saturation and the total hemoglobin concentration. For example, a newborn with cyanotic congenital heart disease and a severe anemia may have an arterial oxygen saturation of only 60 percent, together with a hemoglobin of 6. This infant will have 3.6 gm of oxygenated hemoglobin and 2.4 gm of reduced hemoglobin, and thus by definition will not appear cyanotic, despite the presence of "cyanotic" heart disease.

### Types of Cyanosis

There are two basic types of cyanosis — central and peripheral.<sup>1,2</sup> The clinical picture, pathophysiology, and implications for course and outcome are considerably different (Table 1).

#### Central Cyanosis

Central cyanosis is due to a pathologic process which results in inadequate oxygenation of central arterial blood.<sup>1</sup> It is manifest clinically by the presence of cyanosis of the tongue and mucous membranes, as well as the extremities and nail beds. Beyond the first 20 minutes of life, central cyanosis should *always* be considered abnormal. It is caused by pathology in one of four organ systems: pulmonary, cardiac, central nervous, or hematologic. The infant with central cyanosis will deteriorate, and further evaluation must be pursued immediately to ensure precise diagnosis and appropriate treatment.

#### Peripheral Cyanosis

Peripheral cyanosis is present when the tongue and mucous membranes are pink, but the nail beds and extremities are blue. There is normal arterial oxygen saturation, but increased extraction of oxygen at the tissue level.<sup>1</sup> Peripheral cyanosis is usually "physiologic," but may occasionally result from a pathologic process.

#### Pathophysiology

In order to have normal oxygenation of peripheral tissues, the infant must have: normal ventilation, normal diffusion of oxygen across the alveolar-capillary membrane, normal transport of oxygen by red blood cells, and normal blood flow through the pulmonary and systemic circulations. Alterations in any of these processes can compromise delivery of oxygen to the peripheral tissues and result in a clinical appearance of cyanosis.

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**Table 1. Characteristics of Central and Peripheral Cyanosis**

	Peripheral	Central
Pathophysiology	↑ O <sub>2</sub> extraction at tissue level	central arterial desaturation
Clinical picture	pink tongue blue nail beds	blue tongue blue nail beds
Arterial O <sub>2</sub> saturation	normal	decreased
"Physiologic" causes	hypothermia local venous obstruction vasomotor instability	—
Pathologic causes	shock sepsis myocarditis	pulmonary cardiovascular CNS hematologic

**Central Cyanosis**

There are five basic physiologic mechanisms which cause central arterial desaturation and result in central cyanosis. All infants with central cyanosis have one or more of these mechanisms as causes for their cyanosis:

1. *Alveolar Hypoventilation* – Individual alveoli are not adequately ventilated because of shallow, irregular respiratory effort. Whatever oxygen does reach alveoli diffuses normally into pulmonary capillary blood. (Example – central nervous system disease – intracranial hemorrhage)

2. *Diffusion Impairment* – The process of ventilation is normal but oxygen does not diffuse normally from alveoli into pulmonary capillary blood. (Example – pneumonia)

3. *Right-to-Left Shunt* – Ventilation and diffusion are normal, but a portion of peripheral venous blood bypasses the lungs and joins the systemic circulation, thus having no opportunity to pick up oxygen from the alveoli. (Example – heart defect)

4. *Ventilation-Perfusion Inequality* – Despite normal mechanics of respiration, portions of the alveoli are not well ventilated. However, these portions of the lung are adequately perfused with blood. (Example – atelectasis)

5. *Inadequate Oxygen Transport* – Ventilation and diffusion of oxygen are normal. Blood flow through the lungs is normal. Red blood cells are incapable of transporting oxygen from the lungs to the tissues. (Example – congenital methemoglobinemia)

**Peripheral Cyanosis**

Peripheral cyanosis is due to in-

creased extraction of oxygen at the tissue level. The entire process of oxygenation of the blood is normal and therefore central arterial oxygen saturation is normal. Peripheral cyanosis occurs because of one of two physiologic mechanisms:

1. Decreased flow of blood through the vascular system (Examples – shock, sepsis, myocarditis) results in slow flow through capillary beds and increased extraction of oxygen at the tissue level. This mechanism should be considered a pathologic cause of peripheral cyanosis.

2. Peripheral vasoconstriction (Examples – hypothermia, vasomotor instability) results in slow flow through capillary beds and increased oxygen extraction at the tissue level. This mechanism should be considered a "normal" or "physiologic" cause of peripheral cyanosis. It is encountered in many normal newborn infants.

**Clinical Evaluation**

The initial decision in evaluating a patient with cyanosis should be whether the cyanosis is central or peripheral. This decision is based upon the color of the tongue and mucous membranes. While the extremities and nail beds will be blue in both types of cyanosis, the tongue will be blue in central cyanosis and pink in peripheral cyanosis. The tongue is a high flow, low resistance organ which extracts very little oxygen from the blood perfusing it. For this reason, observing the color of the tongue may be likened to obtaining a central arterial PO<sub>2</sub> from the ascending aorta. If the color of the tongue is pink, the observer

may confidently conclude that the process of oxygenation of the arterial blood is being accomplished normally. By definition, a patient with a pink tongue has peripheral cyanosis. Conversely if the tongue is blue, the observer can be assured that the arterial PO<sub>2</sub> will be decreased and that there is some abnormality in the process of oxygenation of the arterial blood resulting in central cyanosis.

If the infant is determined to have peripheral cyanosis (pink tongue), the next decision should be whether he has a "physiologic" or "pathologic" type of peripheral cyanosis. While this will usually be obvious from physical examination, if there is any question, one of the infant's lower extremities may be placed either into a tub of hot water or wrapped in a hot moist towel for a five-minute period (test the temperature yourself to avoid excessive heat). If peripheral cyanosis is due to a "physiologic" cause such as vasomotor instability or hypothermia, there will be a reflex vasodilatation of blood vessels in *both* lower extremities, and the cyanosis will clear. If cyanosis does not clear with this test, the infant should be suspected of having a "pathologic" type of peripheral cyanosis. Further investigation should be made for pathologic causes.

If the infant has central cyanosis (blue tongue), his respiratory pattern should be carefully evaluated. A characteristic breathing pattern will frequently suggest pathology in a particular organ system. When the central cyanosis is due to alveolar hypoventilation the infant will have a characteristic breathing pattern consisting of periods of apnea, bradypnea, and periodic shallow breathing suggesting an abnormality of the central nervous system. When central cyanosis is due to inadequate oxygen transport (hematologic disease), the respiratory pattern will be normal reflecting a normal process of ventilation. When central cyanosis is due to a cardiovascular abnormality, the pathogenetic mechanism is true right-to-left shunting of blood which bypasses the lungs and prevents normal oxygenation. The infant attempts to compensate by developing a mild increase in rate and depth of breathing without true respiratory distress. Finally, when central cyanosis is caused by pulmonary disease, there is an impairment of diffusion or a ventilation-perfusion

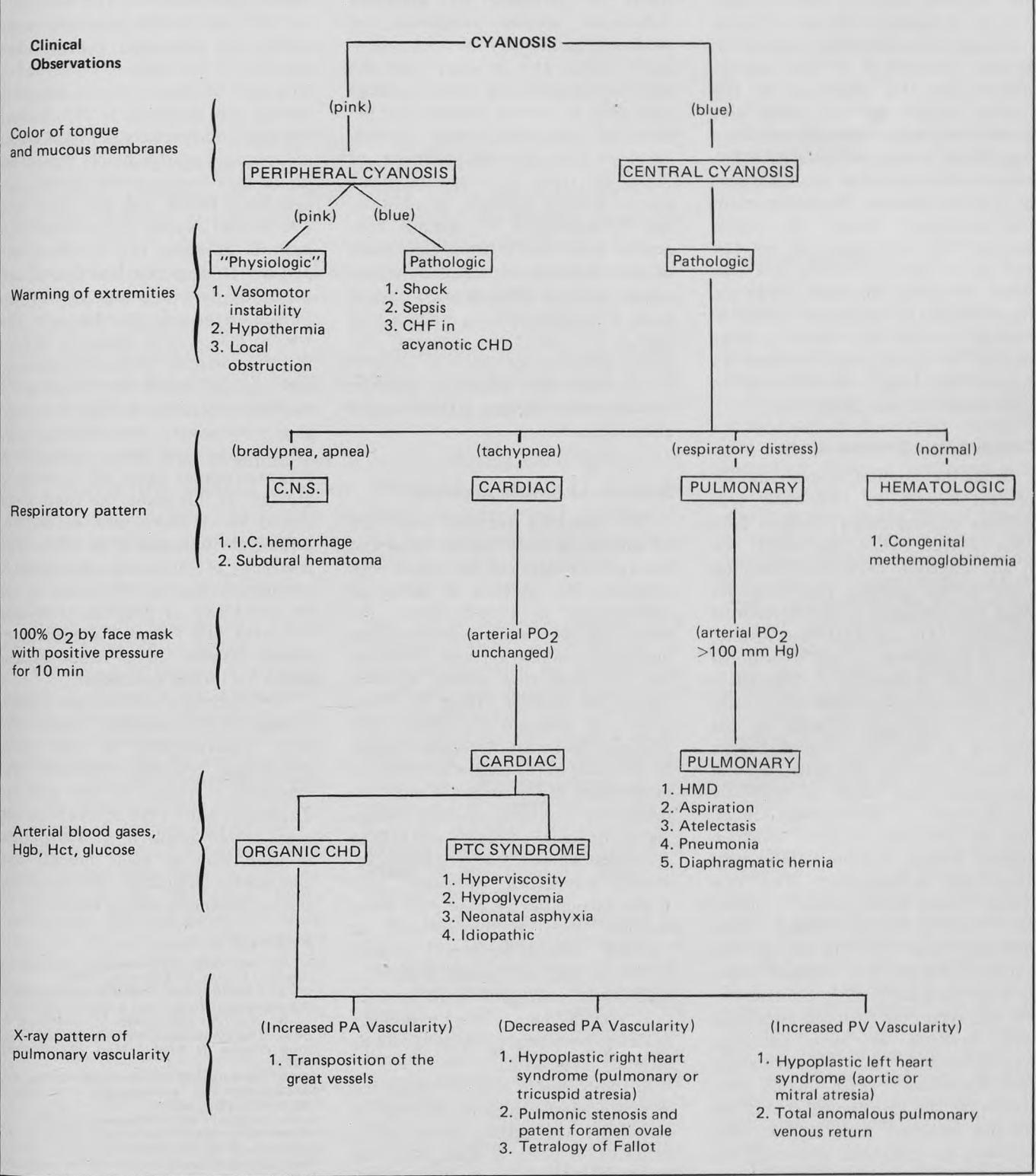
inequality. The breathing pattern is one of respiratory distress with dyspnea, intercostal and subcostal retractions, grunting and nasal flaring.

Those patients with central nervous system and hematologic causes of central cyanosis are usually easily distinguished by their clinical appearance.

The diagnosis of congenital methemoglobinemia can be confirmed by drawing up a few drops of blood onto filter paper and exposing it to the air. Normal blood should become bright red with exposure to air. If the patient has methemoglobinemia, the color of the blood will remain dark.

Difficulty commonly arises in distinguishing pulmonary from cardiovascular cyanosis. Several bedside observations may be helpful in differentiating the two, including the responses to crying and to inhalation of oxygen. In the infant with pulmonary cyanosis, crying will improve the

**Table 2. Flow Sheet for Evaluation of Cyanosis**



process of ventilation, and decreases the cyanosis. Inhalation of oxygen may also improve pulmonary cyanosis, by providing more oxygen to the alveolar-capillary interface. Conversely, for the infant with cardiac disease, an improvement in ventilation caused by crying, or an improvement in oxygen saturation resulting from inhalation of increased oxygen, will not improve cyanosis since a large portion of blood continues to bypass the lungs, never becoming oxygenated. Finally, Shannon et al<sup>3</sup> have demonstrated that the inhalation of 100 percent oxygen by face mask with positive end-expiratory pressure for a ten-minute period will clearly differentiate pulmonary and cardiac causes of central cyanosis. When the infant has pulmonary disease, the central arterial PO<sub>2</sub> will frequently rise 100 mm Hg or more following this test. When the infant has cardiac cyanosis, there will be no significant change in central arterial PO<sub>2</sub> since a large portion of blood will continue to bypass the lungs, never having an opportunity to pick up oxygen.

### Cardiovascular Cyanosis

When the response to breathing 100 percent oxygen by face mask with positive end-expiratory pressure indicates a true right-to-left shunt, the infant is likely to have a cardiovascular cause for his cyanosis. Two categories must be considered in the differential diagnosis: (1) congenital heart disease, or (2) persistence of the transitional circulation syndrome.<sup>4,5</sup> The latter syndrome is characterized by the early onset of striking cyanosis in the absence of anatomic congenital heart disease or primary pulmonary disease, associated with mild to moderate cardiomegaly, congestive heart failure, and an electrocardiogram which is usually normal or demonstrates right ventricular hypertrophy. The syndrome results from persistent pulmonary vasoconstriction causing abnormal right-to-left shunting through the ductus arteriosus and foramen ovale. In most cases the etiology is unknown, but the syndrome has been associated with prenatal or birth asphyxia, hypoglycemia, and hyperviscosity (polythycemia).<sup>4</sup> These infants illustrate that the transitional circulation of the newborn may be adversely affected by metabolic abnormalities. Hemoglobin and dextrostix determina-

tions for glucose level should be performed in every infant with evidence of a true right-to-left shunt.

Anatomic congenital heart disease causing cyanosis in the newborn may be differentiated on the basis of clinical findings, chest x-ray, and electrocardiogram. One way to consider cyanotic congenital heart disease in the newborn is to classify cases on the basis of increased or decreased pulmonary arterial vascularity, or increased pulmonary venous vascularity (Table 2).<sup>2</sup> In some cases the electrocardiogram and clinical findings may help to further differentiate the type of congenital heart disease. However, the clinical diagnosis of individual types of congenital heart disease is often difficult. In addition, the differentiation of cyanotic congenital heart disease from persistence of the transitional circulation syndrome may be difficult on a clinical basis. For these reasons, when a true right-to-left shunt is apparent, the infant should immediately be referred to a center with diagnostic facilities for emergency cardiac catheterization and treatment.

### Summary of Bedside Approach

The principles discussed above can be utilized to carry out a concise and accurate evaluation of any infant with cyanosis. By utilizing a series of observations in proper order, the entire evaluation and a decision regarding further evaluation and treatment can be completed within approximately 30 minutes (Table 2). When called to evaluate an infant with cyanosis, the initial observation should be the color of the tongue and mucous membranes. If the tongue is pink, the infant has peripheral cyanosis. Warming of the lower extremity will help to determine whether the peripheral cyanosis is "physiologic" or "pathologic." If the extremities become pink when warmed, then a "physiologic" or "normal" type of peripheral cyanosis is present and no further evaluation needs to be performed. If the extremities remain blue, then pathologic causes of peripheral cyanosis should be carefully investigated.

If the tongue is blue, the infant has central cyanosis which by definition is pathologic and further evaluation is indicated. A portable chest x-ray can be obtained at this point and while it

is being processed, further clinical observations are made. The infant's respiratory pattern is next evaluated as part of a brief, but complete physical examination. The clinical picture and respiratory pattern may differentiate which organ system is involved. The respiratory pattern may be especially helpful in differentiating those infants with central nervous system disease or hematologic disorders. The most difficult differentiation is between primary cardiac and pulmonary disorders. The response of the infant to crying and to inhalation of oxygen may be helpful in making this diagnosis. If the observer remains unsure as to the etiology of the cyanosis at this point, the infant should have central arterial blood gases performed before and after breathing 100 percent oxygen by face mask with positive pressure for a ten-minute period.<sup>3</sup> Hemoglobin, hematocrit, and dextrostix determinations may be performed on the same blood sample. The arterial PO<sub>2</sub> will be especially helpful in differentiating between pulmonary and cardiac causes of cyanosis. A marked increase in arterial PO<sub>2</sub> suggests a pulmonary cause. If the arterial PO<sub>2</sub> is unchanged, then it is likely that a cardiovascular cause of cyanosis is present. At this point, the chest x-ray should be reviewed, and an electrocardiogram obtained if possible. The presence of acidemia, hypoxemia, hypoglycemia, or polythycemia should be noted and, if possible, treatment instituted for these abnormalities before transfer to a cardiovascular center for further evaluation.

The method of evaluation outlined, if used in a systematic fashion and with understanding of the basic physiologic principles involved, will consistently result in an accurate diagnosis of the type of cyanosis and organ system involved. An appropriate decision may be made quickly and confidently regarding the need for further treatment and/or referral.

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