Neonatal Cyanosis: A Clinical Diagnosis

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Abstract

Neonatal cyanosis is a physical finding characterized by a bluish discoloration of the skin, mucus membranes and nail beds. The word cyanosis derives from the Greek word for dark blue, Kuanos. There are multiple causes and physiologic pathways which lead to this finding. This article will review the diagnosis and pathophysiology of neonatal cyanosis. The recognition of cyanosis and the development of an approach to define the underlying cause is a priority among hospitalized children.

Keywords: Neonatal; Cyanosis; Physical Diagnosis

Introduction

Neonatal cyanosis is a physical finding of bluish discoloration of the skin, lips, mucus membranes and nail beds which is apparent as part of the initial observation of the newborn. The distribution of the discoloration, physiologic basis for cyanosis and determining possible causes, is a complex process necessitating a full evaluation of the newborn and infant. This review will provide i) the process by which a diagnosis may be established, ii) the organization of a differential of possible diagnoses leading to targeted treatment.

Physical findings and distribution of cyanosis

Acrocyanosis and transition to room air

The term acrocyanosis refers to a peripheral distribution of a bluish discoloration of the distal extremities. The infant typically will be otherwise well on physical examination. Acrocyanosis can be associated though with poor perfusion, and if this finding persists, may require further evaluation and treatment.

The transition of the newborn to room air involves multiple changes physiologically leading to expansion of the chest wall and lungs. There is increased negative intrathoracic pressure upon delivery, followed by a decrease in the pulmonary vascular resistance (PVR). If the PVR is high, blood shunts though a patent ductus arteriosus (PDA), for 48 hours or more. In a normal neonate, the PDA has physiologic closure by 48 hours and anatomic closure within two to three weeks [1].

Central cyanosis

Central cyanosis is characterized by generalized blue discoloration of the skin and may involve the nailbeds and mucus membranes. The finding occurs when deoxygenated hemoglobin exceeds 3 - 5 g/dL. Central cyanosis may be life threatening and the possible causes include cardiac, metabolic, neurologic, infectious disease, parenchymal and non-parenchymal pulmonary diseases [2].
Differential cyanosis

Differential cyanosis refers to a distribution of cyanosis with a gradient in oxygen saturation between the upper and lower extremities. Reverse differential cyanosis refers to predominantly lower extremity cyanosis. The differential in oxygen saturation in comparing pre-ductal and post-ductal values, right hand and left foot respectively, can be profound due to the presence of shunting and redirection of pulmonary blood flow.

In considering differential cyanosis, the upper body is cyanotic reflecting the presence of a cardiac condition leading to hypoxemia of the upper extremities. The conditions associated include Co-Arctation of the Aorta (CoA), Patent Ductus Arteriosus, Persistent fetal circulation, Persistent pulmonary hypertension (PPHTN).

Reverse differential cyanosis in contrast is associated with a lower right hand oxygen (O$_2$) saturation, and is found in Transposition of the Great Arteries (TGA) with a PDA with or without a CoA [3].

Physical examination findings

Physical examination (PE) findings of cyanosis may be associated with systemic or focal organ system diseases. The PE involves observation for signs and symptoms of distress, respiratory distress, cardiovascular disease, sepsis and apnea. The infant is examined for perfusion, glucose and temperature instability, muscle tone, alertness, irritability, cry quality, jitteriness, tremors and feeding pattern. Infants with high levels of Hemoglobin variants with abnormal oxygen affinity often will not be in distress [4].

Hypoxemia, oxygen saturation and hemoglobin

A further area of consideration in the evaluation of the cyanotic infant is the use of blood testing to evaluate for hypoxemia. The infant with cyanosis has a level of deoxygenated blood which is elevated.

Cyanosis appears when the level of deoxygenated blood reaches a level of 3 - 5 g/dL. The infant may also have conditions such as anemia, polycythemia or a hemoglobinopathy which alter delivery of oxygen. The use of pulse oximetry is a useful initial indicator of hypoxemia, but the appearance of cyanosis varies depending upon the concentration of hemoglobin.

In normal infants, cyanosis may be detectable at 80 - 85% saturation in room air. In contrast, among infants with high levels of Hemoglobin or polycythemia, cyanosis is apparent at 87% saturation. Anemic infants appear cyanotic at lower levels of O$_2$ saturation, in the mid to low 60s.

Infants are born with high levels of Hemoglobin F, and this will shift the O$_2$ dissociation curve to the left. Newborns compared to older children will have significantly lower paO$_2$ levels, before the finding of central cyanosis. Other conditions such as acidosis and temperature alter the relationship between O$_2$ saturation and paO$_2$ [1].

Diagnostic approaches

Airway, breathing and circulation

The infant with cyanosis may have a complicated and complex pathophysiology, and the diagnostic approach involves a matrix of methods in establishing the diagnosis. The diagnostic steps first involve establishing an airway, breathing and circulation or 'ABCs'. Airway problems may include a variety of upper airway conditions, including choanal atresia, macroglossia or laryngo-tracheomalacia. In a study of 34 infants with choanal atresia or stenosis, 24% presented with cyanosis [5].

Breathing problems include pulmonary parenchymal and non-parenchymal conditions. Some examples of lung diseases causing cyanosis include neonatal pneumonia, respiratory distress syndrome, and pulmonary edema. Non-parenchymal etiologies include collapse of a lung or lobular collapse, and effusion.
Circulatory problems include cardiovascular disease, Hemoglobulinemias and alterations in the concentration of Hemoglobin.

**Temporally related cyanosis**

**Congenital**

Intrinsic diseases involve fetal development and abnormal development of the cardio-pulmonary and hematologic systems. Congenital defects may include cardiac disease resulting in the inadequate delivery of oxygenated blood to the tissues or result in right to left shunting with delivery of deoxygenated blood to the periphery. The presence of cyanosis which worsens after the patent ductus arteriosus (PDA) closes is often found in association with a ductal dependent cardiac lesion. Examples of cyanotic cardiac ductal dependent lesions include left sided defects such as hypoplastic left heart, Aortic stenosis and CoA. A mixing lesion such as TGA is another possible diagnosis particularly in the early newborn period. Right sided lesions involving obstruction to the delivery of blood to the lung, include tricuspid atresia and pulmonic stenosis.

In contrast, cyanosis that worsens with exertion, such as crying or feeding is often present in newborns with pulmonary disease.

Lung hypoplasia or premature lung disease can contribute to deoxygenated blood returning to the left chambers of the heart. Abnormal structure of the brain resulting in seizures and central apnea may also be considered. Upper airway disease may be present and produce obstruction of airflow to the lungs and may be associated with disordered breathing. Anemia, polycythemia and abnormal Hb molecular structure are among the many possible congenital causes of neonatal cyanosis [1,6].

**Extrinsic factors after delivery**

The events that occur after delivery which may lead to neonatal cyanosis are numerous and the maternal history is important in the assessment and determination of the diagnosis. Some common causes include meconium aspiration pneumonitis, pneumonia, sepsis and aspiration pneumonitis. Maternal and newborn drugs may depress the respiratory system, and lead to abnormal ventilator patterns and subsequent poor oxygenation. Upper airway mucus and obstruction of nasal airflow may lead to apnea and hypoxemia. Less commonly, neonatal anaphylaxis may occur and lead to desaturation.

**Mechanistic considerations**

The physiologic mechanisms of central cyanosis in the neonate involve basic functional analysis of the cardio-vascular and pulmonary systems. The four main mechanisms of hypoxemia are: i) Hypoventilation, ii) Ventilation/Perfusion mismatch, iii) Right to Left shunting, iv) Impaired alveolar-arterial diffusion.

Examples of hypoventilation reflect the respiratory center and breathing patterns of the infant. Decreased effort is associated with hypoventilation and may reflect metabolic diseases such as inborn errors of metabolism. Airflow can be decreased in upper airway and neurologic disease. Weakness of chest wall and accessory respiratory muscles can also result in hypoventilation.

Ventilation/Perfusion mismatching can result from pulmonary diseases which result in deoxygenation of blood returning to the left heart chambers. Right to left shunting as a result of cardiac disease and/or elevated pulmonary pressures has a broad differential of congenital conditions and acquired cardiac right ventricular failure [1,7] (Figure 1).

![Figure 1](image-url)
Unexpected episodes of cyanosis

In one study of 49 infants with a gestational age of ≥ 35 weeks who were admitted for central cyanosis, without cardiovascular collapse, reflux was diagnosed among 10% and the majority of infants presented in the first 48 hours of life. Only 23% of events occurred after 48 hours when the PDA is expected to physiologically close. The occurrence of an apparent life-threatening event or ALTE, has now been distinguished from a new definition of Brief Resolved Unexplained Event (BRUE) by the American Academy of Pediatrics (AAP). Lower risk BRUE infants may be observed and have fewer diagnostic tests performed. The lower risk infant is >60 days old; ≥ 32 weeks gestational age with a negative exam and past medical history. BRUE is characterized in contrast to ALTE by marked changes in tone and may also involve episodes of pallor rather than cyanosis [8,9].

Conclusions

The presence of neonatal cyanosis is a physical finding, with many possible single system or multisystem causes. Early diagnosis depends on recognition of the finding and a systematic approach to the infant with cyanosis. The diagnostic approach is based on the presence of deoxygenated Hemoglobin. The determination of the underlying cause first considers the airway, breathing and circulatory systems. The use of diagnostic imaging of the pulmonary and cardiac systems is based on the physical finding, temporal relationship of cyanosis to ductal closure, feeding, exertion and presence of congenital anomalies (Figure 2).

**Figure 2**

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Bibliography