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Approach to Cyanosis in a Neonate

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Introduction

Hello, and welcome to this pedscases podcast on an approach to cyanosis in a neonate. My name is Michelle Fric and I am a fourth-year medical student at the University of Alberta. This podcast was made in collaboration with Dr. Georgeta Apostol, a general pediatrician at the Royal Alexandra Hospital Pediatrics Clinic in Edmonton, Alberta.

Cyanosis refers to a bluish discoloration of the skin or mucous membranes and is a common finding in newborns. It is a clinical manifestation of the desaturation of arterial or capillary blood and may indicate serious hemodynamic instability. It is important to have an approach to cyanosis, as it can be your only sign of a life-threatening illness.

The goal of this podcast is to develop this approach to a cyanotic newborn with a focus on these can't miss diagnoses. After listening to this podcast, the learner should be able to:

1. Define cyanosis
2. Assess and recognize a cyanotic infant
3. Develop a differential diagnosis
4. Identify immediate investigations and management for a cyanotic infant

Background

Cyanosis can be further broken down into peripheral and central cyanosis. It is important to distinguish these as it can help you to formulate a differential diagnosis and identify cases that are life-threatening. Peripheral cyanosis affects the distal extremities resulting in blue color of the hands and feet, while the rest of the body remains pinkish and well perfused. This can occur at a normal systemic oxygen saturation and is commonly seen in healthy newborns for the first 1-2 days of life. This is also referred to as acrocyanosis and is a generally a benign finding. Peripheral cyanosis is thought to represent venous congestion caused by immature control of vascular tone in neonates and this improves as the neonate matures.

In contrast, central cyanosis affects the entire body, but is most evident in the mucous membranes and tongue. It is caused by an increase in the amount of deoxygenated hemoglobin and is associated with a low oxygen saturation. Central cyanosis can be normal in newborns for the first 5-10 minutes after birth, but if it persists, it requires immediate evaluation as it is always a manifestation of a serious underlying condition for the neonate.

Clinical Case

Now that we have the basics down, lets start with a case. You are the junior resident on your NICU rotation and you are called to assess a female newborn named Susie who appeared blue immediately after delivery and has not improved over the past thirty minutes.

You start your assessment by ensuring the baby is stable. Her temp is 37.9, she is tachypneic at 110 breaths/min, 85% SaO2 on RA, tachycardic at 177 beats/min, with a mean blood pressure of 61mmHg .

You get a quick history, paying close attention to gestational and delivery history. She was a 3.9kg female born at term after an uncomplicated pregnancy with regular pre-natal checks. She was delivered vaginally to a G1P1 mom and labour lasted 22hours. Mom was GBS negative and has no other health conditions. The nurse tells you that the amniotic fluid was dark in color and APGAR scores were 4 and 6 at 1 and 5 minutes respectively, with little respiratory effort initially.

On exam, she does not appear to have any dysmorphic features. She has blue but moist mucous membranes and her skin is dusky. She has nasal flaring and intercostal retractions. She has normal S1 and S2 with no murmur. She has decreased air entry bilaterally with coarse breath sounds. She has equal femoral pulses bilaterally. Her abdomen is soft with no hepatosplenomegaly. She is moving her limbs symmetrically and her primitive reflexes are in tact. The rest of your exam is unremarkable.

Lets discuss the approach to a cyanotic newborn a little more while keeping this case in mind.

Pathophysiology

To help better understand the differential of central cyanosis, it can be helpful to understand the pathophysiology. Cyanosis occurs when there is an increase in the absolute amount of deoxygenated hemoglobin in the blood. This is important because cyanosis becomes evident on appearance at an absolute concentration of about 3-5g/dL of deoxygenated hemoglobin, rather than at a specific oxygen saturation. *Normal arterial saturation as measured by pulse oximetery is ≥95%. Depending on the hemoglobin concentration, the degree of desaturation required to produce the same amount of cyanosis varies considerably. For example, an infant or a child with hemoglobin of 20 g/dL will exhibit cyanosis at a saturation of 85% (15% of 20 g/dL is 3 g/dL of deoxygenated hemoglobin), whereas an infant or a child with hemoglobin of 10 g/dL will not exhibit clinical cyanosis until saturation drops to as low as 70% (30% of 10 g/dL is 3 g/dL of desaturated hemoglobin). Thus, in children with anemia with*

hypoxemia, clinical cyanosis may not be recognized until saturations drop below 85%.[5] Therefore, you cannot solely rely on oxygen saturation as an indication for cyanosis, as there are some babies who may present with central cyanosis at a relatively high oxygen saturation. For this reason, you should always look for cyanosis on exam.

You can break down the pathophysiology of increased deoxygenated hemoglobin into 5 processes:

1. Hypoventilation – a problem bringing oxygen into the body
2. V/Q mismatch – a problem with lung oxygenation and perfusion
3. Diffusion abnormalities – a problem with the lungs delivering oxygen
4. Right to left shunt – a problem with the heart pumping oxygenated blood to the body
5. Inadequate oxygen transport – a problem with hemoglobin carrying the oxygen

Each of these situations can lead to *the arterial desaturation of oxygen or hypoxemia, leading to the appearance of cyanosis.*

Differential Diagnosis

First, we will divide our differential diagnosis based on central and peripheral causes of cyanosis.

Central Cyanosis Differential

Central cyanosis can be life-threatening and requires urgent evaluation. The differential is broad, and it is helpful to think about it through a systems based approach. Since the differential is so large, we will focus on major categories:

- Cardiovascular system:
    - There are many cyanotic congenital heart lesions, including: Transposition of the great arteries, Tetralogy of Fallot, truncus arteriosus, and tricuspid atresia. Cyanotic heart disease is life threatening and must be identified early. Cyanosis may be the only clue of a cyanotic heart lesion in an infant who appears to be otherwise well. For more information on cardiac causes, please see the PedsCase podcast on Cyanotic Congenital Heart Disease.
    - You should also keep in mind causes of heart failure, which can cause cyanosis. Heart failure can be secondary to sepsis, myocarditis, supraventricular tachycardia, complete heart block, or other cardiac condition
    - Persistent pulmonary hypertension may be another cardiovascular cause of cyanosis.
- Conditions related to the respiratory system include:
    - Respiratory distress syndrome
    - Transient tachypnea of the newborn
    - Meconium aspiration
    - Diaphragmatic hernia

    - You should also keep in mind airway obstructions, which can include choanal atresia or Pierre Robin Sequence among others.
- Infectious etiologies that cause cyanosis include
    - Pneumonia
    - Meningitis
    - Or sepsis
- Cyanosis can also be caused by decreased respiratory drive and problems with the nervous system including:
    - Maternal sedative drugs (including opioids) causing hypoventilation and apneas in the newborn
    - Asphyxia
    - Intracranial hemorrhage
    - Neuromuscular disease
- Problems with the hematologic system causing cyanosis include:
    - Acute or chronic blood loss
    - Polycythemia
    - Methemoglobinemia, which is a blood disorder with abnormally oxidized hemoglobin which prevents oxygen dissociation to the tissues and can either be hereditary or acquired. Infants are more likely to be affected by acquired forms of methemoglobinemia compared to adults.
- Other causes of cyanosis include endocrinology and metabolic concerns, such as:
    - Hypoglycemia
    - Congenital adrenal hyperplasia
    - Inborn errors of metabolism

This may seem like a huge differential. Later, we will discuss some physical exam findings and investigations that can quickly help you narrow it down. You should also keep in mind the most common causes of cyanosis in a newborn, which are respiratory distress syndrome, sepsis, and cyanotic heart disease.

Peripheral Cyanosis Differential

Peripheral cyanosis can be normal for the first 24 hours of a baby's life if they appear to be otherwise healthy. However, if the cyanosis persists for more than 24 hours, you should re-assess and investigate for a more serious diagnosis. These other causes of peripheral cyanosis include:

- Sepsis
- Cardiogenic shock
- Hypovolemia
- Environmental exposures to air, water

If a baby is born prematurely, they may have benign peripheral cyanosis persisting past the first 24 hours of life. It is still important to rule out the previously mentioned causes of peripheral cyanosis, including sepsis.

Assessment

When doing your physical exam of a newborn, be sure to include an assessment for cyanosis. First, ensure that the baby is stable by assessing ABCs and a full set of vitals. Pulse oximetry should be performed in the right hand and either foot. If the O2% is less than 95%, you should administer supplemental oxygen. Look for signs of respiratory distress, including nasal flaring, chest retractions, tachypnea over 60 breaths/min, stridor, and grunting. If a cyanotic infant is showing signs of increased work of breathing, the cause is more likely related to the respiratory system. A cyanotic neonate could have irregular, weak or absent respirations, which should make you think about central causes of decreased respiratory drive or severe fatigue. Listen for a murmur or abnormal breath sounds, which can help you differentiate between cardiac and respiratory diseases.

With quick inspection of the newborn, you may identify central cyanosis by checking the lips, mucous membranes, perioral region, and nail beds for bluish discoloration or peripheral cyanosis by seeing bluish color of the hands or feet. However, many cases of cyanosis are not so obvious. It is important to be intentional when looking for cyanosis, as it may be subtle or difficult to detect clinically due to factors such as skin color, exposure to light, or presence of jaundice. Furthermore, cyanosis may become apparent only during episodes of crying or feeding, when the saturations decrease further. Ensure you have good lighting and examine the tongue and oral mucosa to prevent missing a cyanotic infant.

To help you differentiate between cardiac and non-cardiac causes, you should perform a hyperoxia test. This compares pulse oximetry with or without an arterial blood gas before and after exposure to 100% inspired oxygen for ten minutes. In general, infants with neurologic or pulmonary causes of cyanosis will have a substantial increase in their oxygen saturation after exposure to 100% FiO2, whereas infants with cardiac causes will show negligible change.

You should make sure you complete a full physical exam on the newborn to identify any other signs that may help with your diagnosis. For example, the abdomen may be scaphoid in cases of diaphragmatic hernias. Make sure you look for dysmorphic features, as that can give you a clue to an underlying syndrome which can often be associated with congenital heart disease.

If you haven't taken a full history from mom yet, make sure you take the time to get a detailed pregnancy history, such as maternal age, gestational diabetes, pregnancy induced hypertension, prenatal screening and ultrasounds. A detailed labour history can give you clues for diagnosis, such as premature rupture of membranes, GBS status, use of sedatives or narcotics, pre-term birth, and presence of meconium.

If you are taking care of a well newborn, make sure they have their oxygen saturation checked before discharging them home. The Canadian Paediatric Society and Canadian Paediatric Cardiology Association recommend that all newborns should have pulse oximetry screening before leaving the hospital after birth to enhance detection of critical congenital heart disease. Changes in pulse oximetry may be able to pick up patients with clinically undetectable cyanosis. O2 saturation <90% is abnormal and should be investigated, whereas an O2sat of 90-94% or hand to foot difference

>3% is borderline and should be reassessed after an hour and if it's still < 95% after 2 repeated screens should be investigated.

Investigations & Management

Now onto the investigations and management for a cyanotic neonate. Once again, cyanosis can indicate a life threatening illness. Always go back to your ABCs and make sure the baby is stable. Signs that the infant needs immediate support include signs of obstructed airway, poor respiratory effort and fatigue, and circulatory collapse indicated by bradycardia, hypotension, and poor perfusion. You may need to consider bag-mask ventilation or intubation. If you suspect that it may be a cardiac lesion, ensure that the ductus arteriosus stays open by administering prostaglandins.

After your thorough history and physical exam, hopefully you have some idea of what system may be the primary cause of your patient's cyanosis.

Initial bloodwork should include an arterial blood gas to determine the severity of respiratory compromise, CBC to assess for anemia and sign of infection. Blood culture may be indicated to investigate sepsis. Blood glucose can be checked to determine presence of hypoglycemia.

A *chest x-ray* should be ordered for a cyanotic neonate. Not only does a chest xray help identify lung pathology, but it is also helpful to assess the cardiac silhouette and pulmonary blood flow.

An *echocardiogram and ECG* should be ordered in the context of a murmur, cardiomegaly on xray, or no improvement with oxygen in order to determine structural heart disease or persistent pulmonary hypertension.

At this point, it would be appropriate to start getting relevant consult services involved, such as cardiology. Once you have your diagnosis, you can initiate definitive management.

Clinical Case

Back to our clinical case… we already know that Susie is showing signs of respiratory distress and cyanosis. Based on what we've learned about cyanosis, we know that cardiac and pulmonary causes are the most common and can be life threatening. We still need to check O2 saturation and get a 4 limb BP. Initially her O2% was 85% on RA. You give her some supplemental oxygen and monitor her saturations for the hyperoxia test. Her saturations improve to 97% after 10 minutes on 2L of oxygen.

Given the positive response to oxygen, her normal cardiac exam, and abnormal respiratory exam, you are leaning more towards a respiratory cause. You order a couple investigations, including chest xray, blood gas, CBC, and blood cultures

Your chest xray images come back quickly but are unreported. The heart appears to be normally shaped and is less than 50% of the mediastinal width. The lungs, however, look abnormal with diffuse patchy areas, no evidence of pneumothorax, and no focal consolidation. Her CBC is within expected range for a newborn and her blood gas shows she is retaining CO2.

Some pertinent positives in your assessment include that she was a term baby, dark stained amniotic fluid, respiratory distress with improvement after supplemental oxygen, and abnormal appearing lungs on CXR. With this in mind, the top of your

differential is meconium aspiration syndrome. You have kept Susie on supplemental oxygen and decided that she is stable without more aggressive forms of respiratory support. You are feeling confident to present to your staff about this interesting case of neonatal cyanosis!

Summary

Now that we have developed an approach to a cyanotic newborn, I want to leave you with some key take home points.

1. Checking for cyanosis should always be part of your newborn exam. Central cyanosis persisting after the first 10 minutes of life must always be investigated. Keep in mind, cyanosis is not always obvious, especially in dark-skinned babies. Make sure to look closely in the mouth with a good light.
2. During the assessment of cyanotic the newborn, it is important to identify the cause of cyanosis on a physiologic basis. It will be helpful to consider if the cyanosis is caused by: cardiac or pulmonary conditions, because these are the most common causes for cyanosis in the newborn and could potentially be life-threating requiring immediate interventions. Other causes to consider are sepsis, hemoglobin abnormalities, hypoglycemia or metabolic diseases.
3. Remember to check the babies response to supplemental oxygen for the Hyperoxia test.
4. Don't be afraid to ask for help from your team or consulting services. Cyanosis can indicate a life-threatening pathology. Ensure that the baby is stable before continuing on with the rest of your exam or investigations.

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