An Approach to Neonatal Cyanosis

General Presentation

Central cyanosis is a bluish discoloration of the skin, mucus membranes and tongue that is observed when deoxygenated hemoglobin is > 3g/dL in arterial blood or > 5g/dL (>3.1mmol/L) in capillary blood. It is associated with a low arterial partial pressure of oxygen (PaO_2) and low hemoglobin oxygen saturation (SaO_2) as measured by oxymetry. Cyanosis is dependent on the absolute concentration of deoxy Hb, not on the ratio of oxy Hb/deoxy Hb. For instance, in a normal neonate with a Hb concentration of 17 g/dL, when hemoglobin oxygen saturation (SaO_2) is 82%, deoxy Hb is > 3g/dL. However, in polycythemia, cyanosis is detectable at a higher value of SaO_2, whereas in anemia, the reverse is true. Thus, in severe anemia, cyanosis cannot be detected by observation.

Another type of cyanosis, called peripheral cyanosis, involves a bluish discoloration of the skin but sparing of the mucus membranes & tongue. In this type, a normal PaO_2 value is detected. In this case, increased oxygen extraction due to sluggish movement through the capillaries leads to increased deoxygenated blood on the venous side. Vasomotor instability, and vasoconstriction caused by cold, low cardiac output and polycythemia can all cause this slow movement through the capillaries. Peripheral cyanosis is often a normal finding in newborns, especially when only the extremities are affected (acrocyanosis) due to vasoconstriction as a result of transient hypothermia; however, it is important to rule out serious causes of peripheral cyanosis, such as sepsis.

Questions to Ask

Explore pregnancy and labor history as suggested below. Also ask about family history of congenital heart disease and fetal ultrasound results, as the latter may reveal structural deformities such as congenital heart disease, diaphragmatic hernia and congenital cystic adenomatoid malformation (CCAM).

Pregnancy Hx	Associated causes of cyanosis
Gestational diabetes mellitus (GDM)	TTN, RDS, hypoglycemia, TGA
Oligohydramnios	Pulmonary hypoplasia
Pregnancy induced hypertension	IUGR, polycythemia, hypoglycemia
Lithium intake (1st trimester)	Ebstein's anomaly
Advanced maternal age	Trisomy 21 associated with many congenital heart defects (cyanotic and acyanotic)

Labor Hx	Associated causes of cyanosis
PROM, fever, GBS +ve	Sepsis
Sedatives/anesthetics	Respiratory depression, apnea
C-section	TTN, PPHN
Preterm infant	RDS
Meconium	MAS (pneumonia)

Abbreviations: TTN = transient tachypnea of the newborn, RDS = respiratory distress syndrome, TGA = transposition of the great arteries, IUGR = intrauterine

growth retardation, PPHN = persistent pulmonary hypertension of the newborn, also known as persistent fetal circulation, MAS = meconium aspiration syndrome

Physical Examination

1) Determine whether the cyanosis is central or peripheral
2) Check the vitals: signs of respiratory distress such as tachypnea, retractions, nasal flaring & grunting usually indicate a respiratory problem congenital heart disease is often accompanied by absent or effortless tachypnea. Sepsis often has the following findings: peripheral cyanosis, ↑ HR, ↑ RR, ↓ BP, ↑/↓ temp (DD_X: left-sided obstructive lesions: hypoplastic left heart syndrome, critical aortic stenosis & severe coarctation of the aorta).
3) Rule out choanal atresia. If in doubt, attempt to insert a catheter through the nares
4) Listen for murmurs: a systolic murmur audible in most forms of cyanotic CHD (exception: d-TGA with intact ventricular septum & no pulmonary stenosis).
5) Assess the abdomen: scaphoid abdomen in diaphgragmatic hernia
6) Consider neurological disorders: observe for apnea and periodic breathing, which may be related to immaturity of the nervous system. Seizures can cause cyanosis if the infant fails to breathe during the episodes.

Differential Diagnosis

To determine the underlying cause of cyanosis in a newborn, it is important to think about the various mechanism of cyanosis. Then, organize your thoughts by anatomical systems.

Ventilation/perfusion mismatch
Airway disease: transient tachypnea of the newborn (TTN), respiratory distress syndrome (RDS), pneumonia, aspiration (meconium, blood, amniotic fluid), atelectasis, diaphragmatic hernia, pulmonary hypoplasia, pulmonary hemorrhage, CCAM
Extrinsic compression of the lungs: pneumothorax, pleural effusion, hemothorax,

Right-to-left shunt
Intracardiac: **The 5 T's: T**etralogy of Fallot, **T**ricuspid atresia, **T**ransposition of the great arteries, **T**otal anomalous pulmonary venous return, **T**runcus arteriosus; and pulmonary atresia, Ebsteins anomaly (abnormal tricuspid valve), hypoplastic left heart
Great vessel level: persistent pulmonary, hypertension of the newborn
Intrapulmonary level: pulmonary arteriovenous malformation

Alveolar Hypoventilation
CNS depression: asphyxia, maternal sedation, intraventricular hemorrhage, seizure, meningitis, encephalitis
Airway obstruction: choanal atresia, laryngomalacia, Pierre Robin syndrome
Neuromuscular disease: phrenic nerve inury, neonatal myasthenia gravis

Diffusion Impairment
Pulmonary edema: left-sided obstructive cardiac disease (aortic stenosis), cardiomyopathy
Pulmonary fibrosis

↓ Hemoglobin O2 affinity

Methemoglobinemia (congenital, drugs)

↓ Peripheral circulation (peripheral cyanosis)
Sepsis, shock of any cause, polycythemia, hypothermia, hypoglycemia, low cardiac output (hypocalcemia, cardiomyopathies, etc)

Investigations:

CBC & diff :
- ↑ or ↓ WBC → sepsis
- hematocrit > 65% → polycythemia

Serum glucose: to detect hypoglycemia

Arterial Blood Gases (ABGs):
- Arterial PO_2: to confirm central cyanosis → SaO_2 not as good an indicator due to ↑ fetal Hb affinity for O_2 (left-shift)
  - ↑ $PaCO_2$: may indicate pulmonary or CNS disorders, heart failure
  - ↓ pH: sepsis, circulatory shock, severe hypoxemia

Methemoglobinemia: ↓ SaO_2, normal PaO_2, chocolate-brown blood

Hyperoxia test: administer 100 % oxygen for > 10 min
- PaO_2 > 100 mmHg: **pulmonary disease** likely
- PaO_2 < 70 mmHg, rise by < 30 mmHg or SaO_2 unchanged: **cardiac** cause (R-L shunt) likely
- Total anomalous pulmonary venous return may respond
- Pulmonary disease with a massive intrapulmonary shunt may not respond

Pre-ductal & Post-ductal PaO_2 or SaO_2 measurements (pre- and post- ductus arteriosus):
- Preductal artery (right radial) PaO_2 10 – 15 mmHg > post ductal artery (umbilical artery line) PaO_2 → R – L ductal shunt (e.g., pulmonary diseases, commonly PPHN)
- SaO_2 can also be measured (right hand & right or left leg) → significant if > 10-15 % difference.

CXR:
- To identify pulmonary causes of cyanosis: pneumothorax, pulmonary hypoplasia, diaphragmatic hernia, pulmonary edema, pleural effusion, etc.
- Useful in evaluating congenital heart disease: e.g., cardiomegaly & vascular congestion → heart failure:
  - TGA → egg-on-a-string (anterior/posterior relationship of great vessels)
  - TOF → boot-shaped heart (RVH)
  - TAPVR → snowman, figure 8 (anomalous drainage chamber in superior mediastinum)

Echocardiography
- Indicated if abnormal cardiac examination suggestive of congenital heart defect, failed hyperoxia test (cardiac disease suspected) or has unclear diagnosis

Initial Management

1) Monitor Airway, breathing, circulation (ABCs)
→ with respiratory compromise, establish an airway & provide supportive therapy (e.g., oxygen, mechanical ventilation)

2) Monitor Vital signs
3) Establish vascular access for sampling blood & administering meds (if needed)
   → umbilical vessels convenient for placement of intravenous & intraarterial catheters
4) If sepsis is suspected or another specific cause is not identified, start on broad spectrum antibiotics (e.g., ampicillin and gentamycin) after obtaining a CBC, urinalysis, blood & urine cultures (if possible). Left untreated, sepsis may lead to pulmonary disease & left ventricular dysfunction.

5) An infant who fails the hyperoxia test & does not have PPHN or a CXR showing pulmonary disease likely has a congenital heart defect that's ductus-dependent. If cardiac disease is suspected, immediately start PGE_1 infusion
   Complications of PGE_1 infusion include hypotension, tachycardia, apnea
   Secure a separate intravenous catheter to provide fluids for resuscitation and ensure accessibility of intubation equipment should they be required.

Conclusion:

Central cyanosis in a newborn is an abnormal finding and one must consider all of the possible etiologies with a complete history, physical examination and relevant investigations. Remember to think about the various mechanisms causing cyanosis and go through each systematically until you have your diagnosis. Prompt management should be undertaken while you are trying to figure out your diagnosis. Putting all of this together, you will be sure not to miss an important diagnosis and keep your patient safe at the same time!

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