PEM GUIDE: CYANOTIC CONGENITAL HEART DISEASE

INTRODUCTION (KELLY CLEARY, M.D. 8/2013)
Congenital heart disease (CHD) is the most common congenital disorder affecting about 1 out of every 115 live births. Of these, approximately 15% are disorders that present with cyanosis in the neonatal period. Cyanosis occurs when the level of deoxygenated hemoglobin in blood exceeds 3-5 gm/dL. In the neonatal period, it is often difficult to differentiate cyanosis that originates from a cardiac etiology versus a non-cardiac cause. Prompt recognition is crucial for early emergency intervention

CYANOTIC HEART LESIONS – "5 T'S +"		
T	Transposition of the Great Arteries (TGA)	Mixing Lesion
T	Tetrology of Fallot (TOF)	R to L Shunt
T	Truncus Arteriosus (TA)	Mixing Lesion
T	Total Anomalous Pulmonary Venous Return (TAPVR)	Mixing Lesion
T	Tricuspid Atresia (TA), Epstein's anomaly	R to L Shunt
+	Double Outlet Right Ventricle (DORV)	Mixing Lesion
+	Pulmonary Atresia/Stenosis (PA/PS)	R to L Shunt

HISTORY – INCREASED RISK OF CHD
Maternal diabetes +/- obesity
Smoking in first trimester
Congenital heart block (mother with SLE - Lupus)
CMV, HSV, Rubella, Coxsackie maternal infection
Hydantoin anticonvulsants (eg Phenytoin), Lithium
Assisted reproductive technology
1st degree relative with CHD

CLINICAL EVALUATION
Cyanotic congenital heart disease should be considered in any neonate or infant that presents critically ill as well as those with cyanosis. Elements of the history, vital signs, physical exam and ancillary testing will aid in the diagnosis.

DIFFERENTIAL DIAGNOSIS – CRITICALLY ILL INFANT		
T	Trauma	Consider intentional trauma
H	Heart disease	Congenital heart disease, arrhythmias
E	Endocrine	Congenital adrenal hyperplasia
M	Metabolic	Hypoxia, hypoglycemia
I	Inborn errors	Acidosis, hyperammonemia
S	Sepsis	Bacterial, viral
F	Formula (Na)	Hypo/hypernatremia
I	Intestinal	Malrotation
T	Toxicants	Methemagobinemia
S	Seizures	Primary, secondary

DIFFERENTIAL DIAGNOSIS - CYANOSIS	
Airway	Obstruction – choanal atresia, larygomalacia, Pierre Robin
Pulmonary	Pulmonary (internal) – transient tachypnea of the newborn, respiratory

	arrest syndrome, pneumonia, aspiration, atelectasis, pulmonary hemorrhage/hypoplasia/edema
	Pulmonary (external) – pneumo/hemothorax, diaphragmatic hernia, pleural effusion
Cardiac	R-L shunts – TET, Tricuspid atresia (TA), Ebstein's anomaly, PA/PS Mixing - Truncus arteriosus, TAPVR, TGV, DORV
	Shock – Hypoplastic left heart, critical aortic stenosis, critical coarctation
Neuro	CNS – asphyxia, sedation (maternal drugs), intraventricular hemorrhage, seizure, meningitis, encephalitis
	Neuromuscular disease – neonatal myasthenia, phrenic nerve injury
Shock	Any cause - sepsis, hypothermia, hypoglycemia
Heme	Methemoglobinemia, polycythemia

PHYSICAL EXAMINATION

VITAL SIGNS - CYANOTIC CARDIAC LESIONS	
Heart Rate	Tachycardia
Blood pressure	BP gradient may exist between upper and lower extremities (coarctation) Infant may be hypotensive (shock)
Respiratory	Varying degrees of respiratory distress Mild tachypnea to severe respiratory distress
O_2 saturation	Low saturation with cyanotic lesions Differential cyanosis (upper half of the body is non-cyanotic and the lower half is cyanotic, or vice versa)

PHYSICAL EXAM FINDINGS
Cyanosis
Murmur
Poor perfusion
Hepatomegaly
Crackles/rales on lung auscultation
Weakened pulses

EVALUATION

Initial work-up should include a chest XRAY (CXR), EKG, arterial blood gas (ABG), pulse oximetry, CBC, and echocardiogram. Often a sepsis work-up is done since the presenting features of neonatal sepsis may mimic those of CHD. On chest XRAY, careful attention should be given to heart size and shape, pulmonary vascular markings and the location of the aortic arch. Echocardiography will provide definitive diagnosis of CHD.

XRAY/EKG FINDINGS WITH CYANOTIC LESIONS				
LESION	CXR HEART	CXR VASCULARITY	EKG	DUCTAL DEPENDANT
TOF	Boot shaped	Decreased	RAD/RVH	YES (possibly)*

TGA	Egg-on-a-string	Increased	RAD/RVH	YES (possibly)*
TAPVR	Snowman	Increased	RAD/RVH	NO
TA (truncus)		Increased	RAD/RVH	NO
TA (tricuspid)		Decreased	LAD/LVH	YES (always)

* Whether or not a lesion is ductal dependent depends on the presence of other lesions (communication between chambers). For example, transposition of the great vessels is not ductal dependent if there is a large atrial or ventricular septal defect (ASD or VSD)

EKG

The EKG in the infant with cardiac disease may be normal or suggestive of atrial or ventricular enlargement, though some lesions are associated with specific EKG patterns The normal neonatal EKG has a right axis deviation(RAD) (QRS +90 to+180) and right ventricular hypertrophy(RVH). EKG of patients with TA and ED will demonstrate pathognomonic superior axis (0 to -90 degree). Cardiac lesions with a small right ventrical (such as TA) will show signs of left axis deviation (LAD), right atrial enlargement (RAE) (tall peaked P waves in lead II) and left ventricular hypertrophy (LVH).

HYPEROXIA TEST

The hyperoxia test is used to help distinguish between cardiac and non-cardiac causes of cyanosis. Neonates with cyanotic congenital heart disease typically do not have a significant increase in the PaO_2 with administration of 100% oxygen. The PaO_2 in patients with pulmonary disease usually increases significantly because V-Q mismatches are overcome by oxygen administration. This test is performed by measuring the arterial oxygen tension in the right radial artery (pre-ductal) while administering room air and then comparing this to the arterial oxygen tension while administering high levels of inspired oxygen (100%) for 10 minutes. A significant increase in the systemic arterial oxygen saturation or PaO_2 (above 150mmHg) suggests pulmonary disease as an etiology. The pre-ductal oxygen tension while breathing 100% oxygen rarely exceeds 150mmHg in patients with cardiac lesions.

HYPEROXIA TEST – RESPONSE TO SUPPLEMENTAL OXYGEN	
Normal	Increased PaO_2
Methemaglobinemia	Increased PaO_2, yet remains cyanotic
Pulmonary disease	Some increased $Pa0_2$
Cyanotic Congenital Heart	No increase $Pa0_2$

MANAGEMENT

Assess and manage airway, breathing and circulation. Consider early intubation, support with inotropes (Dopamine, Dobutamine) as needed, obtain adequate vascular access

PROSTAGLANDIN E1 - If there is clinical suspicion for a ductal-dependent cardiac lesion, prostaglandin E1 (PGE1) should be used immediately to maintain a patent ductus arteriosus. The initial dose is 0.05 – 0.1 mcg/kg/min. Complications of PGE1 are listed below. The clinician should be prepared to intubate and support hemodynamics after its administration. Patients being transported to an outside institution should be intubated prior to transport.

PGE1 COMPLICATIONS
Hypotension
Tachycardia / bradycardia

Apnea
Seizure
Hyperthermia
Rash / skin flushing
Thrombocytopenia

Decreasing pulmonary vascular resistance and oxygenation stimulate closure of the ductus arteriosus at birth. Patients with ductal dependent lesions may present with an acute onset of deterioration when the ductus closes. The right-sided ductal dependent lesions typically present with cyanosis while the left sided lesions typically present with signs of congestive heart failure – trouble feeding, breathing, sweating, irritability, rales, hepatomegaly, weak or absent pulses, signs of poor distal perfusion

Note that not all cyanotic lesions are ductal dependent (complete mixing lesions – truncus arteriosus, TAPVR) and that some non-cyanotic lesions may be ductal dependent (eg coarctation of the aorta). In addition, whether or not a lesion is ductal dependent depends on the presence of other lesions (communication between chambers) For example, transposition of the great vessels is not ductal dependent if there is an ASD or VSD present. In fact, treatment for a ductal dependent TGV is the creation of an ASD (atrial septostomy) through a catheter. Oxygen administration may worsen ductal dependent lesions by promoting closure of the ductus. Right to left lesions will become more cyanotic and left to right lesions will develop worsening congestive heart failure. If a ductal dependent lesion is suspected the patient should me managed on room air

DUCTAL DEPENDENT CARDIAC LESIONS
RIGHT SIDED LESIONS
Depend on ductus for pulmonary blood flow (Right to Left)
Presentation – cyanosis
• Pulmonary Atresia (PA)
• Critical pulmonary stenosis (PS)
• Tricuspid Atresia (TA)
• Tetrology of Fallot (TET)
LEFT SIDED LESIONS
Depend on ductus for systemic blood flow (Left to Right)
Presentation – weak or absent femoral pulses, cardiogenic shock
• Coarctation of the aorta
• Critical Aortic stenosis (AS)
• Hypoplastic left heart
RIGHT AND LEFT SIDED CIRCULATION SEPARATED

Depends on ductus to connect separate circulations
Presentation - Cyanosis
• Transposition of the great arteries (TGA)

ANTIBIOTICS: Infants with cyanotic cardiac lesions often present in extremis with cyanosis, left ventricular dysfunction and tachypnea after the ductus closes. Given that these symptoms mimic neonatal sepsis, these infants are often empirically started on broad-spectrum antibiotics.

SPECIFIC CYANOTIC HEART LESIONS

TRANSPOSITION OF THE GREAT ARTERIES - This is the most common congenital cyanotic lesion diagnosed in the newborn period, affecting approximately 5% of patients with congenital heart defects. (TOF is the most common overall, but usually diagnosed later). In TGA, the aorta arises from the morphologic right ventricle and the pulmonary artery arises from the left ventricle. With normal cardiac anatomy, pulmonary and systemic circulations run in series; with TGA, two parallel systems without connection exist. The clinical scenario that results is severe hypoxemia secondary to deoxygenated venous blood traversing through the right atria and right ventricle just to be returned to the systemic system deoxygenated. This lesion is incompatible with life if mixing between the pulmonary and systemic systems does not occur.

Cyanosis, +/- a murmur are the most common presenting clinical findings. An electrocardiogram shows right axis deviation and right ventricular hypertrophy (RVH), which is not specific given that this is typical of a newborn EKG. Chest X-ray may show increased pulmonary vascular markings as well as an “egg on a string” pattern (narrow mediastinum due to a small thymus and anterior/posterior positioning of the great vessels as opposed to the usual right/left positioning of the vessels.) Echocardiography can provide the definitive diagnosis. Immediate stabilization is provided by PGE1 administration. If inadequate oxygenation or acidosis persists despite PGE1 an atrial septostomy may be indicated/ (Definitive treatment is an arterial switch procedure with re-implantation of the coronary arteries.)

TRUNCUS ARTERIOSUS is a non-ductal dependent cardiac lesion in which one great vessel emerges from the heart; the aorta, pulmonary arteries and coronary arteries all originate from ascending portion of a single vessel. The vessel has combined output from the left and right ventricles. Symptomatology is dependent on the amount of pulmonary blood flow (PBF); the greater the PBF, the greater the degree of congestive heart failure (CHF) that develops. CXR findings include increased pulmonary vascular markings and cardiomegaly. Initial emergent treatment includes management of CHF; definitive treatment is closure of the VSD, separating the pulmonary arteries from the trunk and creating a conduit to the right ventricle (Rastelli procedure).

TOTAL ANOMALOUS PULMONARY VENOUS RETURN - There are four types of TAPVR; supracardiac, cardiac, infracardiac, and mixed lesions. In all lesions, the pulmonary veins fail to connect to the left atrium and therefore systemic circulation. A right to left shunt is necessary for survival to distribute oxygenated blood to the body. The degree of cyanosis is dependent upon the degree of mixing as well as any obstruction of the pulmonary veins.

TAPVR SUBTYPES	
Supracardiac	Pulmonary veins connect to SVC
Cardiac	Pulmonary veins drain into RA directly

Infracardiac	Pulmonary veins drain into portal vein->hepatic vein->IVC
Mixed	Combination of the above

In cases of TAPVR, an EKG will likely show RVH and RAH. The CXR will show increased pulmonary vascular markings, and in cases of supracardiac TAPVR may have a “snowman” or “figure of 8” appearance. This is caused by a dilated superior vena cava (SVC) and vertical vein (formed by the pulmonary veins joining together.)

TETROLOGY OF FALLOT - This is the most common cyanotic heart lesion when considering all groups. Clinical presentation is dependent on the severity of the pulmonary outflow obstruction. “Pink TETS”, those with mild ventricular outflow obstruction tract obstruction, may present with CHF due to pulmonary over circulation. However, as the degree of pulmonary stenosis increases, the pulmonary blood flow decreases, and the degree of cyanosis increases.

TETROLOGY OF FALLOT	
1	RV Outflow Tract obstruction
2	VSD
3	Right Ventricular Hypertrophy
4	Overriding aorta

A loud systolic ejection murmur may be detected (due to right ventricular outflow tract (RVOT) obstruction) at the left sternal border. The second heart sound may be diminished as the aorta overrides the pulmonary artery. EKG may show nonspecific RVH. CXR may show decreased pulmonary vascular markings and a “boot shaped” heart due to an absent or decreased pulmonary artery segment.

Treatment of TOF initially includes PGE1 if the patient is cyanotic and pulmonary blood flow is ductal dependent. Surgical intervention includes initial modified Blalock-Taussig shunt (Gortex conduit connecting of the subclavian artery to a branch pulmonary artery). Definitive treatment includes repair of the RVOT obstruction with augmentation and / or repair of the pulmonic stenosis and closure of the VSD.

Patients may develop cyanotic or hypoxic spells, which consist of sudden onset of increased cyanosis, excessive crying, hypoxemia, acidosis, dyspnea, syncope, rarely seizures, and occasionally death if untreated. (See PEM Guide – Tetrology of Fallot Spells). During these “Tet” spells, there is increased right-to-left shunting due to obstructed pulmonary outflow tract and / or decreased systemic vascular resistance.

Treatment of TET spells includes increasing pulmonary blood flow by:

1. Increase systemic venous resistance (SVR) to increase systemic venous return,
   Knee-chest position, squatting, intravenous fluids and Phenylephrine increase SVR
2. Decrease pulmonary vascular resistance (PVR)
   Calming the infant and sedation with Morphine or Ketamine decreases PVR.
3. Reduce the degree of right ventricular outflow tract (RVOT) obstruction.
   Propranolol reduces heart rate, relaxes the RVOT

Severe cases may require abdominal aorta compression and emergent Blaylock-Taussig shunt placement, Sodium bicarbonate may be required to correct acidosis.

TRICUSPID ATRESIA - No communication is present between the right atrium and ventricle; therefore a hypoplastic right ventricle is present. A patent foramen ovale or ASD is necessary for survival. Severe cyanosis is the rule. EKG will show pathognomonic superior axis (0 to -90 degree), Right atrial and left atrial enlargement, , and left ventricular hypertrophy. Initial

management includes prostaglandin; balloon septostomy may be necessary followed by a Blalock Taussig shunt.

EBSTEIN ANOMALY - This lesion is referred to as “atrialization” of the right ventricle; there is inferior displacement of the tricuspid valve. In its most severe form, the tricuspid leaflets may extend into the right ventricular outflow tract. Chest X-ray shows a large right atrium and massive cardiomegaly (due to atrial enlargement), and EKG may show right bundle branch block, large P waves, and sometimes first degree atrio-ventricular block or Wolf-Parkinson-White syndrome. Treatment is usually palliative. Cyanosis from the right-to left atrial shunting typically improves as PVR decreases in the neonatal period.

PULMONARY ATRESIA - With this lesion, pulmonary blood flow is a ductal dependent; depending on blood flow from the aorta to the pulmonary artery through a patent ductus arteriosus (PDA). Initial treatment includes stabilization with PGE-1. Definitive treatment includes opening the pulmonary valve via cardiac catheterization or surgical repair to create a right ventricular to pulmonary artery connection.

**DOUBLE OUTLET RIGHT VENTRICLE - ** Both the pulmonary artery and aorta arises from the right ventricle. DORV always includes a VSD. Children with this lesion often present in CHF. DORV is treated surgically.