**Embryology**

- **Tetralogy of Fallot (TOF)**
  - Most common cause of cyanotic congenital heart disease (CHD)
  - Incidence of 7-10% of all CHD
  - TOF-PA
    - Accounts for about 2% of CHD; incidence of 0.07 per 1000 live births
    - Accounts for 20.3% of all forms of TOF
    - With multiple aortopulmonary collaterals (MAPCAs)
      - Is the most extreme form of TOF
      - Accounts for 20% of all cases of TOF

- **Normal development**
  - Lungs develop from foregut and carry nutrient supply from the paired dorsal aorta
  - Paired 6th aortic arches give rise to branches that fuse with the pulmonary vascular tree at 27 days gestation
  - Branches from the descending thoracic arch regress and 6th aortic arch enlarges
  - Aorta and pulmonary arteries (PAs) form from the distal bulbus cordis
  - Truncus arteriosus (TA) positioned above the right ventricle (RV)
  - Bulbotruncal ridges separate the great arteries
Aortic component rotates posteriorly

- Abnormal development of TOF-PA
  - Occurs between 5th-6th week gestation
  - Faulty rotation of bulbus-truncus results in incomplete transfer of aorta above the left ventricle (LV)
  - Posterior malalignment of infundibular septum results in ventricular septal defect (VSD)
  - Infundibular stenosis developmental theories
    - Anterior displacement of the bulbotruncal region, or
    - Underdevelopment of the subpulmonic infundibulum resulting in conal septum hypoplasia

- The RV outflow obstruction often multi-level
  - Anterior and cephalad deviation of the infundibular septum results in subvalvar obstruction
  - Hypertrophy of muscular bands can cause further subvalvar obstruction
  - Pulmonary valve (PV) annulus usually hypoplastic, but may be normal size
  - PV can be bicuspid and stenotic
  - May have supravalvar narrowing in the main pulmonary artery (MPA) at the sinotubular ridge
  - Further obstruction at the branch PAs due to hypoplasia or focal areas of stenosis
    - Commonly at the proximal branch pulmonary arteries
    - Especially ? Usually (better word?) the proximal left pulmonary artery (LPA) near the site of ductal insertion

- Associated genetic syndromes
  - Genetic testing
    - Recommended for all patients with TOF
    - Must be done prior to cardiopulmonary bypass (CPB)
  - Conotruncal defect
  - High incidence of 22q11 deletion (DiGeorge Syndrome)
    - Up to 50%

Anatomy (See illustration below for TOF)

- Characterized by the combination of four anatomic malformations:
  - Ventricular Septal Defect (VSD) (Number 4 in illustration below)
  - Overriding aorta, overriding the muscular ventricular septum (Number 2 in illustration below)
  - Obstruction of RV outflow tract (Number 1 in illustration below)
  - PAs usually confluent (Number 3 in illustration below) #3 looks like it refers to RV, not PAs
  - RV hypertrophy (Area of arrows in illustration below)
Tetralogy of Fallot


- **TOF with PA**
  - More severe anatomical variant
    - Solid tissue forms in place of the pulmonary valve
    - Prevents any valve opening
  - Pulmonary blood flow occurs through the PDA
    - About 70% of TOF with PA
  - PAs typically confluent
    - Branch PAs confluent in 85%
    - Non-confluent in 15%

- **TOF with PA and MAPCAs**
  - Pulmonary blood flow is multifocal
    - Via MAPCAs
    - PAs often non-confluent (70%)
  - MAPCAs
    - Typically arise from the descending aorta
    - May arise from any vessel including:
      - Ascending aorta
      - Head and neck vessels
      - Coronary arteries
  - MAPCAs
    - Create highly variable patterns:
      - PA size and arborization
      - Origin of collateral vessels
      - Number of vessels
• Course of vessels
  ▪ Connections between the PA and collaterals
    ▪ Unpredictable
    ▪ Change as the patient grows.
  ▪ Can become irregularly shaped, thickened, kinked, or stenotic

**Physiology**
- In TOF
  o Four cardinal anatomic structures and degree of presentation
    ▪ Determine physiology
    ▪ Determine clinical presentation
  o Degree of RV outflow tract obstruction determines
    ▪ Pulmonary blood flow
    ▪ Degree of left to right shunting through the VSD
    ▪ Degree of cyanosis
- In TOF with PA
  o Complete obstruction of the RV outflow tract obstruction
    ▪ Must have alternate source of blood flow to the pulmonary arteries
    ▪ May be either via the PDA or by MAPCAs
  o Pulmonary blood flow via the PDA
    ▪ Prostaglandins (PGE) required to ensure pulmonary blood flow
  o Pulmonary blood flow via MAPCAs
    ▪ May or may not require PGE; depends on:
      ▪ Anatomy of the MAPCAs
      ▪ Presence of PDA
- Clinical Manifestations
  o Cyanotic at birth
    ▪ Degree of cyanosis depends on PDA and MAPCAs
  o Heart sounds
    ▪ Murmur
      ▪ Usually not heard
      ▪ May be a faint continuous murmur of PDA/MAPCAs
      ▪ Single, loud S2
  o Electrocardiogram (ECG)
    ▪ RV hypertrophy with right axis deviation
    ▪ Prominent R waves anteriorly and S waves posteriorly
    ▪ Upright T wave in V1
    ▪ May also see a qR (?QR) pattern in the right sided chest lead
  o Chest X-ray
    ▪ Normal-sized, boot-shaped heart
    ▪ Decreased pulmonary vascular markings
    ▪ A concavity in the region of the main pulmonary artery
    ▪ Right-sided aortic arch – 26-50%
  o Echocardiogram (ECHO)
    ▪ Parasternal-long axis view
      ▪ Large aortic valve (AV) that overrides a large malalignment VSD
- Color flow demonstrates lack of patency of RV outflow tract
- Suprasternal and high parasternal views evaluate:
  - Pulmonary trunk
  - Right and left pulmonary artery size
  - Confluence of PAs

**Procedures and Interventions**

- **Diagnostic Procedures**
  - Required as anatomy of the PAs and the source of pulmonary blood supply may vary widely
  - 2-dimenasional (2-D) ECHO with color flow and 2-D doppler
    - Main diagnostic tool
    - Identifies
      - Sources of PA blood flow - includes PDA and MAPCAs
      - Significant hypoplasia of the central pulmonary arteries
      - Presence of a small PDA
        - Highly predictive of the presence of MAPCAs
        - If present, further imaging by MRI or angiography likely
  - Magnetic Resonance Imaging (MRI)
    - Non-invasive tool
    - Visualize PAs and collateral supplies
  - Cardiac catheterization and angiography
    - Delineate all sources of pulmonary blood supply
    - Facilitates surgical planning

- **Interventions**
  - Cardiac catheterization
    - Diagnostic
      - Evaluation for surgical intervention
      - Identify sources of obstruction to pulmonary blood
      - Evaluate ventricular size, structure
    - Intervention
      - Initial evaluation of RV/PA connection
        - Possible radiofrequency ablation (RFA) of membranous PV
        - Balloon dilation of pulmonary stenosis (PS)/pulmonary atresia
        - Stent placement
          - PV annulus
          - PDA
      - Repeat catheterizations
        - Balloon dilation/stent placements in stenotic pulmonary artery segments
        - Coil embolization dual source of pulmonary blood supply
        - Coil embolization of MAPCAs
  - Surgical repair
    - Options depend on PA anatomy and presence/extent of MAPCAs
• Single stage repair
  • Considered when PAs confluent and of good size
  • MAPCAs
    o Ligated at the aorta
    o Mobilized toward the posterior mediastinum to construct a pulmonary artery confluence
    o Conduit placed between confluence and RV
  • PAs reconstructed to relieve any surgically accessible stenotic areas
  • VSD closure
  • Mortality rate - 5-20%
• Staged repair
  • Depends on PA anatomy
    o May be required if PAs
      ▪ Hypoplastic
      ▪ Non-confluent
      ▪ Supplied by extensive MAPCAs.
  • Stage 1 – Palliative shunting
    o Induces enlargement and growth of the native PAs
    o Shunt types - Blalock-Taussig shunt, central shunt, or RV to PA conduit
  • Stage 2 Early unifocalization
    o Direct MAPCAs into a central pulmonary artery confluence
    o Improve long-term outcomes
      ▪ Maximize the recruitment of lung segments
      ▪ Increase likelihood of definitive repair
      ▪ Eliminate dual blood supply to a lung segment
        • Coil occlude MAPCA in cardiac catheterization laboratory (cath lab)
        • Ligate at time of unifocalization
    o Objectives
      ▪ To recruit as many of the perfused lung segments as possible
      ▪ Maximize the cross-sectional area of the pulmonary vascular bed
      ▪ Manage unprotected lung segments with a large blood supply
        • At risk for developing pulmonary vascular disease by four to six months of age if untreated
  • Stage 3- Final stage (See illustration below)
    o Complete intracardiac repair with VSD closure (Number 2 in illustration below)
    o Placement/replacement of a RV to pulmonary artery conduit (Number 1 in illustration below)
PA reconstruction as needed to meet following requirements:
- Central pulmonary arterial area should be greater than 50% of normal
- Presence of predominantly left-to-right intracardiac shunting
- Equivalent of an entire lung must be supplied by the central pulmonary artery confluence
- Stenotic lesions in the pulmonary artery outflow must be addressed

Specific Considerations
- Preoperative
  - Pulmonary blood flow supplied by:
    - PDA, MAPCAs, or both
    - Alternative sources of pulmonary blood flow accounts for variable clinical presentation
  - Neonates
    - With insufficient pulmonary blood flow, usually present with:
      - Cyanosis - PGE necessary to maintain ductal patency to improve/maintain pulmonary blood flow
      - Hypoxemia
- Metabolic acidosis
  - With adequate pulmonary blood flow
    - Large, unobstructed MAPCAs
      - With unrestricted blood flow
      - May lead to congestive heart failure
    - As pulmonary vascular resistance (PVR) decreases
      - Pulmonary blood flow may become excessive
      - Results in congestive heart failure
    - MAPCAs may provide pulmonary blood flow, but are prone to stenosis
  - Require screening for chromosomal anomalies
    - Common with conotruncal defects
    - Frequently see 22q11 deletion (DiGeorge syndrome)
      - Abnormal function of parathyroid glands leads to hypocalcemia
      - Immunodeficiency from abnormal T-cell-mediated response predisposes to increased infection risk
      - Physical defects include:
        - Palatal defects causing feeding difficulties
        - Kidney abnormalities
        - Gastrointestinal issues including abnormal motility which may lead to constipation
        - Dysmorphic facies (microstomia, micrognathia, unusually shaped ears, long nose)
      - Learning and psychiatric disorders

- Intraoperative
  - Operative goals:
    - Tailored to specific anatomy
    - Provide adequate, separate pulmonary and systemic circulations
  - Irradiated blood only if DiGeorge or absent thymus
  - Anticipate coagulopathies with severe cyanosis and polycythemia

- Postoperative (See Peds/Neo Problem Guidelines for Postoperative Care)
  - Concerns differ depending on repair
    - Palliation versus correction
    - Multi-staged repair versus one-stage repair
  - Residual defects
    - VSD or VSD patch leak
    - RV outflow tract obstruction
  - RV dysfunction may result in low cardiac output; may be caused by:
    - Increased RV volume loading
    - Ventriculotomy if performed
    - Lower compliance of neonatal myocardium
  - Arrhythmias (See Peds/Neo Problem Guidelines for Arrhythmia Management)
    - Complete Heart Block (CHB)
      - Requires temporary pacing
      - Possible permanent pacemaker, incidence is rare
- Junctional ectopic tachycardia (JET)
  - Potential for significant hemodynamic compromise
  - Reduce degree of hemodynamic impairment
    - Early recognition
    - Prompt treatment
      - Cooling to core temperature less than 36 degrees
      - Antiarrhythmic medications
  - Elevated RV pressure
    - May result from residual defects
      - Stenosis in pulmonary arteries
      - Stenosis at anastomosis sites
      - Residual MAPCAs
    - If prolonged, cardiac catheterization may be required
      - Dilation of stenotic pulmonary arteries
      - Embolization of residual MAPCAs
- Respiratory complications
  - Increased occurrence with unifocalization of MAPCAs
  - Bronchospasm related to dissection around bronchopulmonary tree
  - Reperfusion injury in patients with preoperative stenosis of MAPCAs
  - Pulmonary complications such as pneumonia, pulmonary hemorrhage, large airway compression
  - Prolonged respiratory failure requiring prolonged ventilation
- Genetic syndrome
  - 22q11 deletion (DiGeorge)
    - Anticipate hypocalcemia
      - May require frequent calcium replacement or infusion
    - Immune deficiencies
      - Require use of irradiated blood
      - Increased incidence of infections (See Peds/Neo Problem Guidelines for Infection Prevention)
- Provide parental education and support

**Routine Care**
- Lifelong disease requires careful follow-up through adulthood
  - Follow-up at least annually with adult CHD (ACHD) trained cardiologist/NP
  - Potential for additional surgical and interventional procedures
- Infants require frequent follow-up by pediatric cardiologist/NP trained in CHD
  - Prior to and evaluation of surgical intervention(s)
  - ECHO
    - Monitor RV pressure and function
    - Monitor pulmonary circulation
      - Conduit function
      - Evaluation for increasing stenosis/flow in MAPCAs
      - Evaluation for development of aortopulmonary collaterals
  - Repair with RV to PA conduits
    - Require conduit replacement
Risk for conduit stenosis and/or conduit valve degradation
  - Cardiac catheterization
  - Hemodynamic evaluation of RV function, PA stenosis
    - Intervention balloon dilation of PAs/ stent placement
    - Coil MAPCAs.
- Subacute Bacterial Endocarditis prophylaxis (See American Heart Association recommendations for Adult and Pediatric SBE Prophylaxis, 2015)

**Long-term Complications/Problems** (See Adult Problem Guidelines on Arrhythmia Management, Ventricular Dysfunction)
- Abnormal RV physiology secondary to chronic pulmonary regurgitation
  - Ventricular arrhythmias
  - Decreased RV compliance
  - Need for PV/conduit replacements
  - Exercise Intolerance
- Related to DiGeorge
  - Learning disabilities
  - Behavioral & mental health problems
  - Immune disorders
  - Poor vision and hearing
  - Velopharyngeal insufficiency
  - Mypoatic facies
  - Short stature

**References**


12/2015