Cardiovascular Pathophysiology: Left To Right Shunts
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Learning Objectives
• Learn the relationships between pressure, blood flow, and resistance
• Review the transition from fetal to mature circulation
• Correlate clinical signs and symptoms with cardiac physiology as it relates to left to right shunt lesions:
  – VSD, PDA, ASD
• Discuss Eisenmenger’s Syndrome

Pressure, Flow, Resistance
• Perfusion Pressure: Pressure gradient across vascular bed
  – Δ Mean Arterial - Venous pressure
• Flow: Volume of blood that travels across vascular bed
• Resistance: Opposition to flow
  – Vessel diameter
  – Vessel structure and organization
  – Physical characteristics of blood
Poiseuille equation

\[ Q = \frac{\Delta P \pi r^4}{8nl} \]
\[ R = \frac{8nl}{\pi r^4} \]

\( \Delta P \) = pressure drop
\( r \) = radius
\( R \) = resistance
\( n \) = viscosity
\( l \) = length of tube
\( Q \) = flow

Hemodynamics

Flow (Q) = \( \frac{\Delta \text{Pressure}}{\text{Resistance}} \)
Resistance = \( \frac{\Delta \text{Pressure}}{\text{Flow}} \)

Two parallel fetal circulations

- Placenta supplies oxygenated blood via ductus venosus
- Foramen ovale directs ductus venous blood to left atrium (40%)
- Pulmonary blood flow minimal (<10%)
- Ductus arteriosus allows flow from PA to descending aorta (40%)
**Ductus Venosus and Streaming**

- Ductus venosus diverts $O_2$ blood through liver to IVC and RA
  - Amount varies from 20-90%

- Streaming of blood in IVC
  - $O_2$ blood from the DV $\rightarrow$ FO $\rightarrow$ LA $\rightarrow$ LV
  - De-$O_2$ blood from R hep, IVC $\rightarrow$ TV $\rightarrow$ RV

- SVC blood flows across TV $\rightarrow$ RV
  - $<5\%$ SVC flow crosses FO

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**$O_2$ blood to high priority organs**

- RV pumps De-$O_2$ blood to PA $\rightarrow$ DA $\rightarrow$ DescAo $\rightarrow$ lower body and placenta

- LV pumps $O_2$ blood to AscAo $\rightarrow$ coronary + cerebral circ

- Aortic isthmus connects the two separate vascular beds

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**Fetal Shunts Equalize Pressure**

- RAp = LAp due to FO
- RVp = LVp due to DA

Unlike postnatal life unless a large communication persists...
RV is “work horse” of fetal heart

- RV pumps 66% CO
  - 59% goes to DA
    • (88% RV CO)
  - 7% goes to lungs
    • (12% RV CO)
- LV pumps 34% CO
  - 31% goes to AscAo
- Only 10% total CO crosses Ao isthmus

Transition from Fetal to Neonatal Circulation

- Lose placenta
  - ↑SVR
- Lungs expand mechanically
- ↑O₂ vasodilates pulm vasc bed
  - ↓PVR
- ↑PBF + ↑LA venous return
  - ↑LAp
- DV constricts
  - ↓RAP

Three Fetal Shunts Close

- LAP > RAP
  - FO closure
- ↑O₂ and ↓PGE₁
  - DA and DV constrict
- RV CO ↓
  - RV wall thickness ↓
- LV CO ↑
  - LV hypertrophies

RV CO = LV CO
Postnatal circulation in series
### Regulation of Pulmonary Vascular Tone

- **Vasoconstriction**
  - Hypoxia/acidosis
  - High blood flow and pressure
  - Failure of vessel maturation (no regression of medial hypertrophy)
- **Vasodilation**
  - Improved oxygenation
  - Prostaglandin inhibition
  - Thinning of vessel media (regression of medial hypertrophy)

### Fetal Pulmonary Vascular Bed

- Placenta is the organ of gas exchange
- Goal to bypass the fetal lungs
- **Pulmonary Pressure >> Ao Pressure**
  - Low O₂ tension causes Vasoconstriction
  - Medial wall hypertrophy
- **Pulmonary blood flow << Ao flow**
- **Pulmonary resistance >> Ao resistance**
  - Encourages shunting via DA to aorta

### Neonatal Pulmonary Vascular Bed

- **Pulmonary Pressure ≈ Ao Pressure**
  - Arterial vasodilation
  - Medial wall hypertrophy persists
- **Pulmonary Blood flow = Aortic Flow**
  - Ductus arteriosus closes
  - Neonatal RV CO = LV CO
- **Pulmonary resistance ≈ Ao Resistance**
Adult Pulmonary Vascular Bed

- Pulmonary Pressure << Ao Pressure
  - 15 mmHg vs. 60 mmHg
  - Arterial Vasodilation
  - Medial wall hypertrophy regresses - remodeling

- Pulmonary Blood Flow = Aortic Flow

- Pulmonary Resistance << Ao Resistance
  - Resistance = $\frac{\Delta \text{Pressure}}{\text{Flow}}$

Pulmonary Vascular Bed: Transition from Fetal to Adult

Re-Cap: Fetal to Postnatal

- Fetus
  - Shunts exist
  - Lungs collapsed
  - RV CO > LV CO (Parallel circ)
  - Pulmonary pressure and resistance high

- Newborn
  - Shunts close
  - Lungs open
  - RV CO = LV CO (Series circ)
  - Pulmonary pressure and resistance drop
## Left to Right Shunts

- Anatomic Communication between Pulmonary and Systemic circulations
- Excess blood flow occurs from the Systemic (Left) to the Pulmonary (Right) circulation

## Qp:Qs

- Extra flow is represented by the ratio of pulmonary blood flow (Qp) to systemic blood flow (Qs)
- Qp:Qs = 1:1 if no shunts
- Qp:Qs >1 if left to right shunt
- Qp:Qs <1 if right to left shunt
- Qp:Qs of 2:1 means pulmonary blood flow is twice that of systemic blood flow

## Why do we care?

- Already oxygenated pulmonary venous blood is recirculated through the lungs
- Excess PBF causes heart failure (CHF)
- Size of the shunt and the amount of PBF (Qp) determine how much CHF
- Shunt size determined by:
  - Location of communication
  - Size of communication
  - Age of the patient
  - Relative resistances to blood flow on either side of the communication
**Pulmonary Effects of L to R Shunt**

- ↑ PBF = ↑ extravascular lung fluid
  - transudation of fluid across capillaries faster than lymphatics can clear
- Altered lung mechanics
  - Tidal volume and lung compliance ↓
  - Expiratory airway resistance ↑
- Pulmonary edema results if Qp and Pulm Venous pressure very high
- Tachypnea

**Neurohumoral Effects of L to R Shunt**

- Sympathetic nervous system and renin-angiotensin system activation
  - plasma [NE] and [Epi] ↑
  - cardiac hormone B-type natriuretic peptide (BNP) ↑
- Tachycardia
- Diaphoresis

**Metabolic Effects of L to R Shunt**

- Acute and chronic malnutrition
- Mechanism not clear
  - ↑ metabolic expenditures (↑ O2 consumption) due to ↑ respiratory effort and myocardial work
  - ↓ nutritional intake
- Poor growth/ Failure to thrive
**Pulmonary Hypertension: End Stage**

- ↑ PBF causes sustained ↑ PAp
- Pulm vascular bed fails to remodel
  - Alveolar hypoxia may exacerbate
- Gradual effacement of the pulm arterioles
  - Overgrowth of vascular smooth muscle
  - Intimal proliferation
- Abnormal local vascular signaling
- Impaired endothelial function
- Pulm bed loses normal vasoreactivity
  - fixed pulmonary HTN and irreversible pulmonary vascular disease

**Re-Cap**

- Flow, Resistance, Pressure
- Fetal and Transitional Circulation
- Left to Right Shunts and CHF
- VSD
- PDA
- AVC
- ASD
- Eisenmenger

**“Top 4” Left to Right Shunt Lesions**

- Ventricular Septal Defect (VSD)
  - Left ventricle to Right ventricle
- Patent Ductus Arteriosus (PDA)
  - Aorta to Pulmonary artery
- Atrioventricular Canal Defect (AVC)
  - Left ventricle to Right ventricle
  - Left atrium to Right atrium
- Atrial Septal Defect (ASD)
  - Left atrium to Right atrium
VSD most common CHD (20%)

- 2/1000 live births
- Can occur anywhere in the IVS
- Location of VSD has no effect on shunt

- Perimembranous most common (75%)
- Muscular (15%) most likely to close
- Outlet (5%) most likely to involve valves
  - ↑ incidence in Asian pop (30%)
- Inlet (5%) assoc with AVC

Ventricular Septal Defect

VSD: Determinants of L to R shunt

- Size of VSD
- Difference in resistance between Pulmonary and Systemic circulations
- Difference in pressure between RV and LV
VSD: Determinants of L to R shunt

- Small (restrictive) VSD: L to R shunt flow limited by size of hole
- Large (unrestrictive) VSD: L to R shunt flow is determined by Pressure and Resistance
  - If RVp < LVp, L to R shunt occurs
  - If RVp = LVp, L to R shunt occurs if pulmonary < aortic resistance
- Shunt flow occurs in systole

Transitional Circulation: Effects on L to R shunt in large VSD

- Fetus: bidirectional shunt
- At Birth: No shunt
- Transition 1-7 wks
  - PA/RVp ↓ to < LVp
  - PA resistance ↓ to < Systemic
  - L to R shunt ↑

Large VSD: Hemodynamic Effects

- Flow LV→ RV→ PA
- ↑ Pulm Venous Return
- LA/LV volume overload
- ↑ LV SV initially by Starling mechanism
- ↑ LV dilation leads to systolic dysfxn & CHF
- ↑ Pulm circ leads to pulm vascular disease
VSD: Signs/Symptoms

• Asymptomatic at birth: PA = Ao Pressure and Resistance
• Signs of congestive heart failure as pulmonary pressure and resistance ↓
  – Poor feeding
  – Failure to thrive (FTT) with preserved height and low weight
  – Tachypnea
  – Diaphoresis
  – Hepatomegaly
  – Increased respiratory illness

VSD: Physical Exam

• Harsh Holosystolic murmur
  – Loudest LLSB radiating to apex and back
  – Smaller VSD = louder murmur
• Precordial Thrill 2° turbulence across VSD
• Mid-Diastolic rumble 2° ↑ trans-Mitral flow
• LV heave 2° LV dilation
• Signs of CHF
  – Gallop (S3), Hepatomegaly, Rales
• Signs of Pulm Vasc Disease
  – ↓murmur, RV heave, loud S2, cyanosis

VSD: Laboratory Findings

• CXR: Cardiomegally, ↑PVM
  – Pulm Vasc Dz: large PAs
• EKG: LAE, LVH
  – Pulm Vasc Dz: RVH
• ECHO: Location/Size VSD
  – Amount/direction of shunt
  – LA/LV size
  – Estimation RV pressure
• CATH: only if suspect ↑PVR
  – O2 step up in RV
VSD: Management

• Does the patient have symptoms?
  – size of the defect, RV/LV pressure, Pulm/Ao resistance
• Will the VSD close or ↓ in size?
• Is there potential for complications?
  – Valve damage, Pulm HTN
• Will the surgery be difficult? Will the surgery be successful?

VSD: Management

• Medical
  – Digoxin
  – Lasix
  – Increased caloric intake
  – 50% VSD size ↓ and CHF resolves
• Surgical
  – Persistent CHF
  – ↑ pulmonary vascular resistance
  – Valve damage
  – Within first two years of life
• Catheter
### VSD: Endocarditis Prophylaxis
- Not for isolated VSD
- Yes for 1st 6 mo following repair of VSD with prosthetic material or device
- Yes for life if there is a residual defect at or adjacent to the site of a prosthetic device
- For dental and respiratory tract procedures ONLY
  - no longer for GI or GU procedures

### Patent Ductus Arteriosus (PDA)
- Communication between Aorta and Pulmonary Artery
- 1/2500-5000 live births
- Risk factors: prematurity, rubella, high altitude

### PDA: Determinants of L to R shunt
- Magnitude L to R shunt depends on
  - Length and diameter of ductus
  - Relative resistances of Ao and PA

- ↑ L to R shunt as Pulm resistance ↓
  - Volume overload of PA, LA, LV

- Shunt flow occurs in systole and diastole
PDA: Signs/Symptoms

- Small PDA: asymptomatic
- Large PDA: CHF
  - Diaphoresis
  - Tachypnea
  - Poor feeding
  - FTT
  - Hepatomegaly
  - Respiratory infections
- Moderate PDA: Fatigue, Dyspnea, palpitations in adol/adults
  - Afib 2º to LAE

PDA: Physical Exam

- Continuous machine-like murmur at left subclavian region
  - Ao>PA pressure in systole and diastole
- Congestive heart failure

PDA: Laboratory Studies

- CXR: cardiomegally, ↑ PVM
- EKG: LAE, LVH
- ECHO: measures size PDA, shunt and gradient, estimate PAp
- CATH: O2 step up in PA
PDA: Management

• Indications for Closure
  – CHF/failure to thrive
  – Pulmonary hypertension

• Closure Methods
  – Indomethacin if preemie
  – Surgical ligation
  – Transcatheter closure
    • Coil
    • Device

PDA Coil Closure

Atrioventricular Canal Defect/Endocardial Cushion Defect

• Atrial Septal Defect (Primum)
• Inlet VSD
• Common Atrioventricular Valve
**AVC: Management**

- Closure always indicated
- Timing of surgery (elective by 6 mos.)
  - Congestive Heart Failure
    - Large left to right shunt
    - Mitral insufficiency
    - Pulmonary hypertension
- Surgical repair
  - ASD, VSD closure
  - Repair of AV-Valves

**Summary: VSD, PDA and AVC**

- Asymptomatic in fetus and neonate
- Progressive ↑ in L to R shunt from 3-8 wks of life as pulmonary pressure and vascular resistance ↓
- Indications for intervention
  - Congestive heart failure: FTT
  - Pulmonary vascular disease
- End stage: Eisenmenger’s syndrome

**Atrial Septum Formation**

- Septum Primum grows downward
- Ostium Primum obliterates
- Fenestration in septum primum forms ostium secundum
- Septum secundum grows downward and fuses with endocardial cushions
  - Leaves oval-shaped opening Foramen ovale
- Superior edge of septum primum regresses
  - Lower edge becomes flap of FO
Atrial Septal Defect

- Persistent communication between RA and LA
- Common: 1/1500 live births
  - 7% of CHD
- Can occur anywhere in septum
- Physiologic consequences depend on:
  - Location
  - Size
  - Association with other anomalies

Atrial Septal Defect (ASD)

ASD Types

- **Ostium Secundum ASD (70%)**
  - 2:1 F>M
  - Familial recurrence 7-10%
    - Holt-Oram syndrome - upper limb defects
  - Region of FO
  - Defect in septum primum or secundum

- **Ostium Primum ASD**
  - Inferior portion of septum
  - Failure of fusion between septum primum and endocardial cushions
  - Cleft in MV or CAVC
### ASD Types

- **Sinus Venosus ASD (10%)**
  - Incomplete absorption of sinus venosus into RA
  - IVC or SVC straddles atrial septum
  - Anomalous pulmonary venous drainage

- **Coronary Sinus ASD**
  - Unroofed coronary sinus
  - Wall between LA and coronary sinus missing
  - Persistent L-SVC

### Patent Foramen Ovale

- **Prevalence 30% of population**

- **Failure of fusion of septum primum and secundum (flap of FO)**

- **Remains closed as long as LAp>RAp**
  - LAp<RAp
    - Pulmonary HTN / RV failure
    - Valsalva
    - Paradoxical embolism and STROKE

### ASD: Manifestations

- **L to R shunt between LA and RA**
  - Amount of flow determined by:
    - Size of defect
    - Relative compliance of RV / LV
  - Shunt flow occurs only in diastole
  - L to R shunt ↑ with age
    - RV compliance ↑
    - LV compliance ↓

- **RA and RV volume overload**
ASD: Signs/Symptoms

- Infant/child usually asymptomatic
  - DOE, fatigue, lower respiratory tract infections
- Adults (prior age 40)
  - Palpitations (Atrial tach 2º RAE)
  - ↓ stamina (Right heart failure)
  - Survival less than age-matched controls (5th-6th decade)

ASD: Physical Exam

- Small for age
- Wide fixed split S2
- RV heave
- Systolic murmur LUSB
  - ↑ flow across PV
- Mid-Diastolic murmur LLSB
  - ↑ flow across TV

ASD: Laboratory Studies

- CXR: cardiomegally, ↑ PVM
- EKG: RAD, RVH, RAE, IRBBB
  - Primum ASD: LAD
- ECHO: RAE, RV dilation, ASD size, location, amount and direction of shunt
- CATH: O2 step up in RA
ASD: Management

- Indications for closure
  - RV volume overload
  - Pulmonary hypertension
  - Thrombo-embolism

- Closure method
  - Surgical
  - Catheter Delivered Device
    - Cardioseal
    - Amplatzer septal occluder

Eisenmenger’s Syndrome

- Dr. Victor Eisenmenger, 1897
- Severe pulmonary vascular obstruction 2º to chronic left to right shunts
- Pathophysiology
  - High pulmonary blood flow → Shear Stress
  - Medial hypertrophy + intimal proliferation leads to ↓ cross-sectional area of pulm bed
  - Perivascular necrosis and thrombosis
  - Replacement of normal vascular architecture
- Pulmonary vascular resistance increases
  - Right to left shunt
  - Severe cyanosis

Medial Hypertrophy
Eisenmenger’s Syndrome
R to L flow via VSD

- Pressure:
  - Pulmonary = Aortic
- Resistance
  - Pulmonary > Aorta
- RV hypertrophy
- Blood flow: RV to LV
- Cyanosis
- Normal LA/LV size

Eisenmenger’s: Signs/Symptoms

- Infancy:
  - CHF improves with ↓ left to right shunt
- Young adulthood:
  - Cyanosis/Hypoxia: DOE, exercise intolerance, fatigue, clubbing
  - Erythrocytosis/hyperviscosity: H/A, stroke
  - Hemoptysis 2º to infarction/rupture pulm vessels

Eisenmenger’s: Physical Exam

- Clubbing
- Jugular venous a-wave pulsations
  - ↑RV pressure during atrial contraction
- Loud S2
- RV heave (RV hypertension)
- Diastolic pulm insufficiency murmur
- No systolic murmur
Eisenmenger’s: Lab findings

- No LV volume overload / ↑ RV pressure
- CXR: Clear lung fields, prominent PA segment with distal pruning, small heart
- EKG: RAE, RVH ± strain
- ECHO: RV hypertrophy, right to left shunt at VSD, PDA, or ASD

EKG: Eisenmenger’s Syndrome

Eisenmenger’s Syndrome: CXR
Eisenmenger’s: Management

- Avoid exacerbating right to left shunt
  - No exercise, high altitude, periph vasodilators
  - Birth Control: 20-40% SAB, >45% mat mortality

- Medical Therapy:
  - Pulmonary vasodilators: Calcium channel blocker, PGI2, Sildenafil
  - Inotropic support for Right heart failure
  - Anticoagulation

- Transplant
  - Heart-Lung vs Lung transplant, heart repair

- Do NOT close Defect
  - VSD/PDA/ASD must stay open
  - Decompress high pressure RV, prevent RV failure and provide cardiac output

Learning Objectives

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- Review the transition from fetal to mature circulation
- Correlate clinical signs and symptoms with cardiac physiology as it relates to left to right shunt lesions:
  - VSD, PDA, ASD
- Discuss Eisenmenger’s Syndrome