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
  - $\Delta$ 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

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Poiseuille equation

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

$\Delta P$ = pressure drop
$r$ = radius
$n$ = viscosity
$l$ = length of tube
$Q$ = flow

$$R = \frac{\Delta P}{Q}$$
Hemodynamics

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

\text{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
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 \( \approx \) Ao Pressure
  - Arterial vasodilation
  - Medial wall hypertrophy persists

- Pulmonary Blood flow = Aortic Flow
  - Ductus arteriosus closes
  - Neonatal RV CO = LV CO

- Pulmonary resistance \( \approx \) 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 = \( \frac{\Delta \text{Pressure}}{\text{Flow}} \)
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 \( \therefore \) the amount of PBF (\( Q_p \)) 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**

- \( \uparrow \) PBF = \( \uparrow \) extravascular lung fluid
  - transudation of fluid across capillaries faster than lymphatics can clear
- **Altered lung mechanics**
  - Tidal volume and lung compliance \( \downarrow \)
  - Expiratory airway resistance \( \uparrow \)
- **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 $\rightarrow$ RV $\rightarrow$ 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
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

• **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
  - Hemothysis 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, Sidenafil
  - 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

- 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