Cardiovascular Pathophysiology: Left To Right Shunts
Ismee A. Williams, MD, MS
iib6@columbia.edu

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

Poiseuille equation

$$Q = \frac{\Delta P \pi r^4}{8n l}$$

$$R = \frac{8n l}{\pi r^4}$$

$\Delta P = \text{pressure drop}$

$r = \text{radius}$

$n = \text{viscosity}$

$l = \text{length of tube}$

$Q = \text{flow}$
Hemodynamics

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

\[
\text{Resistance} = \frac{\Delta \text{Pressure}}{\text{Flow}}
\]

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 → FO → LA → LV
  - De-$O_2$ blood from R hep, IVC → TV → RV

- SVC blood flows across TV → RV
  - <5% SVC flow crosses FO

O$_2$ blood to high priority organs

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

- LV pumps $O_2$ blood to AscAo → 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
- ↑\(O_2\) vasodilates pulm vasc bed
  - ↓PVR
- ↑PBF + ↑LA venous return
  - ↑LAp
- DV constricts
  - ↓RAp

Three Fetal Shunts Close

- LAp > RAp
  - FO closure
- ↑\(O_2\) and ↓PGE\(_1\)
  - 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 $O_2$ 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

\[ R = \frac{\Delta P}{Q} \]

- **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 ($Q_p$) to systemic blood flow ($Q_s$)
- $Q_p:Q_s = 1:1$ if no shunts
- $Q_p:Q_s >1$ if left to right shunt
- $Q_p:Q_s <1$ if right to left shunt
- $Q_p:Q_s$ 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: Electrocardiogram

VSD: CXR
VSD: Echocardiogram

Membranous Ventricular Septal Defect, Apical 4 Chamber View, Inverted

VSD: Angiogram

LA
RA
RV
LV
A
MPA
LV
VSD
C
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

- \( \uparrow \) L to R shunt as Pulm resistance \( \downarrow \)
  - 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 2\(^{o}\) 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

#### 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 2° 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, 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