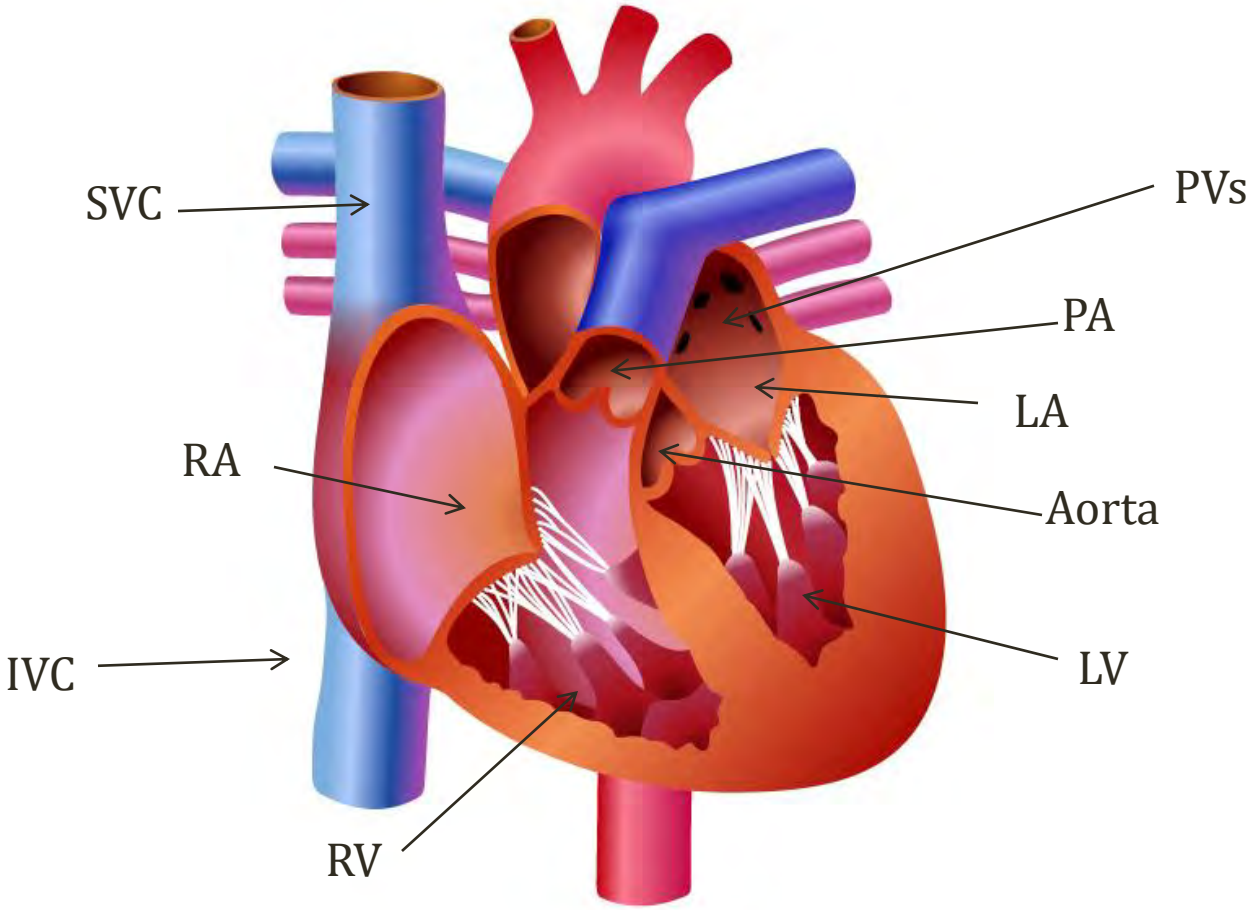
# Cardiac Anatomy

Jason Ryan, MD, MPH

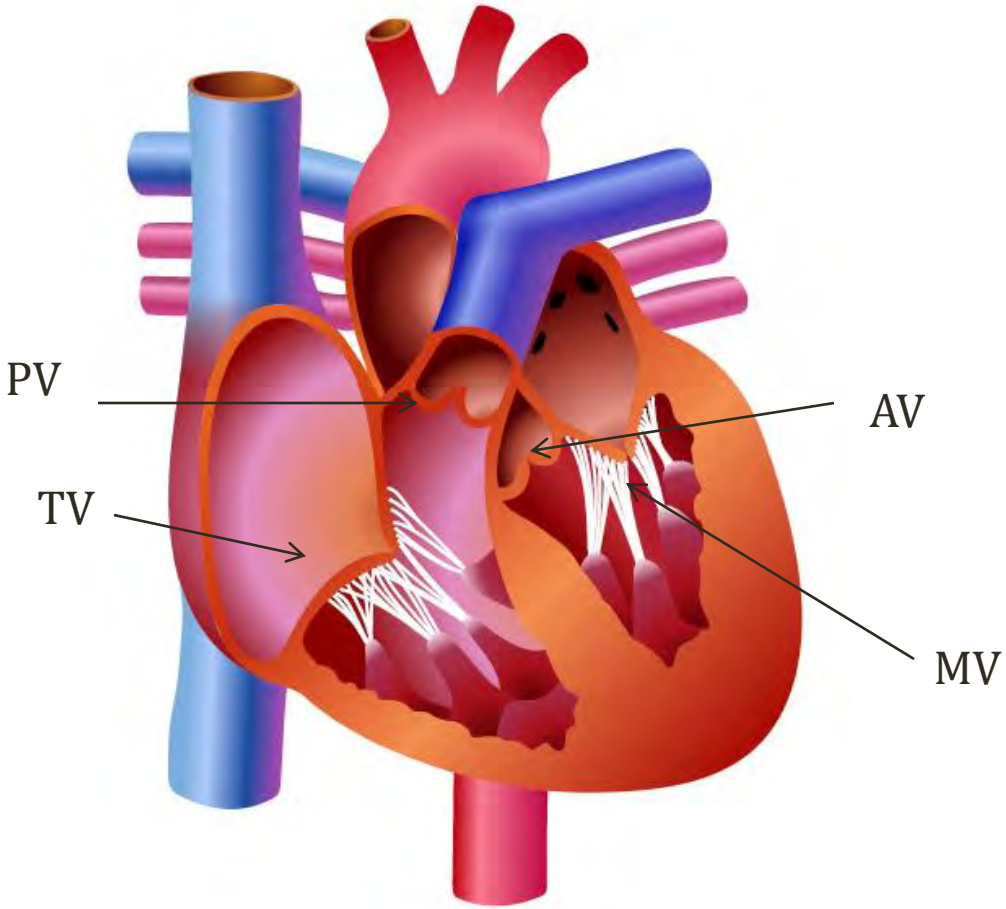
# The Heart

## Chambers

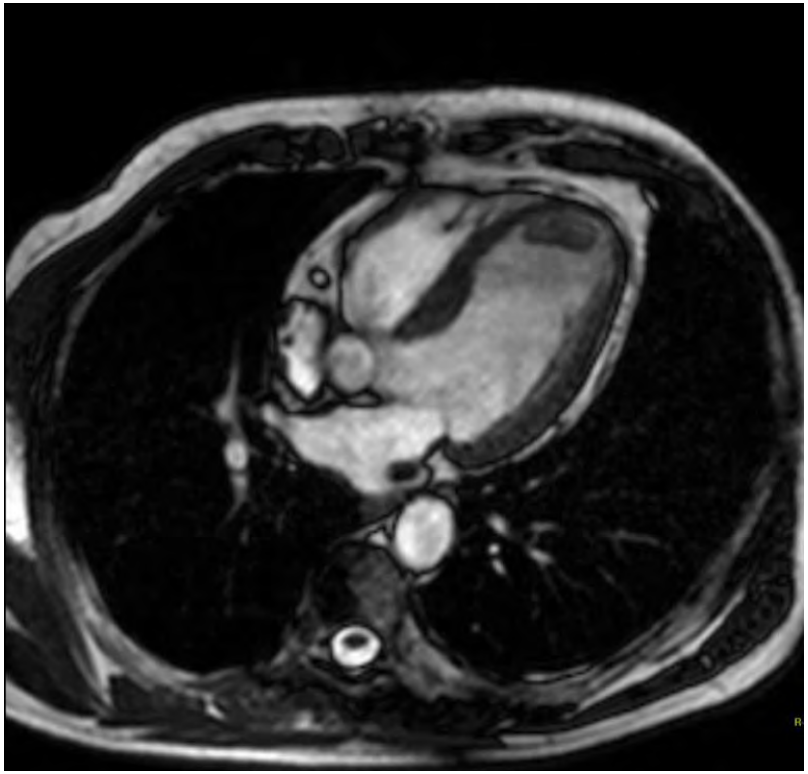


# The Heart

## Valves



# Anterior-Posterior Structures



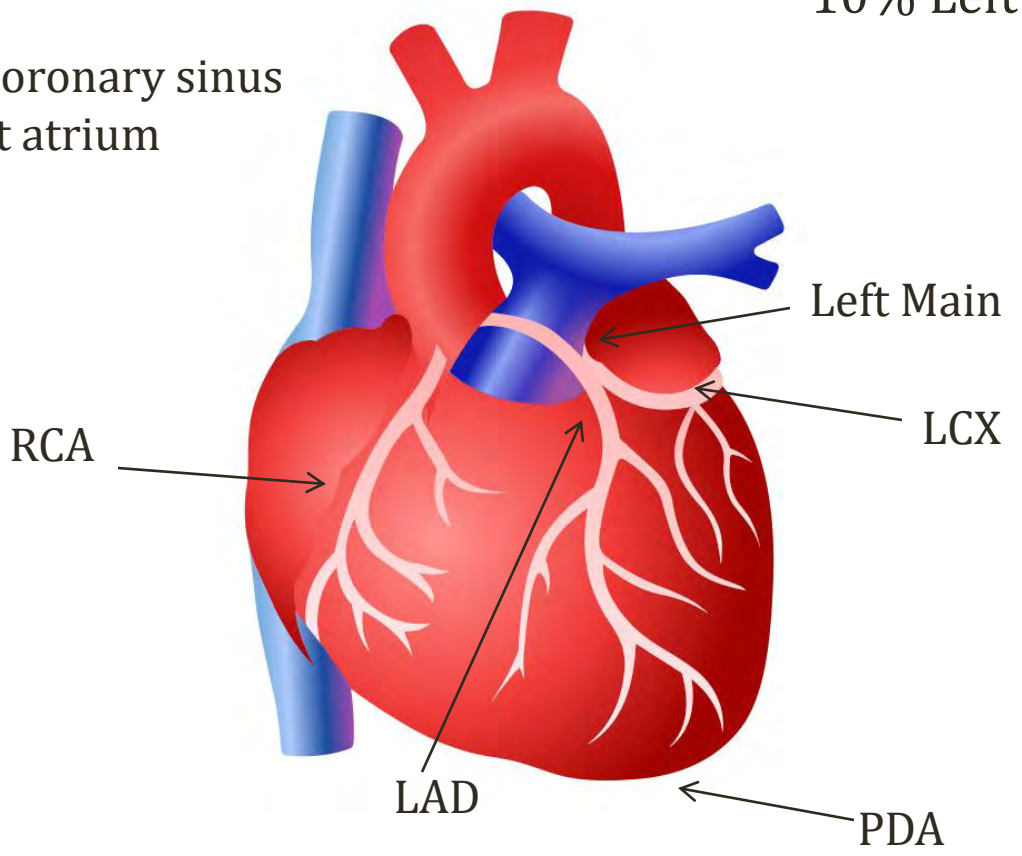
Right Ventricle → Anterior

Left atrium → Posterior

# Coronary Arteries

**90% Right dominant**
10% Left dominant

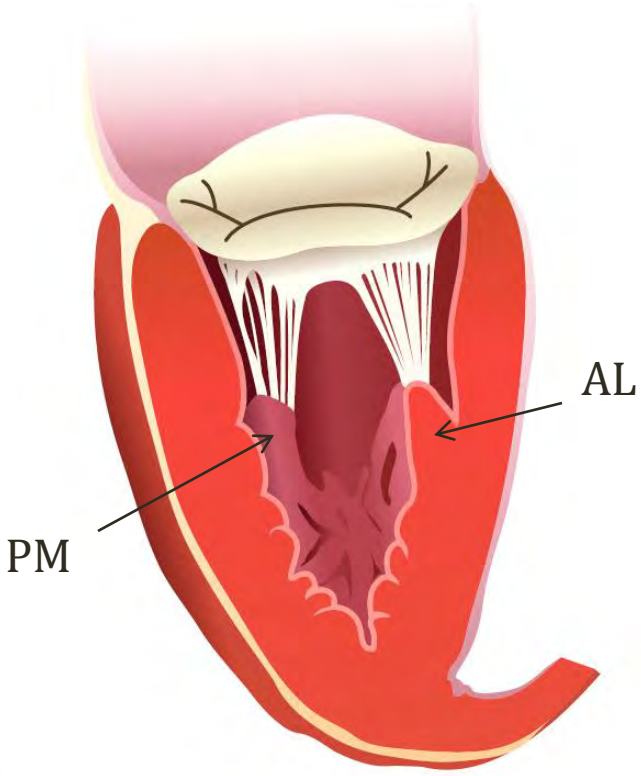
Heart drains to coronary sinus
CS → Right atrium



# Coronary Artery Territories

- Anterior wall, anterior septum, apex → LAD
- Lateral wall → LCX
- Inferior wall, inferior septum → PDA
  - RCA 90% of the time
  - 10% of people "left dominant" - LCX supplies PDA
- Occlusion occurs LAD>RCA>LCX

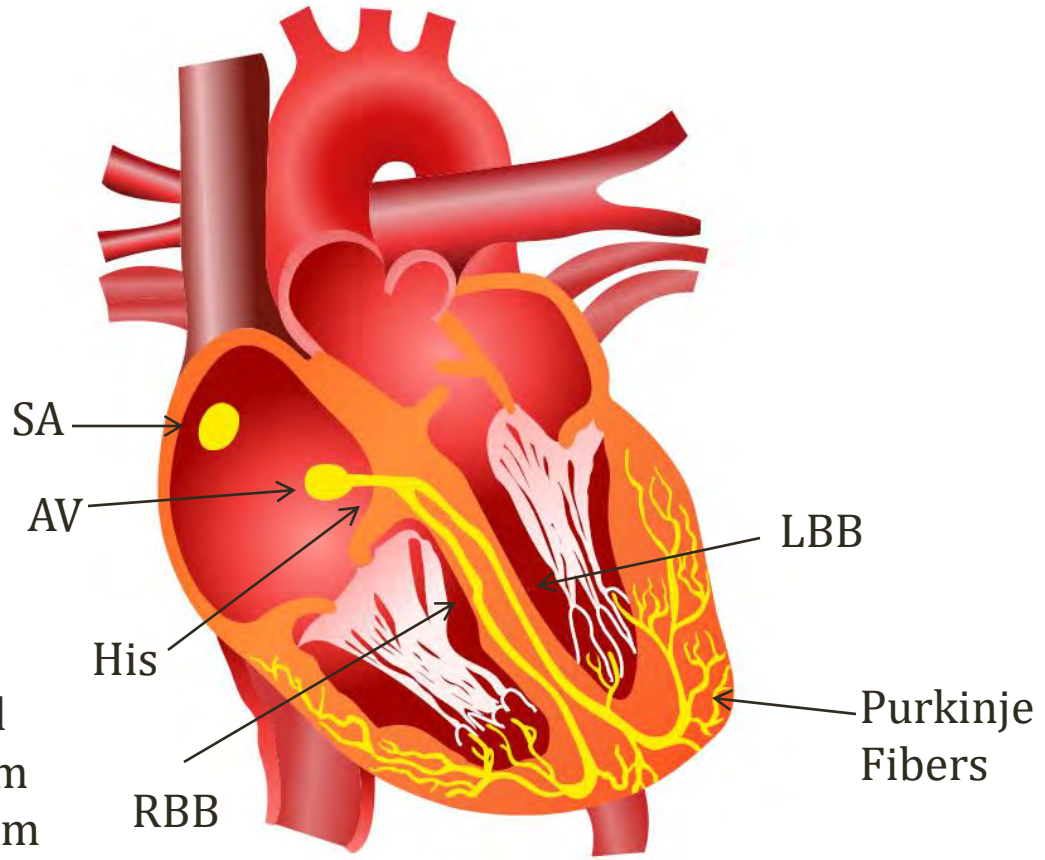
# Mitral Valve




- Two papillary muscles
  - Anterolateral (AL)
  - Posteromedial (PM)
- AL has dual blood supply
  - LAD/LCX
- PM →single blood supply
  - RCA (or LCX)
- Inferior infarction can lead to rupture of PM pap
  - Severe mitral regurgitation
  - Acute heart failure

# Cardiac Electrical System

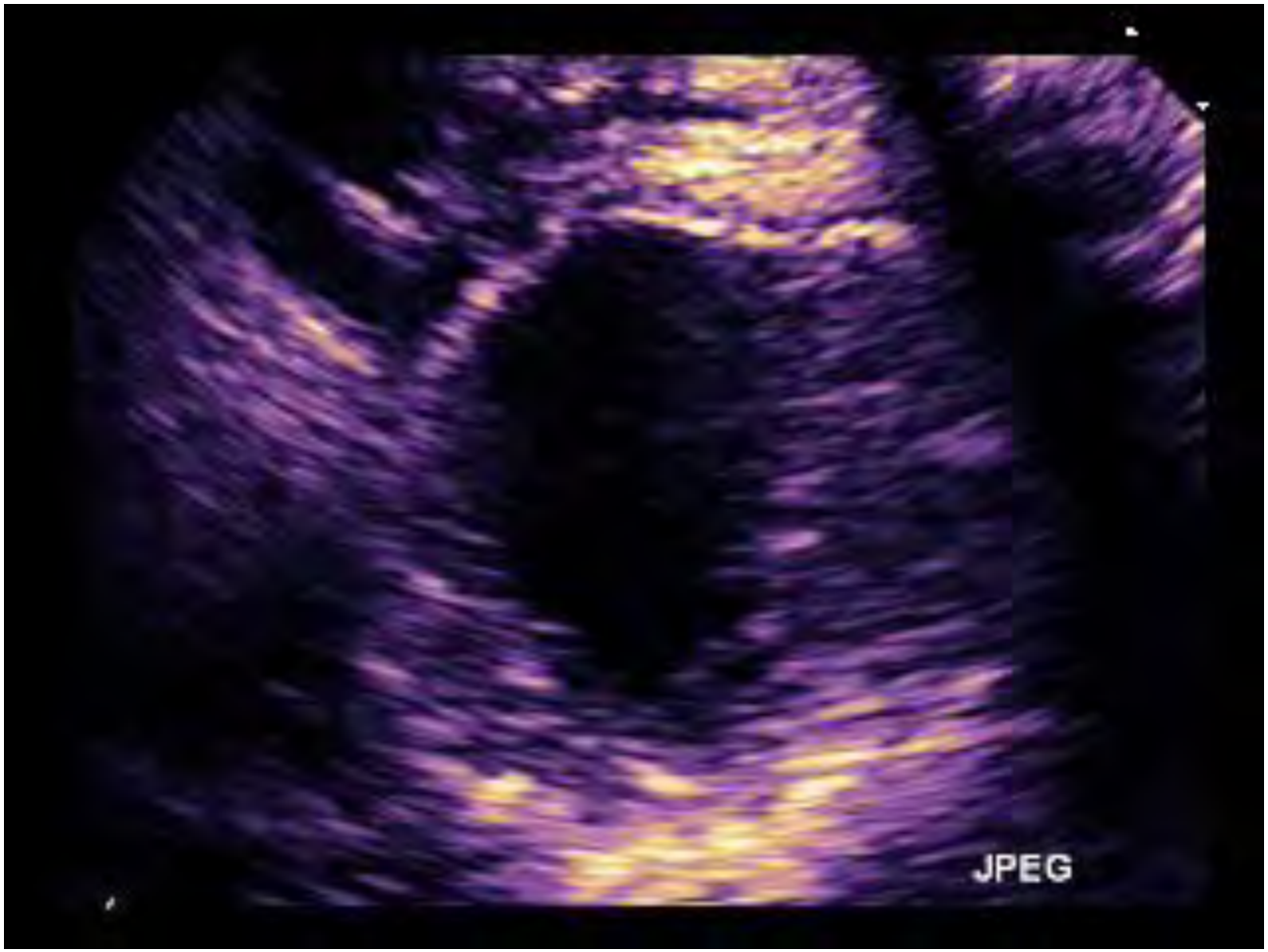
SA/AV node
Usually supplied
by RCA



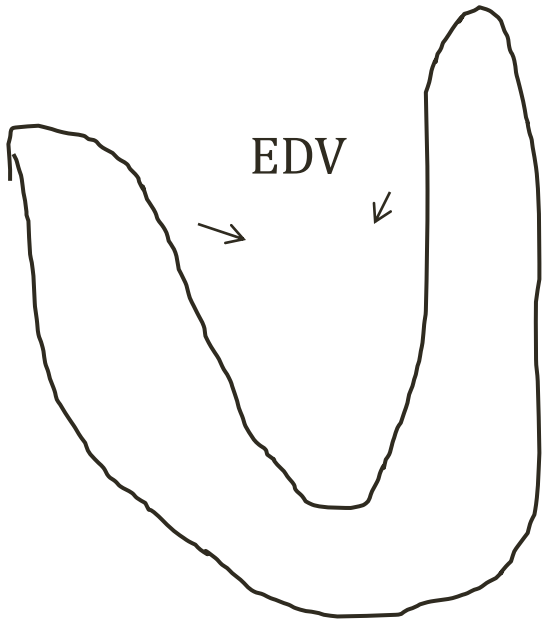

SA Node – Right atrial wall
AV Node –Interatrial Septum
HIS – Interventricular septum

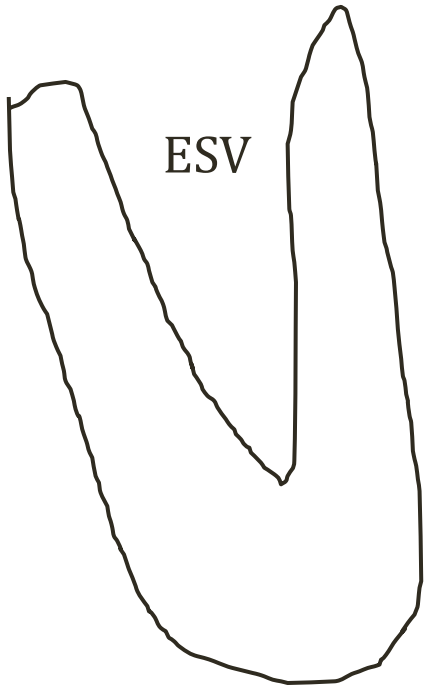
# Cardiac Physiology

Jason Ryan, MD, MPH



# Heart Volumes




**End diastolic Volume**
Filling completed
Contraction beginning

**End systolic Volume**
Emptying completed
Relaxation beginning

# Important Terms

- Stroke Volume (SV) = EDV - ESV
- Ejection Fraction (EF) = SV / EDV
- Cardiac Output (CO) = SV * HR

# Important Terms

- Venous Return (VR)
  - Blood returned to left ventricle
  - Should be equal to the cardiac output
- Total peripheral resistance
  - Resistance to blood flow from peripheral structures
  - Vasoconstriction → ↑ TPR
  - Vasodilation → ↓ TRP

# Blood Pressure Terms

- Systolic Blood Pressure (SBP)
  - Largely determined by stroke volume
- Diastolic Blood Pressure (DBP)
  - Largely determined by TRP
- Pulse pressure
  - SBP – DBP
  - Proportional to SV

# Blood Pressure Terms

- **Mean arterial pressure (MAP)**
  - DBP + 1/3 (SBP – DBP)
- Example: SBP 120/80
  - MAP = 80 + 1/3 (40) = 93.3

# Cardiac Output

- Very important physiology parameter
- Must rise to meet demands
- More cardiac output = more work/O2
  - CO = HR x SV
  - More beats per minute = more work
  - More volume per beat = more work

# Cardiac Output

## Determinants

1. Preload
2. Afterload
3. Contractility
4. Heart rate

# Preload

- **Amount of blood loaded into left ventricle**
- Also how much stretch is on fibers prior to contraction
  - Some books say “length” instead of “stretch”
- More preload = more cardiac output
- More preload = more work the heart must do
  - $\uparrow O_2$ required

# To INCREASE Preload

1. **Add volume** (blood, IVF)
2. **Slow heart rate** → more filling → more volume
3. **Constrict veins**
   - Veins force blood into heart
   - Veins hold LARGE blood volume
   - Response to blood loss → venous constriction
   - Sympathetic stimulation → α1 receptors in veins

# To DECREASE Preload

1. **Remove volume** (bleeding, dehydration)
2. **Raise heart rate** (opposite mechanism above)
3. **Pool blood in veins**
   - Mechanism of action of nitrates
   - Relieve angina
   - Lower preload → less work for heart

# Preload

## Important Terms

- **LVEDV**
  - Volume of blood in the left ventricle when filled
- **LVEDP**
  - Pressure in the left ventricle when filled

# Afterload

- **Forces resisting flow out of left ventricle**
- Heart must squeeze to increase pressure
- Needs to open aortic valve → push blood into aorta
- This is harder to do if:
  - Blood pressure is high
  - Aortic valve is stiff
  - Something in the way: HCM, sub-aortic membrane

# To INCREASE Afterload

1. **Raise mean blood pressure**
2. **Obstruct outflow of left ventricle**
   - Aortic stenosis, HCM

# To DECREASE Afterload

1. **Lower the mean blood pressure**
2. **Treat aortic valve disease, HCM**

- More afterload = more work
  - More oxygen required

# Contractility

- **How hard the heart muscle squeezes**
- Ejection fraction = index of contractility
- Major regulator: **sympathetic nervous system**
  - Also increases heart rate

# To INCREASE Contractility

- Sympathetic nervous system activity
  - Sympathetic innervation to heart
  - Circulating catecholamines (epinephrine, norepinephrine)
  - ↑ calcium release from sarcoplasmic reticulum
  - Triggers: **stress, exercise**
- Sympathomimetic drugs
  - Dopamine, dobutamine, epinephrine, norepinephrine
- Digoxin
  - Inhibits Na-K pump → ↑ calcium in myocytes

# To DECREASE Contractility

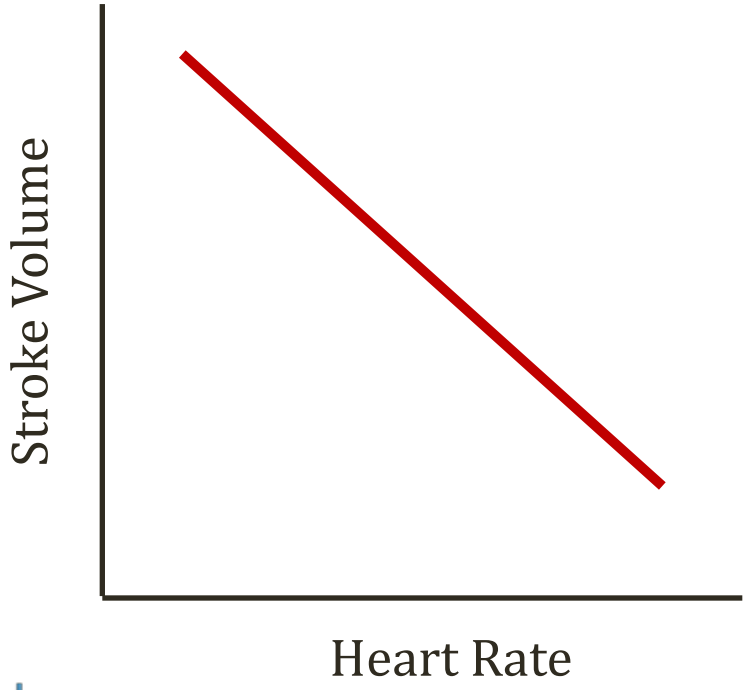
- **Sympathetic system blocking drugs**
  - Beta blockers
- Calcium channel blockers
  - Verapamil, diltiazem
  - Less calcium for muscle contraction
- Heart failure
  - Disease of myocytes

# Heart Rate

- Increases cardiac output under physiologic conditions
- Mainly regulated by **sympathetic nervous system**
- Also increased by **sympathomimetic drugs**
- Decreased by beta blockers and calcium blockers

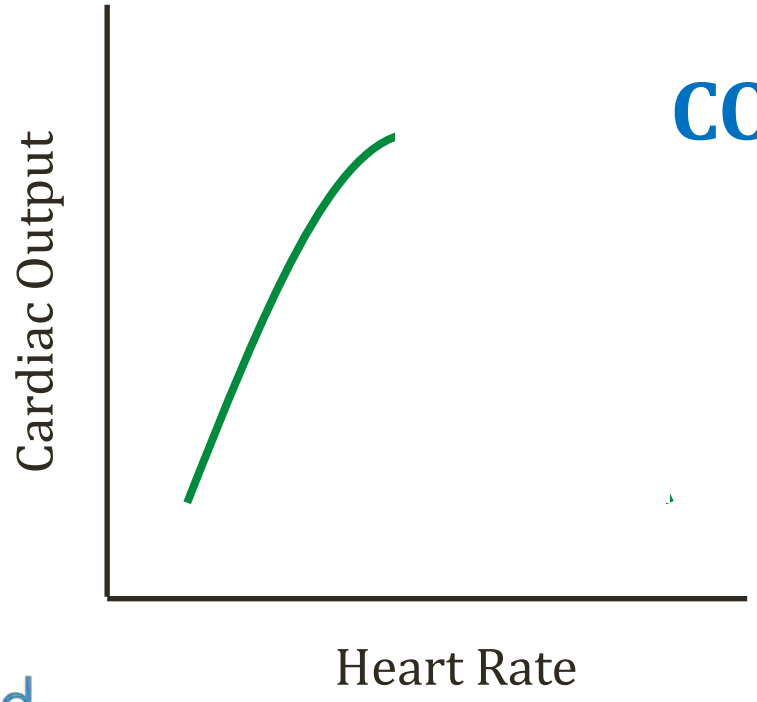
# Heart Rate

- ↑ HR = **↓ stroke volume** (less filling time)



# Heart Rate

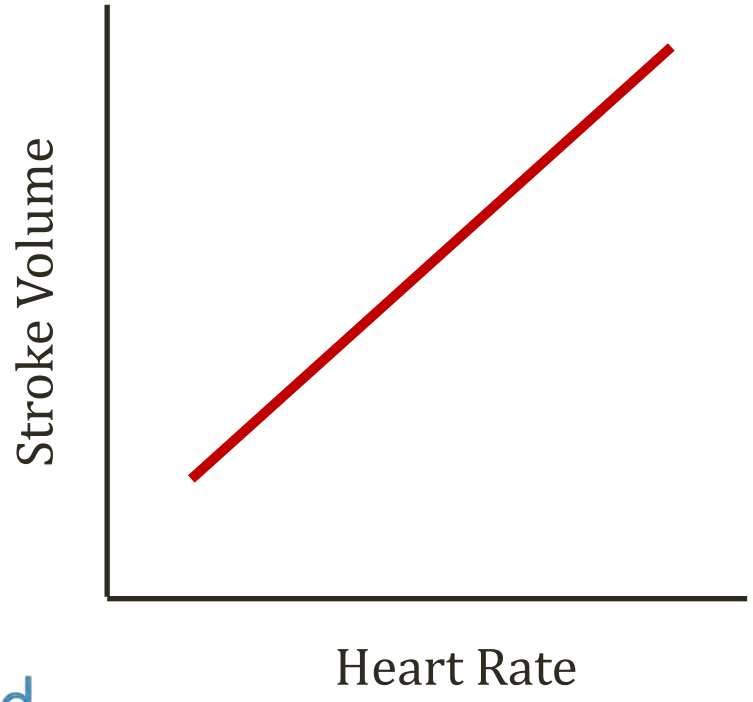
- ↑HR = **↑ cardiac output**




**CO = SV * HR**

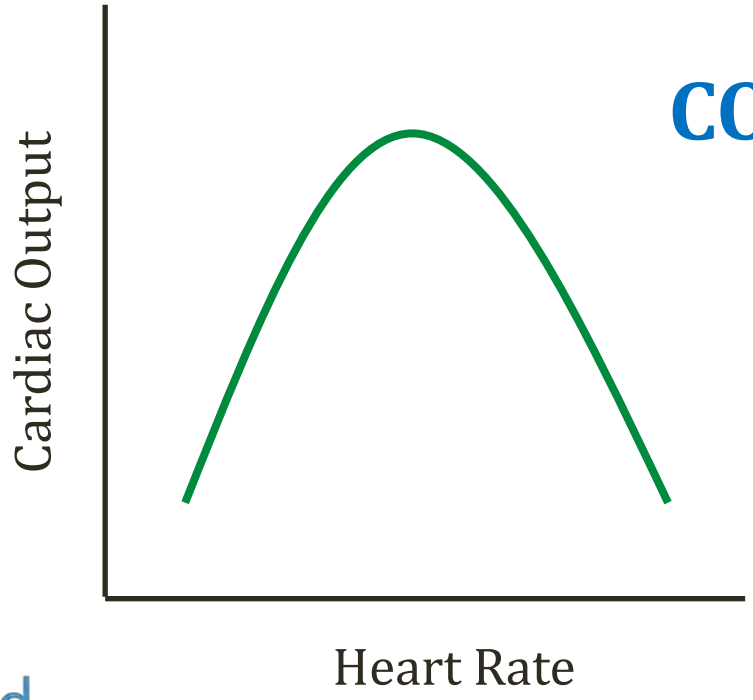
# Heart Rate

- Sympathetic nervous system: ↑HR and ↑contractility
- Stroke volume rises with increased HR



# Heart Rate

- At pathologic heart rates **↑ HR = ↓ CO**
- High heart rate with arrhythmia can lead to ↓CO




**CO = SV * HR**

# Work of the heart

## Myocardial O2 demand

- Preload (LVEDV/P)
- Afterload (MAP)
- Contractility (EF)
- Heart Rate

Hearts starved for O2 → Reduce O2 demand

Low output → Need to increase work

# Cardiovascular Response to Exercise

Jason Ryan, MD, MPH

# Response to Exercise

- Body's overall goal:
  - Maximize perfusion skeletal muscles and heart
  - Minimize perfusion all other areas
- Initiator: **Muscle hypoxia**
- Mediator: **Sympathetic nervous system**

# Response to Exercise

- Process begins with **muscle contraction**
- ATP consumed → oxygen consumed (need more ATP)
- Result: Local hypoxia in muscle tissue
- Vasodilation occurs
  - Multiple mediators released into plasma
  - Adenosine generated from ATP consumption
  - Lactate
  - Carbon dioxide, potassium
- **Lowers total peripheral resistance (TPR)**

# Response to Exercise

- **Sympathetic nervous system** activated
- ↑contractility (stroke volume)
- ↑HR
- Net result: **↑ cardiac output**
- Results in **↑ systolic blood pressure (SBP)**
- Vasoconstriction in some areas (gut, skin)
  - Redistributes blood to important areas (i.e. heart/muscles)

# Response to Exercise

## Blood Pressure Summary

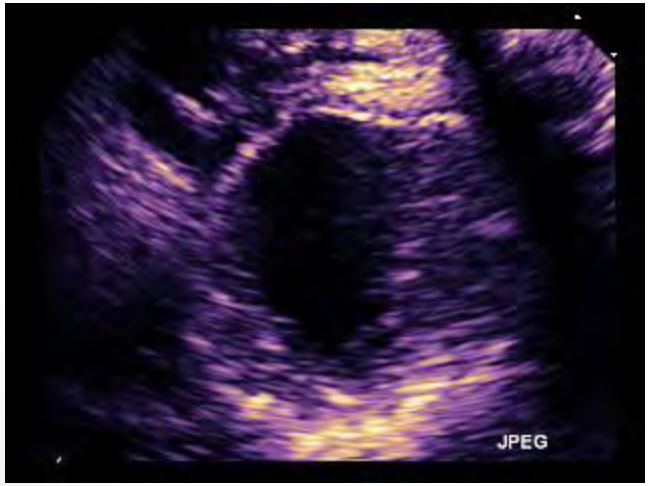
- **SBP rises**
  - More CO = more blood in arteries = more pressure
  - Primary determinant systolic BP = cardiac output
- **DBP decreases slightly or stays normal**
  - Local dilation of skeletal muscles
  - Primary determinant diastolic BP = peripheral resistance
- Pulse pressure increases
- TPR goes down

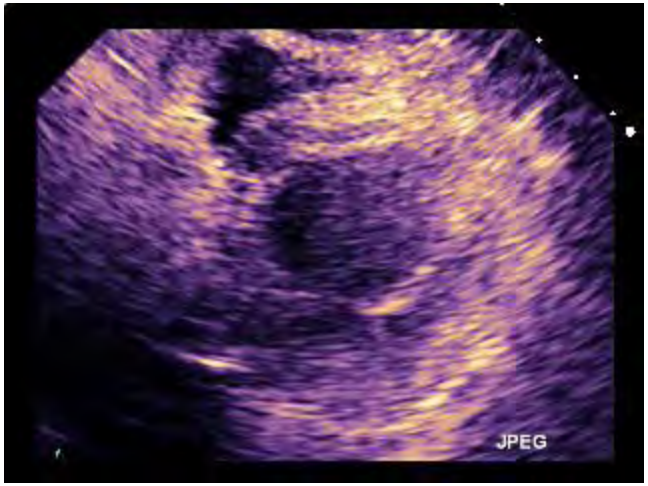
# Response to Exercise

## Ejection Fraction

$$EF = \frac{EDV - ESV}{EDV}$$

- **LVEF increases**
  - More vigorous contraction
  - Major impact: ESV decreases
  - EDV effects minor/variable
  - More preload but less filling time at fast heart rates



# Response to Exercise

## Coronary Perfusion

- Fast HR shortens diastole
- **LESS** coronary filling time
- Coronary vasodilation → increased blood flow
  - Only way to get more oxygen
  - Cannot extract more $O_2$
  - Cardiac tissue extracts maximum oxygen from RBCs
  - Cannot extract more to meet increased demand

# Response to Exercise

## Preload

- **Preload rises with exercise**
- Sympathetic stimulation → **venous contraction**
- Increases preload/EDV
- Contributes to rise in cardiac output
  - Along with increased heart rate and contractility

# Lusitropy

- Lusitropy = **myocardial relaxation**
  - Opposite of contractility
- Increased with exercise
- Contributes to increased preload → ↑ cardiac output

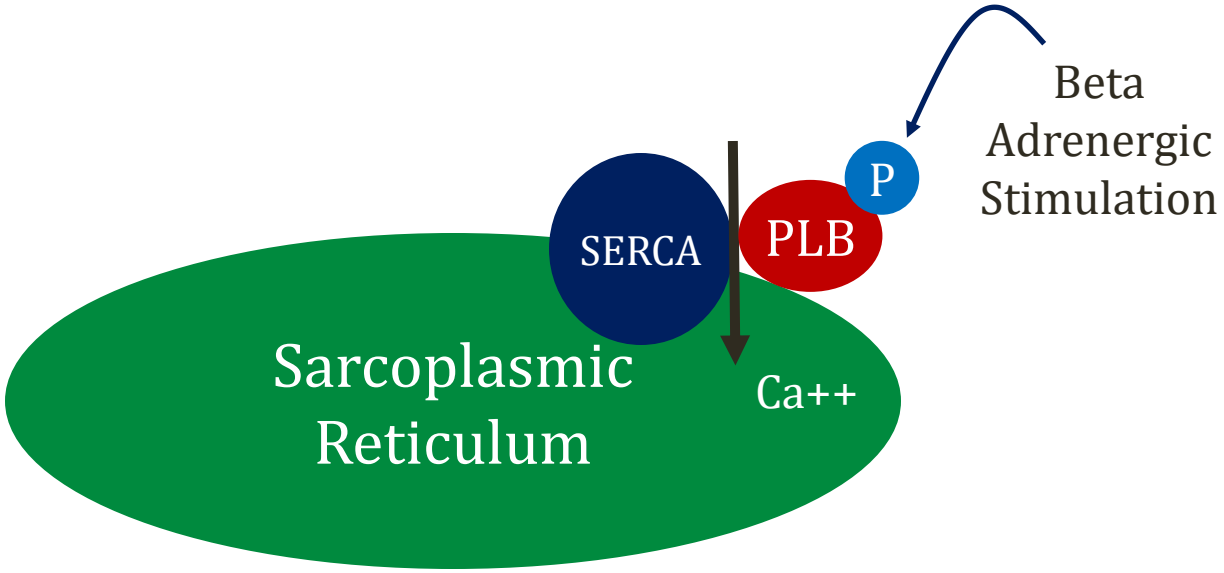
# Lusitropy

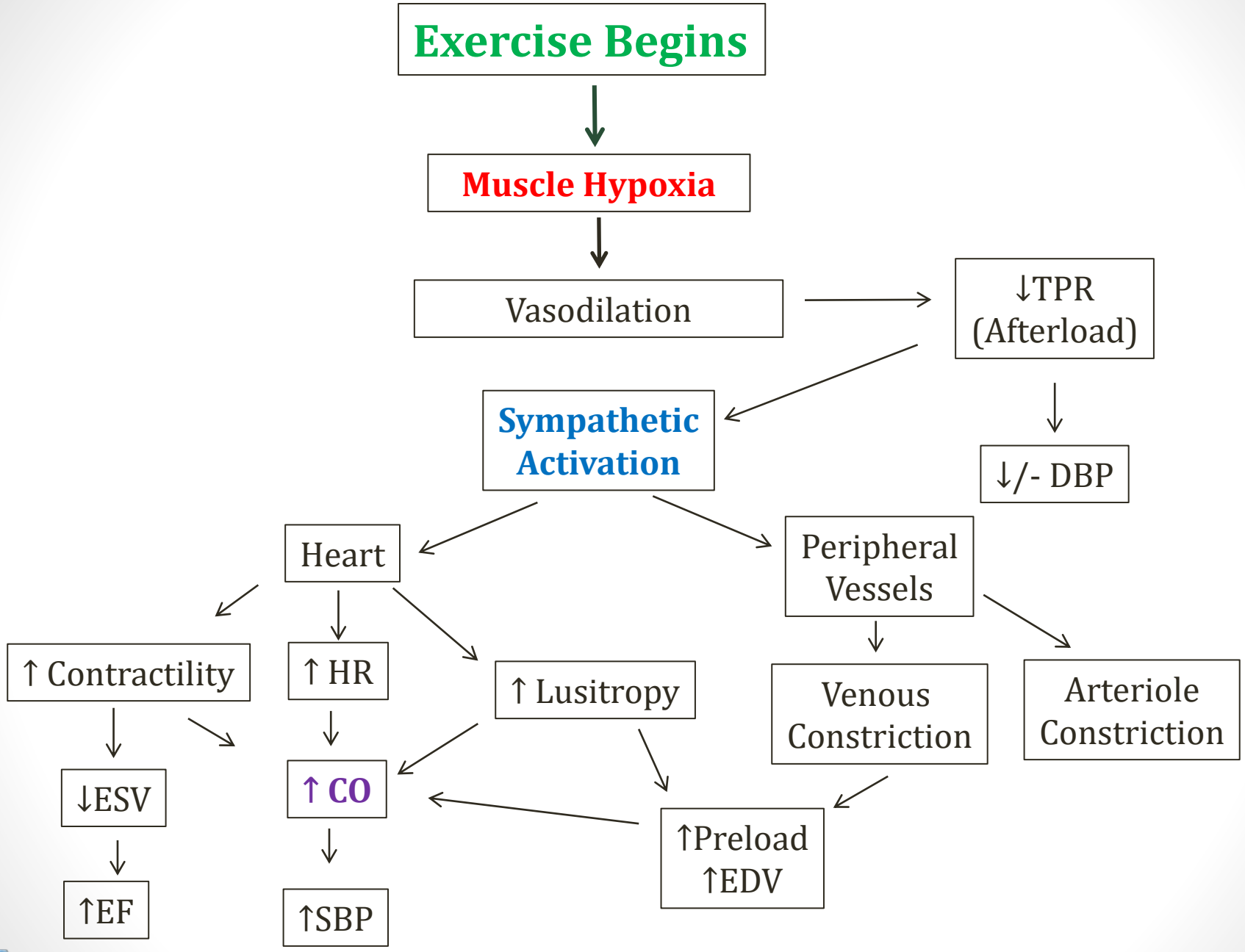
- Key regulatory protein: Phospholamban
  - **Inhibitor:** sarcoplasmic reticulum Ca2+-ATPase (SERCA)
  - Phosphorylated via beta adrenergic stimulation
  - Stops inhibiting SERCA
  - Result: SERCA takes up calcium → relaxation

# SERCA

## Sarco/endoplasmic reticulum $Ca^{2+}$-ATPase

- Sympathetic stimulation → phosphorylates PLB
- Inactivates PLB (relieves inhibitory effect)
- Allows SERCA to uptake more calcium





# Blood Flow Mechanics

Jason Ryan, MD, MPH

# Flow Equations

Ohm's Law $V = I R$

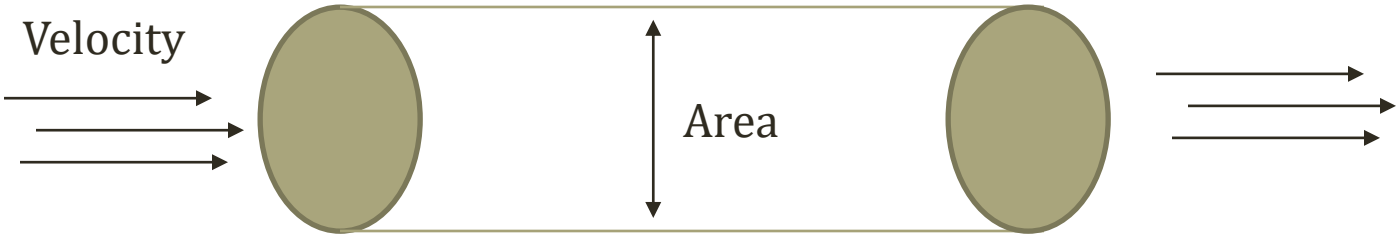
For fluids: $\Delta P = Q \times R$

CO = Q for body

TPR = total peripheral resistance

**$\Delta P = CO * TPR$**

# Flow Equations




**Velocity * Area = Flow**

$(m/s) * (m^2) = (m^3/s)$

# Resistance and Compliance

Resistance = resistance to flow
Compliance = distensability of vessels

**Stiff Vessels**
↑ resistance
↓ compliance

**Stretchy Vessels**
↓ resistance
↑ compliance

High resistance = low compliance (vice versa)

# Pulse Pressure

- Systolic BP – diastolic BP
  - Normal = 120 – 80 = 40mmHg
- Older patients = ↑ pulse pressure
- Hypertensive patients = ↑ pulse pressure
- Related to **vessel compliance**
- **↓ compliance = ↑ pulse pressure**

# Pulse Pressure

- Compliance = Δ volume / Δ pressure
- Stiff vessel → ↓ compliance → ↑ pulse pressure
  - Small change in volume for given pressure applied to walls
- Stretchy vessel → ↑ compliance → ↓ pulse pressure
  - Large change in volume for given pressure applied to walls

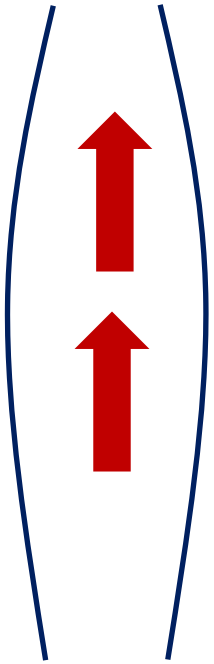
$$C = \Delta V / \Delta P$$

$$\downarrow$$

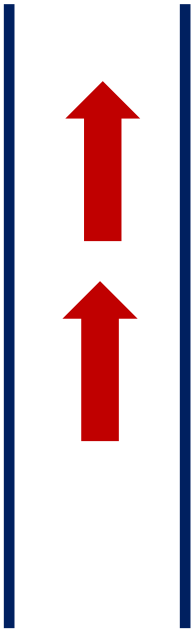
$$\Delta P = \Delta V / C$$

# Pulse Pressure

- **Pulse pressure varies with vessel compliance**
- Stiff vessels → ↓ compliance



Distensible
Vessel
120/80



Stiff
Vessel
170/100

# Flow Equation

## Total Peripheral Resistance

$$\Delta P = CO * \mathbf{TPR}$$

↑ resistance = ↑ pressure to maintain flow

↑ pressure = ↑ cardiac work

# Total Peripheral Resistance

- Easy to push blood out of heart → less $O_2$ required
- Resistance to flow → more work for heart
- What resists forward flow out of heart?
  1. Types of vessels (i.e. pipes/tubes)
  2. Thickness of blood (viscosity)

# Types of Vessels

- Aorta: SBP 100mmHg
- Large arteries: Falls few mmHg
- Small arteries: 10-20mmHg
- **Arterioles: 35mmHg**
- Capillaries: 25mmHg

# Types of Vessels

- **Arterioles = "resistance vessels"**
  - Major determinant of total peripheral resistance
  - Large pressure drop
  - Vasoconstriction = ↑ TPR
  - Vasodilation = ↓ TPR

# Viscosity

- Thickness of blood
- Low viscosity
  - Anemia
- High viscosity
  - Polycythemia
  - Multiple myeloma
  - Spherocytosis

# Poiseuille's Law

- $\Delta P = Q \times R$

$$R = \frac{\Delta P}{Q} = \frac{8\,\eta\,(\text{viscosity})\,L\,(\text{length})}{\Pi\, r\,(\text{radius})^{4}}$$

Changes in radius → large change in resistance

# Series and Parallel Circuits

Human organs arranged **in parallel**

Resistances add up differently in series than in parallel

$$\frac{1}{R_{total}} = \frac{1}{R_1} + \frac{1}{R_2}$$

Parallel

$$R_{total} = R_1 + R_2$$

Series

# Series and Parallel Circuits

For two resistances (2 and 2), what is total R?

$$\frac{1}{R_{total}} = \frac{1}{R_1} + \frac{1}{R_2}$$

$$R_{total} = R_1 + R_2$$

**$R_{total} = 2 + 2 = 4$**

$$\frac{1}{R_{total}} = \frac{1}{2} + \frac{1}{2}$$

**$R_{total} = 1$**

# Flow Equation

$$\Delta P = Q * R$$

- Used to calculate resistance, CO, or ΔP
- Often applied to **body** and **lungs**
  - For both systems Q = Cardiac Output (CO)

# Flow Equation

$$\Delta P = Q * R$$

- Body
  - ΔP = Arterial pressure – right atrial pressure
  - R = Total peripheral resistance (TPR)
  - R = **Systemic vascular resistance** (SVR)
- Lungs
  - ΔP = Pulmonary artery pressure – left atrial pressure
  - R = **Pulmonary vascular resistance** (PVR)

# Mean Arterial Pressure

- Diastolic plus 1/3 (Systolic – Diastolic)
- Total body
  - Arterial blood pressure = 120/80 mmHg
  - Mean arterial pressure = 80 + 1/3 (40) = 93 mmHg
- Lungs
  - Pulmonary artery pressure = 40/20 mmHg
  - Mean pulmonary artery pressure = 20 + 1/3 (20) = 27 mmHg

# Total Body

$$\Delta P = CO * TPR$$

- R = TPR
- ΔP = MAP – RAP
  - MAP = mean arterial pressure
  - RAP = right atrial pressure
- CO of 5L/min; BP 155/80 (MAP 105), RA 5

$$TPR = \frac{\Delta P}{CO} = \frac{MAP - RAP}{5} = \frac{105 - 5}{5} = 20$$

# Lungs

$$\Delta P = CO * TPR$$

- R = PVR
- ΔP = PA – LAP
  - PA = mean pulmonary artery pressure
  - LAP = left atrial pressure
- CO of 5L/min; PA 40/10 (MAP 20), LA 5

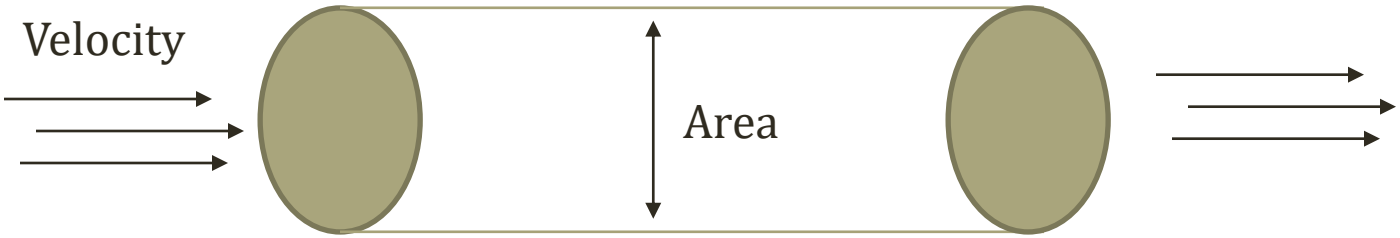
$$PVR = \frac{\Delta P}{CO} = \frac{PA - LAP}{5} = \frac{20 - 5}{5} = 3$$

# Lung and Body Flow Variables

| | Lung | Body |
|---|---|---|
| Flow | CO | CO |
| Resistance | PVR | TPR |
| Start Pressure | PA | AoP |
| End Pressure | LA | RA |
| ΔP | PA – LA | Ao - RA |

# Velocity and Area

- Flow = Velocity * Area
- Changes as blood moves through vessels
  - Aorta → arterioles → capillaries → veins
  - Cardiac output moves through system (same flow)
  - Different vessels → different area, velocity
  - Area ↑↑, velocity ↓↓




**Flow = Velocity * Area**

$(m^3/s) = (m/s) * (m^2)$

# Flow Properties of Blood Vessels

| Property | Highest | Lowest |
|---|---|---|
| Flow | -- | -- |
| Area | Capillaries | Large arteries |
| Velocity | Large Arteries | Capillaries |
| Resistance | Arterioles | Veins |
| ΔP | Arterioles | Veins |

$$\text{Flow} = \text{Vel} * \text{Area}$$

$$\Delta P = Q \times R$$

# Law of Laplace

- Wall tension or wall stress
- Applies to vessels and cardiac chambers
- ↑ tension → ↑ O2 demand → ischemia/angina

$$\text{Tension} \propto \frac{P * r}{2h}$$

# Wall Tension

- Afterload: Increases **pressure** in left ventricle
  - Hypertension, aortic stenosis
  - Will increase wall tension
  - “Pressure overload”

$$\text{Tension} \propto \frac{P * r}{2h}$$

# Wall Tension

- Preload:  Increases **radius** of left ventricle
  - Chronic valvular disease (aortic/mitral regurgitation)
  - Will increase wall tension
  - “Volume overload”

$$\text{Tension} \propto \frac{P * r}{2h}$$

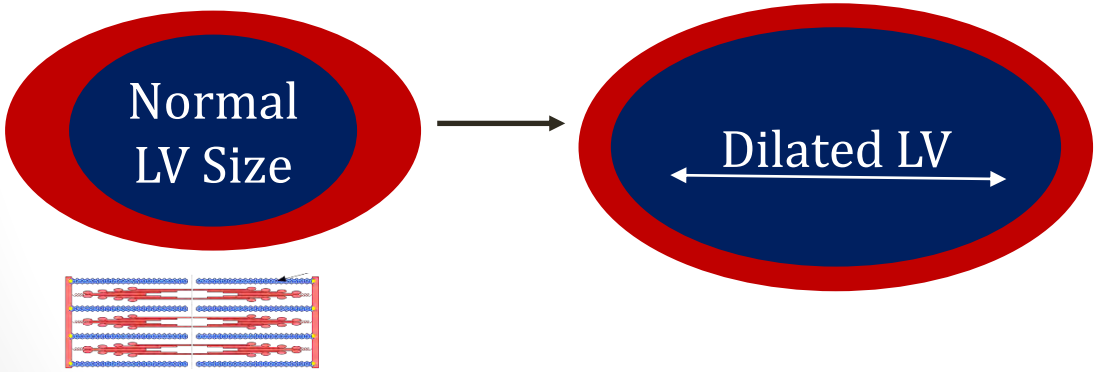
# Wall Tension

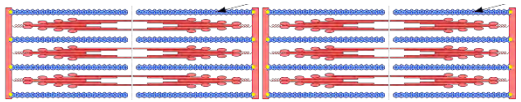
- Hypertrophy: Compensatory mechanism
  - Will **decrease** wall tension
  - Force distributed over more mass
  - Occurs with chronic pressure/volume overload

$$\text{Tension} \propto \frac{P * r}{2h}$$

# Eccentric Hypertrophy

- Longer myocytes
- Sarcomeres added in series
- Left ventricular mass increased
- Wall thickness NOT increased



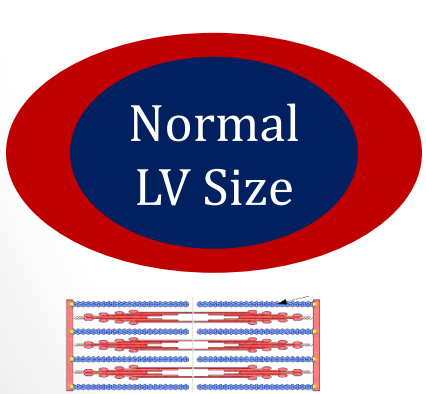
Increased myocyte size
Sarcomeres in series
Normal wall thickness

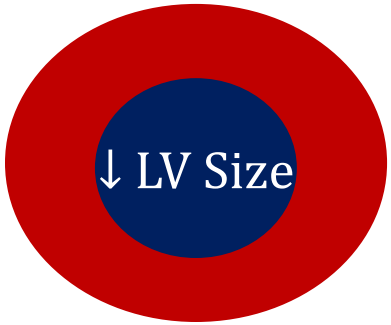
# Eccentric Hypertrophy

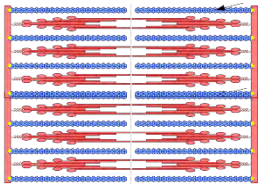
- Volume overload of left ventricle
  - Aortic regurgitation
  - Mitral regurgitation
- Cardiomyopathy
  - Ischemic and non-ischemic

# Concentric Hypertrophy

- Pressure overload
- Chronic ↑↑ pressure in ventricle
- Sarcomeres added in parallel
- Left ventricular mass increased
- Wall thickness increased



Increased myocyte size
Sarcomeres in parallel
Increased wall thickness

# Concentric Hypertrophy

- Classic causes: Hypertension, Aortic stenosis
  - Both raise pressure in LV cavity
- Decreased compliance (stiff ventricle)
- Often seen in diastolic heart failure

# Regulation of Blood Pressure

Jason Ryan, MD, MPH

# Blood Pressure

- Required for perfusion of tissues
- Varies with sodium/water intake
- Regulated by nervous system

# Baroreceptors

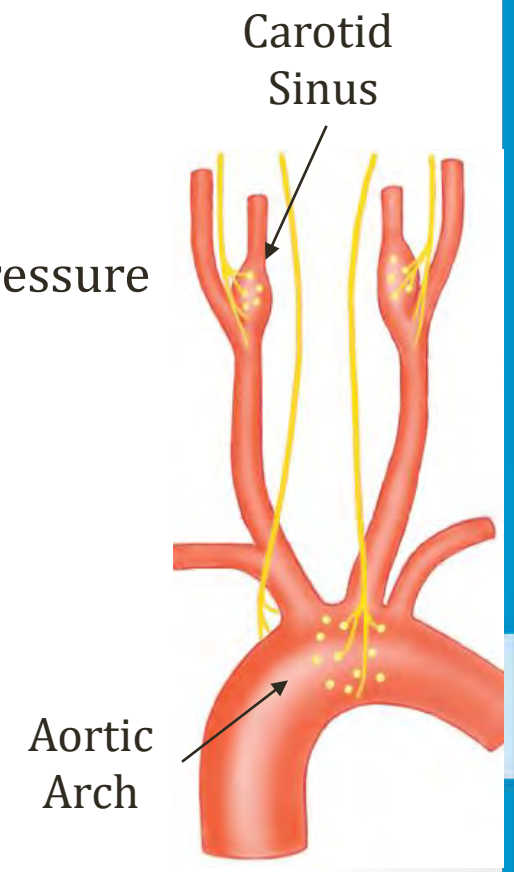
- Blood pressure sensors via **stretch**
- Signal central nervous system (brain)
- Response via **autonomic nervous system**
  - Sympathetic and parasympathetic
- Modify:
  - Heart rate/contractility
  - Arterial tone (vasoconstriction)
  - Venous tone (more tone = more preload to ventricle)
  - Renal renin release

# Baroreceptors

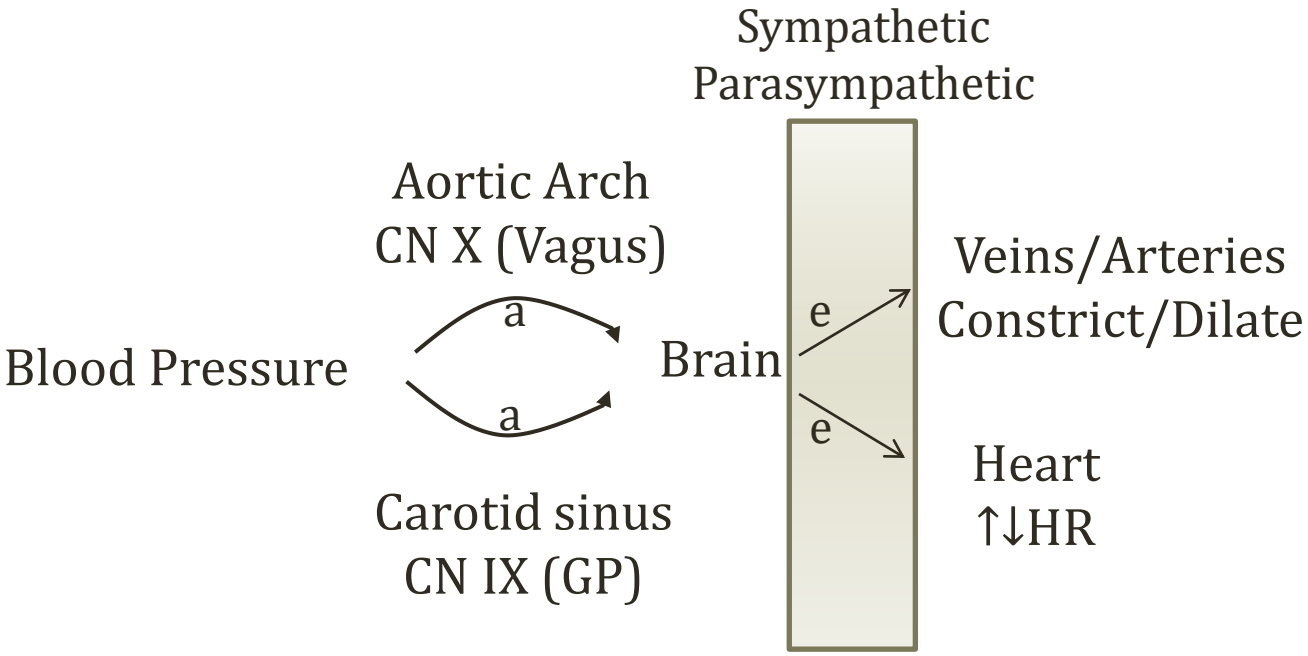
- **Aortic arch and carotid sinus**
  - Quick response to changes in blood pressure
  - Rapid response via autonomic nervous system
- Kidneys (renin release)

# Baroreceptors

- Aortic arch
  - Senses **elevated blood pressure**
  - Poor sensing of low blood pressure
- Carotid sinus
  - Most important baroreceptor
  - Modifies signals over wider range of blood pressure
  - Senses **low and high blood pressure**

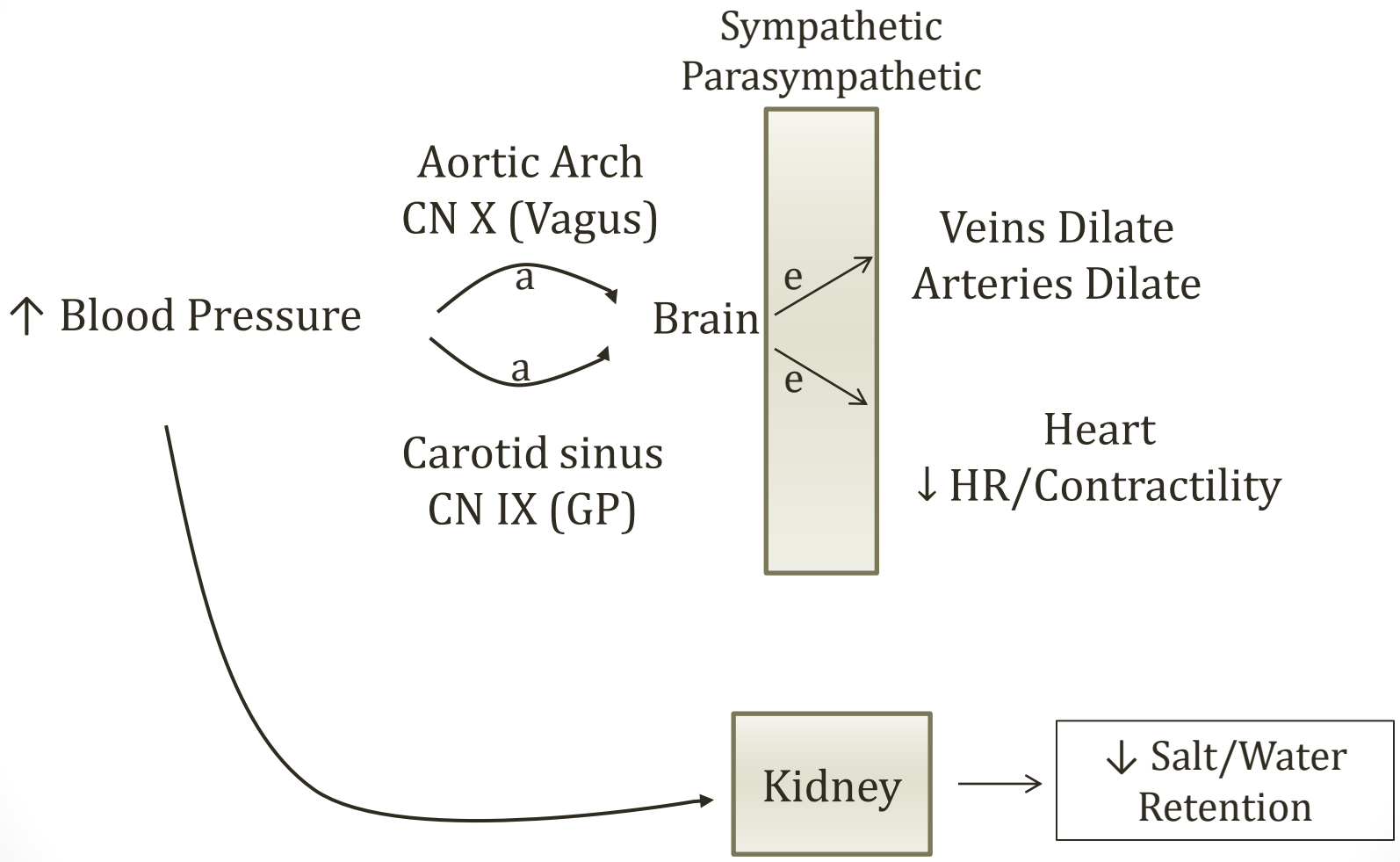


# Blood Pressure Control

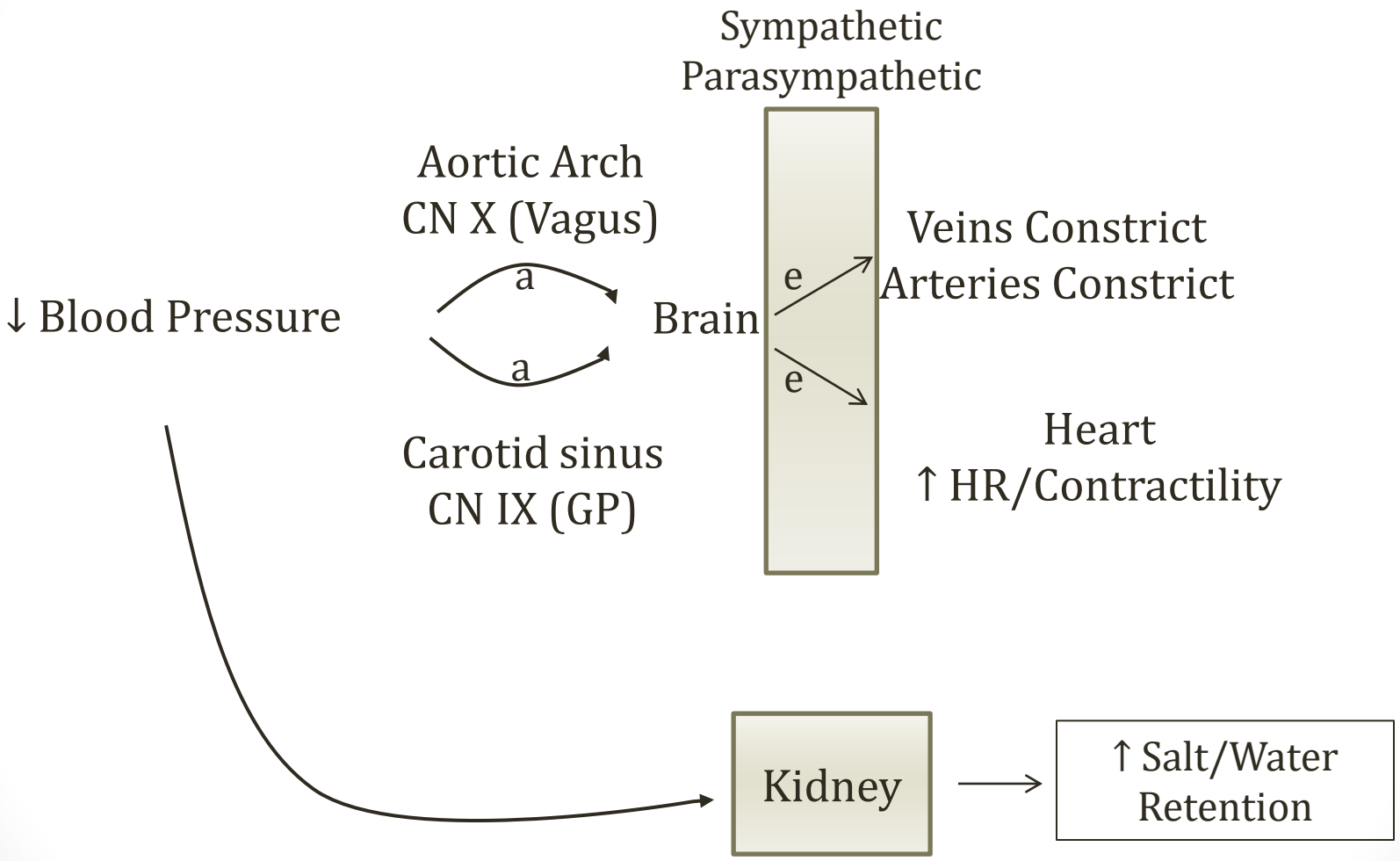



Afferent = Arrive at the brain
Efferent = Exit the brain
Nucleus Solitarius

# High Blood Pressure

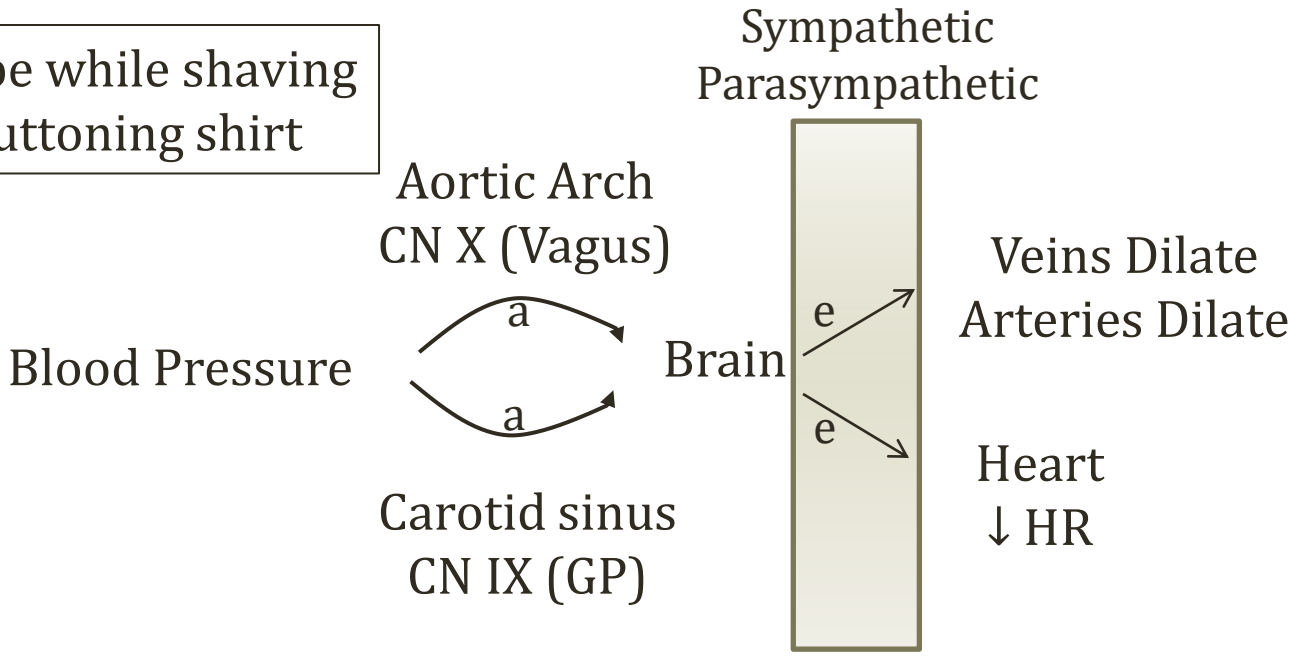


# Hemorrhage



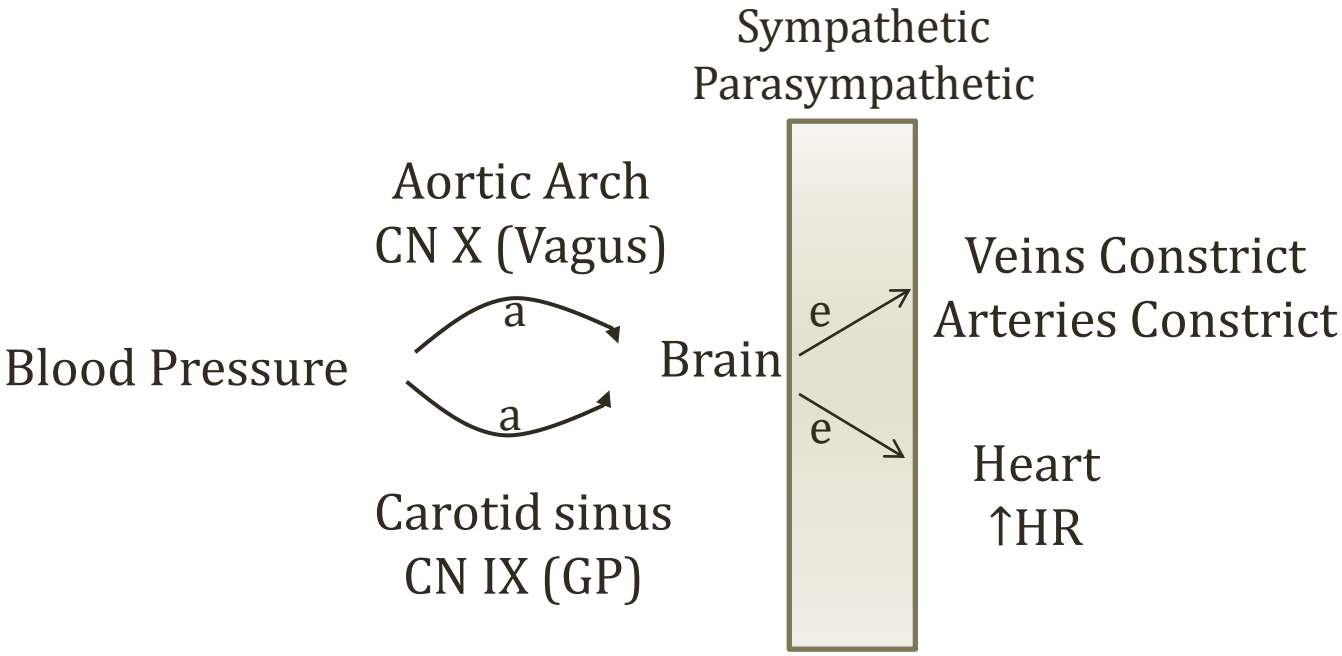
# Carotid Massage

Syncope while shaving or buttoning shirt



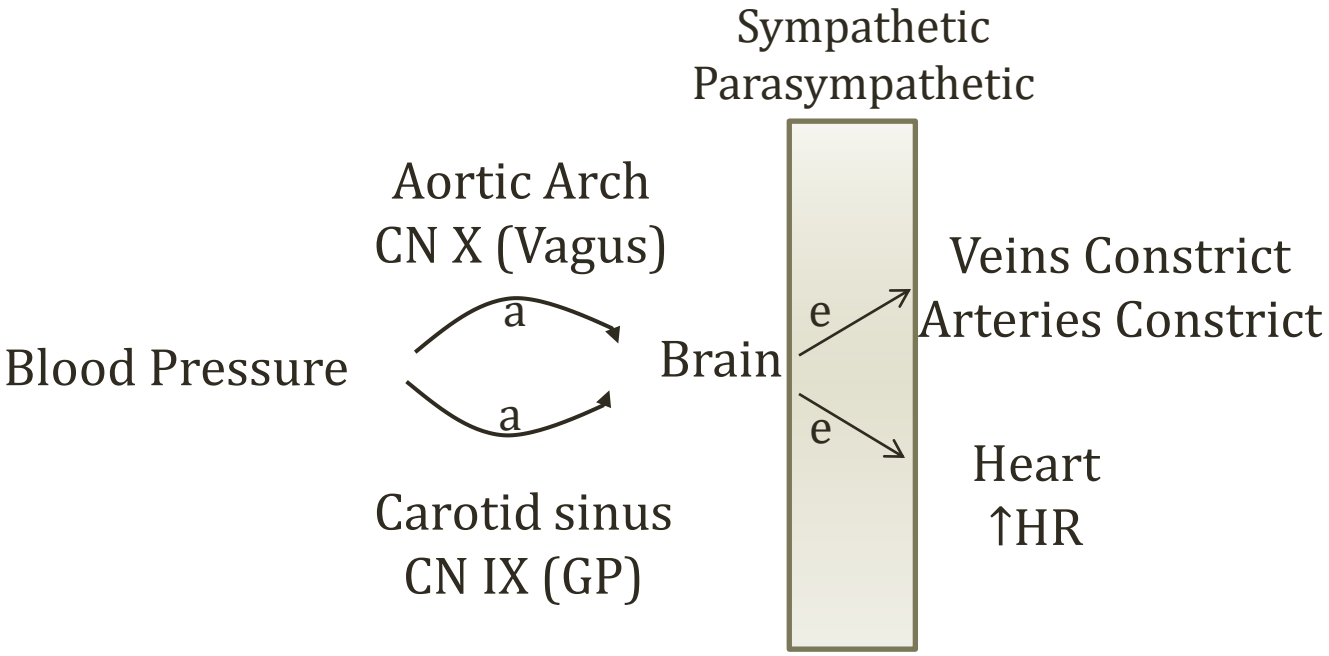

Tricks carotid sinus into thinking ↑ BP
Result: ↓ HR, Vasodilation, ↓ BP

# Carotid Occlusion



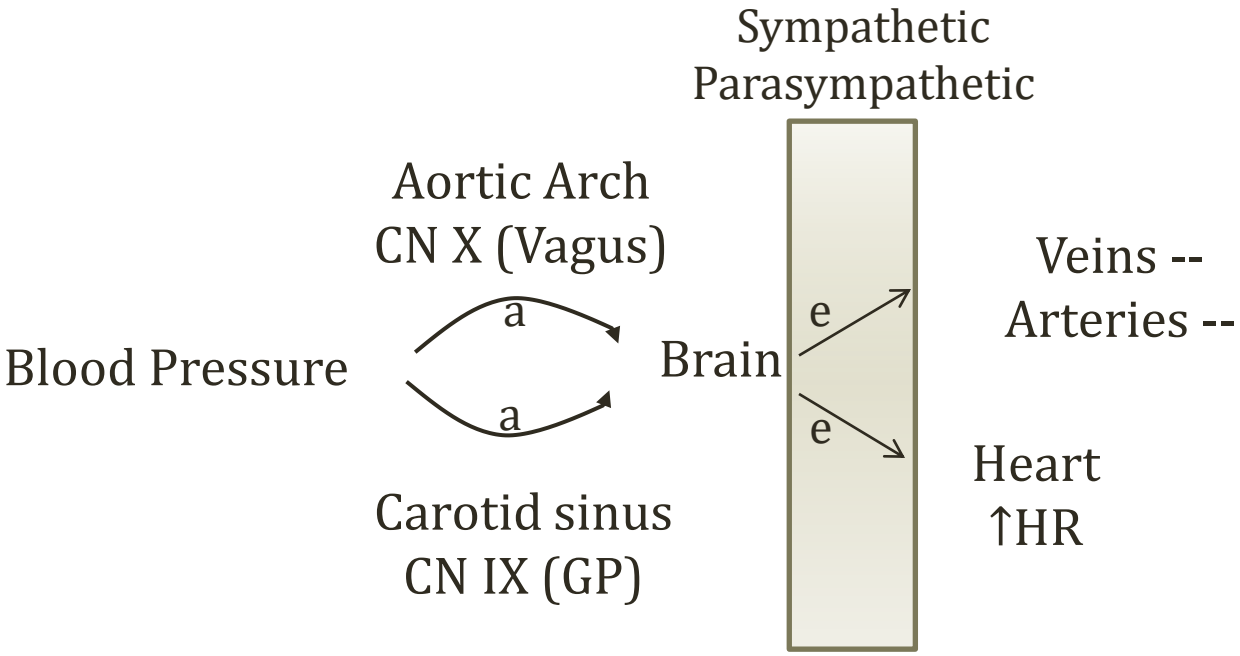

Tricks carotid sinus into thinking ↓ BP
Result is ↑HR, Vasoconstriction, ↑BP

# Severing CN IX




Tricks brain into thinking ↓ BP
Result is ↑ HR, Vasoconstriction, ↑BP

# Severing CN X

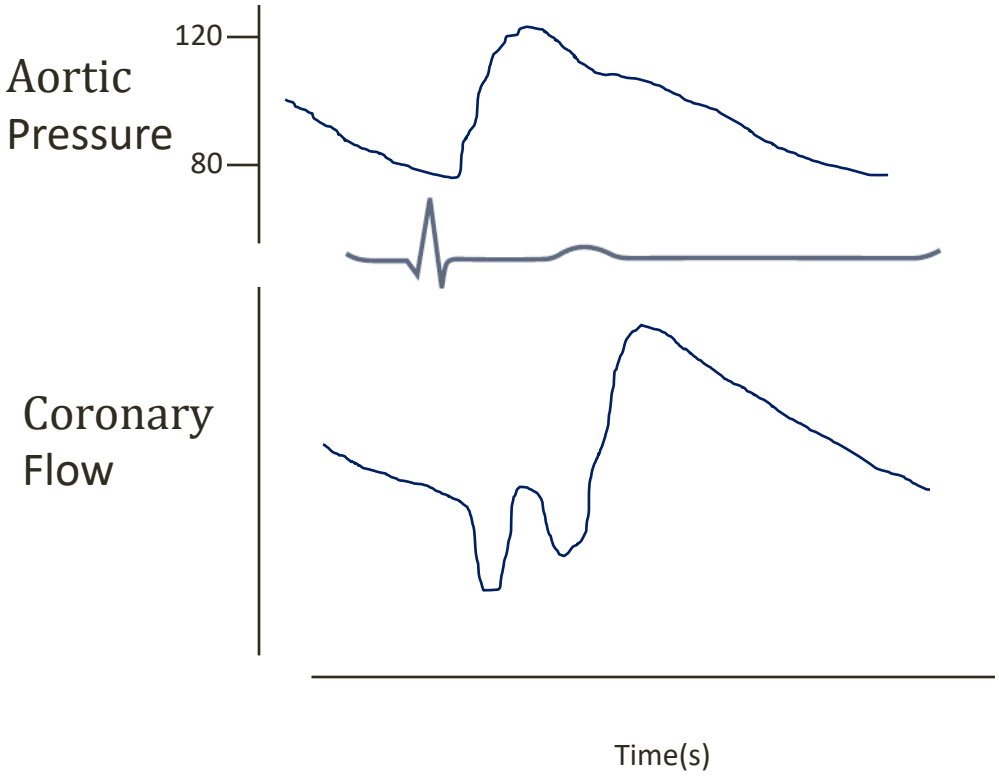



Vagotomy
Unopposed Sympathetic Cardiac Stimulation
Result is ↑ HR

# Summary of Techniques

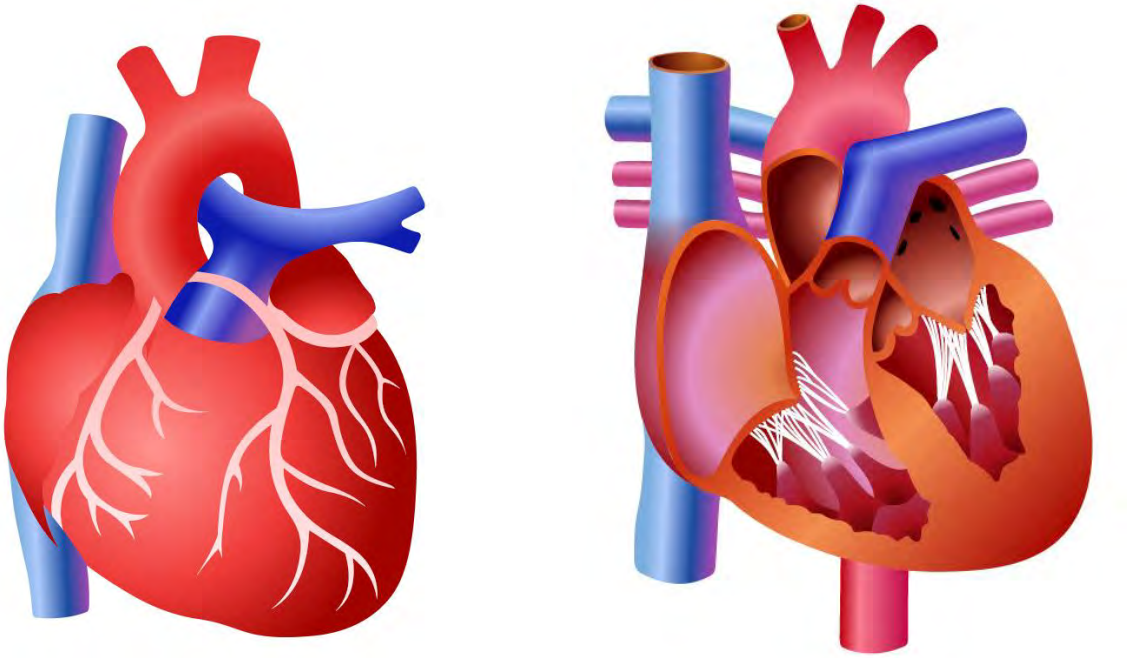
| Technique | Interpretation | Result |
|---|---|---|
| Carotid Massage | ↑BP | ↓HR,↓BP |
| Carotid Occlusion | ↓BP | ↑HR, ↑BP |
| Sever CN IX | ↓BP | ↑HR, ↑BP |
| Sever CN X | -- | ↑HR |

# Coronary Blood Flow




- In tachycardia, less time in diastole → less flow

# Regional Blood Flow



- Epicardium → site of coronary arteries
- Subendocardium receives smallest amount blood flow

# Organ Circulation

| Organ | Key Features |
|---|---|
| Lung | 100% of Cardiac Output |
| Liver | Largest Systemic Blood Flow |
| Kidneys | Highest blood flow by weight |
| Heart | Largest Δ02 (80%)<br>↑ demand vasodilation |

# Autoregulation

- Some tissue beds maintain **constant blood flow**
- ↑ BP → ↑ flow → vasoconstriction → ↓ flow (normal)
- Use local metabolites to sense blood pressure

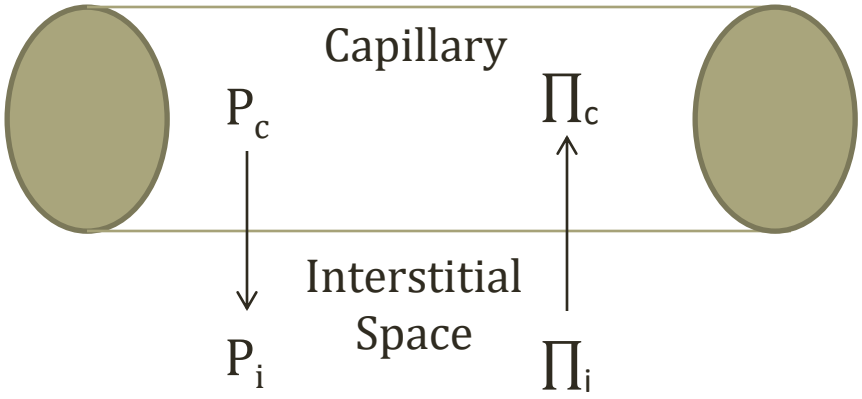
# Autoregulation

| Organ | Key Control Variables |
|---|---|
| Heart | CO2, Adenosine, NO |
| Brain | CO2, pH |
| Kidneys | BP and NaCl feedback |
| Lungs | Hypoxia → Vasoconstriction |
| Skeletal Muscle | Lactate, adenosine, K+ |
| Skin | Sympathetic stimulation |

Kidney, brain, heart: Excellent autoregulation systems
Skin: Poor autoregulatory capacity

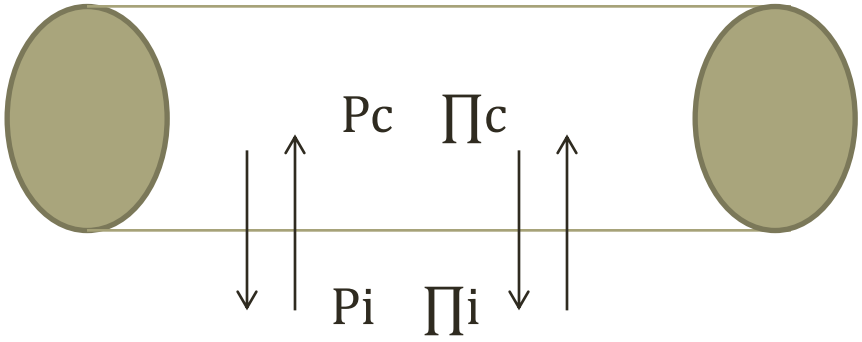
# Capillary Fluid Exchange

- Two forces drive fluid into or out of capillaries
- Hydrostatic pressure (P)
  - Molecules against capillaries walls
  - Pushes fluid out
- Oncotic pressure ($\Pi$)
  - Solutes (albumin) drawing fluid into capillaries



# Capillary Fluid Exchange

- Hydrostatic pressure – fluid PUSHING against walls
  - High pressure drives fluid TOWARD low pressure
- Oncotic pressure –solutes PULLING fluid in
  - High pressure draws fluid AWAY from low pressure

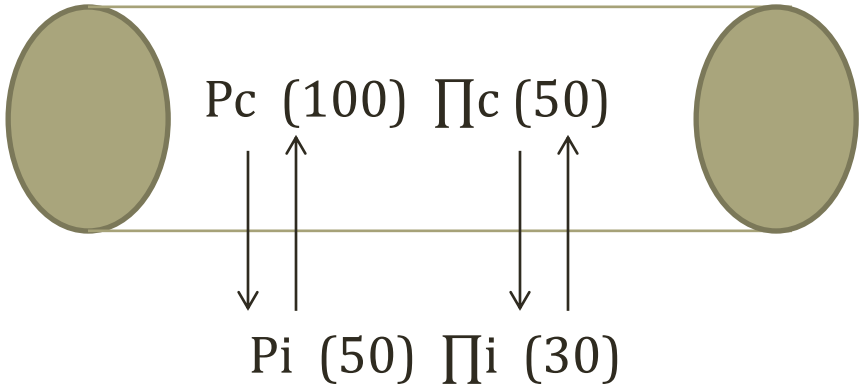



Net Pressure (NP) = (Pc –Pi) - (∏c - ∏i)

Flow = (NP) Kf

# Capillary Fluid Exchange

- Hydrostatic pressure – fluid PUSHING against walls
  - High pressure drives fluid TOWARD low pressure
- Oncotic pressure –solutes PULLING fluid in
  - High pressure draws fluid AWAY from low pressure

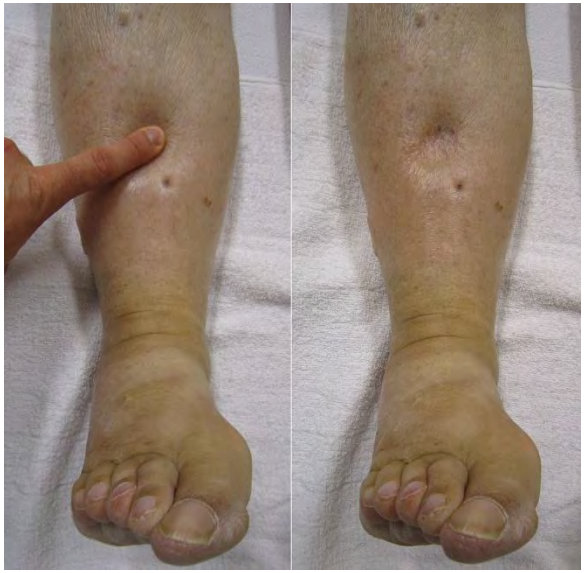



Net Pressure (NP) = 50 - 20
= 30

Flow = (NP) Kf

# Edema

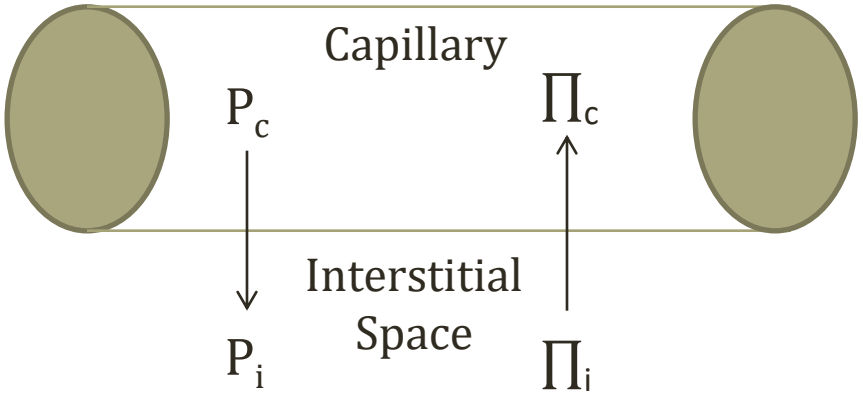
- Excess fluid movement out of capillaries
- Tissue swelling
- Lungs: Pulmonary edema
- Systemic capillaries: Lower extremity edema



James Heilman, MD

# Edema

Net Pressure (NP) = (Pc –Pi) + (∏i - ∏c)




↑ capillary pressure, ↑ Pc (heart failure)
↓ plasma proteins, ↓ ∏c (nephrotic syndrome, liver failure)
↑ capillary permeability, ↑Kf (toxins, infections, burns)
↑ interstitial osmotic pressure, ↑ ∏i (lymphatic blockage)

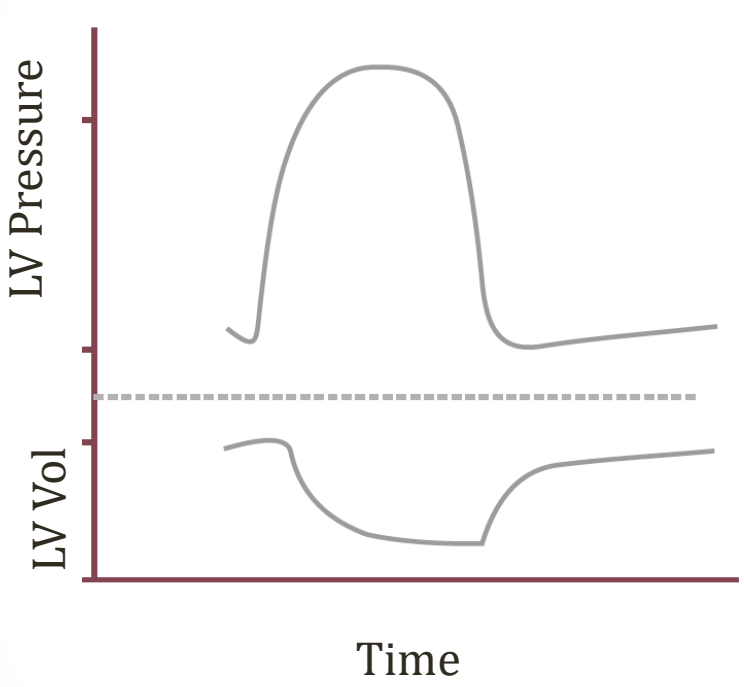
# 3rd Spacing

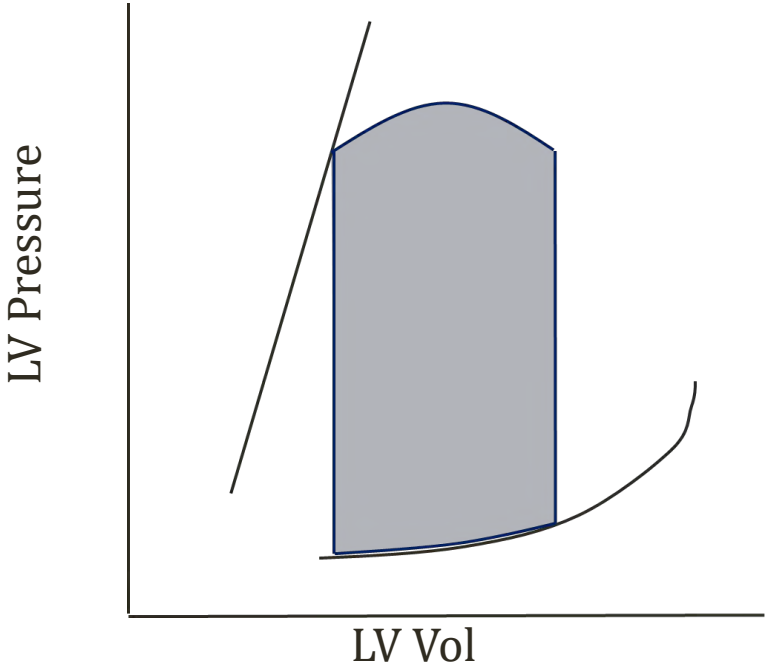
- Intracellular fluid – 1st space
  - About 2/3 body fluid
- Extracellular fluid – 2nd space
  - About 1/3 body fluid
- Third spacing - fluid where it should NOT be
  - Pleural effusions
  - Ascites
  - Cerebral edema
  - Low intravascular volume/High total volume
- Occurs post-op, sepsis

# Pressure Volume Loops

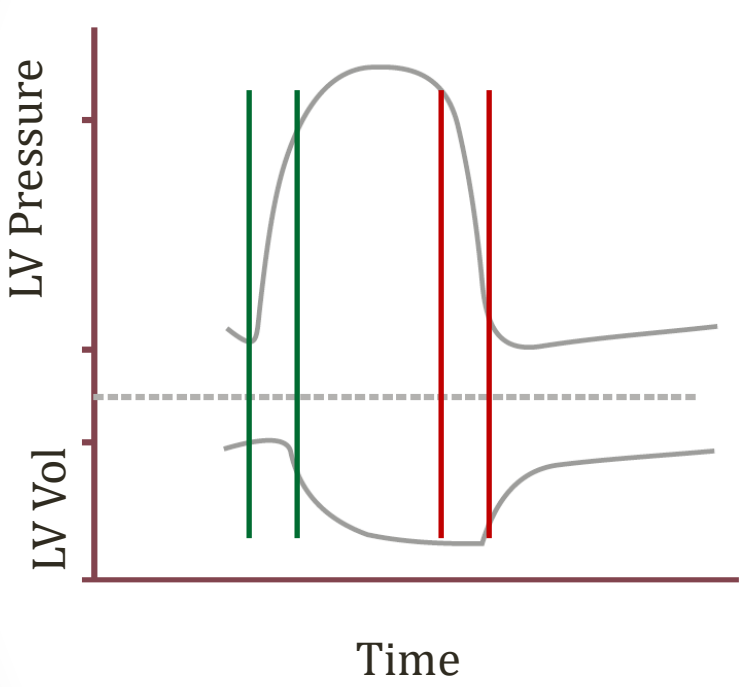
Jason Ryan, MD, MPH

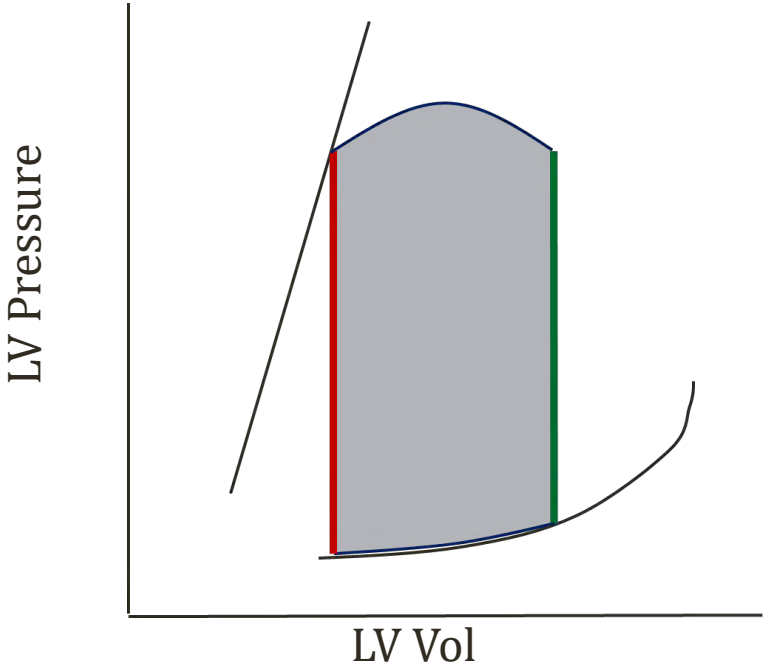
# PV Loops



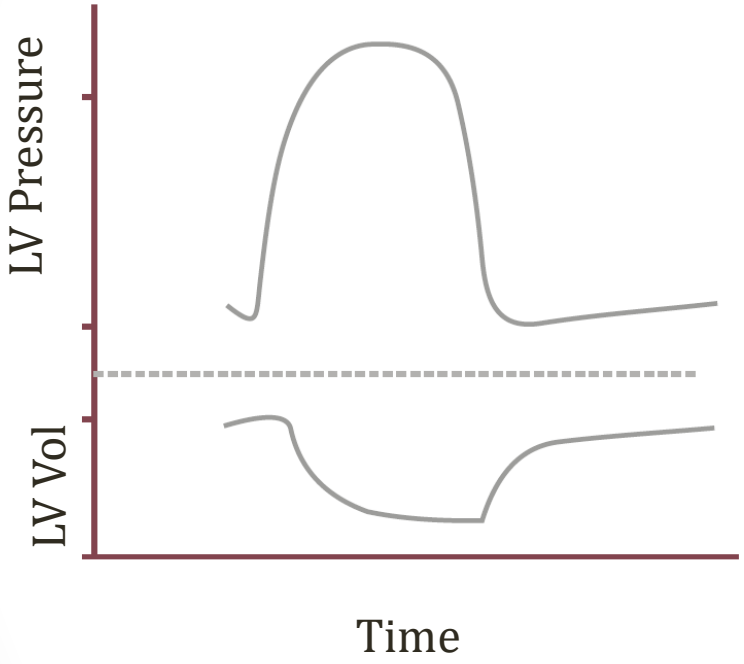



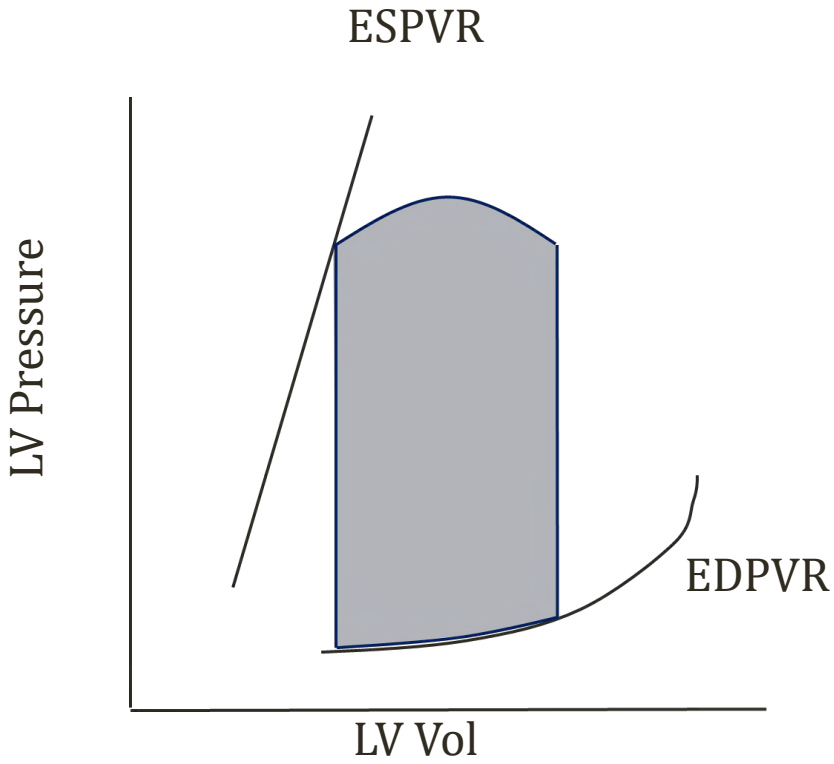
# PV Loops



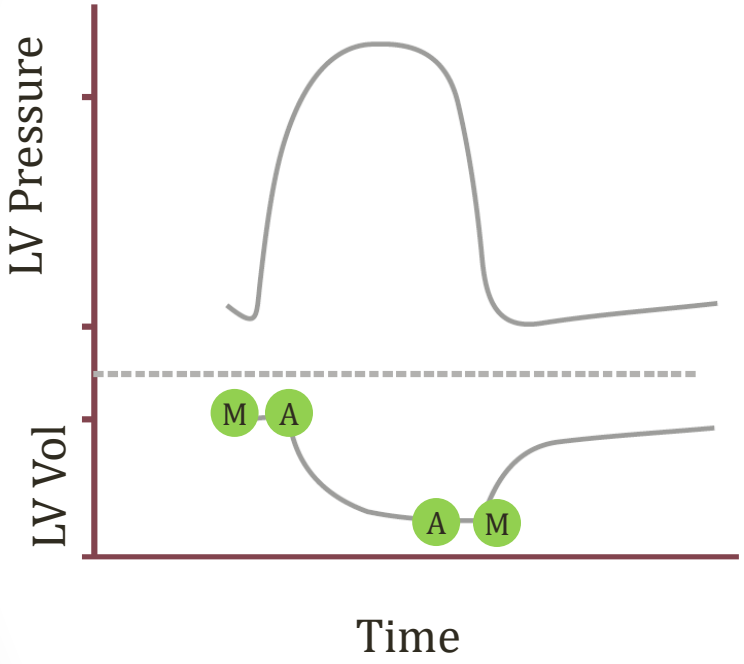



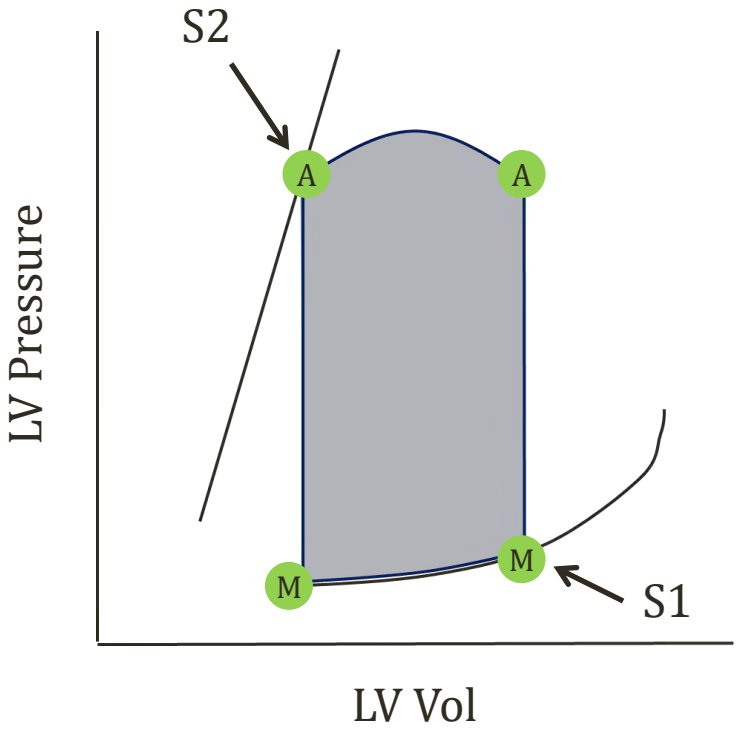
# PV Loops

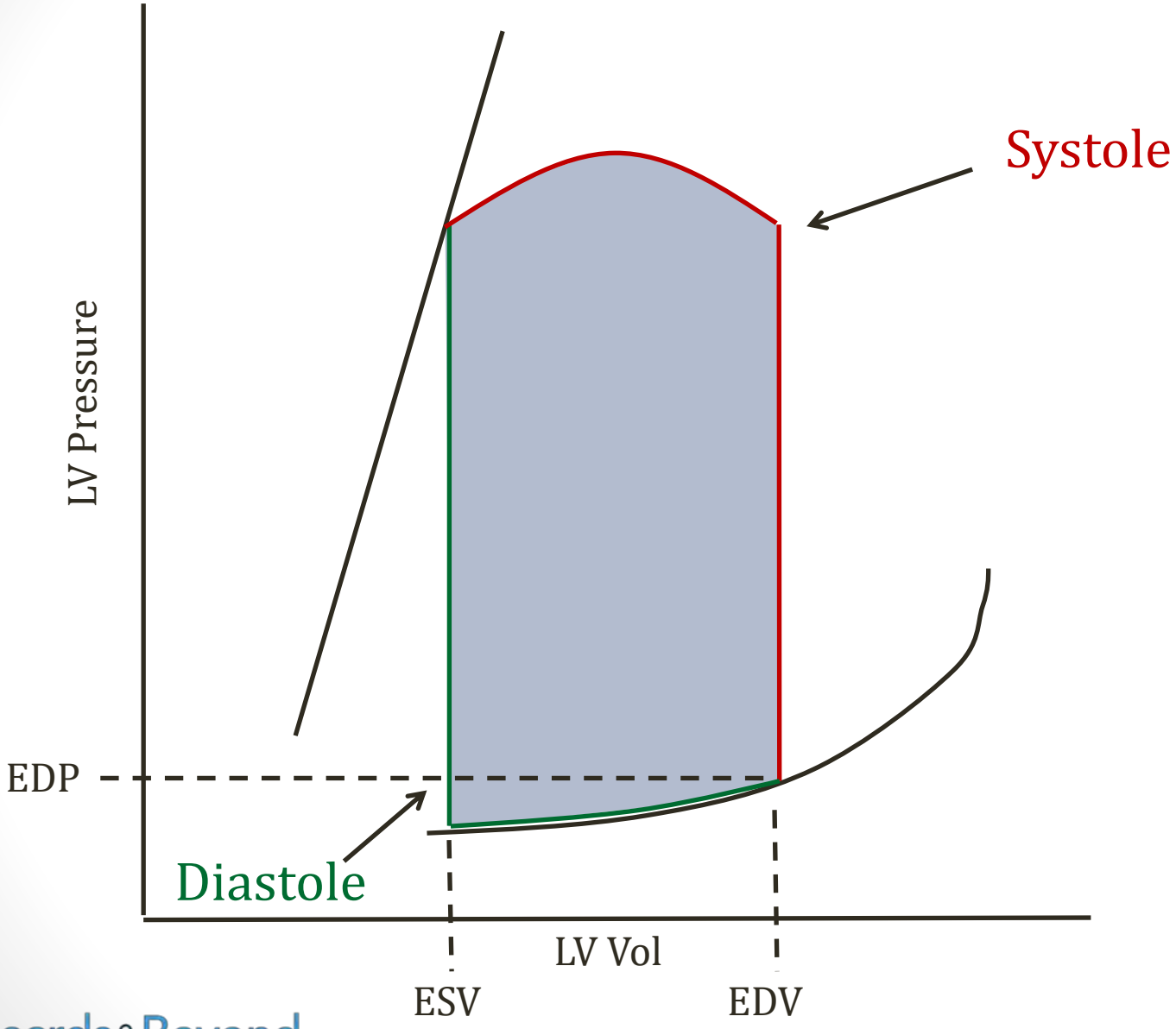


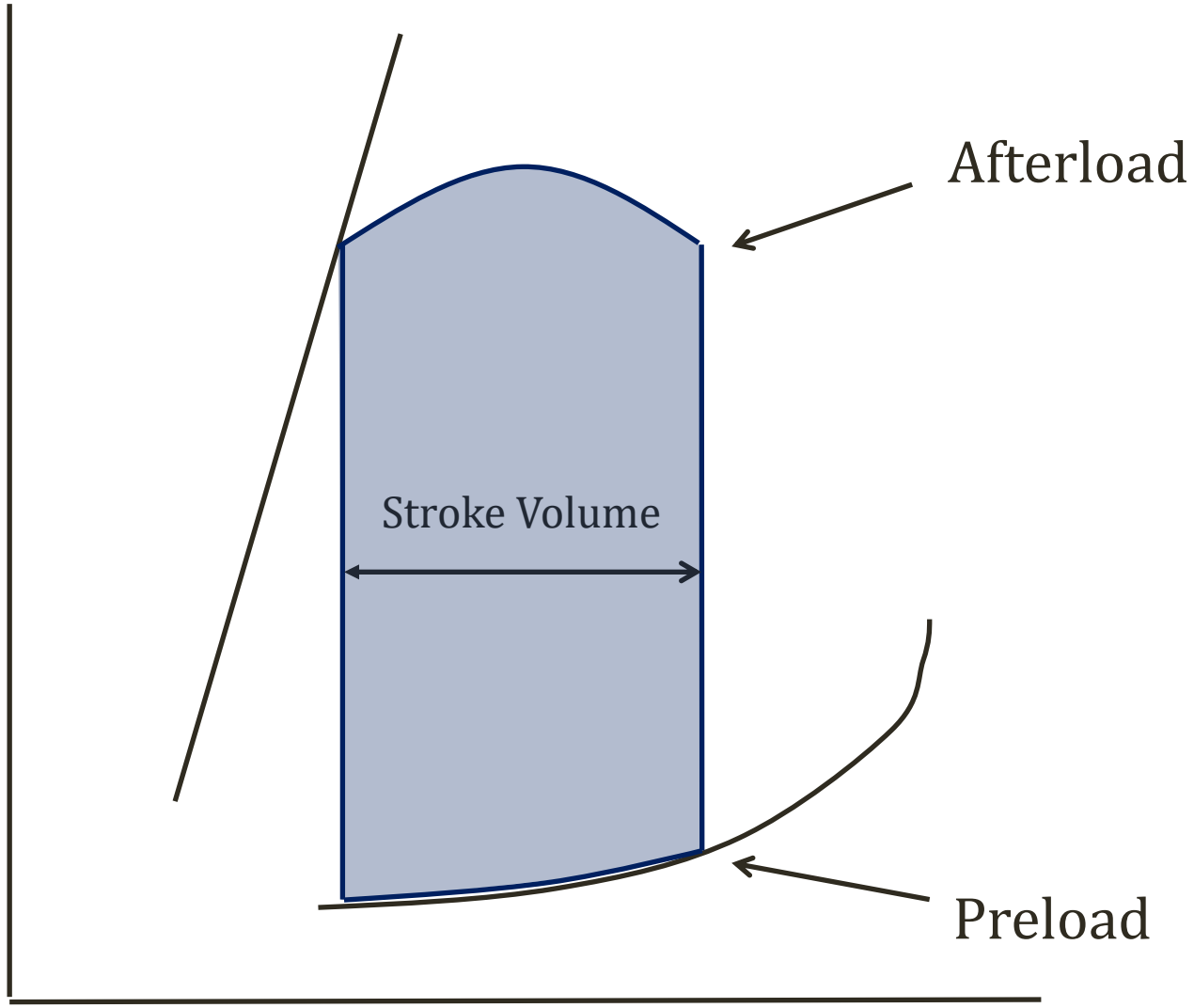



# PV Loops





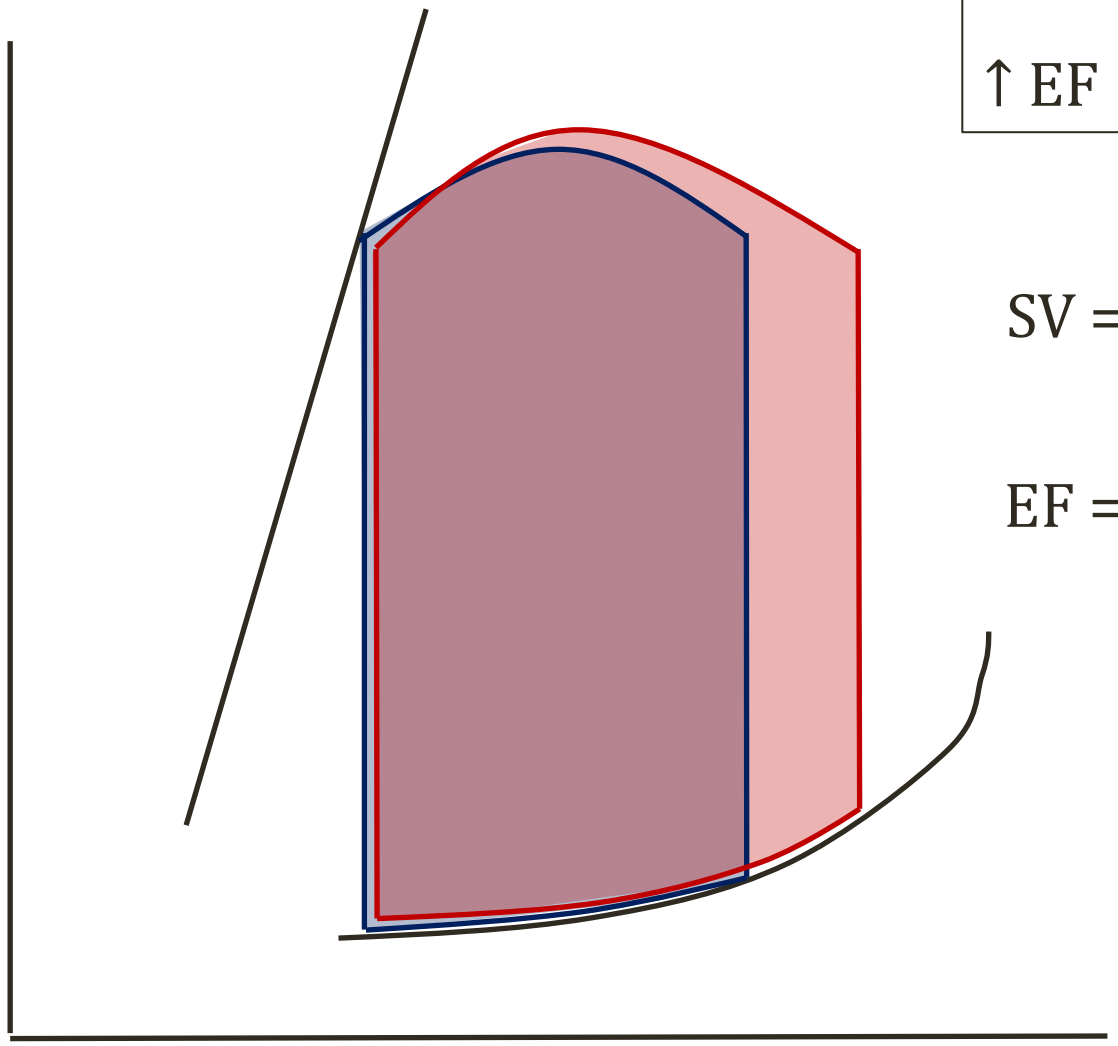


# PV Loop Parameters

- Changes in preload
- Changes in afterload
- Changes in contractility
- Changes in compliance
- In reality, these are inter-related
  - Example: ↑ preload → ↑ contractility (Frank-Starling)

# Preload Changes

## Increase



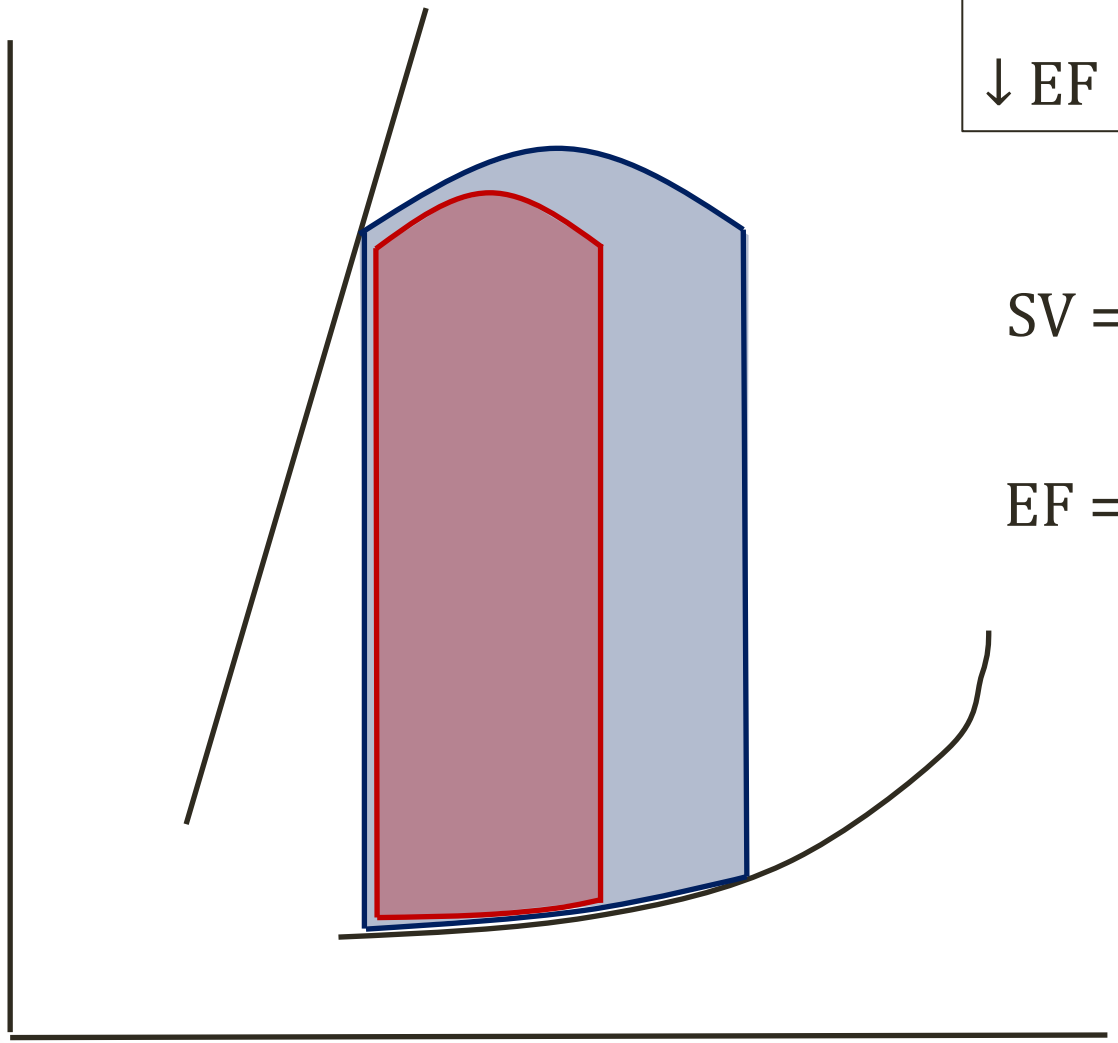
↑ EDV
↑ SV
↑ EF (slightly)

$$SV = EDV - ESV$$

$$EF = \frac{EDV - ESV}{EDV}$$

# Preload Changes

## Decrease



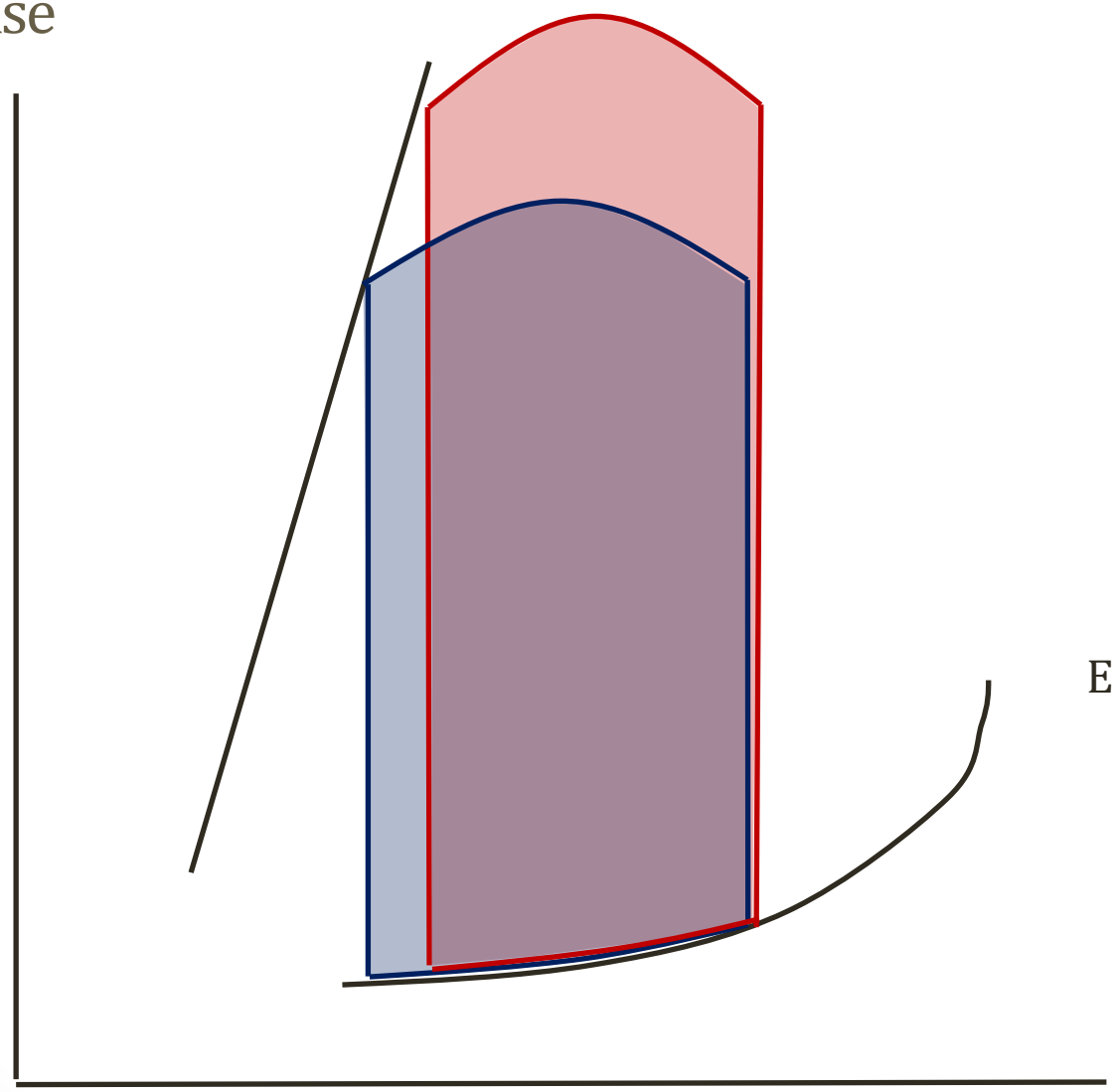
↓ EDV
↓ SV
↓ EF (slightly)

$$SV = EDV - ESV$$

$$EF = \frac{EDV - ESV}{EDV}$$

# Afterload Changes

## Increase

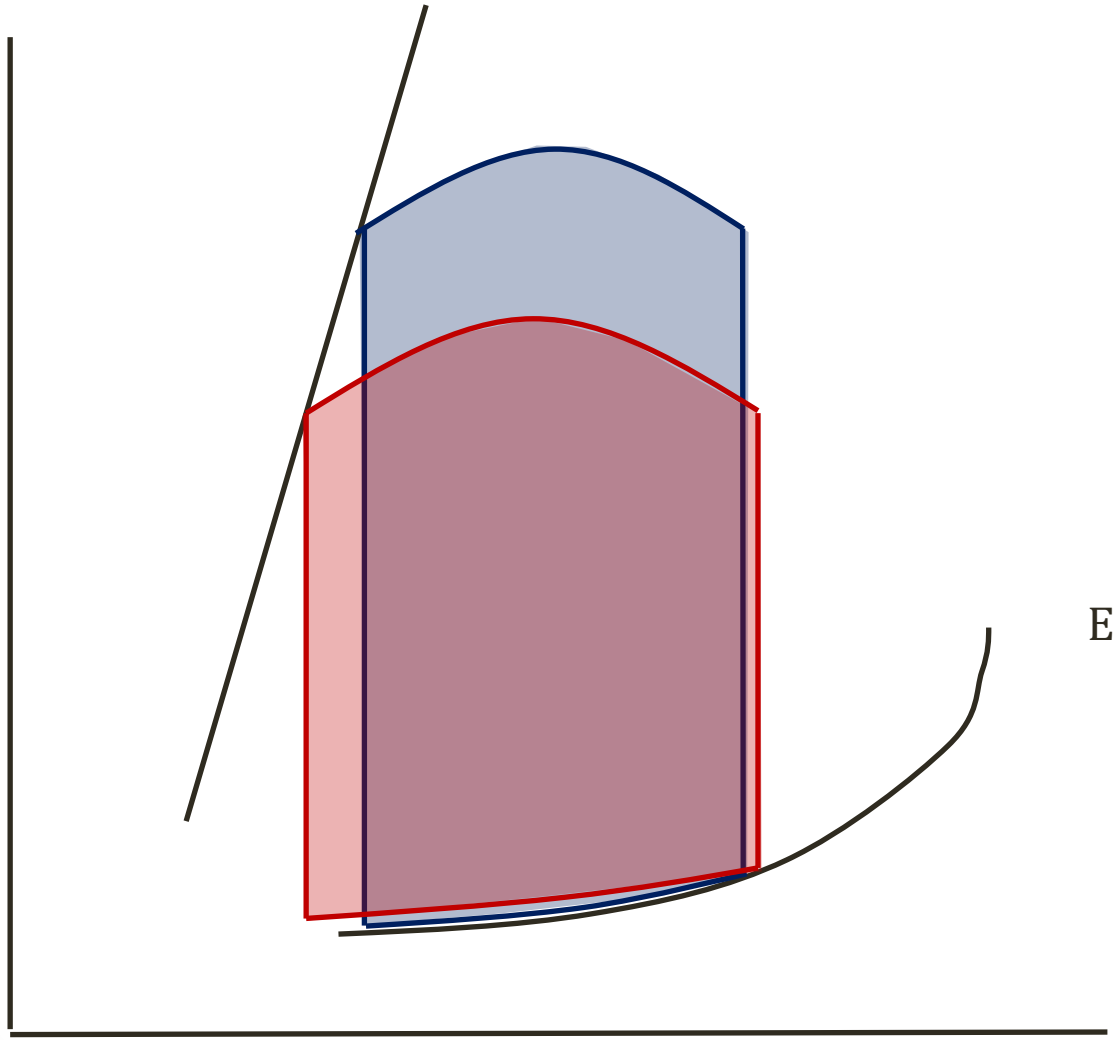


↑ ESV
↓ SV
↓EF

$$EF = \frac{EDV - ESV}{EDV}$$

# Afterload Changes

## Decrease

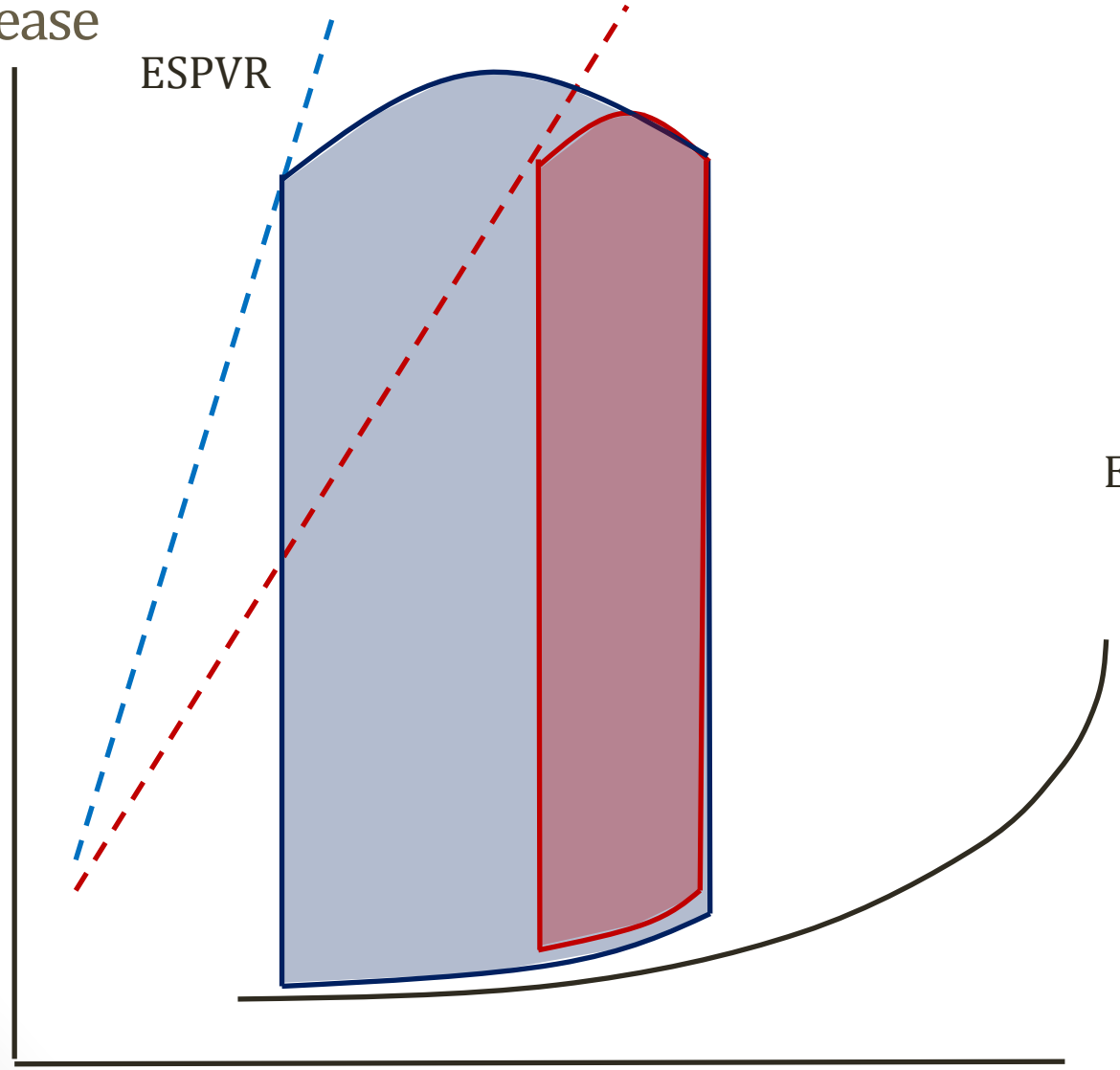


↓ ESV
↑SV
↑EF

$$EF = \frac{EDV - ESV}{EDV}$$

# Contractility Changes

## Decrease

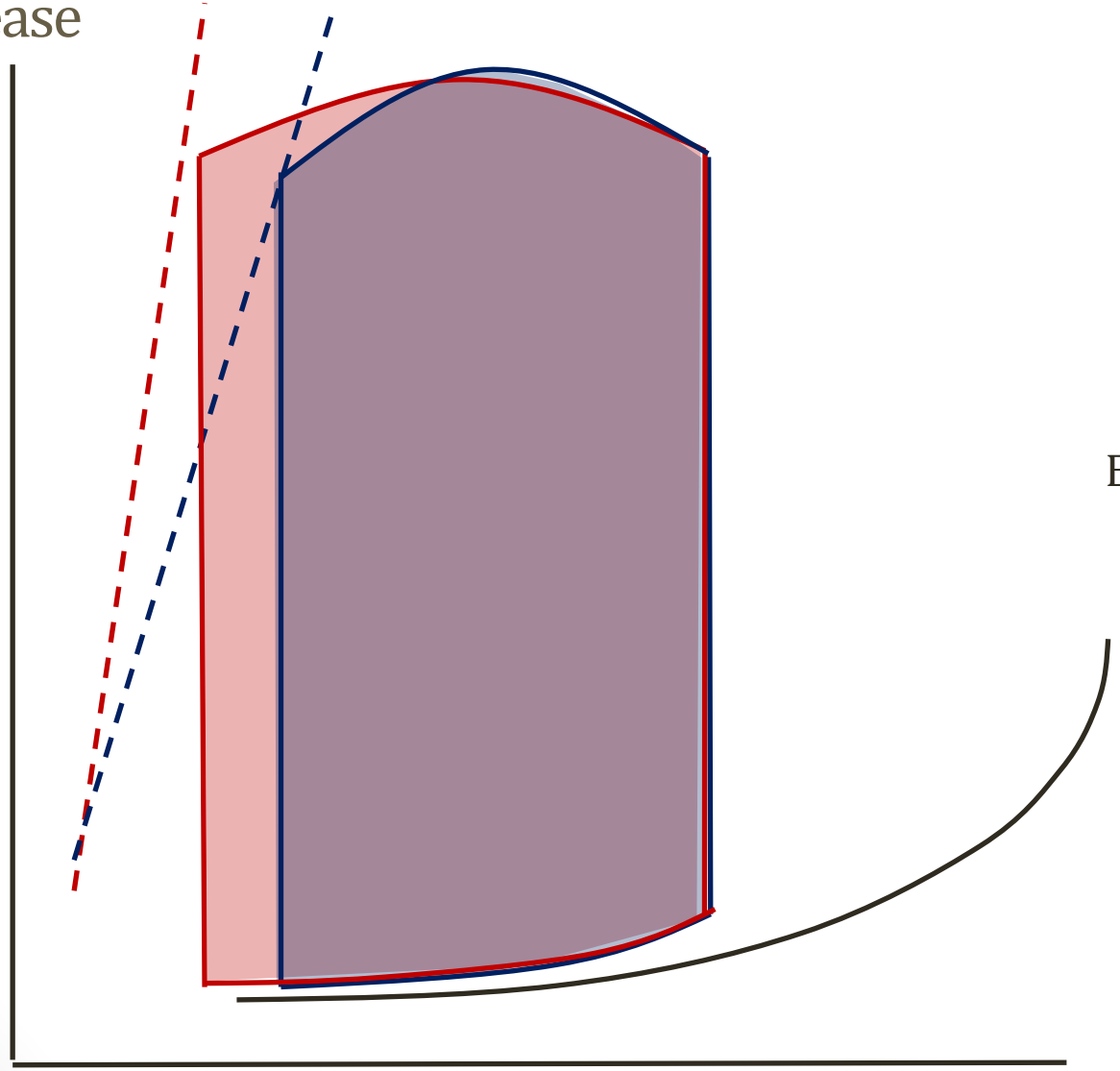



↑ ESV
↓ SV
↓ EF

$$EF = \frac{EDV - ESV}{EDV}$$

# Contractility Changes

Increase

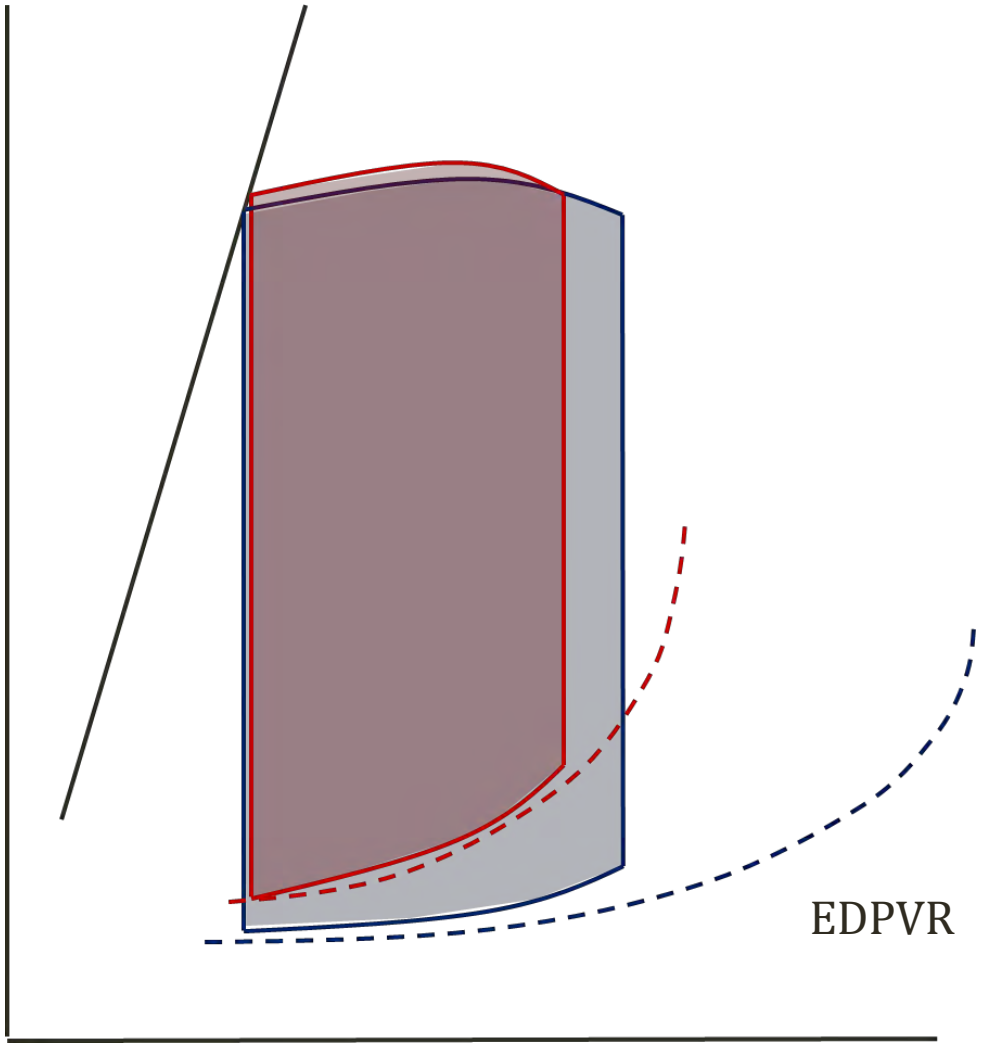


↓ ESV
↑ SV
↑ EF

$$EF = \frac{EDV - ESV}{EDV}$$

# Compliance Changes

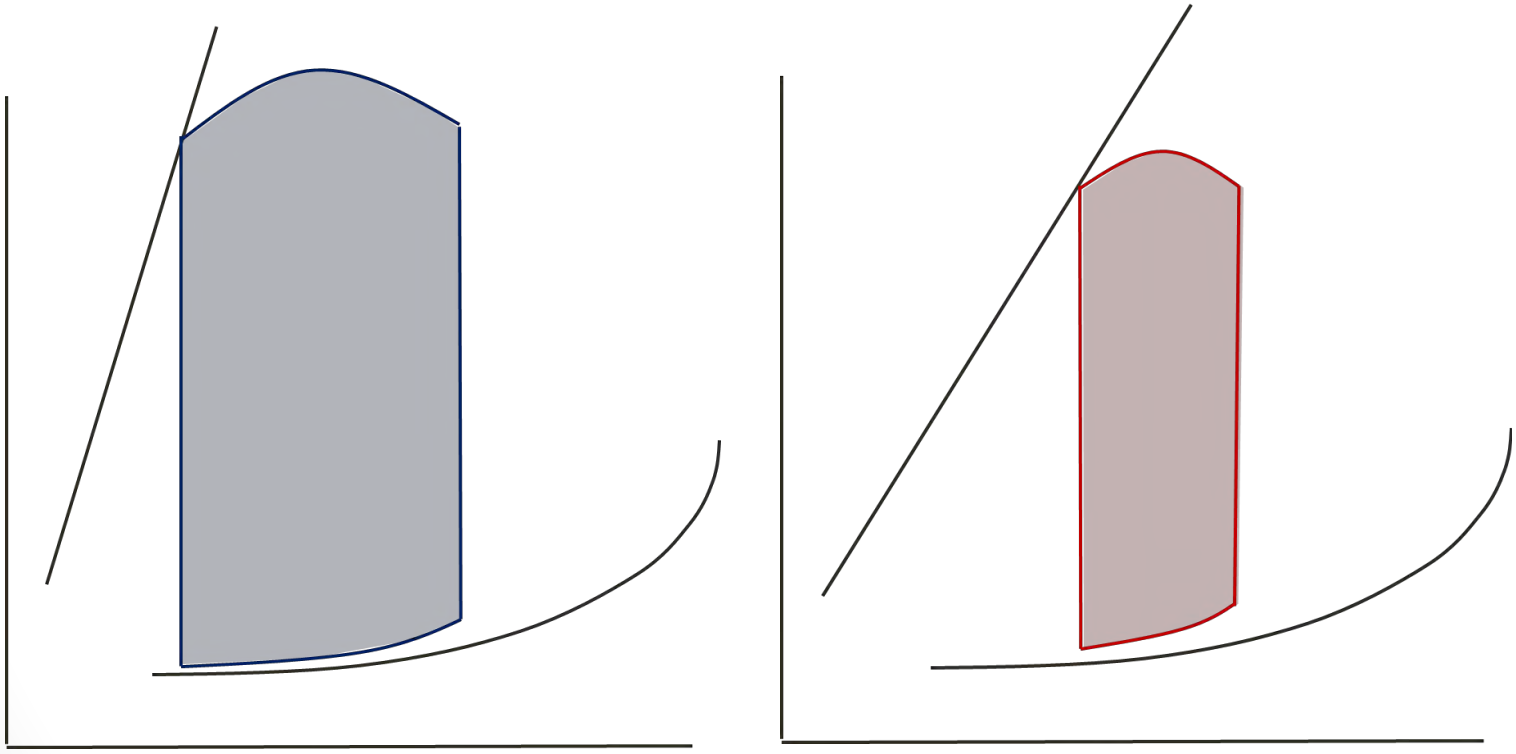
## Decreased Compliance




↓EDV
↑ EDP

# Work of the Heart

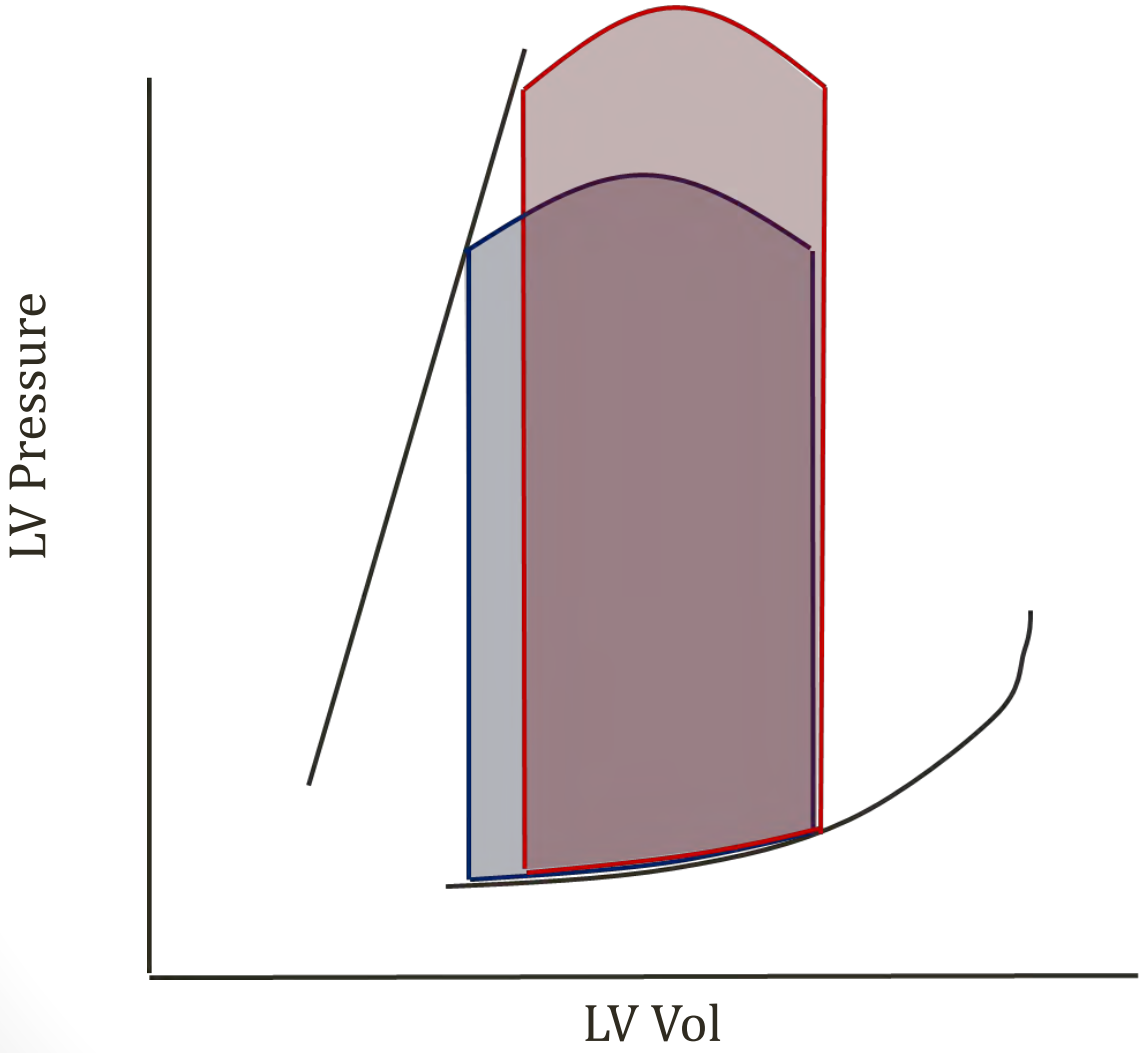
More area = More work



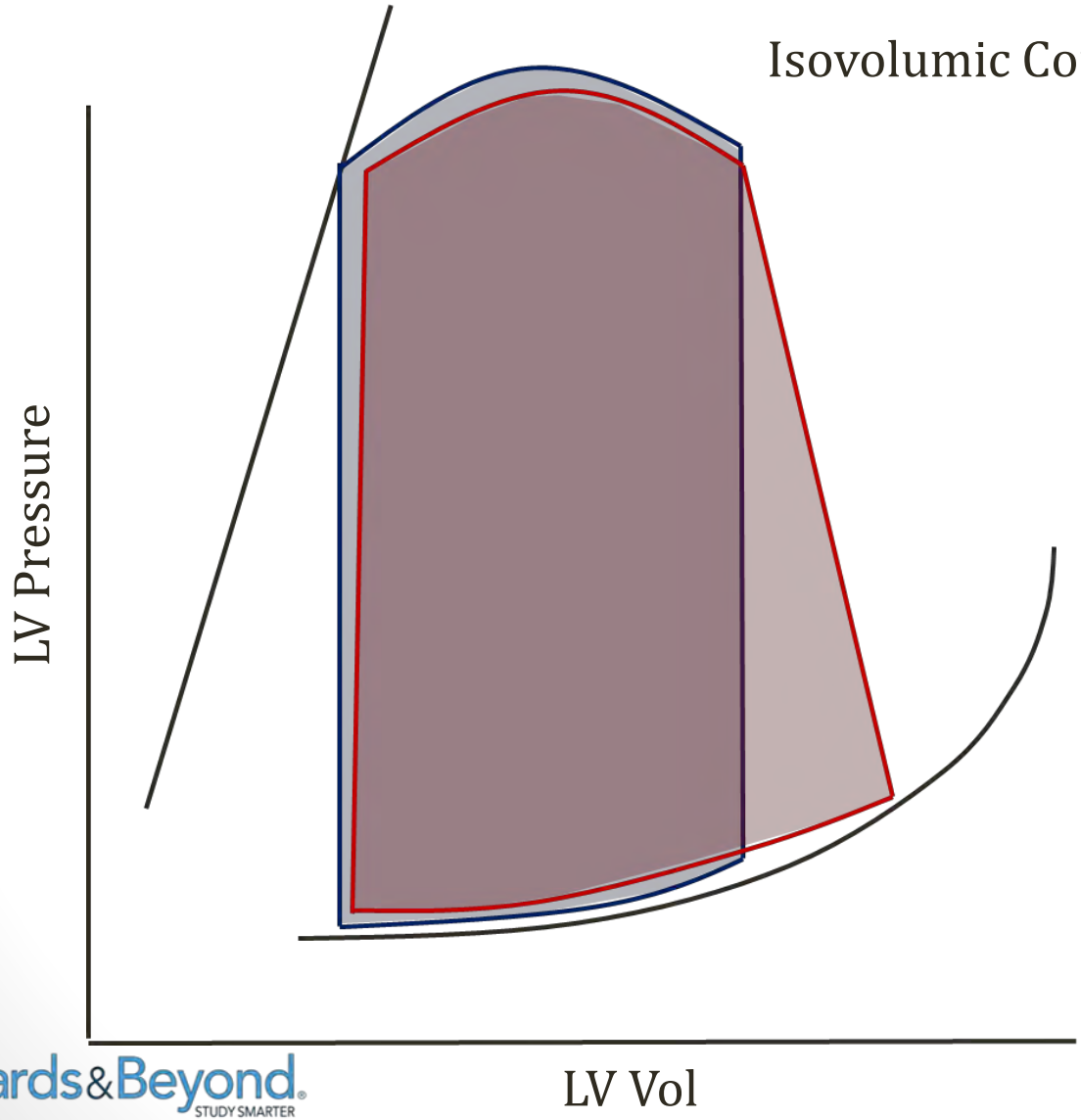
# Commonly Tested PV Loops

- Aortic Stenosis
- Mitral Regurgitation
- Aortic Regurgitation
- Mitral Stenosis

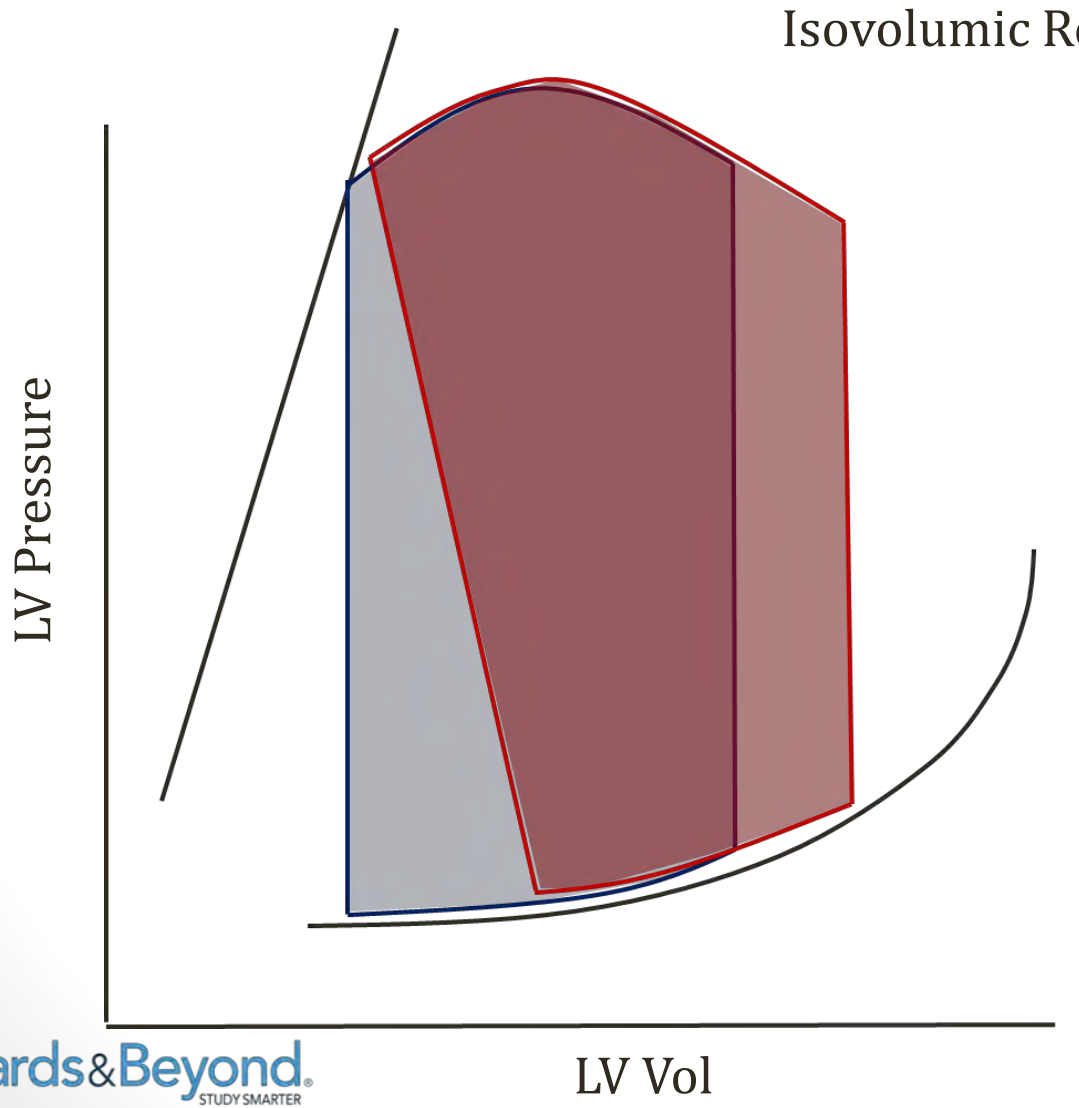
# Aortic Stenosis



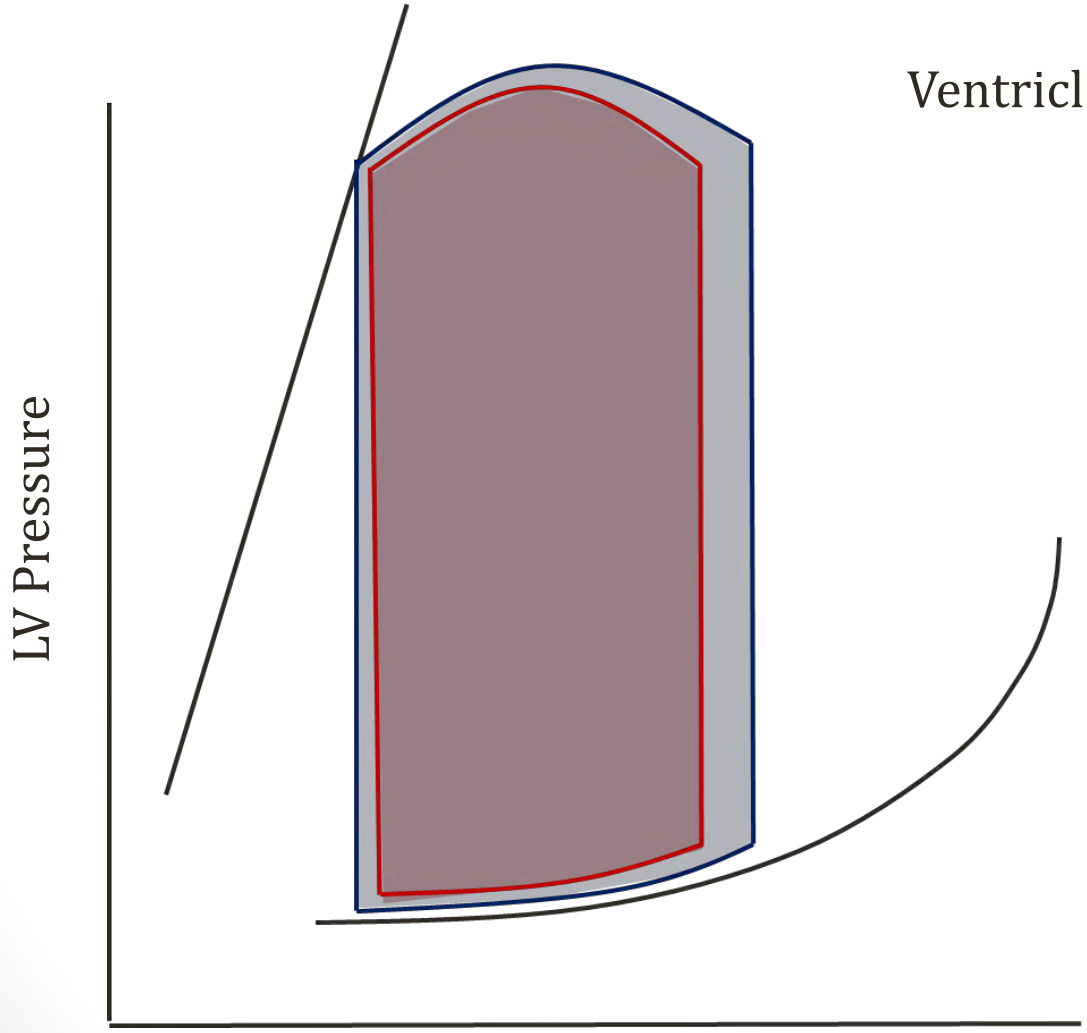
# Mitral Regurgitation



# Aortic Regurgitation



# Mitral Stenosis

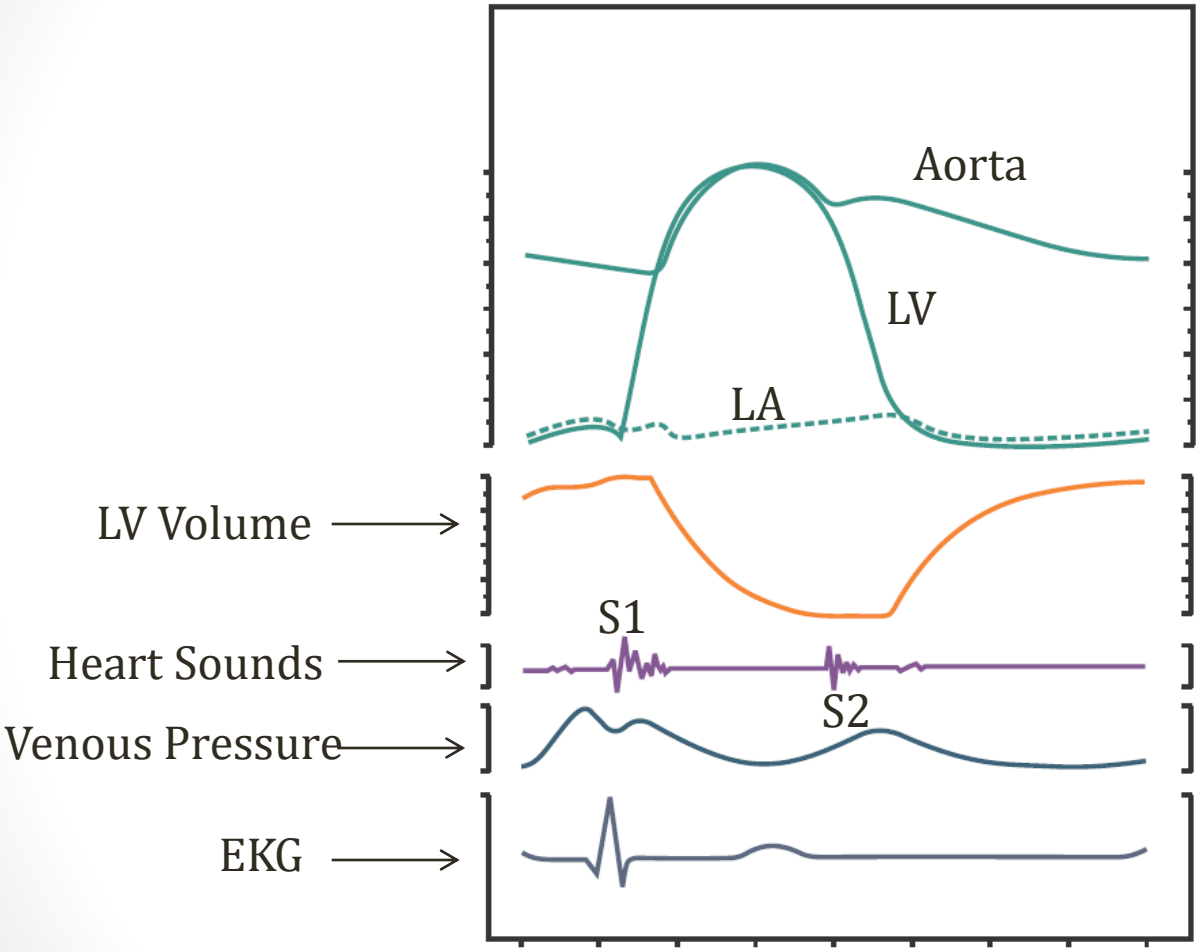



Ventricle can't fill properly

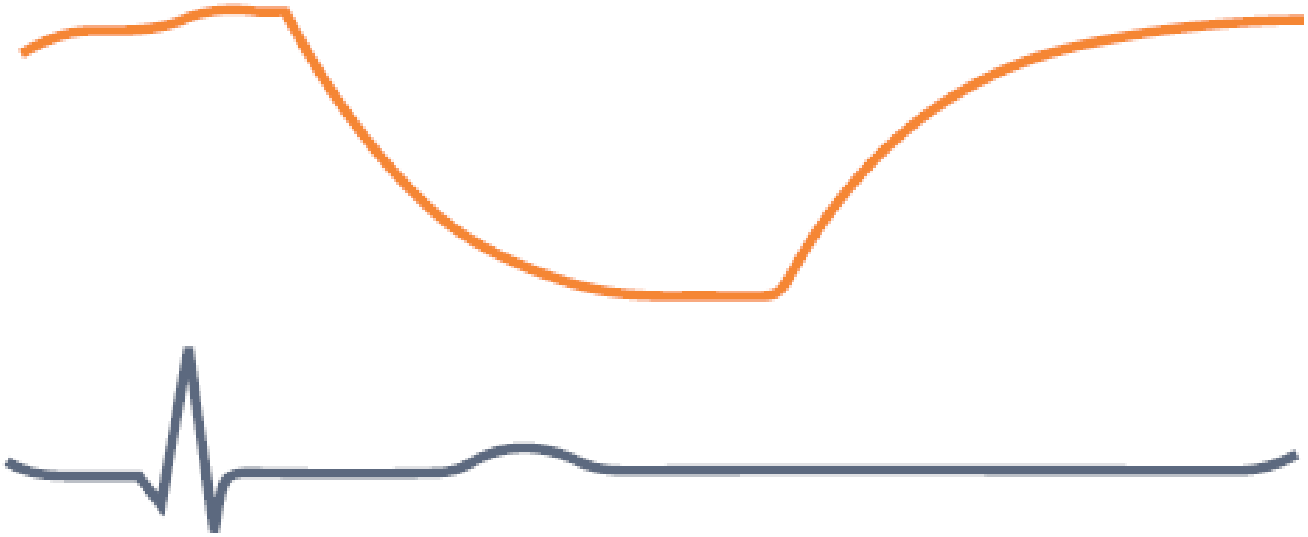
# Wiggers' Diagram

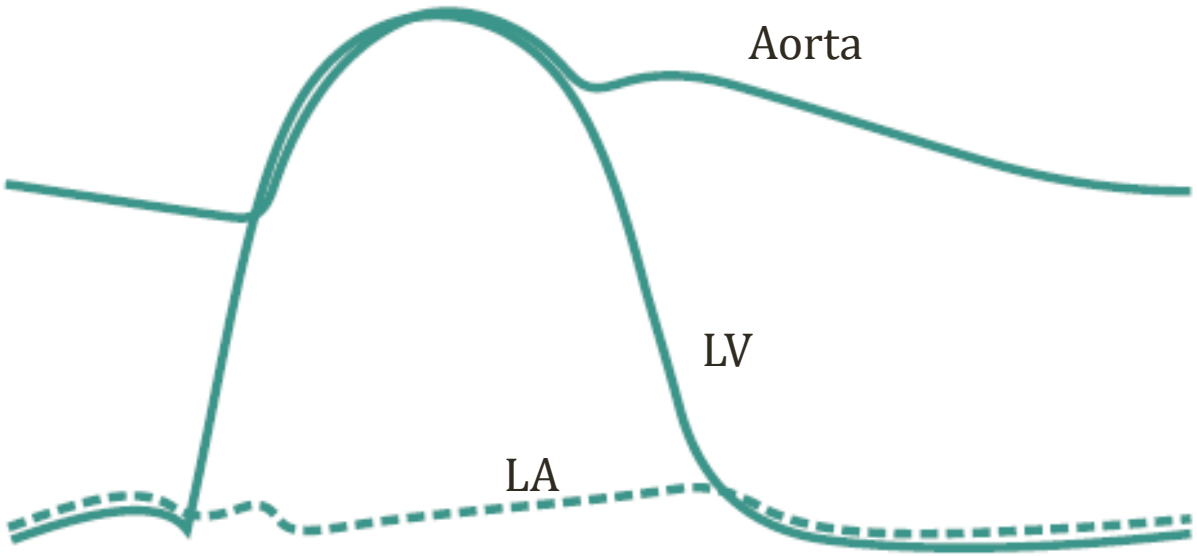
Jason Ryan, MD, MPH

# Wiggers' Diagram

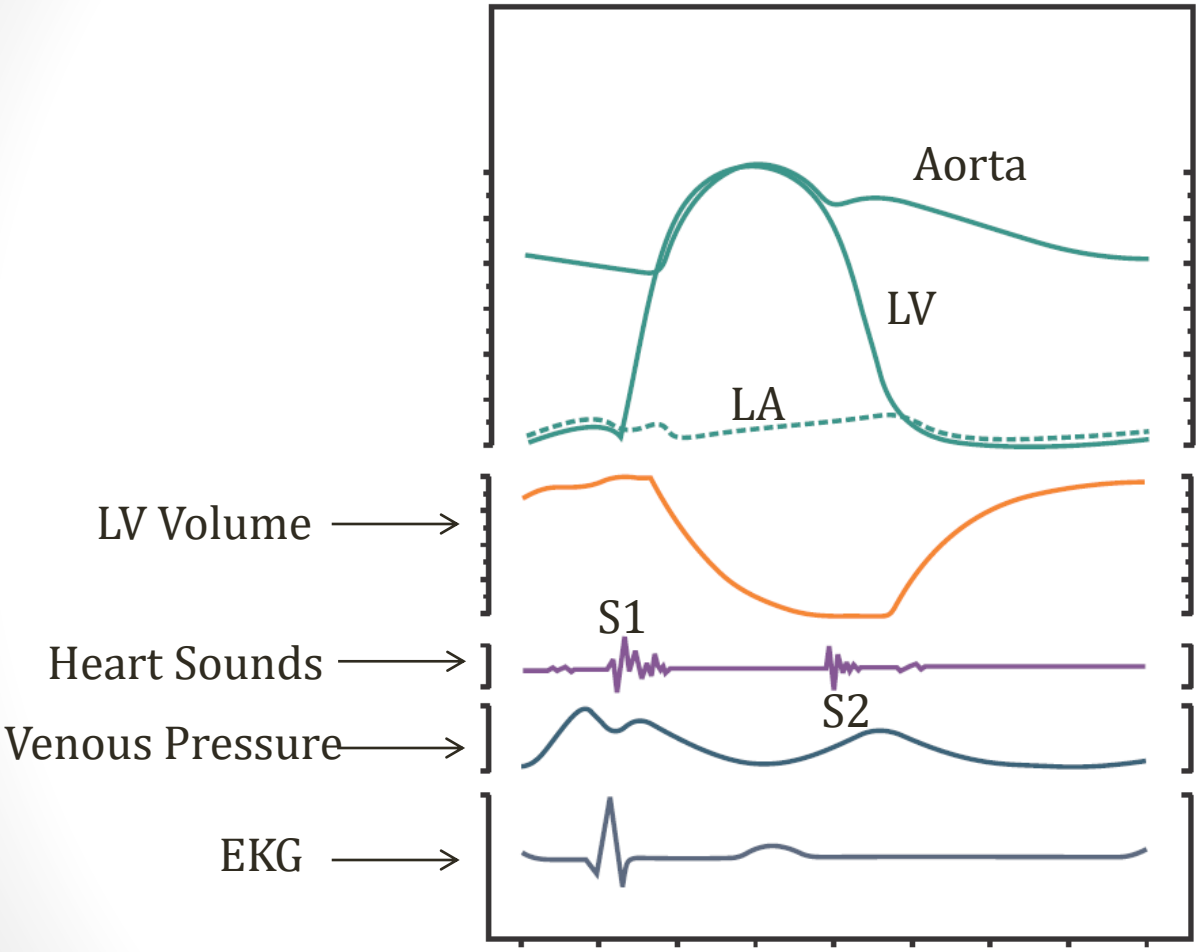


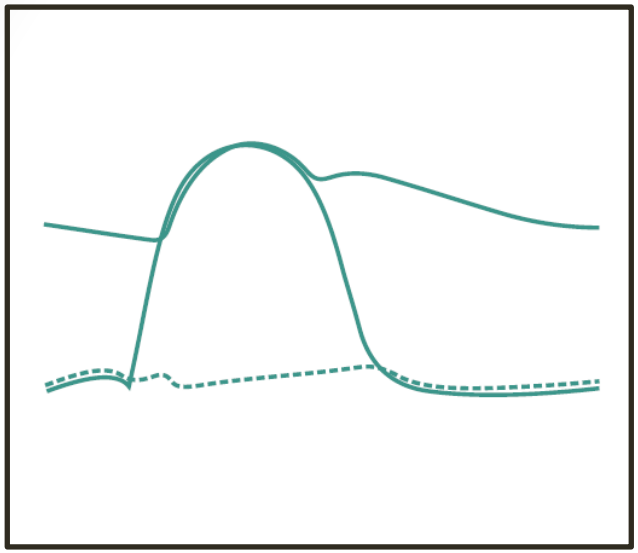
# Left Ventricular Volume



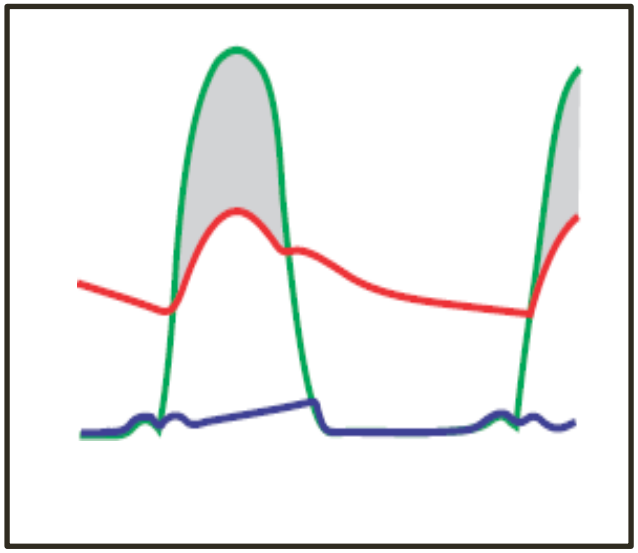


# Wiggers' Diagram



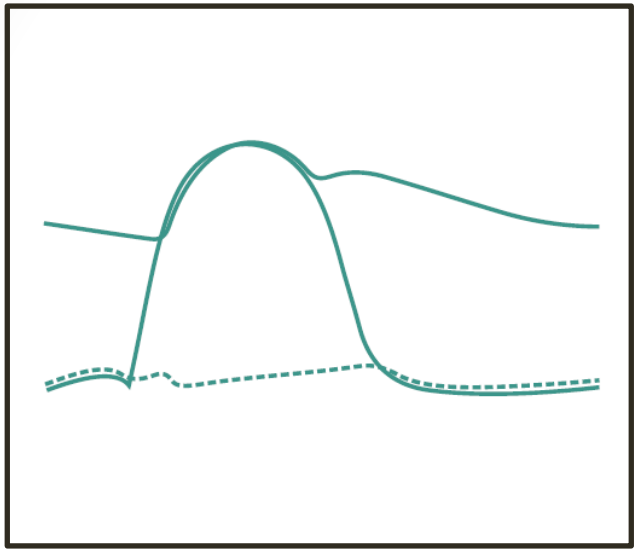


Normal Heart

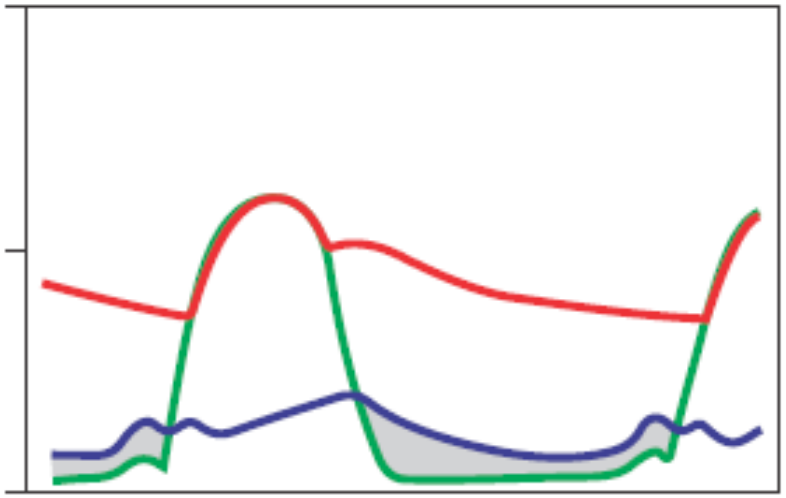


Diseased Heart

# Aortic Stenosis

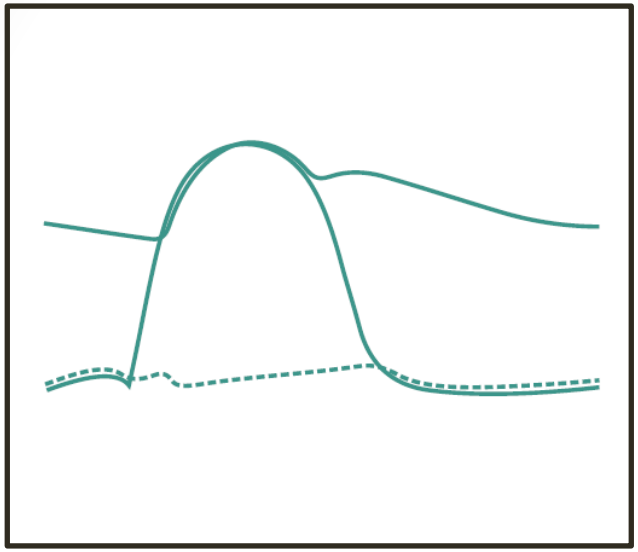


Normal Heart

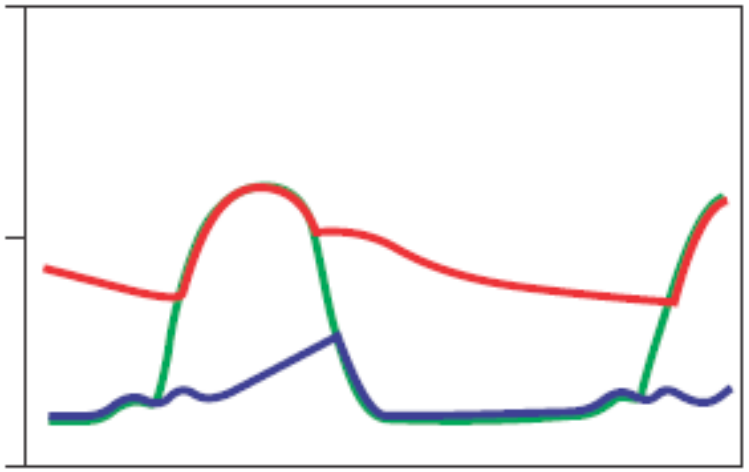


Diseased Heart

# Mitral Stenosis

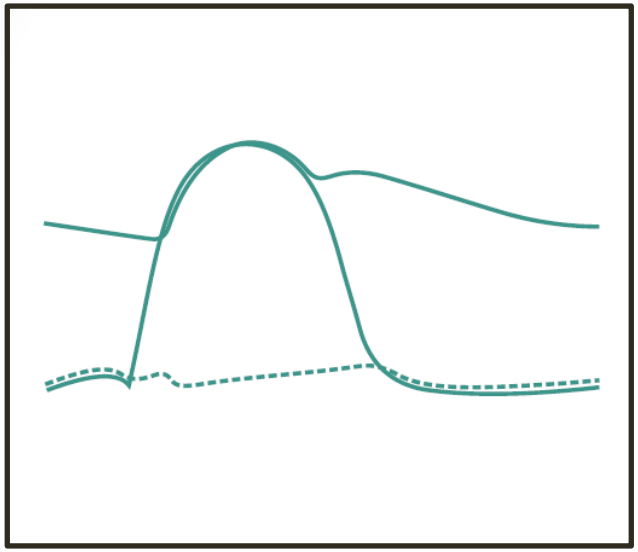


Normal Heart

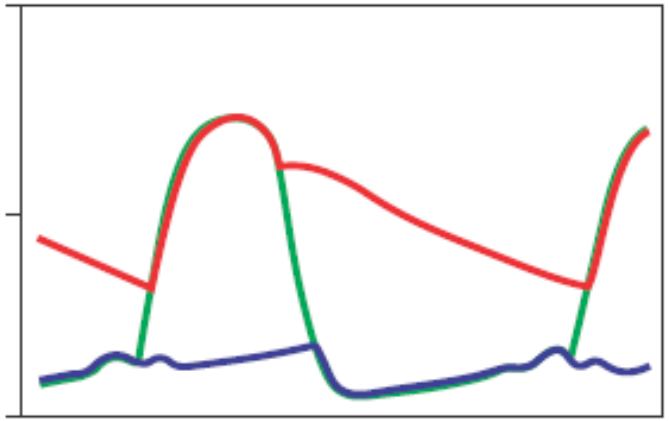


Diseased Heart

# Mitral Regurgitation



Normal Heart



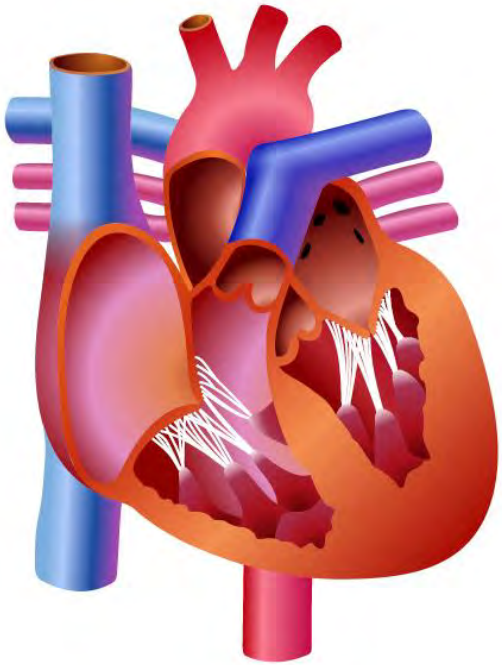
Diseased Heart

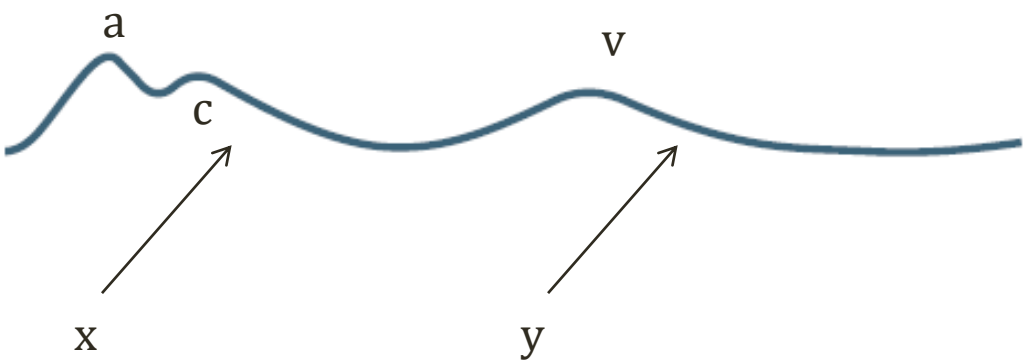
# Aortic Regurgitation

# Venous Pressure Tracings

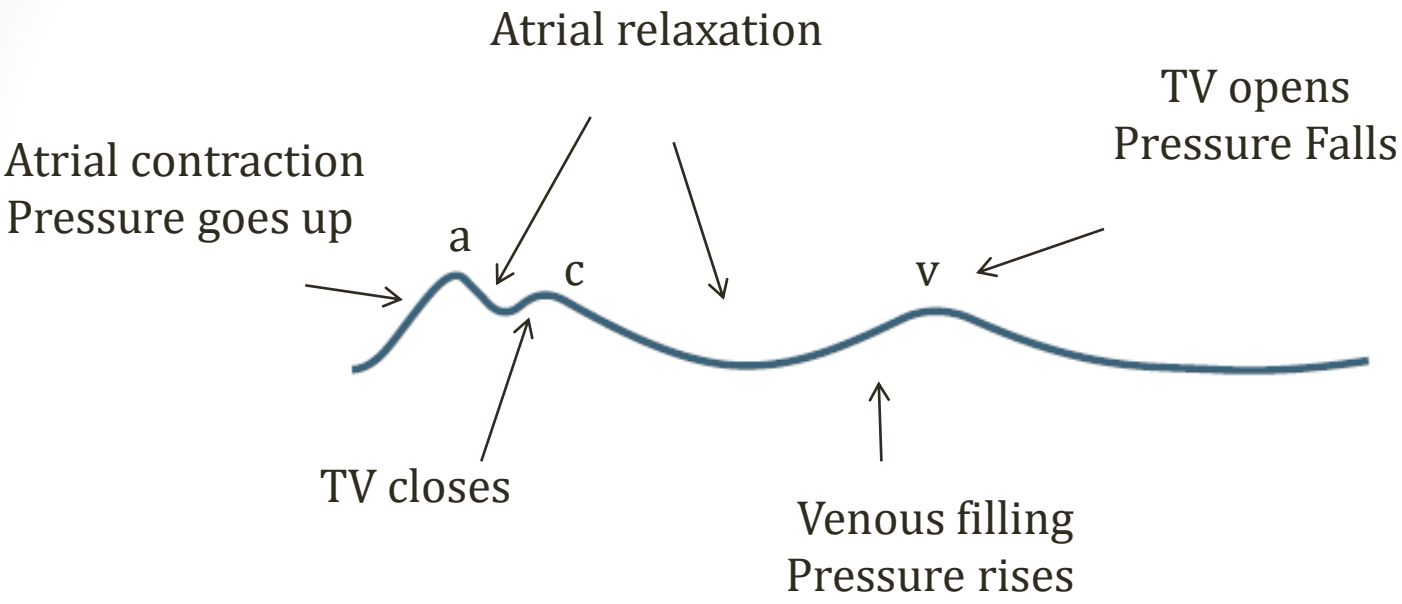
Jason Ryan, MD, MPH

# Venous Pressure





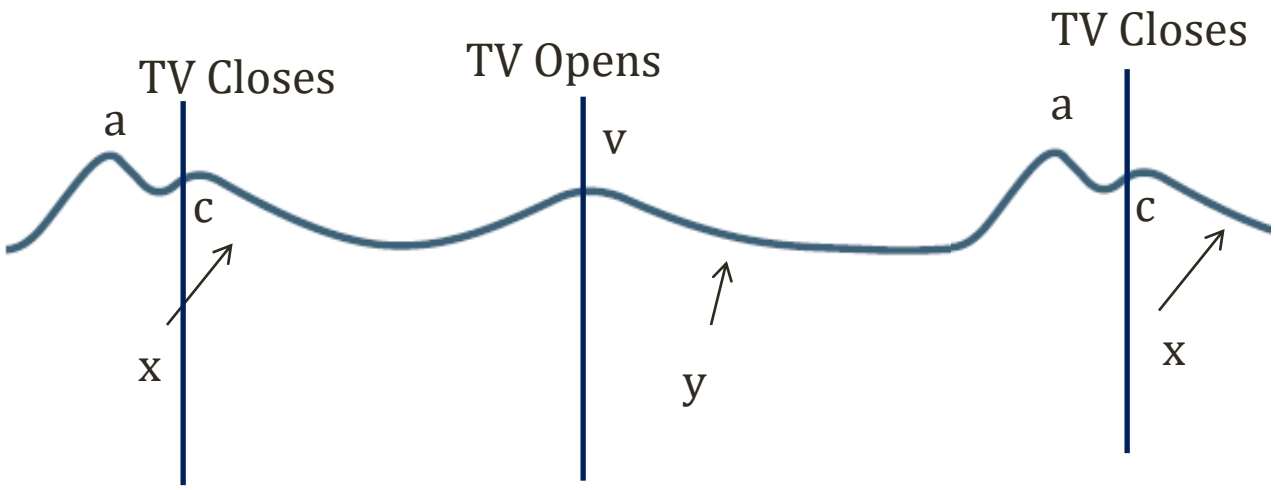
# Venous Pressure



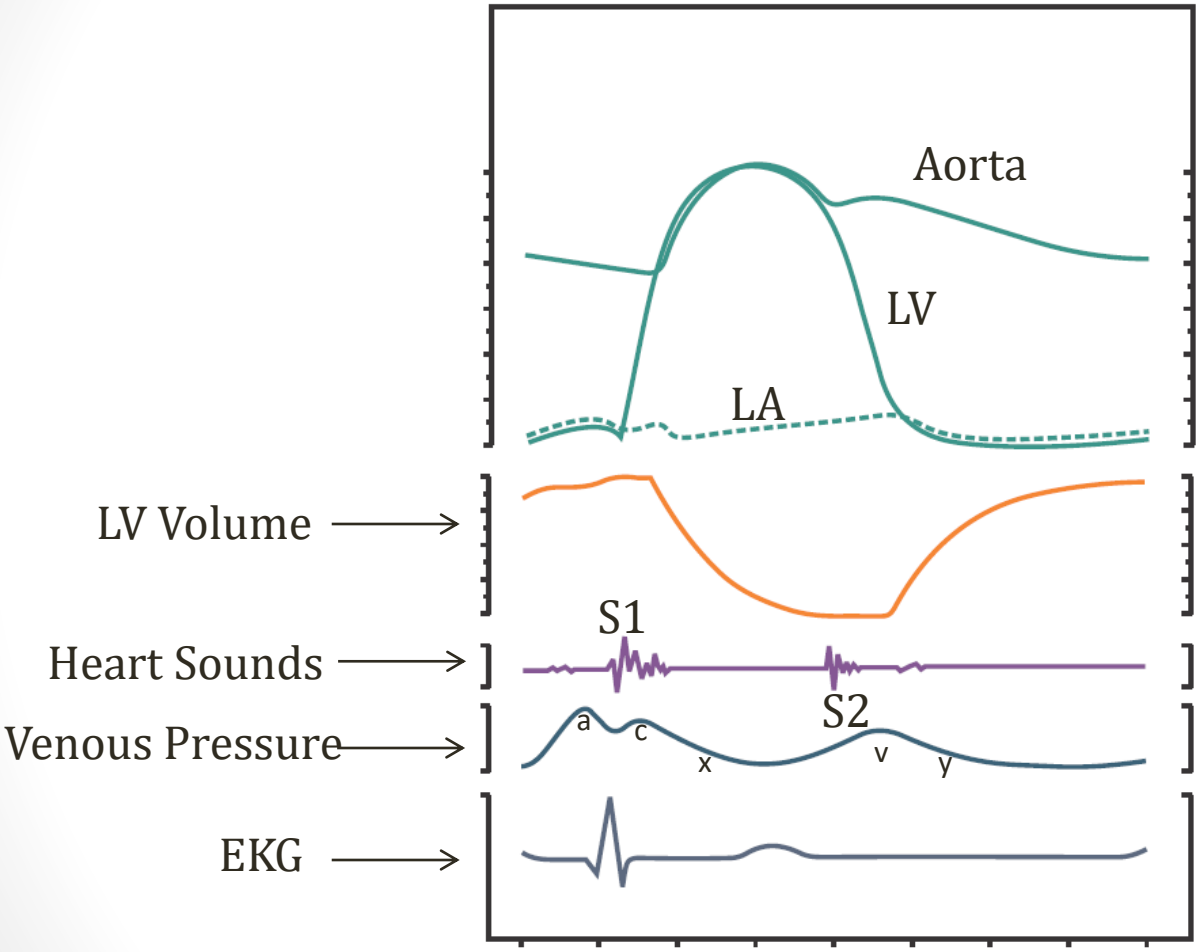

**a** wave = **A**trial contraction
**v** wave = **V**enous filling
**c** wave = tri**C**uspid valve
**x** descent = atrial rela**X**ation
**y** descent = empt**Y**ing of the atrium

# Venous Pressure

## Tricuspid valve



# Wiggers' Diagram

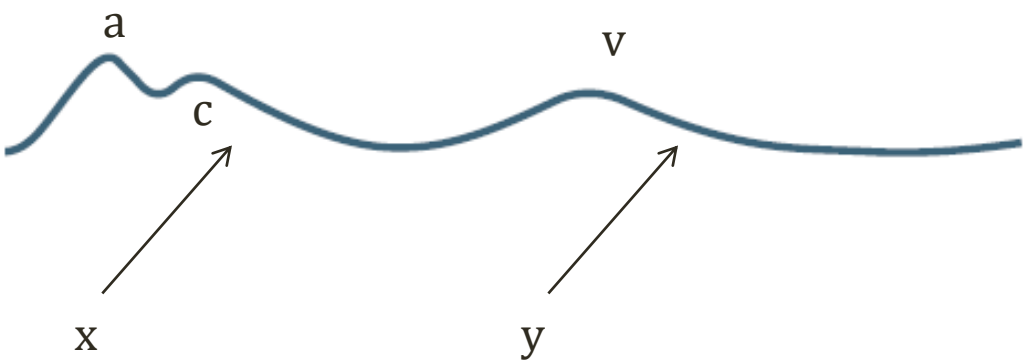


# Classic Findings

- Large a wave
- Cannon a wave
- Absent a waves
- Large v waves

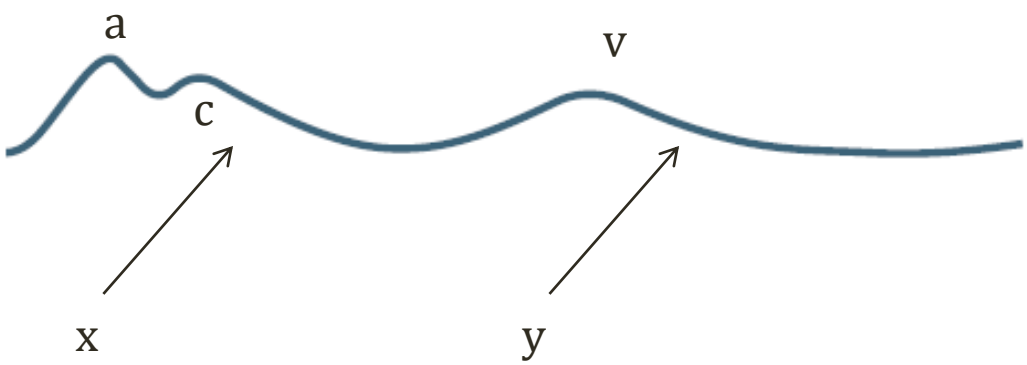
# Large a wave

## Tricuspid stenosis



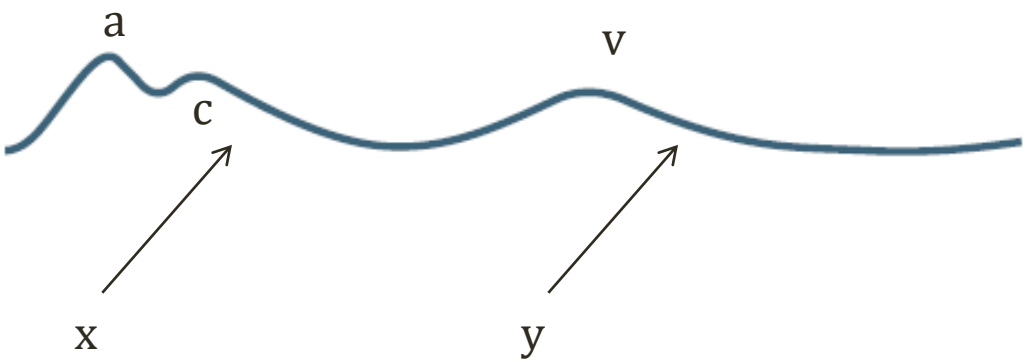
# Cannon a wave

## AV dissociation



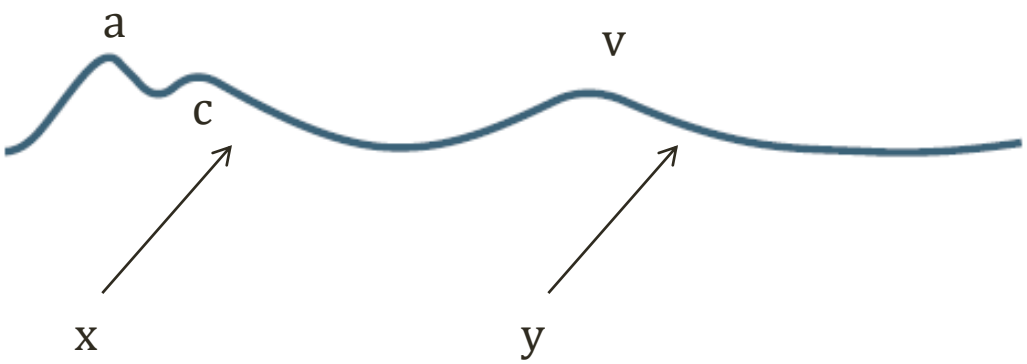
# Absent a wave

## Atrial fibrillation



# Giant v wave

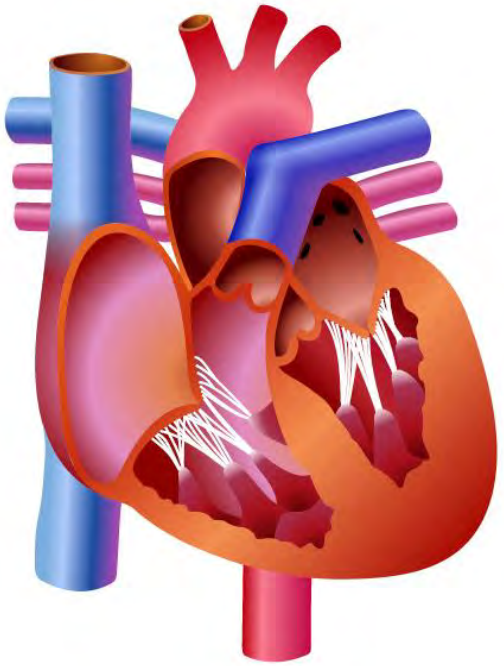
## Tricuspid regurgitation

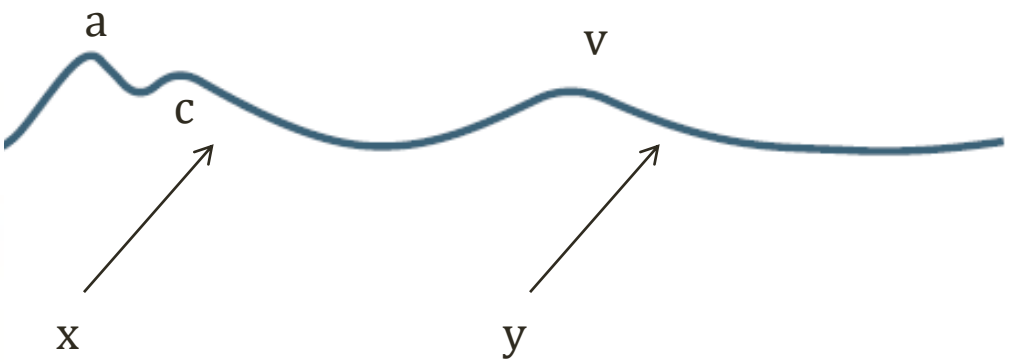


# High Yield Findings

- Large a wave (increased atrial contraction pressure)
  - Tricuspid stenosis
  - Right heart failure/Pulmonary hypertension
- Cannon a wave (atria against closed tricuspid valve)
  - Complete heart block
  - PAC/PVC
  - Ventricular tachycardia
- Absent a wave (no organized atrial contraction)
  - Atrial fibrillation
- Giant V waves
  - Tricuspid regurgitation

# Left Atrial Pressure

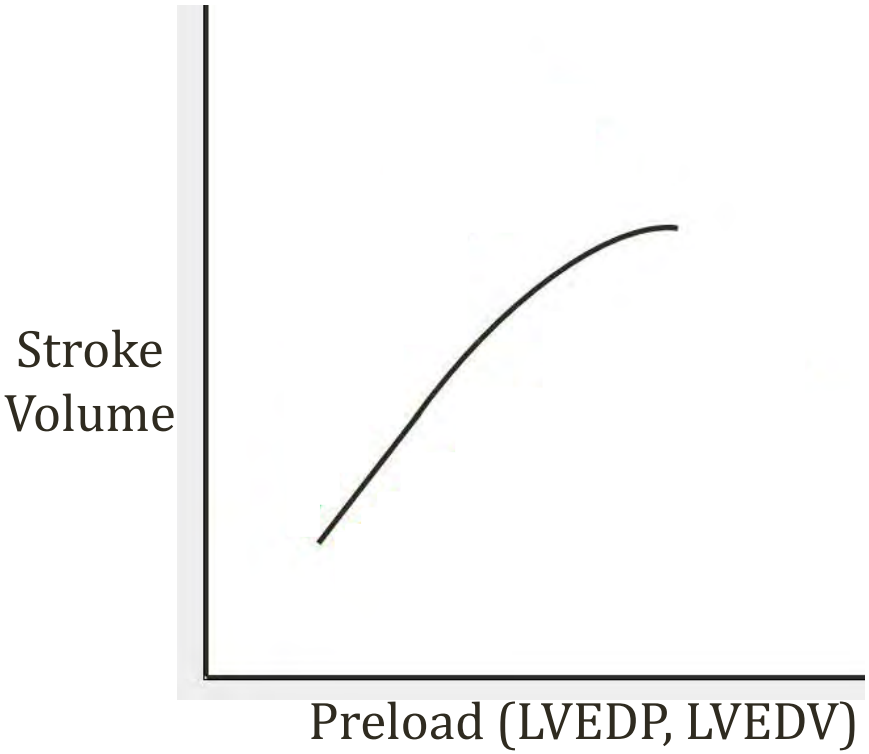




# Starling Curves

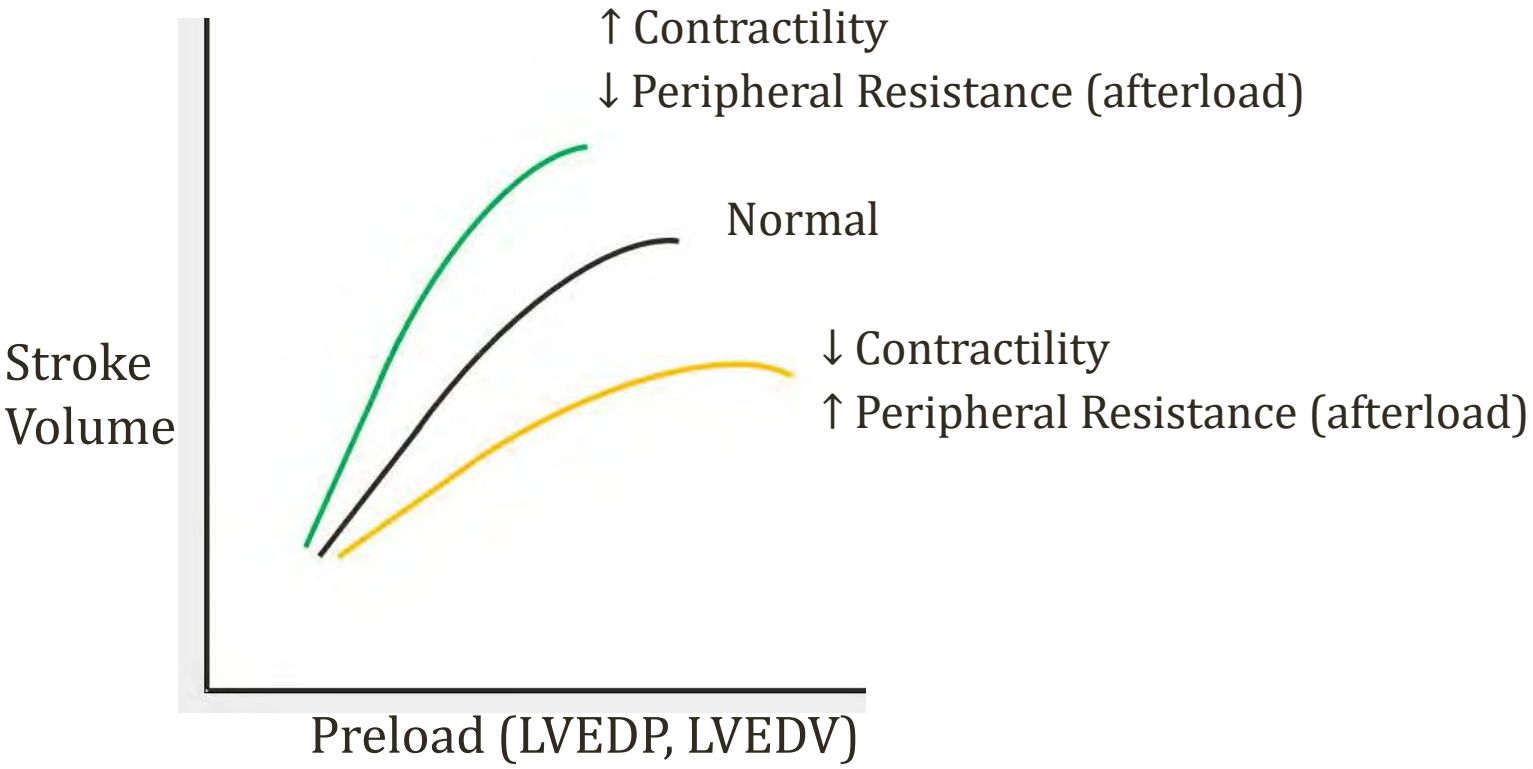
Jason Ryan, MD, MPH

# Frank-Starling Curve



# Frank-Starling Curve

## Left and Right Shifts

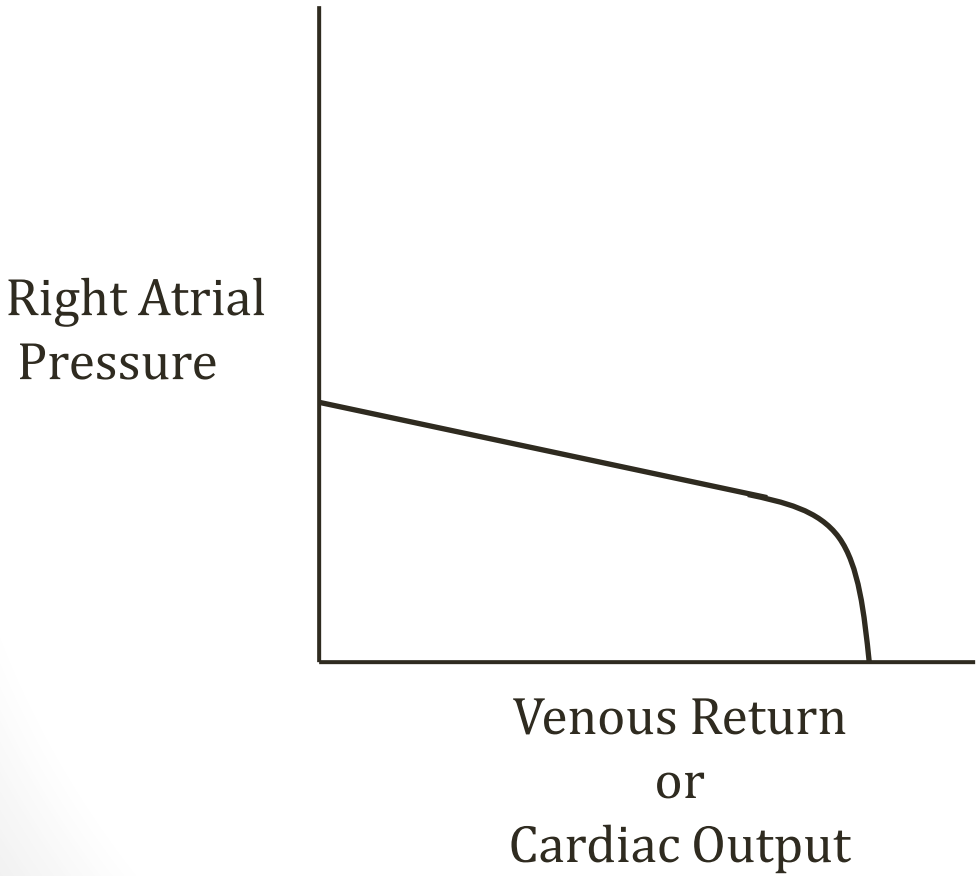


# Frank-Starling Curve

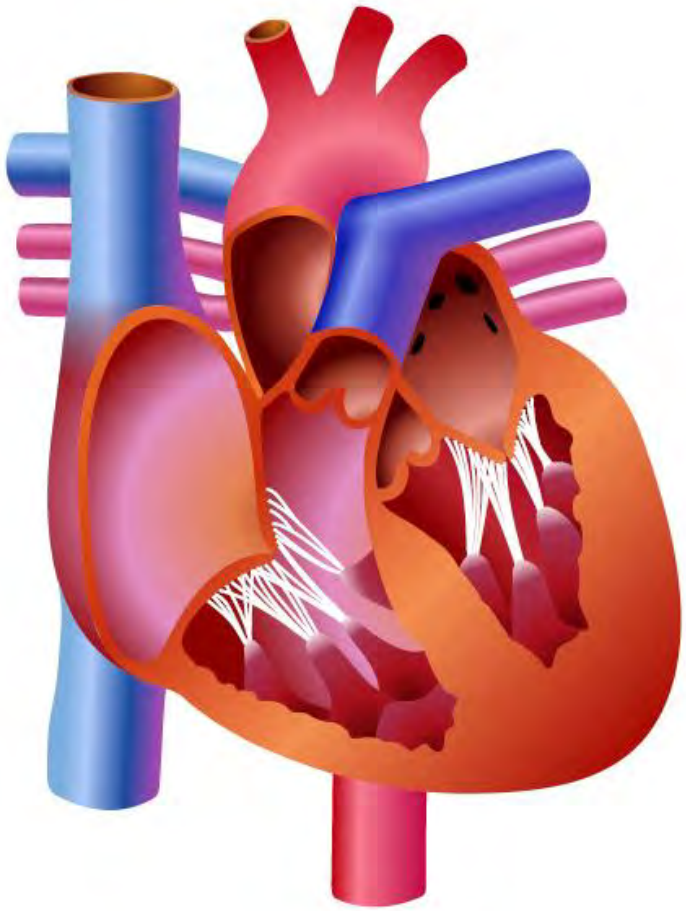
## Left and Right Shifts

- Contractility
  - Increase: Exercise, inotropes
  - Decrease: Myocardial infarction, heart failure
- Peripheral resistance:
  - Total peripheral resistance (TPR)
  - Systemic vascular resistance (SVR)
  - Increase: Vasopressors
  - Decrease: Vasodilators, sepsis

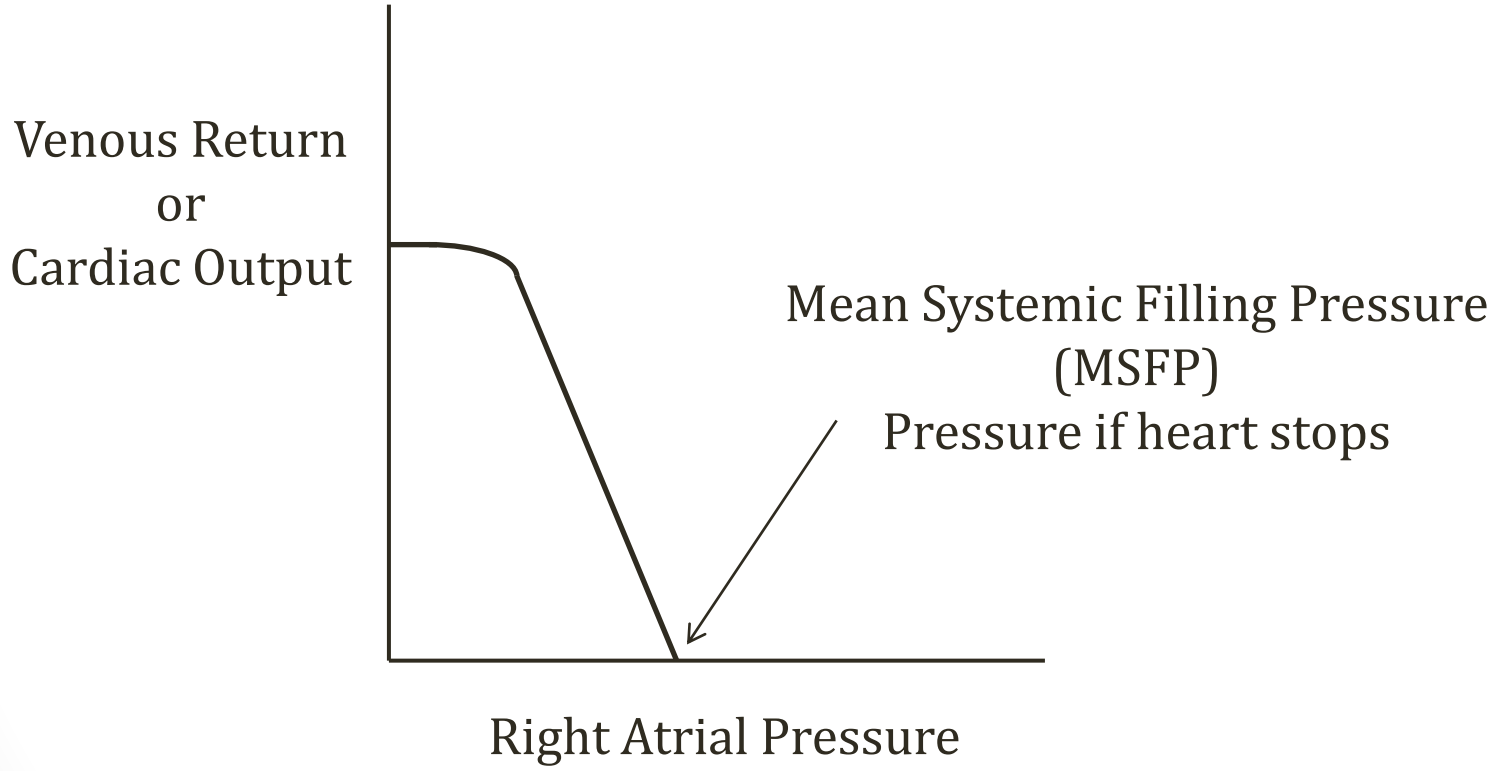
# Venous Return Curve



# Right Atrial Pressure



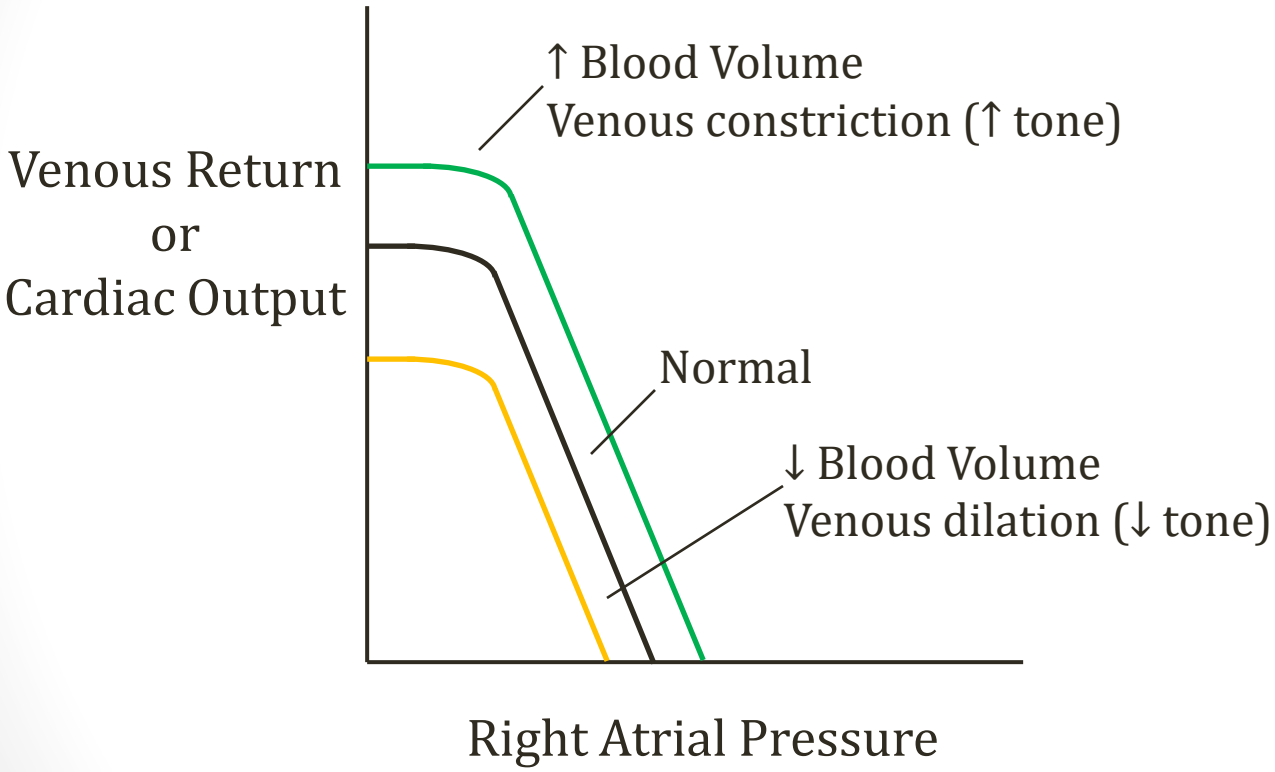
# Venous Return Curve



# Venous Return Curve

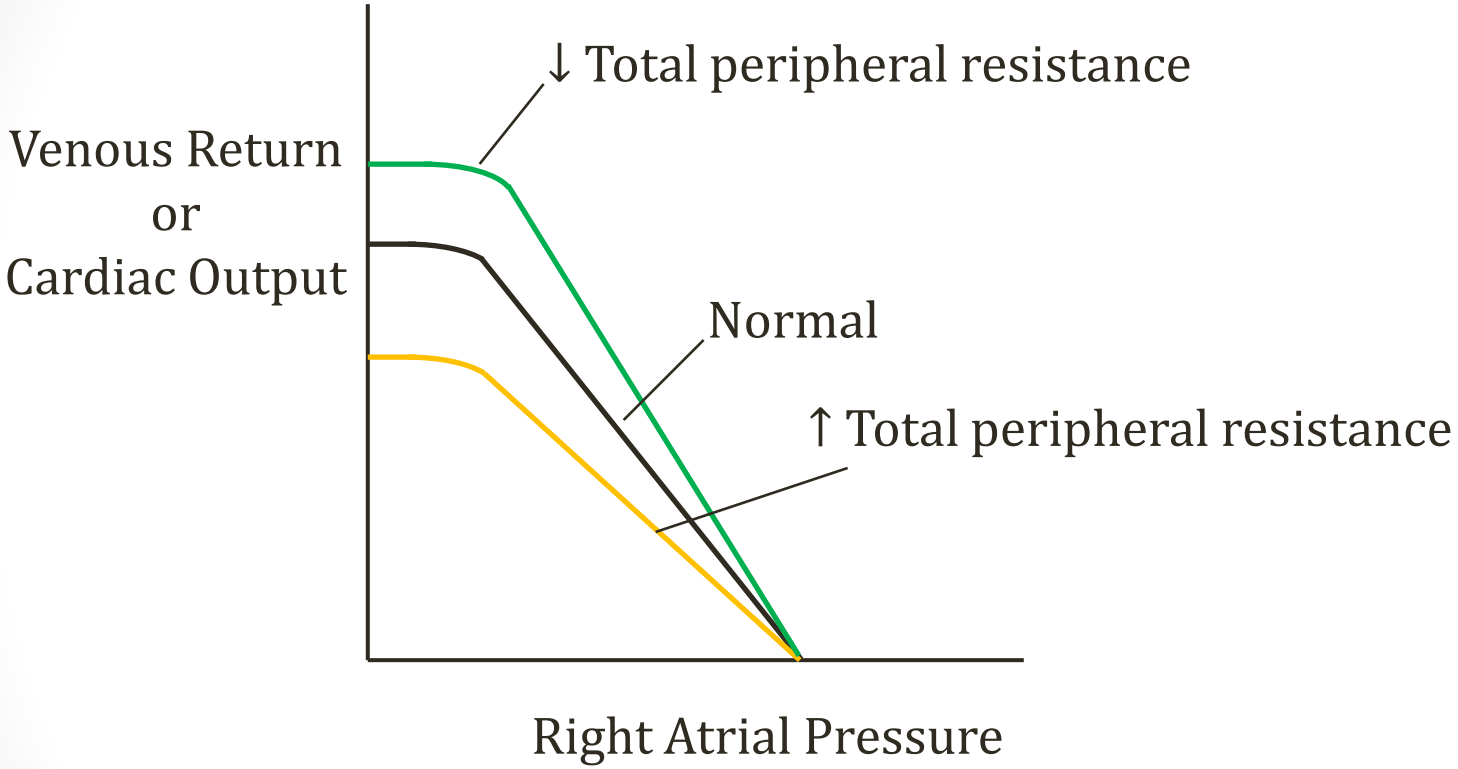
## Left and Right Shifts

**Volume**
**Venous Tone**



# Venous Return Curve

## Changes in Slope



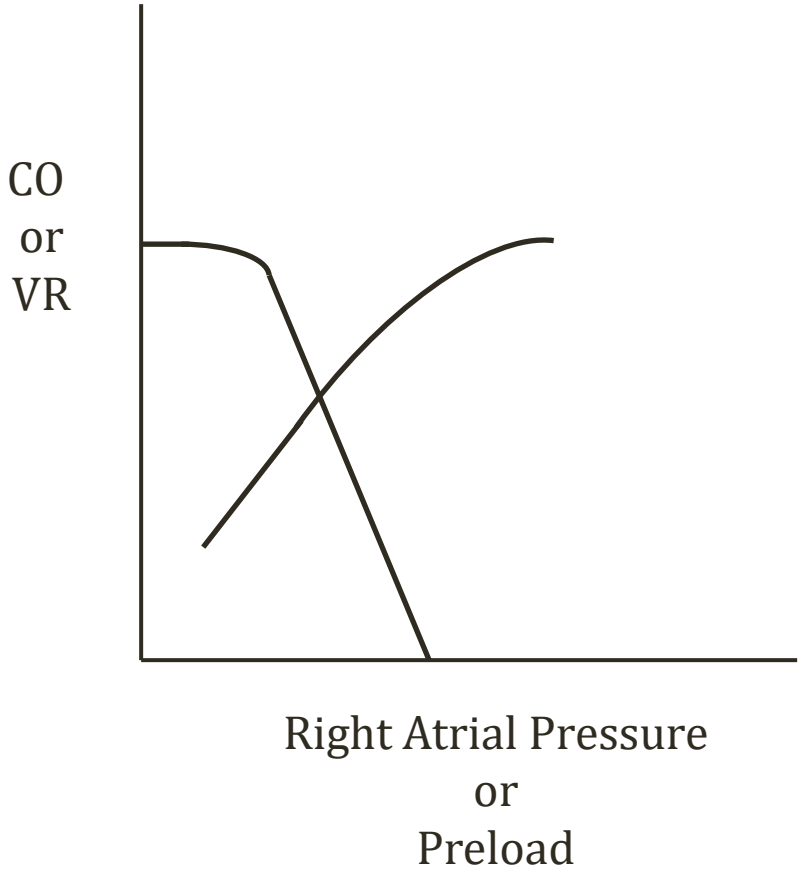

TPR change shifts curve right/left

No change in MSFP

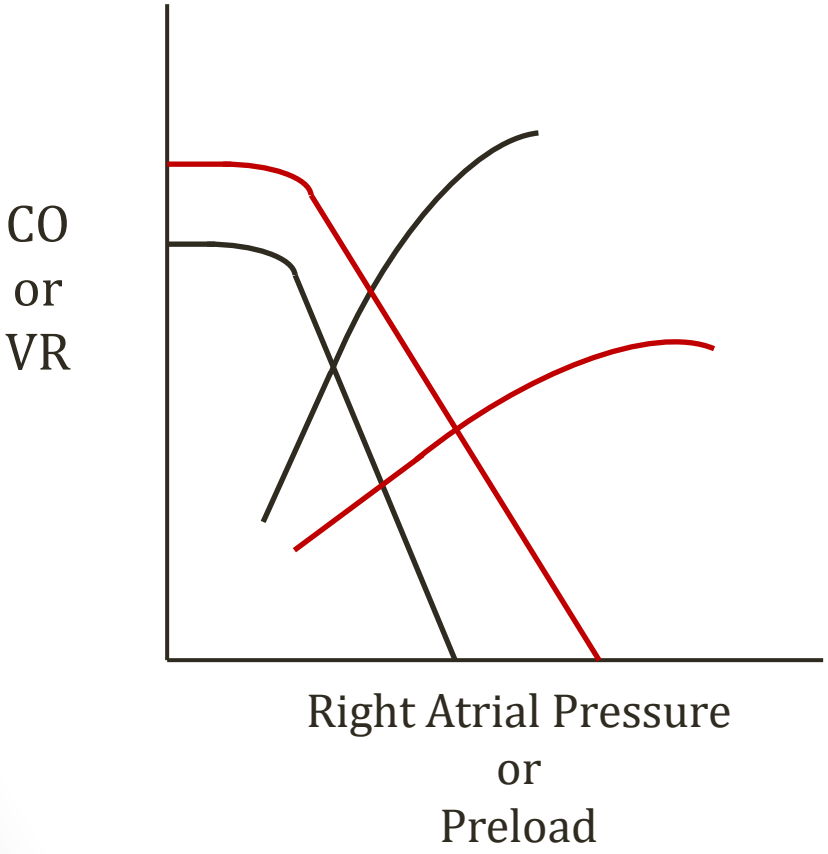
Result: change in **slope** of Venous Return curve

# Combined Curves

## Starling and Venous Return



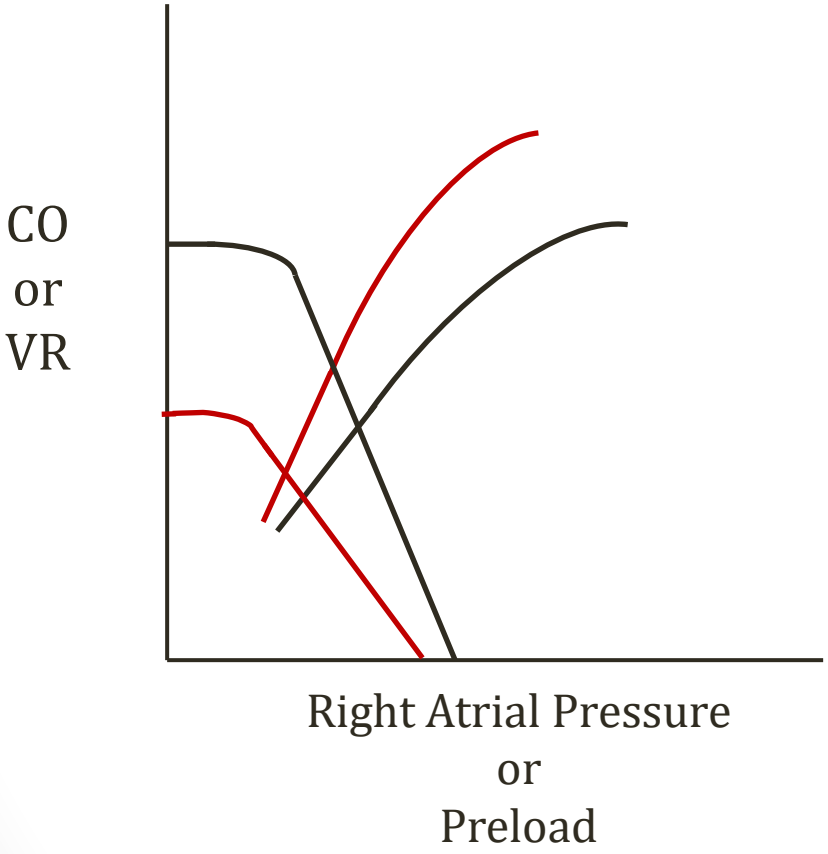
# Heart Failure




↓contractility
↑ TPR
↑ Fluid volume

* Black = normal

# Hemorrhage

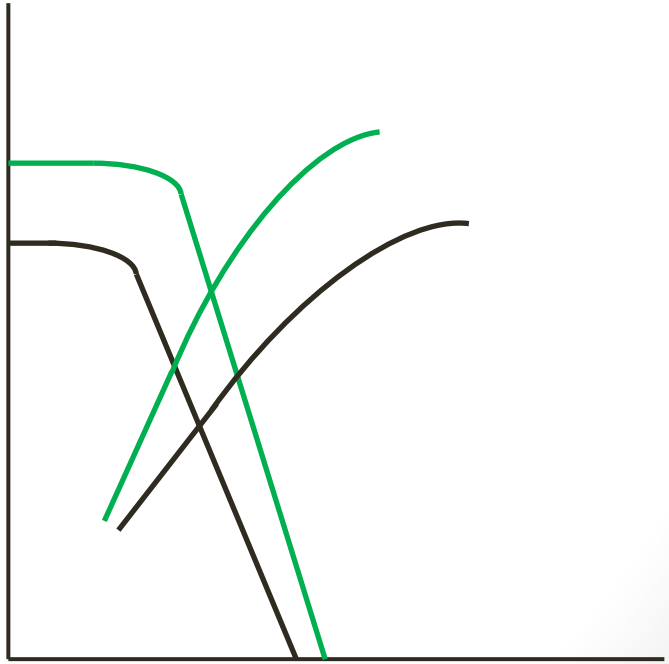



Blood loss
↑ TPR
↑ Contractility

* Black = normal

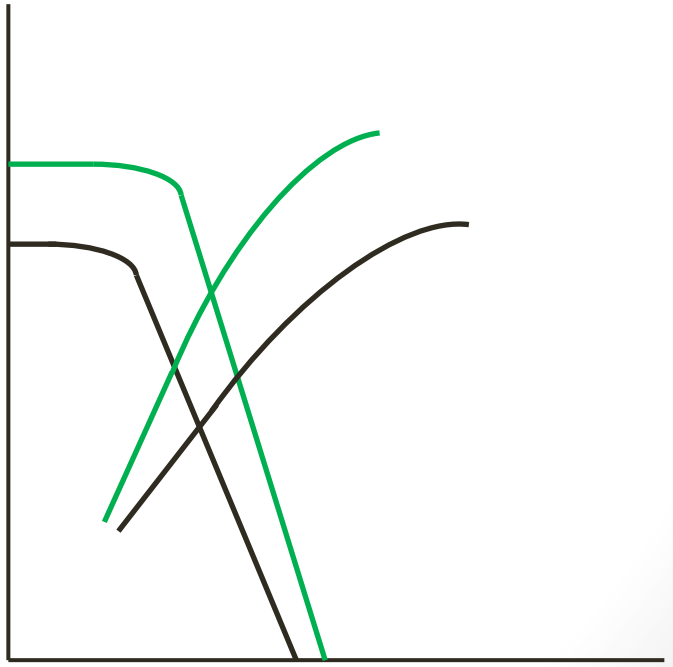
# Exercise

- Decreased afterload (TPR)
- Venous contraction
- Increased contractility
- Net result = increased CO



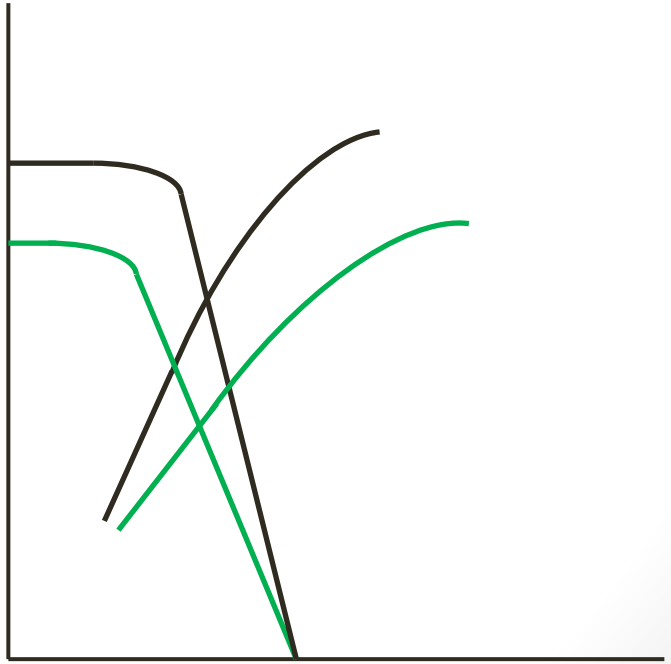
# AV Fistulas

- Decreased afterload (TPR)
- Increased contractility
- Venous contraction
- Net result = increased CO



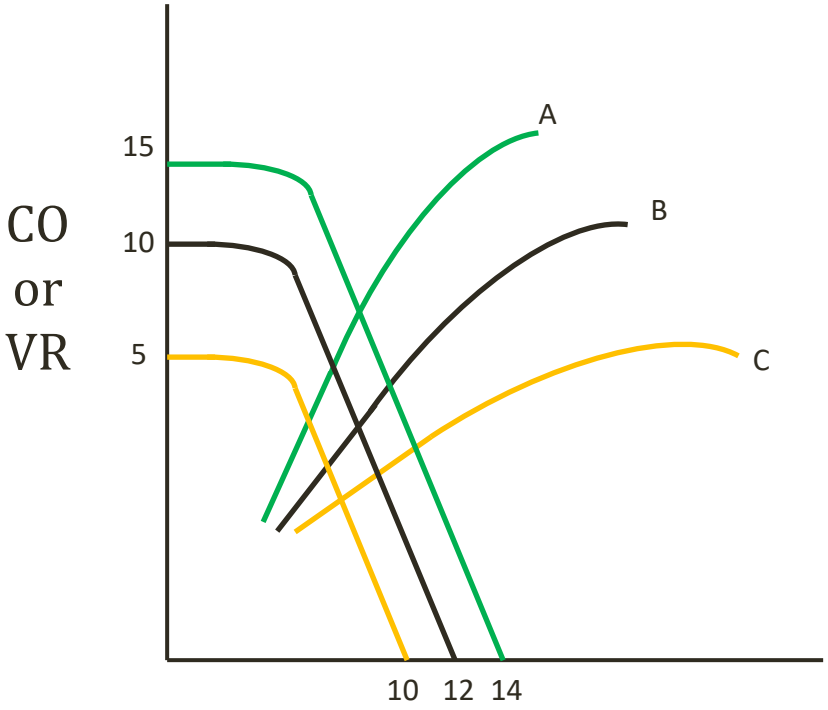
# Vasopressors

- Increased afterload (TPR)
- Alters VR and Starling Curves
- Net result = decreased CO



# Combined Curves

## Starling and Venous Return




* Black = normal

For a patient on starling curve A with a MSFP of 10 what is the cardiac output?

# Atherosclerosis

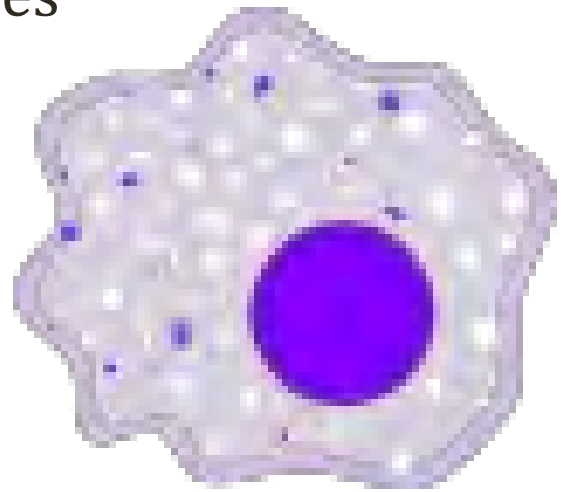
Jason Ryan, MD, MPH

# Vocabulary

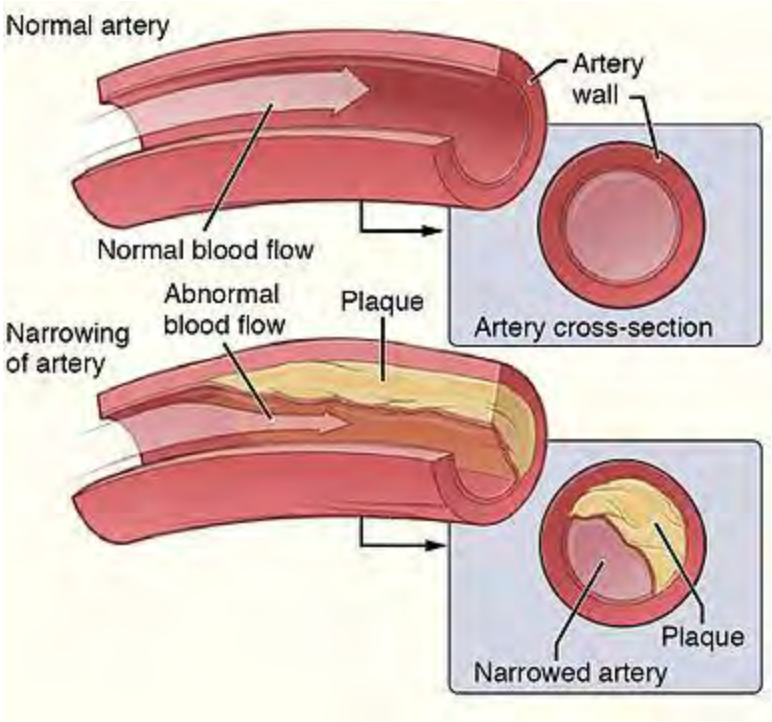
- **Arteriosclerosis**
  - Hardening of arteries
  - Hyaline
  - Hyperplastic
- **Atherosclerosis**
  - Form of arteriosclerosis
  - Most common type

# Atherosclerosis

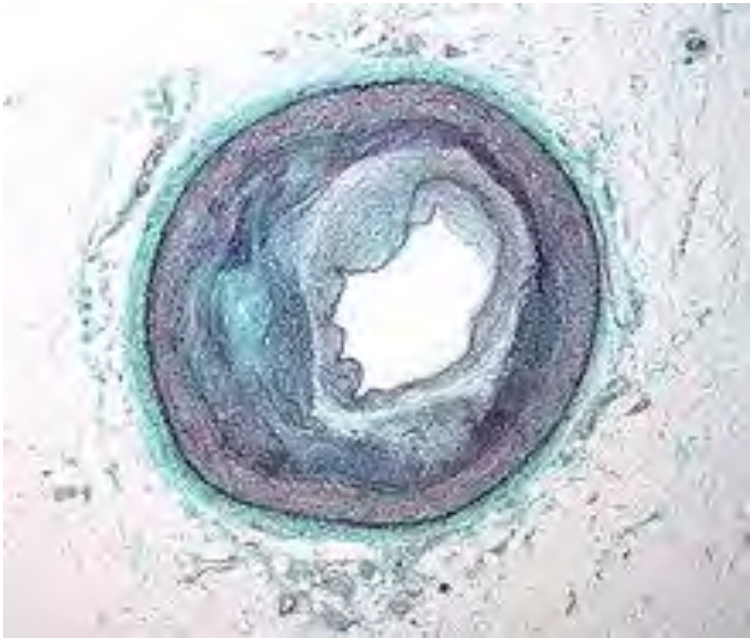
- **Plaque accumulation** in arterial walls
- Chronic inflammatory process
- Involves **macrophages**, T-cells
- Accumulation of **lipoproteins especially LDL**
- Underlying cause of many diseases
  - Myocardial infarction
  - Stroke
  - Peripheral vascular disease



A. Rad et al./Wikipedia



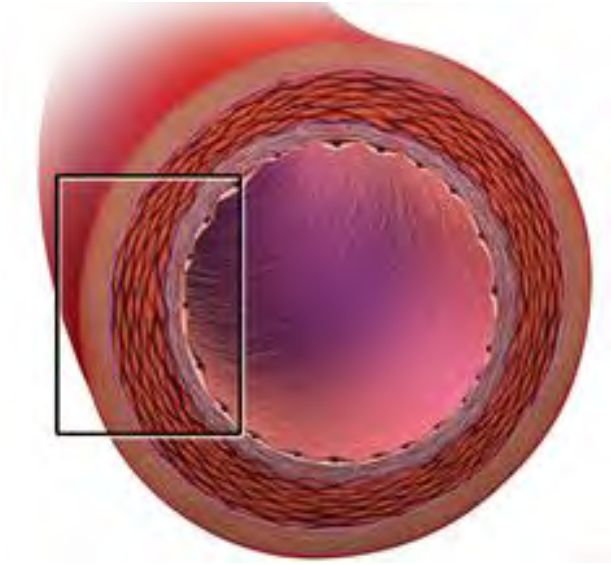

OpenStax College/Wikipedia



Nephron/Wikipedia

# Arterial Structure

- Intima
  - Single layer of endothelial cells
  - Basement membrane
- Media
  - Smooth muscle cells
  - Elastin
- Adventicia
  - Connective tissue
  - Vasa vasorum (blood supply to artery wall)
  - Nerve fibers



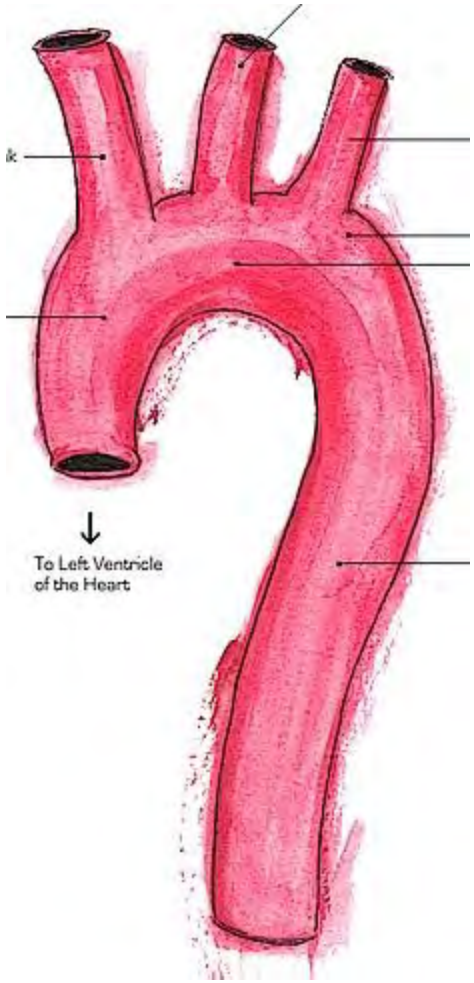
Bruce Blaus/Wikipedia

# Type of Arteries

- **Elastic**
  - Large amounts of **elastin** in media layer
  - Expansion in systole, contraction in diastole
  - Aorta, carotid arteries, iliac arteries
- **Muscular**
  - Layers of smooth muscle cells
  - Vasoconstriction/vasodilation to modify blood flow
  - Arterioles: smallest muscular vessels (most flow resistance)

# Atherosclerosis

- **Large elastic arteries**
  - Aorta, carotid arteries, iliac arteries
- **Medium-sized muscular arteries**
  - Coronary, popliteal




Luke Guthman/Wikipedia

# Atherosclerosis

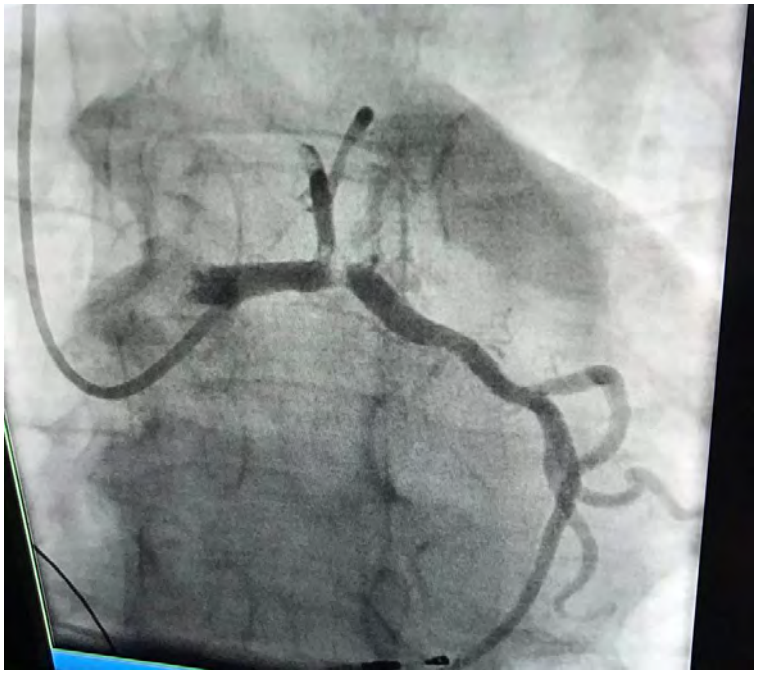
## Pathogenesis

- **Endothelial injury or dysfunction**
  - Details incompletely understood
  - Believed to be related to risk factors
  - Cigarette smoke
  - High blood pressure
  - High cholesterol

# Atherosclerosis

## Pathogenesis

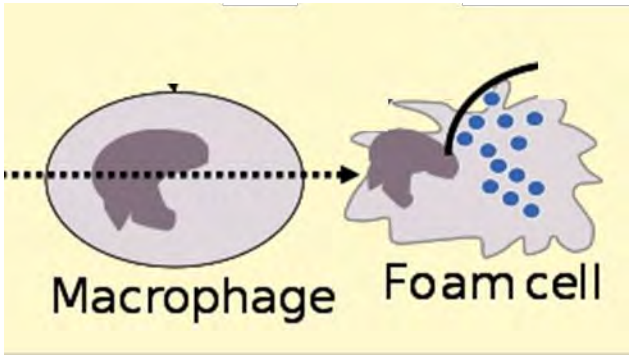
- **Branch points** and **vessel origins** (ostia)
  - Common sites of plaque
  - Turbulent flow → endothelial stress



# Atherosclerosis

## Pathogenesis

- Lipids
  - **LDL accumulation** in intima
  - Oxidized by free radicals
  - Oxidized LDL scavenged by macrophages
  - Cannot be degraded
  - Macrophages become foam cells




Public Domain

# Atherosclerosis

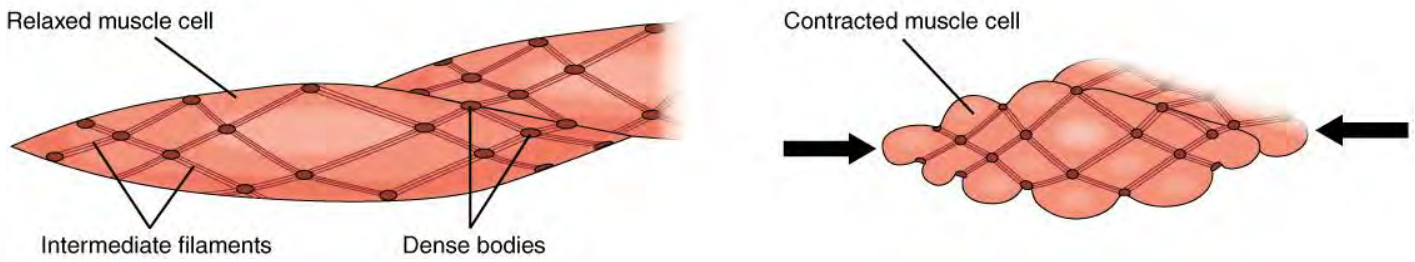
## Pathogenesis

- **Chronic inflammation**
  - LDL oxidized from free radicals
  - Damages endothelium, smooth muscle
  - Macrophages release cytokines

# Atherosclerosis

## Pathogenesis

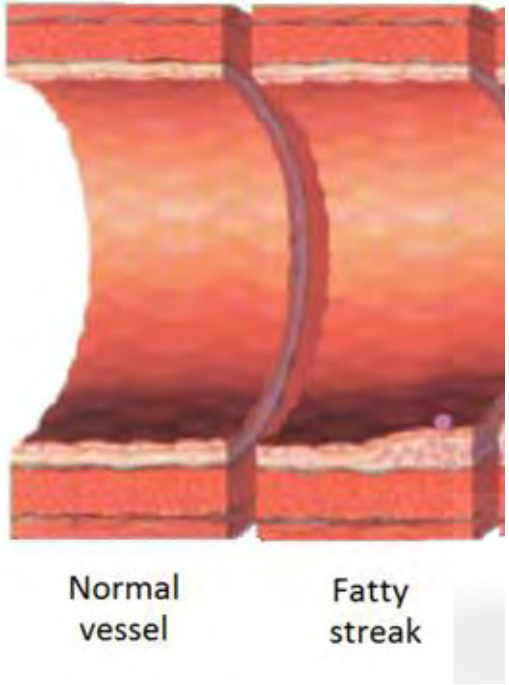
- **Smooth muscle cells** proliferate in intima
- Lay down extracellular matrix
- Key growth factor: **PDFG**
  - Platelet-derived growth factor




OpenStax College/Wikipedia

# Atheroma Growth

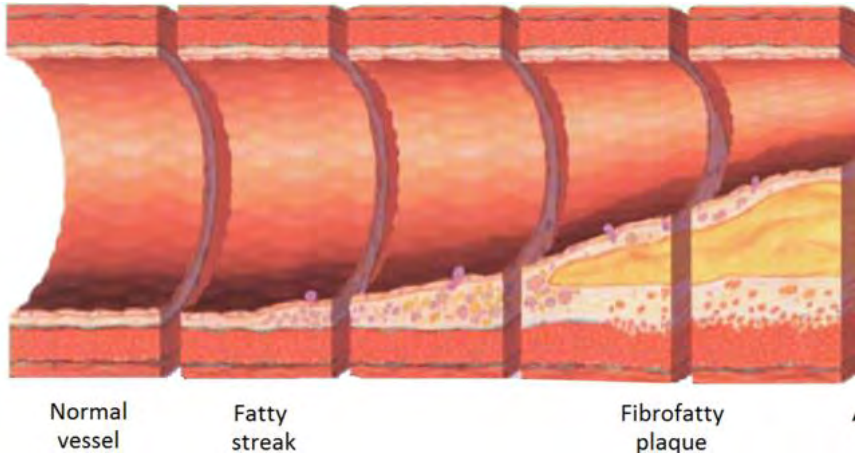
- **Fatty streaks**
  - Macrophages filled with lipids
  - Form line (streak) along vessel lumen
  - Do not impair blood flow
  - Can be seen in children, adolescents
  - Not all progress



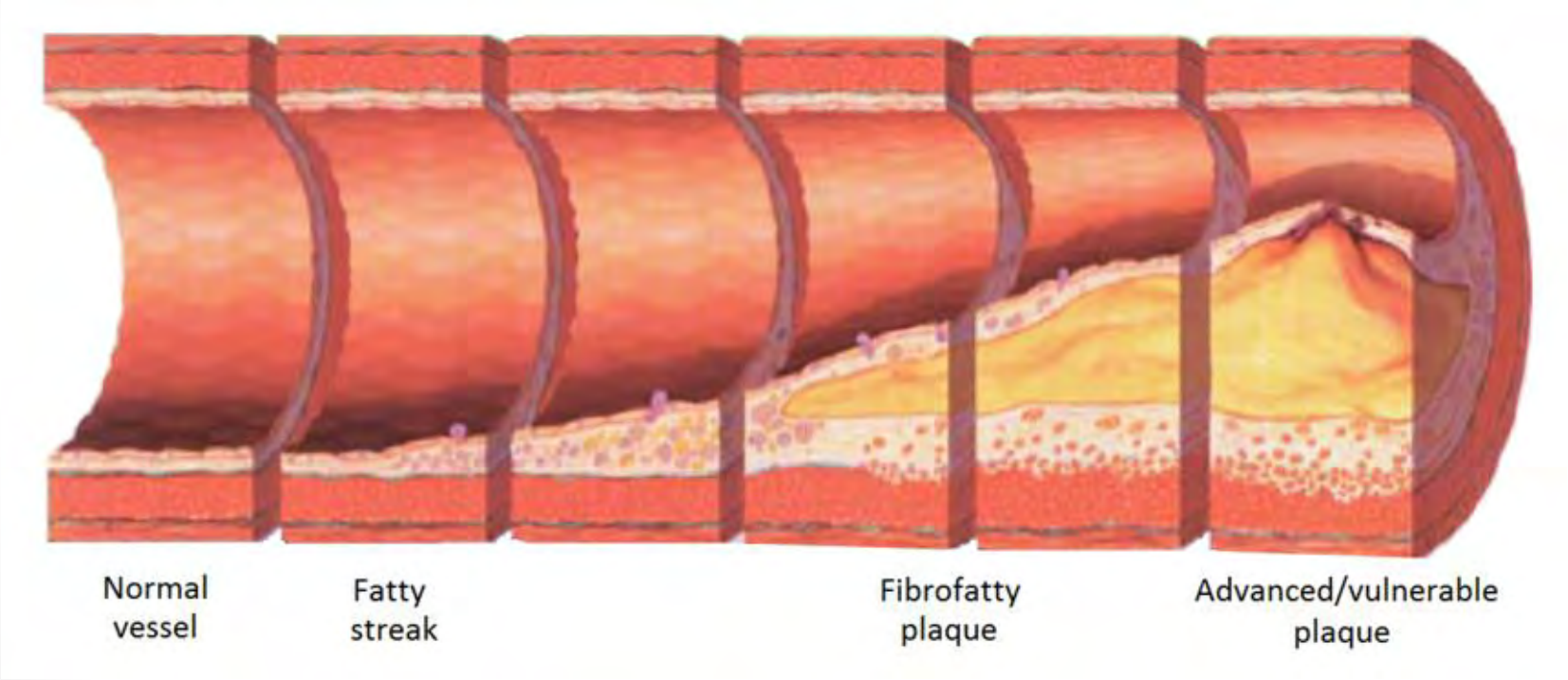

Npatchett/Wikipedia

# Atheroma Growth

- **Atherosclerotic plaques**
  - Intima thickens
  - Lipids accumulate
  - Usually patchy along vessel wall
  - Rarely involve entire vessel wall
  - Usually eccentric



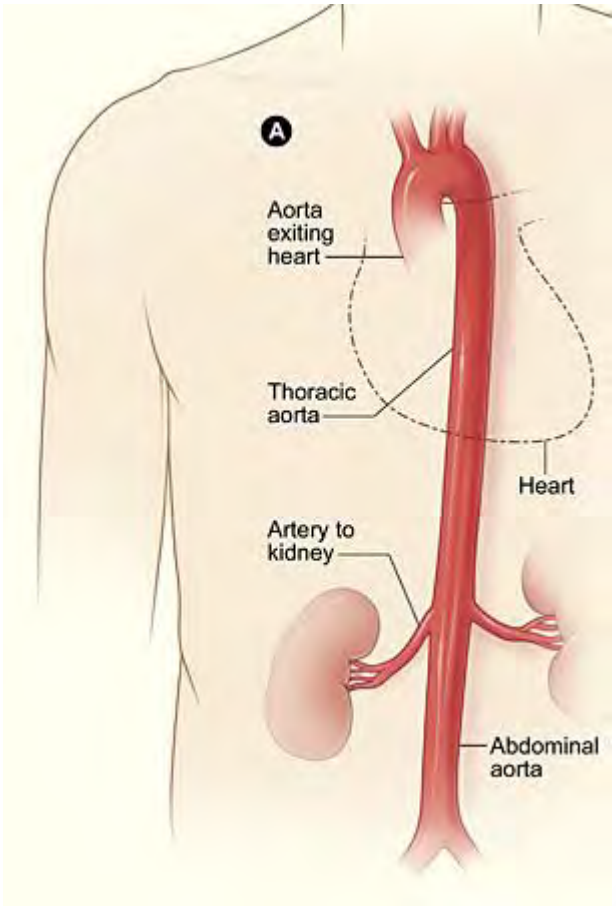

Npatchett/Wikipedia




Npatchett/Wikipedia

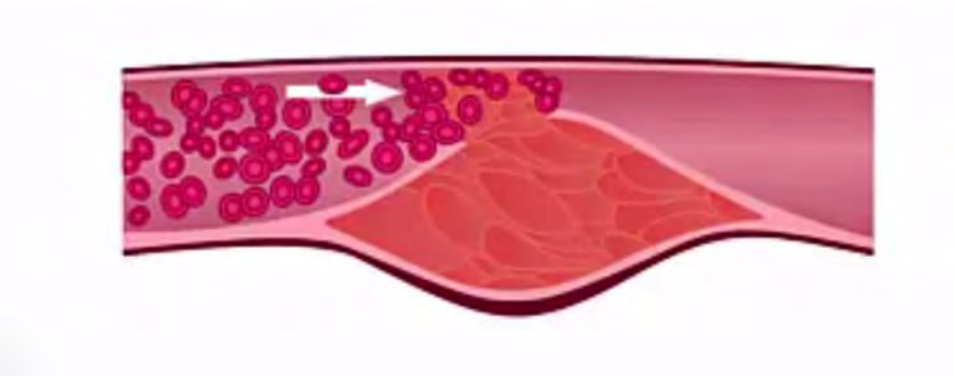
# Locations

- Abdominal aorta (large vessel)
- Coronary arteries
- Popliteal arteries
- Internal carotid
- Circle of Willis



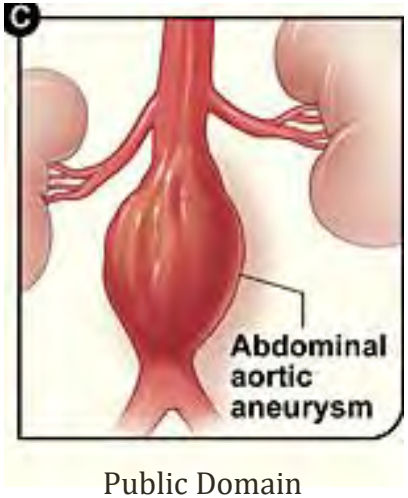
# Atherosclerosis Complications

- **Ischemia**
- Plaque rupture
  - Exposes thrombogenic substances
  - Clot formation
  - May cause acute vessel closure (STEMI)
  - Thrombus may embolize (stroke from carotid plaque)



# Atherosclerosis Complications

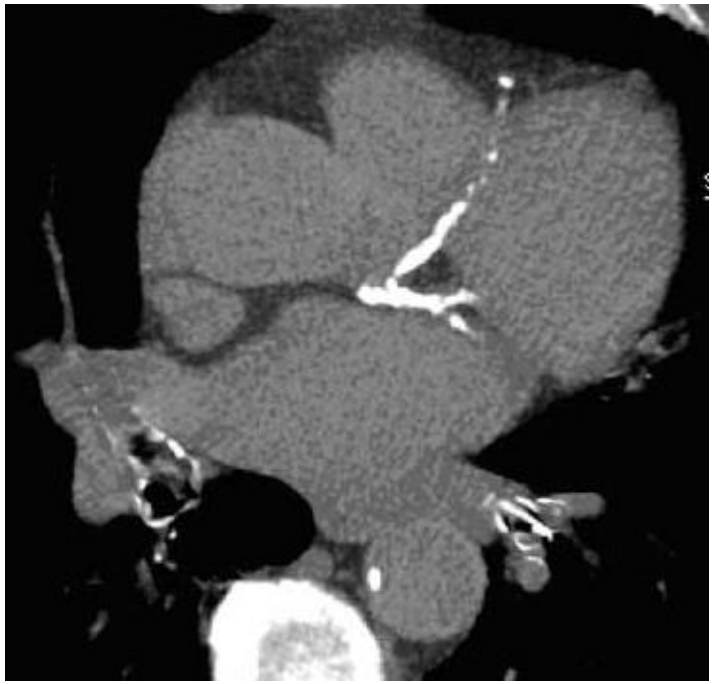
- **Hemorrhage into plaque**
  - Lesions: proliferating small vessels ("neovascularization")
  - Contained rupture may suddenly expand lesion
- Aneurysm
  - Lesions may damage underlying media
  - Plaque associated with abdominal aortic aneurysms




Public Domain

# Dystrophic Calcification

- Commonly seen in atheroma
- Result of chronic inflammation
- Basis for “coronary CT scans”

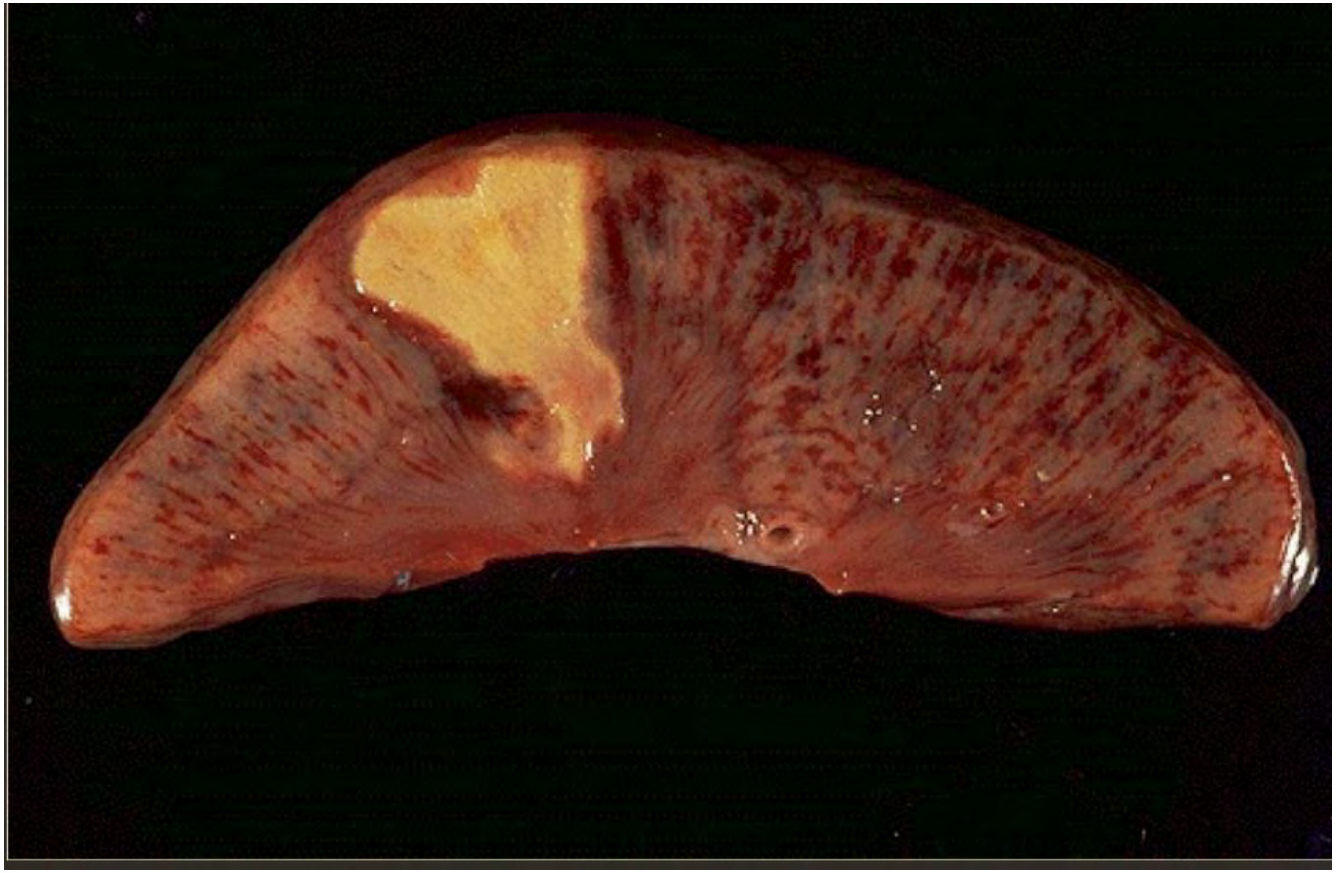


# Infarction

- Area of ischemic necrosis
- Two types: white and red
- **White infarcts**
  - Occlusion of arterial supply to a solid organ
  - Common in heart, kidneys, spleen
  - Limited blood seepage from healthy tissue
  - Tissue becomes pale (white)

# White Infarct

## Renal Infarction



Ryan Johnson/Flikr

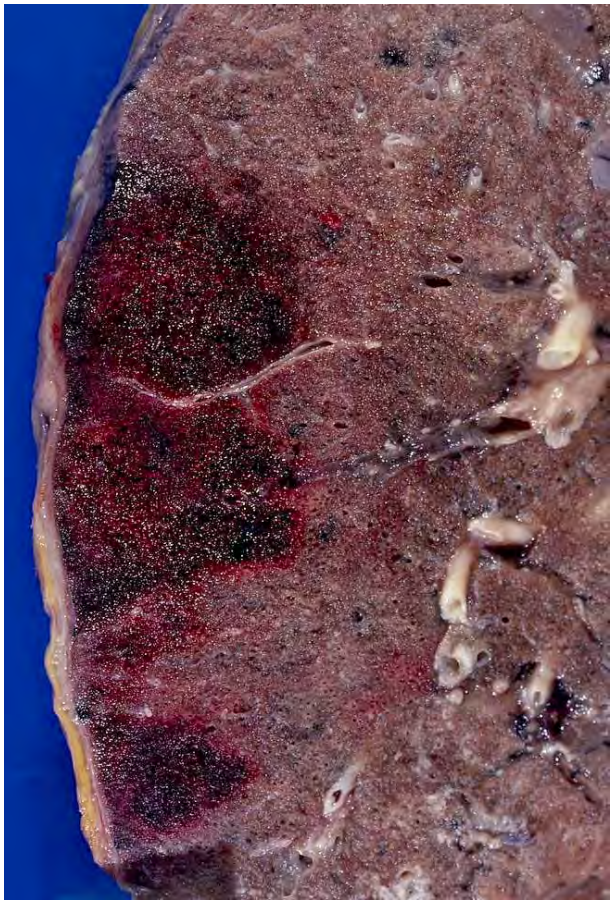
# Red Infarcts

## Hemorrhagic Infarct

- Blood enters ischemic tissue
- Blockage of venous drainage
  - Testicular torsion
- Tissues with dual circulation
  - Blood flow from 2$^{nd}$ supply floods ischemic area
  - Classic location: Lung (diffuse blood supply)
  - Small intestine
- Flow re-established to necrotic area
  - Angioplasty restores flow in coronary artery

# Red Infarct

## Lung Infarction



Yale Rosen/Wikipedia

# Cardiac Ischemia

Jason Ryan, MD, MPH

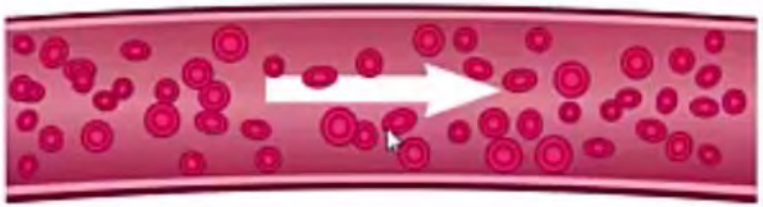
# Cardiac Ischemia

- Caused by coronary atherosclerosis
- **O2 SUPPLY << O2 DEMAND = ISCHEMIA**
- Typical symptoms
  - **Chest pain (angina)**
  - Dyspnea
  - Diaphoresis

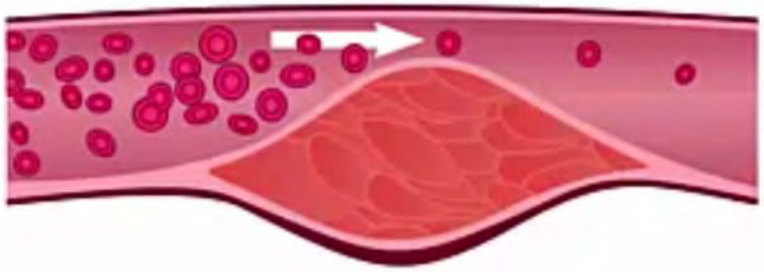
Freestocks.org

# Stable Angina

- Stable atherosclerotic plaque
  - No plaque ulceration
  - No thrombus
- Must occlude ~75% of lumen to cause symptoms



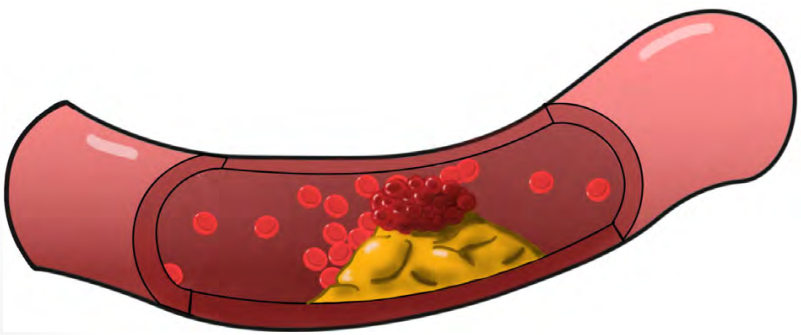
NO SYMPTOMS



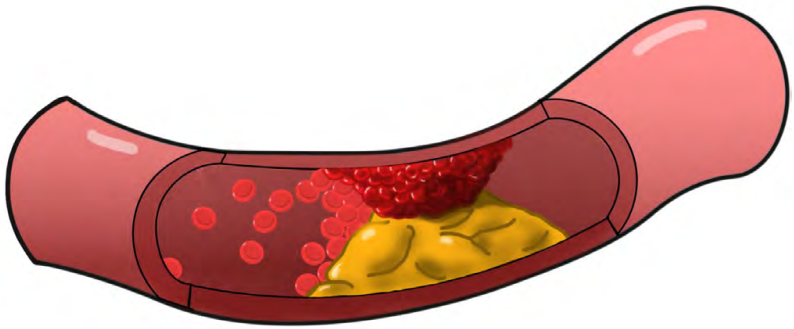
SYMPTOMS WITH EXERTION
(EXERTIONAL ANGINA)

# Acute Coronary Syndromes

- Plaque rupture → thrombus formation
- Subtotal occlusion
  - Unstable angina
  - Non-ST elevation myocardial infarction
- Total occlusion (100%)
  - ST-elevation myocardial infarction (STEMI)



Subtotal Occlusion



Total Occlusion

# Sudden Death

- Common complication of CAD
- Plaque rupture → **arrhythmias**
- CAD is **most common cause of sudden death adults**
  - Younger patients: Hypertrophic cardiomyopathy (HCM)

# Risk Factors

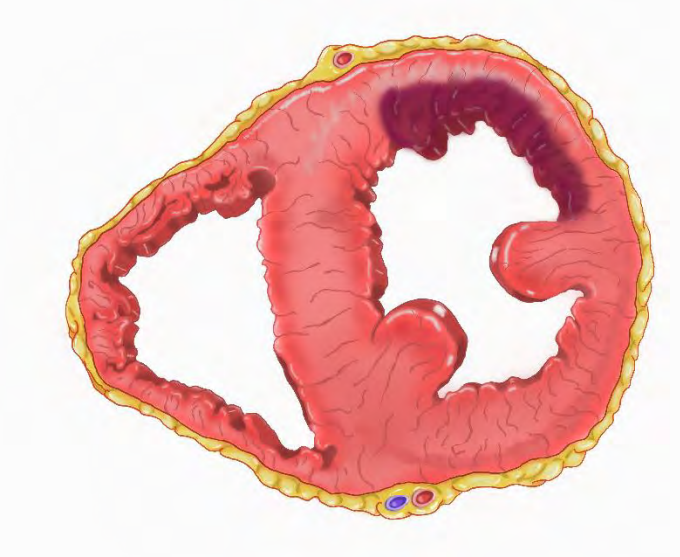
- Major risk is **prior coronary disease**
- Coronary risk equivalents
  - Diabetes
  - Peripheral artery disease
  - Chronic kidney disease

# Risk Factors

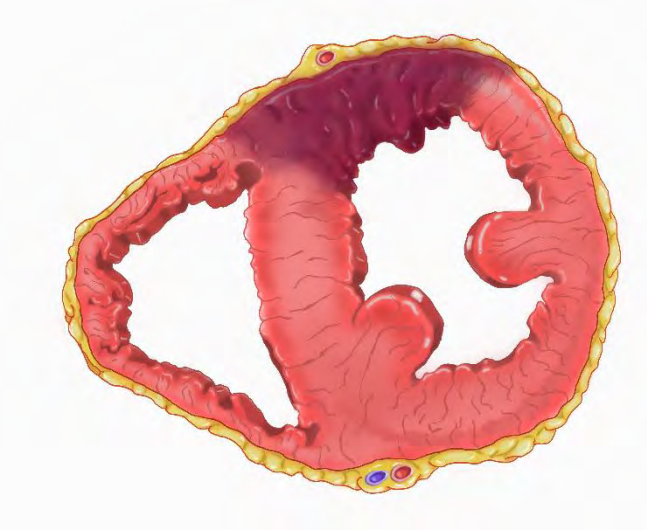
- Hypertension
- Hyperlipidemia
- Family History (1° relative, M<50, F<60)
- Smoking
- Obesity, sedentary lifestyle

# Extent of Ischemia

- **Transmural ischemia**
  - Occurs with complete 100% flow obstruction (STEMI)
- **Subendocardial ischemia**
  - Occurs with flow obstruction but some distal blood flow
  - Stable angina, unstable angina, NSTEMI

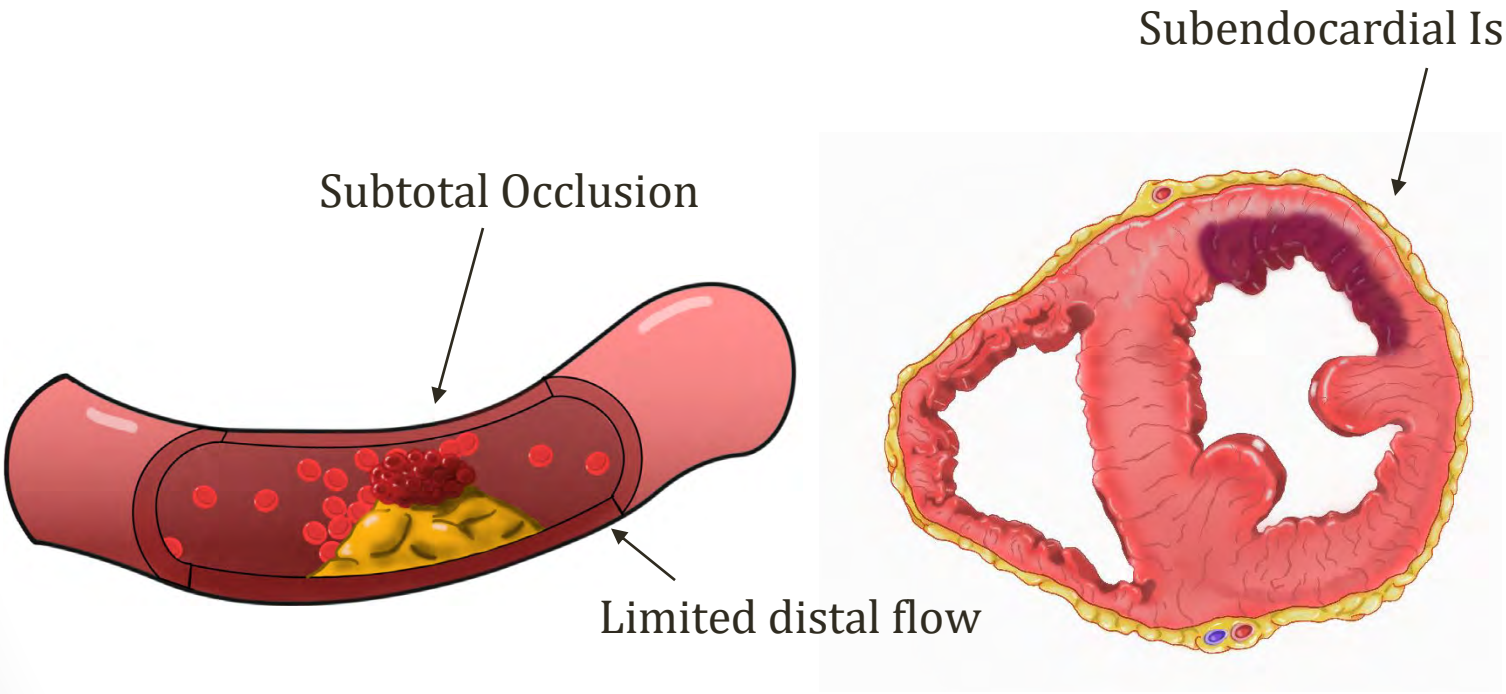


Subendocardial Ischemia

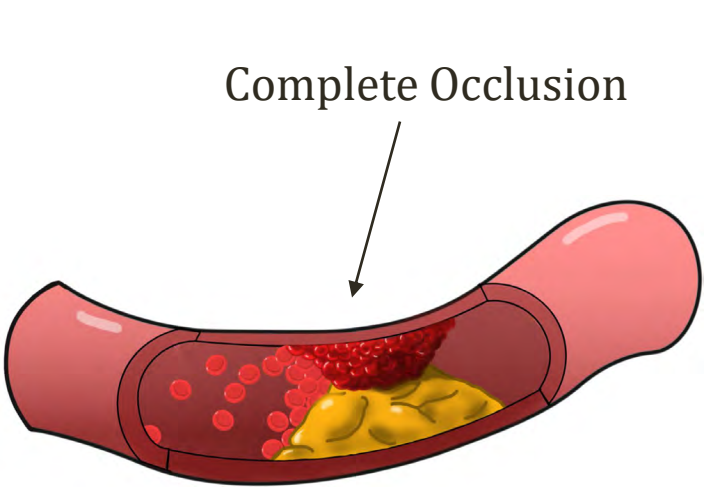


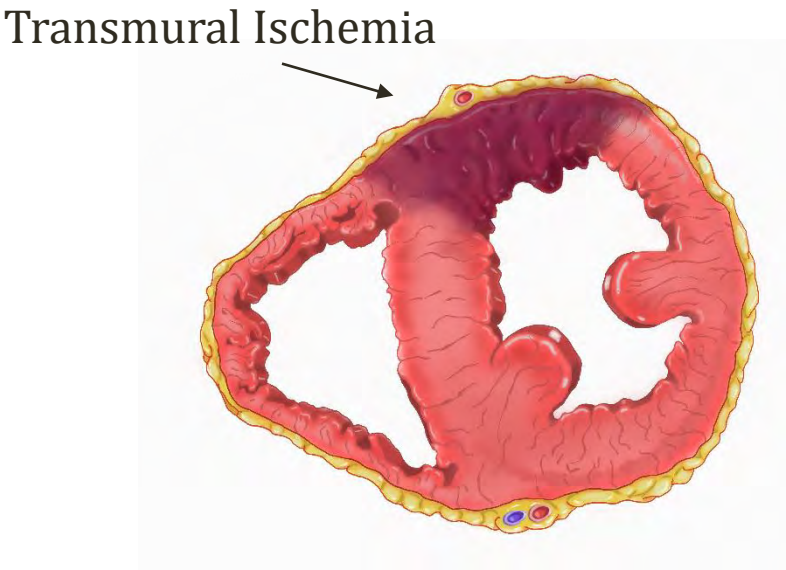
Transmural Ischemia

# Subendocardial Ischemia



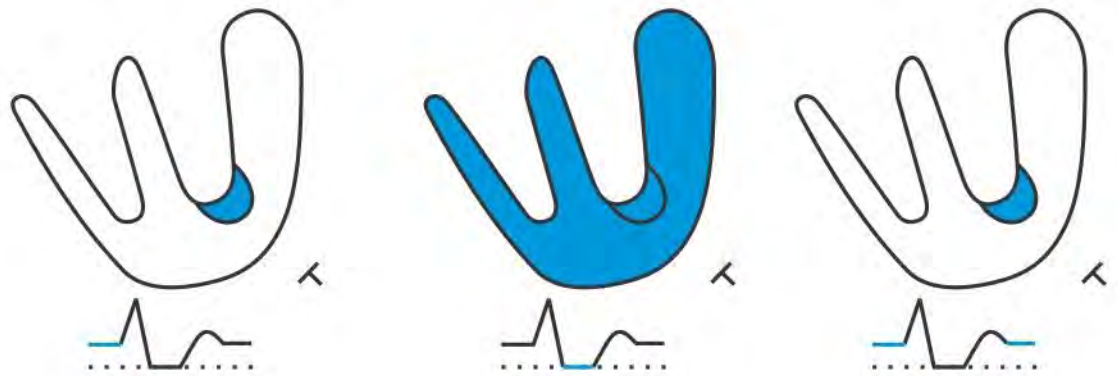
# Transmural Ischemia



# Ischemic EKG changes

## ST depressions

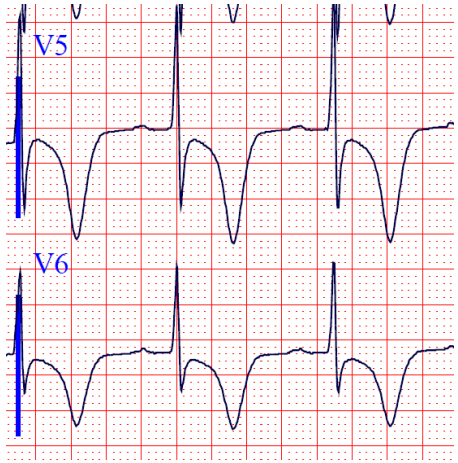


Subendocardial Ischemia

# Ischemic EKG changes

## T wave inversions

- Many causes other than CAD
- Raised ICP
  - Cerebral T waves
- Resolving pericarditis
- Bundle branch blocks
- Ventricular hypertrophy



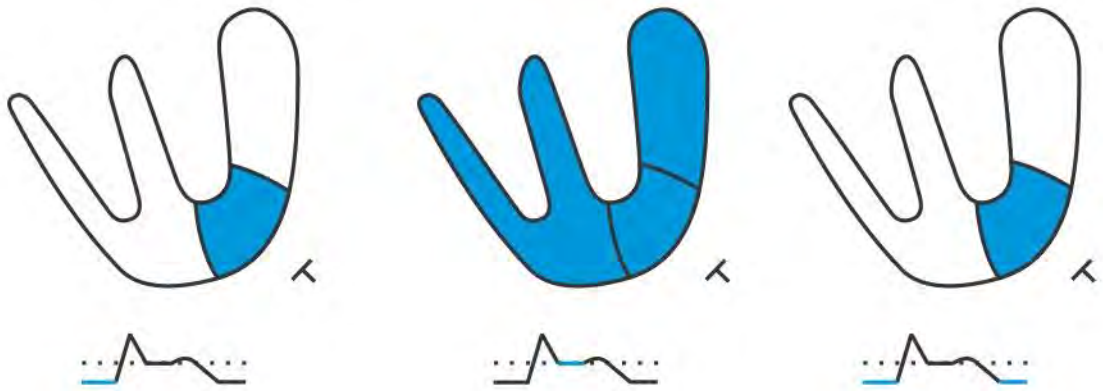
# Ischemic EKG changes

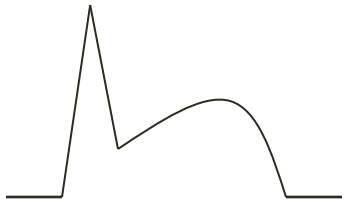
## T wave inversions

Subendocardial Ischemia

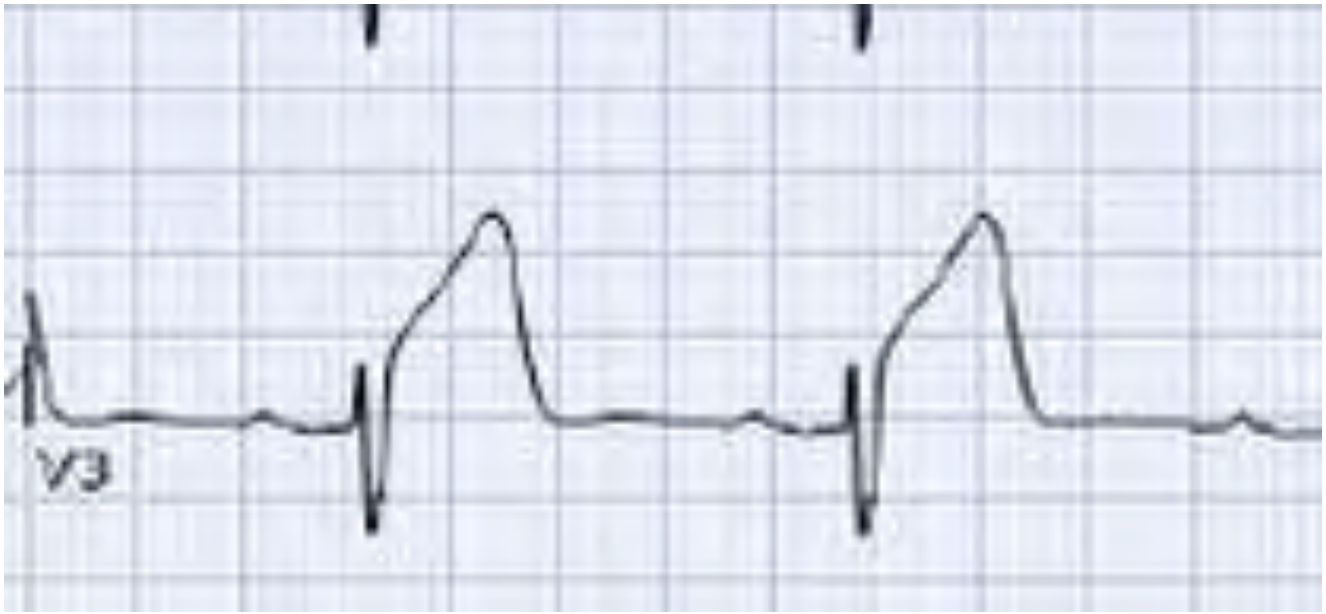
# Ischemic EKG changes

## ST Elevations



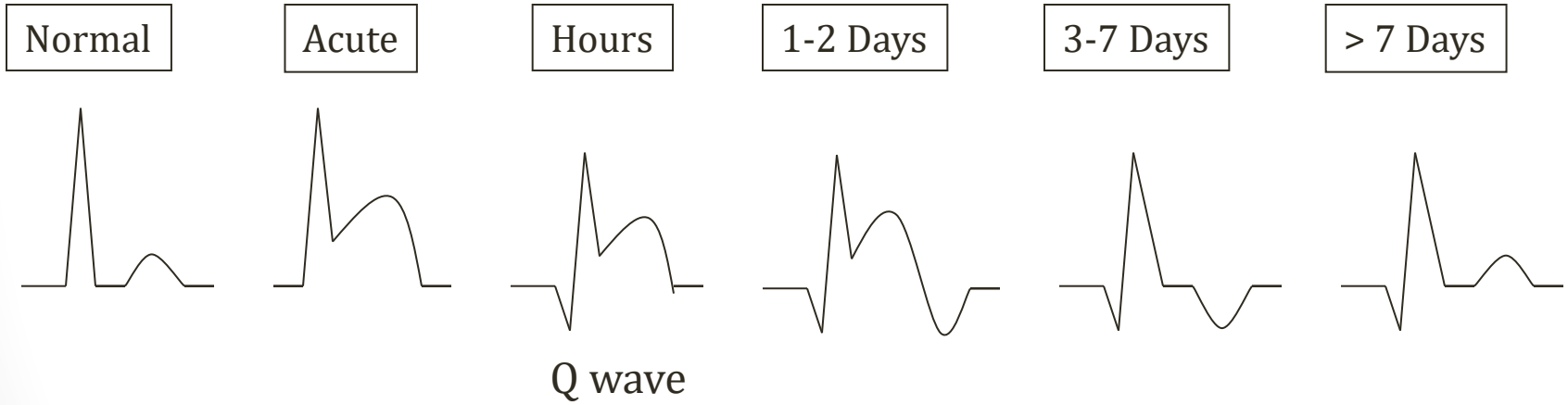


Seen only with transmural ischemia



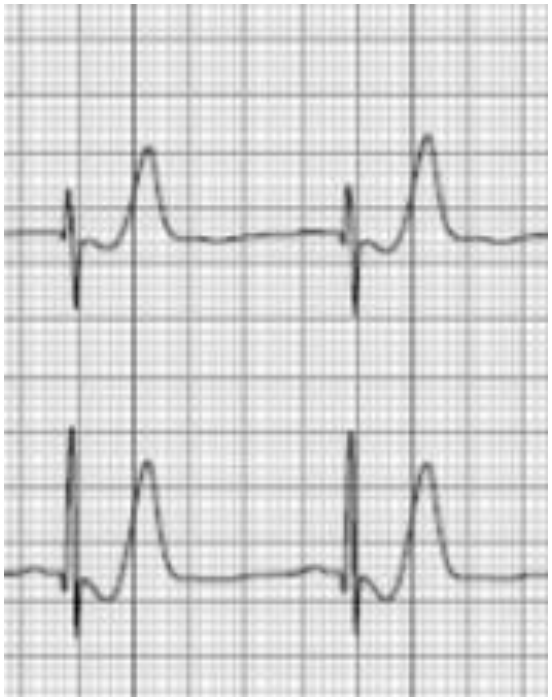
# Evolution of EKG changes

## STEMI



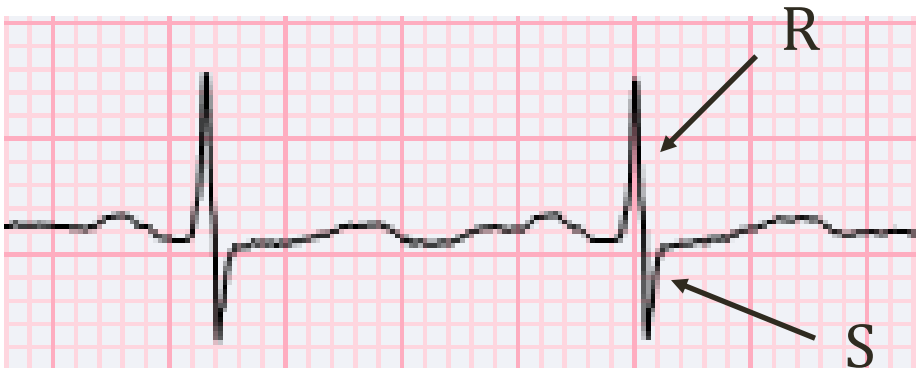
# Hyperacute T waves

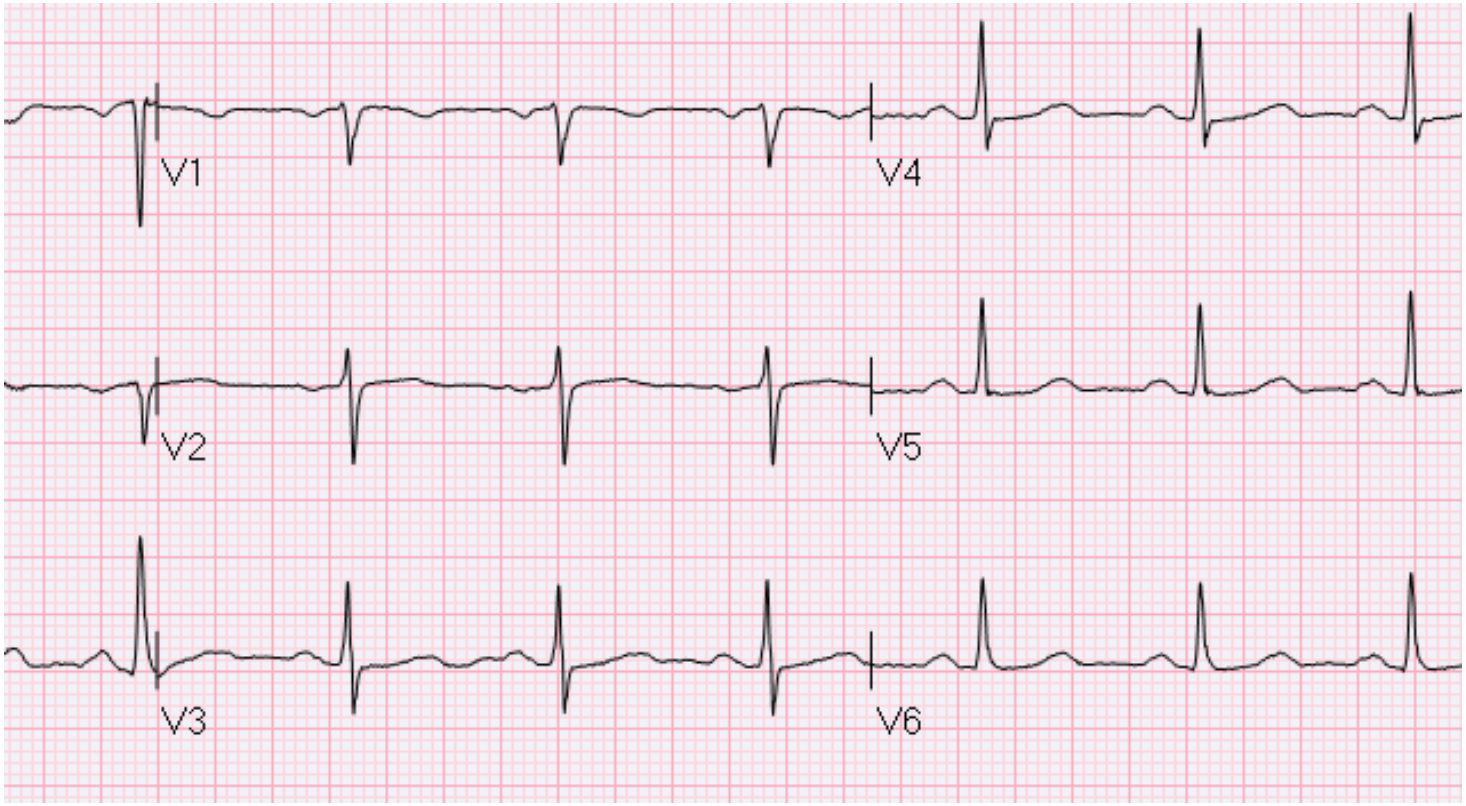
- Seen in transmural ischemia
- Early sign of ischemia
- Seen before ST elevations

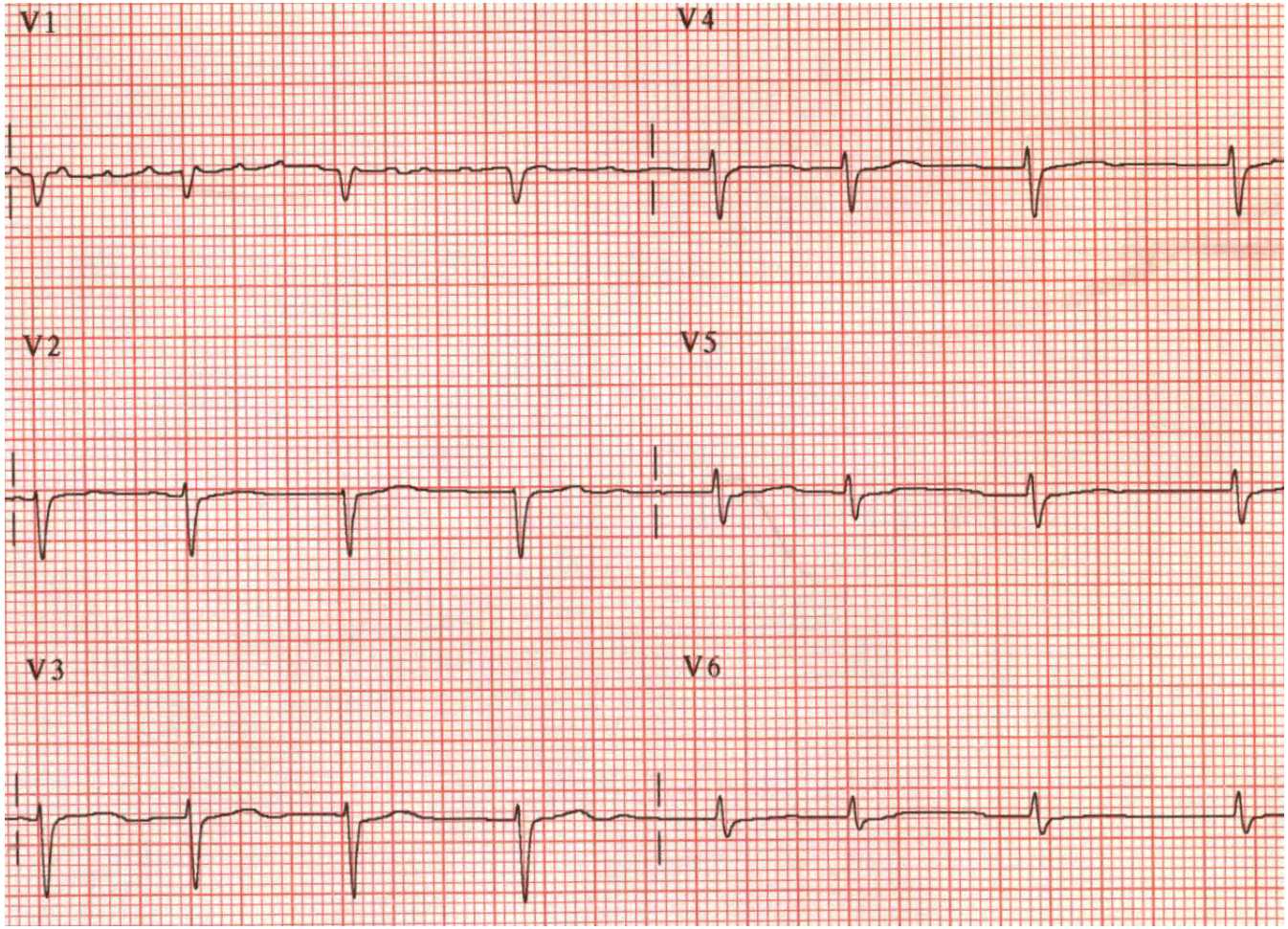


# Poor R Wave Progression

- R wave increases (progresses) in size V1-V6
- Normally R>S waves seen by lead V3
- Poor progression seen in **anterior ischemia**
  - Acute or prior infarction



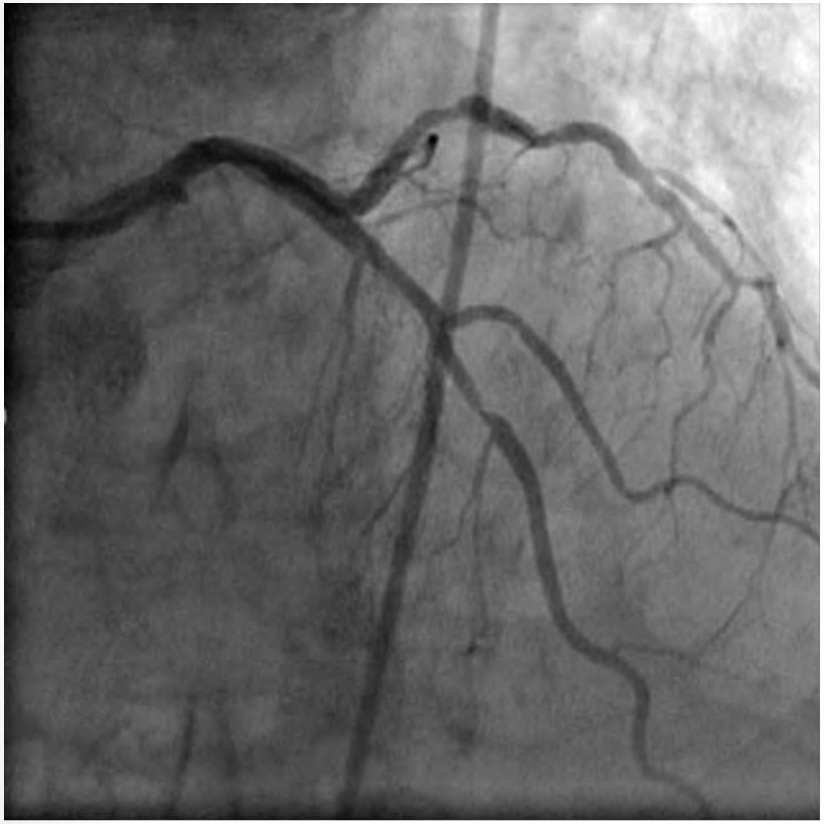




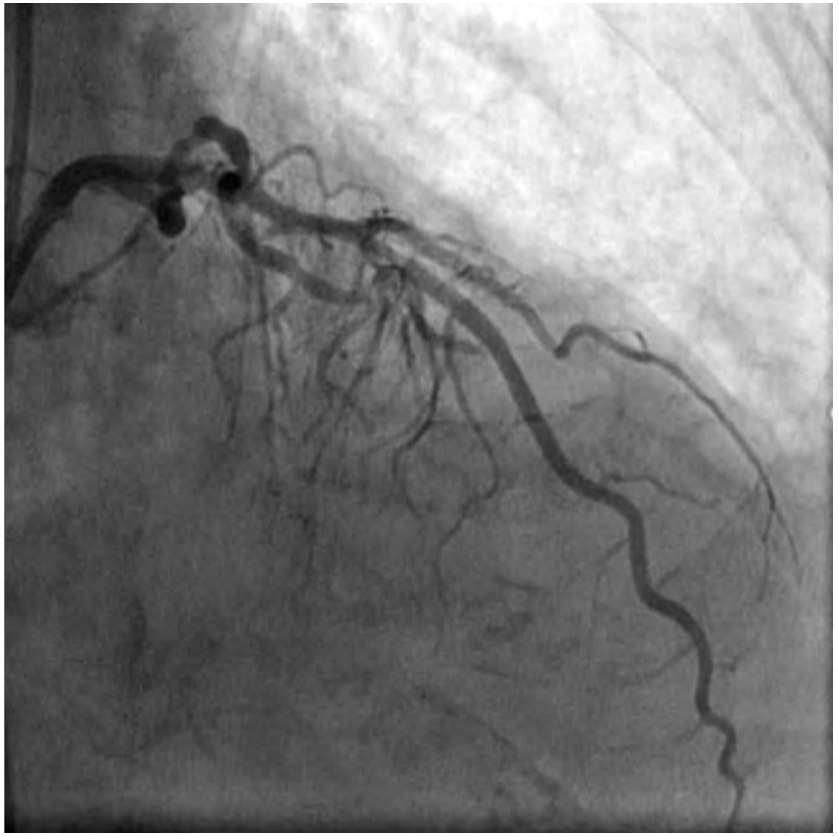
# Terminology

- Revascularization
- Angioplasty
- Coronary stenting
- Coronary bypass surgery

# Revascularization



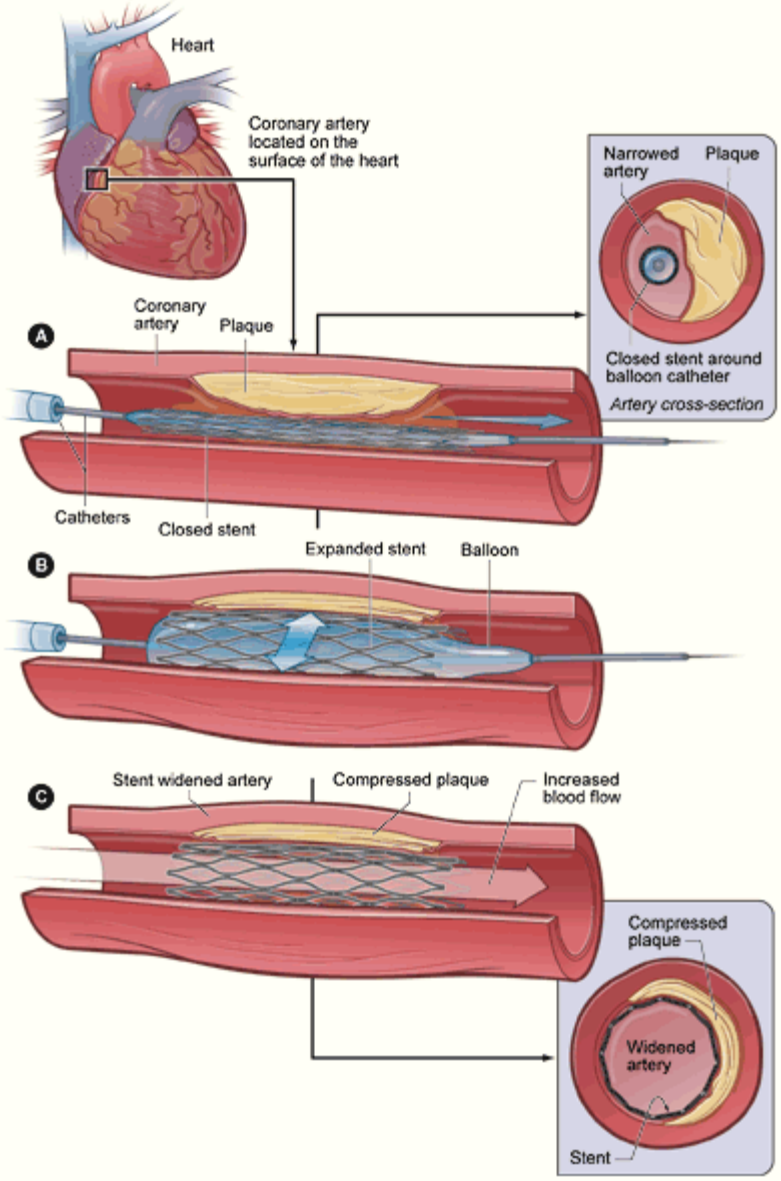
Coronary angiogram: Before



Coronary angiogram: After

# Coronary Stents

- Angioplasty: Reshape vessel
- Balloon angioplasty: Balloon inflation to open vessel
- Percutaneous Coronary Intervention (PCI)
- Stent placement
- About 600,000 stents/year implanted US

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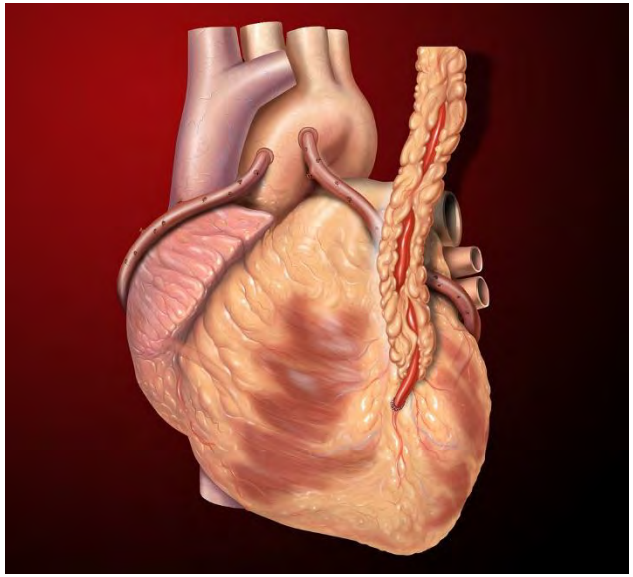
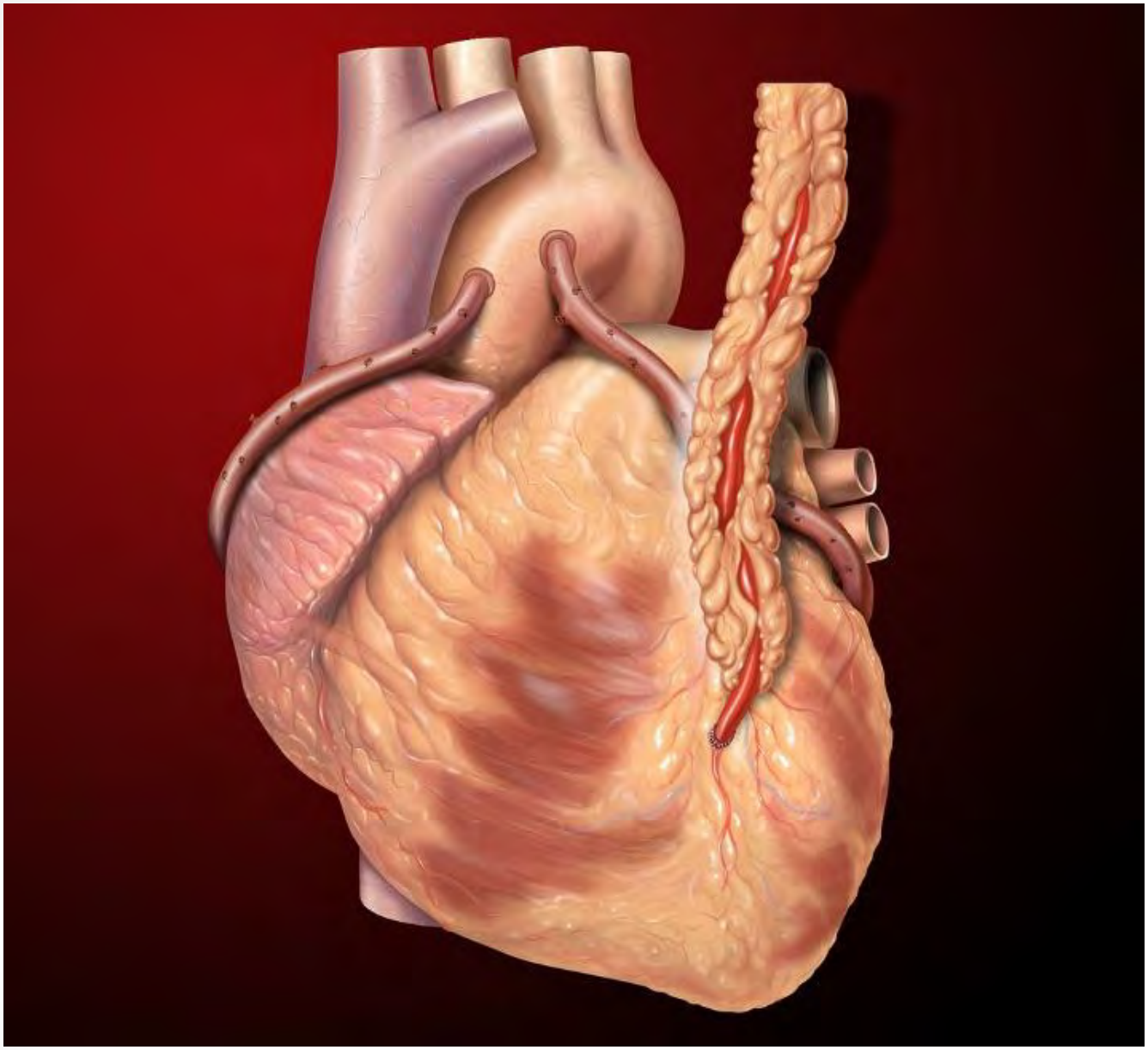
# CABG

## Coronary Artery Bypass Surgery

- “Bypass Surgery”
- Left Internal Mammary Artery (LIMA) Graft
- Saphenous (leg) Vein Grafts
- Radial (arm) Artery Grafts



Patrick J. Lynch/Wikipedia



Patrick J. Lynch/Wikipedia

# Revascularization

## Major Indications

- Angina
- Myocardial infarction
- Systolic dysfunction
  - Hibernating myocardium

# Ischemic Pathologic Changes

## Myocardium

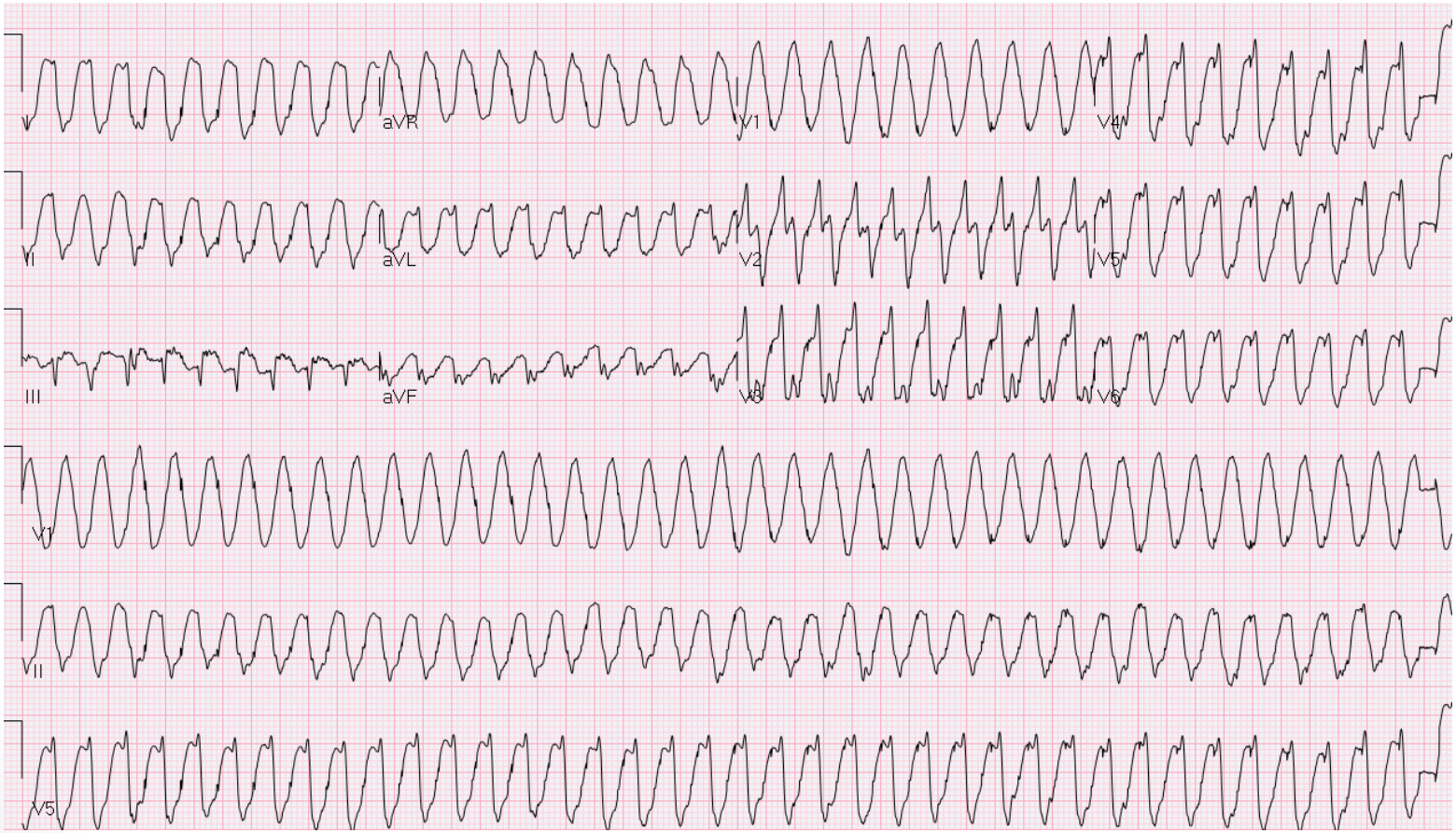
- Zero to 4 hrs
  - **No changes!**
- 4 – 12 hrs
  - Gross: Mottled
  - Micro: Necrosis, edema, hemorrhage
- 12-24 hrs
  - Gross: Hyperemia
  - Micro: Surrounding tissue inflammation
- 5 – 10 days
  - Gross: Central yellowing
  - Micro: Granulation tissue
- 7 weeks
  - Gross: Gray-white scar
  - Micro: Scar

# Complications of Ischemia

- First 4 days
  - Arrhythmia
- 5 – 10 days
  - Free wall rupture
  - Tamponade
  - Papillary muscle rupture
  - VSD (septal rupture)
- Weeks later
  - Dressler's syndrome
  - Aneurysm
  - LV Thrombus/CVA

# Cause of Death

## 0 – 4 days after MI



# Cause of Death

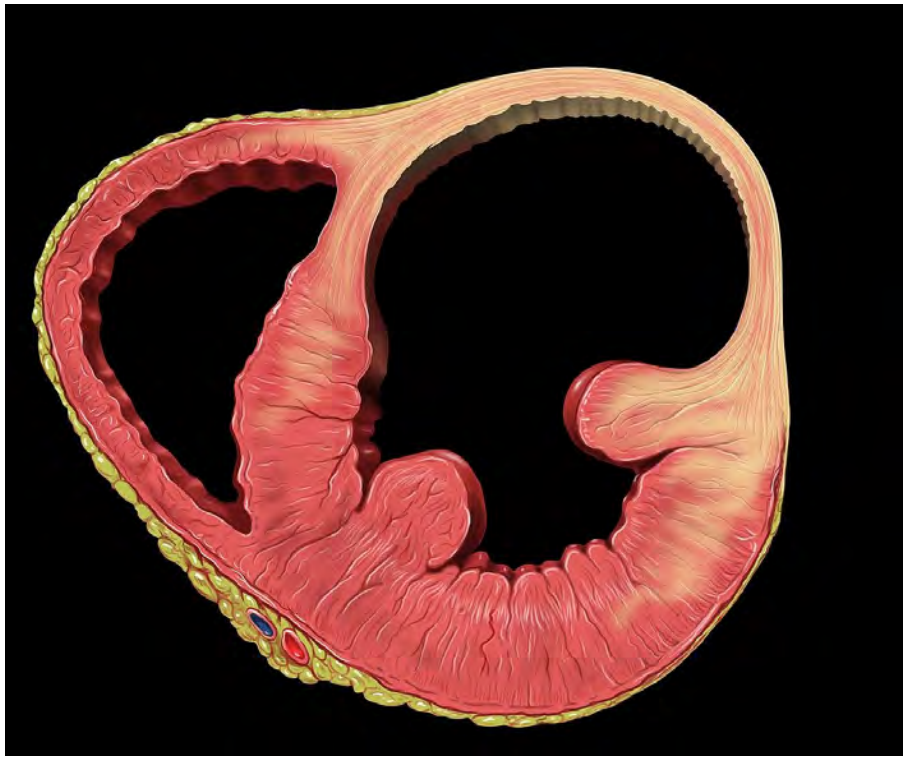
## 5-10 days after MI

- **Free wall rupture**
  - Usually fatal – sudden death
  - May lead to tamponade
- **Papillary muscle rupture**
  - Acute mitral regurgitation (holosystolic murmur)
  - Heart failure, respiratory distress
  - More common inferior MIs
- **Septal rupture – VSD**
  - Loud, holosystolic murmur (thrill)
  - Hypotension, right heart failure (↑ JVP, edema)

# Ventricular Aneurysm

## Weeks after MI

- More common **anterior infarction**
- Risk of thrombus → stroke, peripheral embolism



Patrick J. Lynch, medical illustrator/Wikipedia

# Ventricular Pseudoaneurysm

- **Rupture contained by pericardium/scar tissue**
- Not a true aneurysm
  - No endocardium or myocardium
- May rupture
- Presents as chest pain or dyspnea
- Often seen in the **inferior wall**
- Occurs earlier (<2 weeks) than true aneurysm

# Dressler's Syndrome

## Weeks to months after MI

- Form of pericarditis
  - Chest pain
  - Friction rub
- Immune-mediated (details not known)
- Treatment: NSAIDs or steroids

# Fibrinous Pericarditis

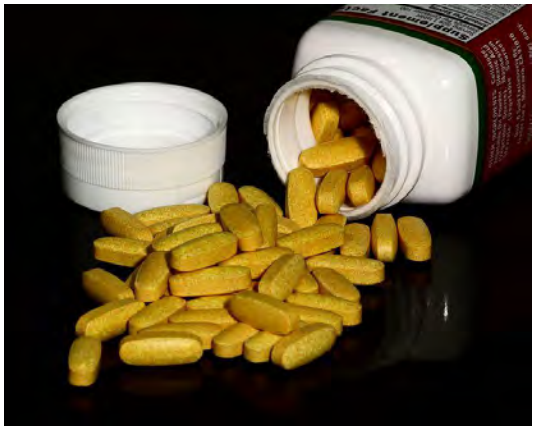
- Occurs ***days*** after MI
  - Sometimes called "post-MI" pericarditis
  - Not autoimmune
  - Extension of myocardial inflammation
- Dressler's occurs ***weeks*** after MI
  - Sometimes called "post cardiac injury" pericarditis
- Rarely life-threatening

# Secondary Prevention

- Any CAD → ↑ risk of recurrent events
  - STEMI, NSTEMI, stable angina
- Preventative therapy used to lower risk
- Even in asymptomatic patients

# Secondary Prevention

- Several proven therapies for risk reduction
- **Aspirin**
- **Statins**
  - Atorvastatin, Rosuvastatin
- **Beta blockers**
  - Used in patients with prior infarction (STEMI/NSTEMI)

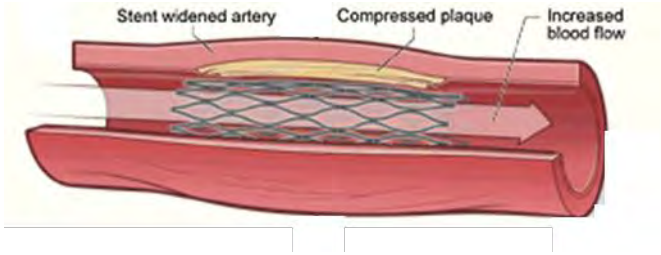


Ragesoss/Wikipedia

# Stent Complications

## Restenosis

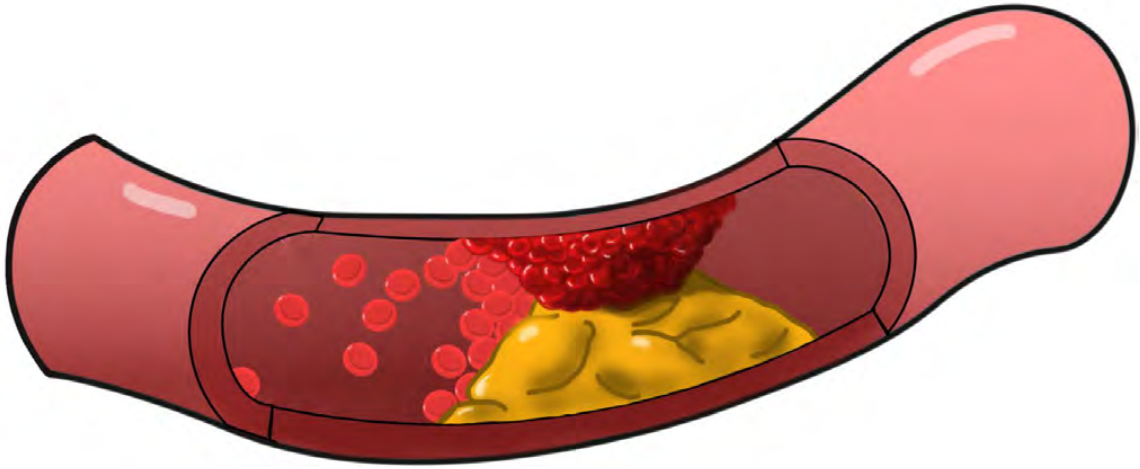
- Slow, steady growth of scar tissue over stent
- "Neo-intimal hyperplasia"
- Re-occlusion of vessel
- Rarely life-threatening
- Slow, steady return of angina
- Most stents coated "drug eluting stents"
  - Metal stent covered with polymer
  - Polymer impregnated with drug to prevent tissue growth
  - Sirolimus



# Stent Complications

## Thrombosis

- Acute closure of stent
- Same as STEMI: life-threatening event
- Dual anti-platelet therapy for prevention
- Associated with **missed medication doses**



# Stent Thrombosis Prevention

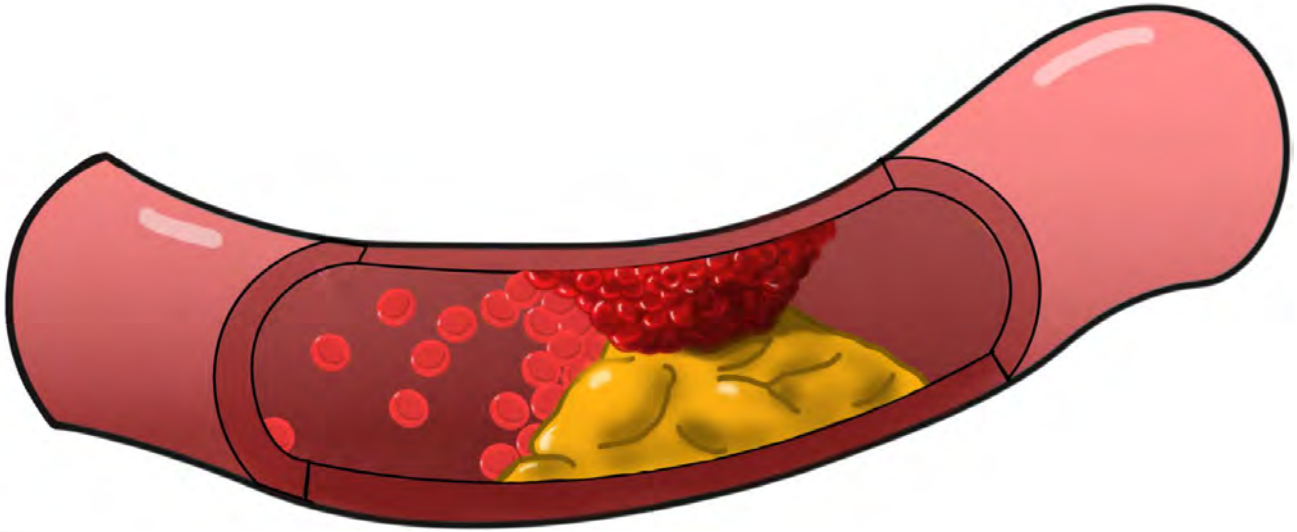
- "Dual antiplatelet therapy"
- Typically one year of:
  - Aspirin
  - Clopidogrel, Prasugrel or Ticagrelor
- After one year, stent metal no longer exposed to blood
  - "Endothelialization"
  - Risk of thrombosis is lower (but not zero)
  - Most patients take aspirin only

# ST-Elevation Myocardial Infarction (STEMI)

Jason Ryan, MD, MPH

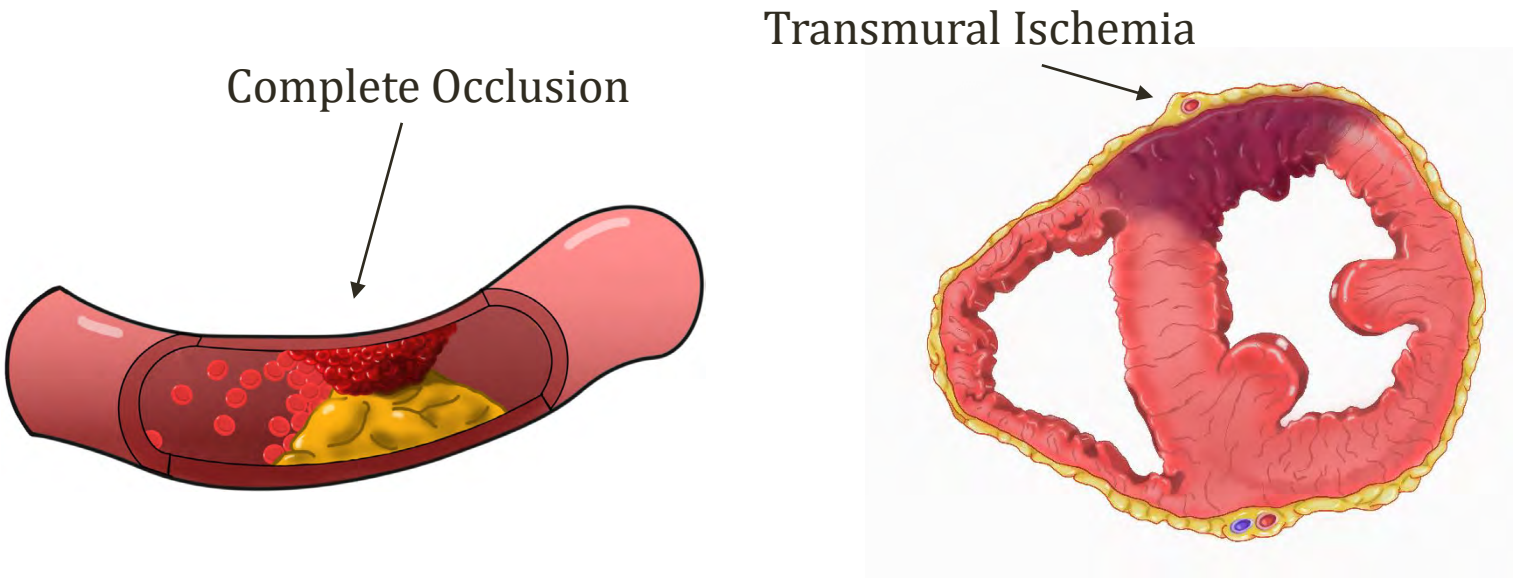
# STEMI

- Atherosclerotic plaque rupture
- Thrombus formation
- Complete (100%) vessel occlusion
- Ischemic chest pain
- ST-elevations on ECG



# STEMI

- **Transmural ischemia**



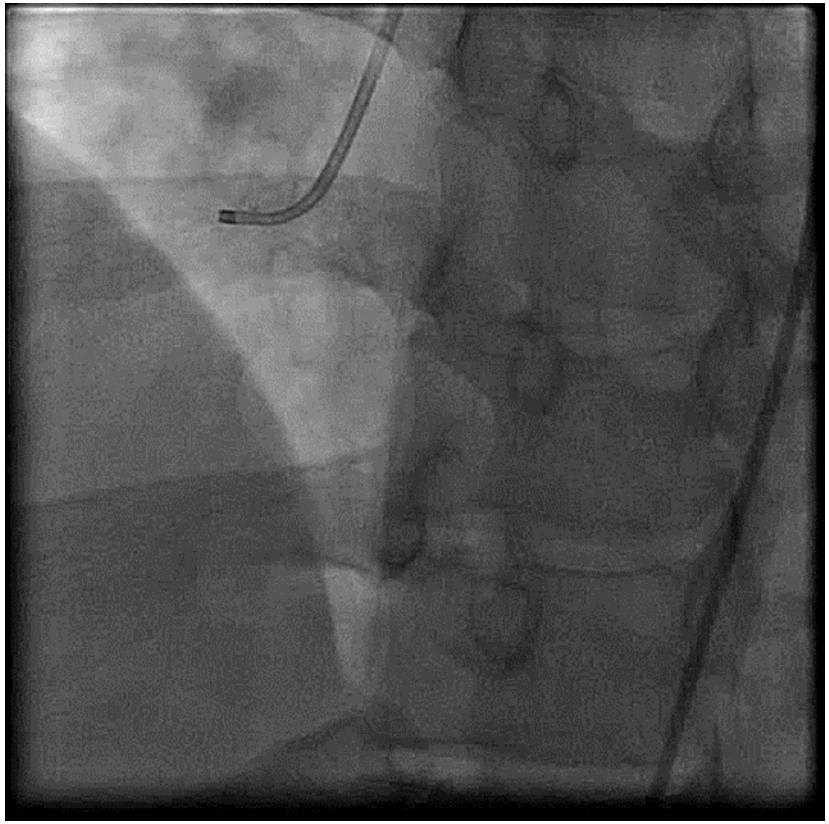

**ST-elevation Myocardial Infarction**

Ulcerated Plaque – Thrombus

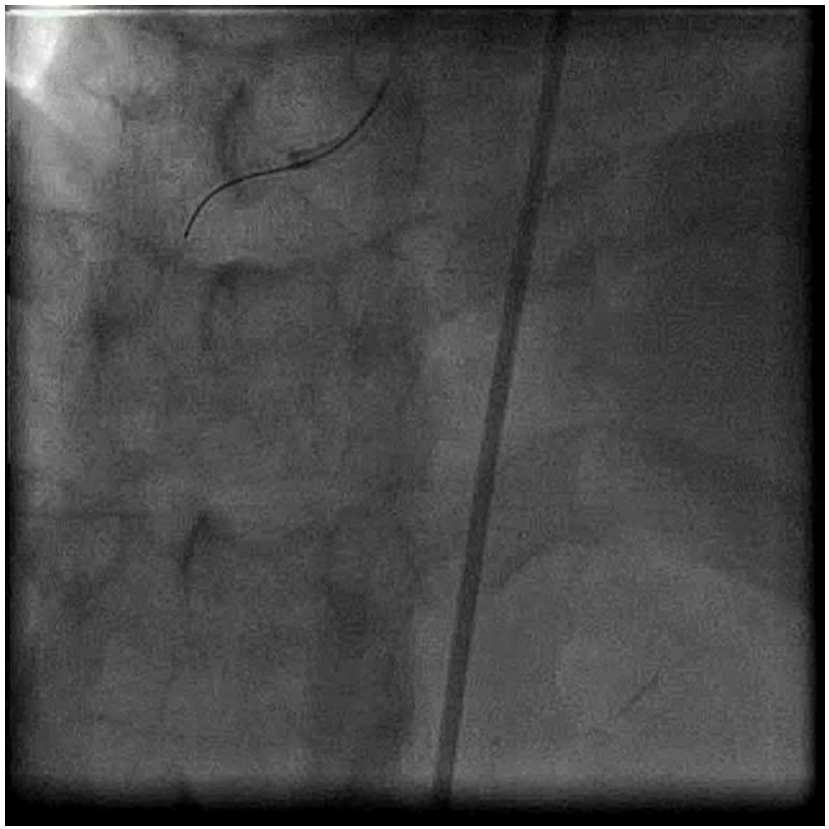
Complete occlusion

No distal blood flow

# STEMI

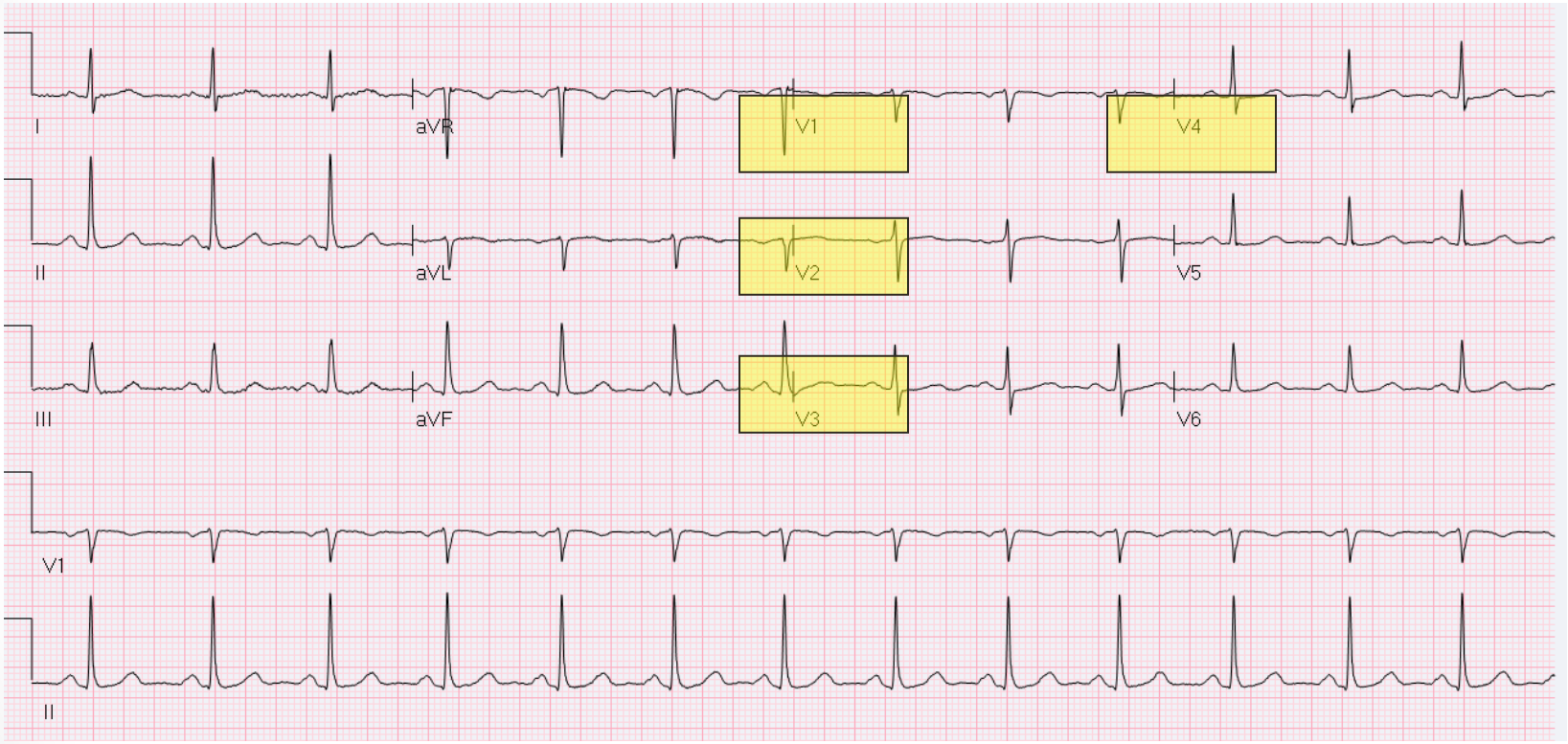


# STEMI



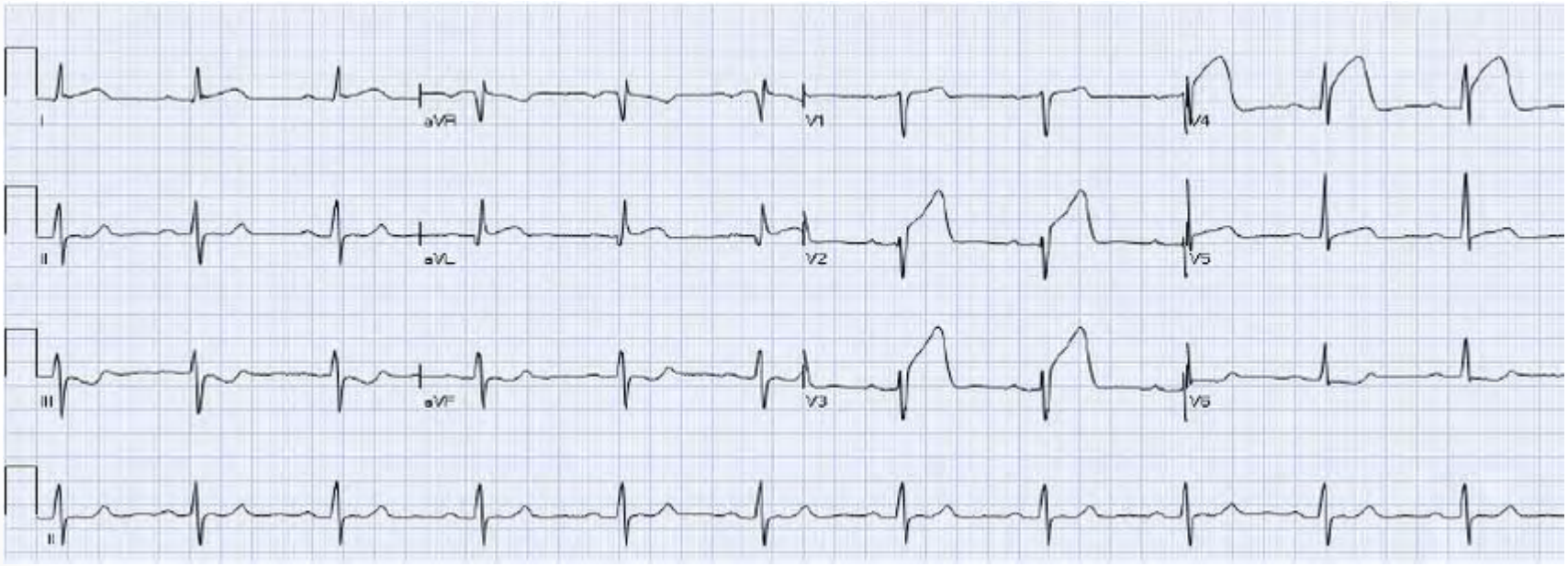
# Leads go together

## ST Elevations - Anterior



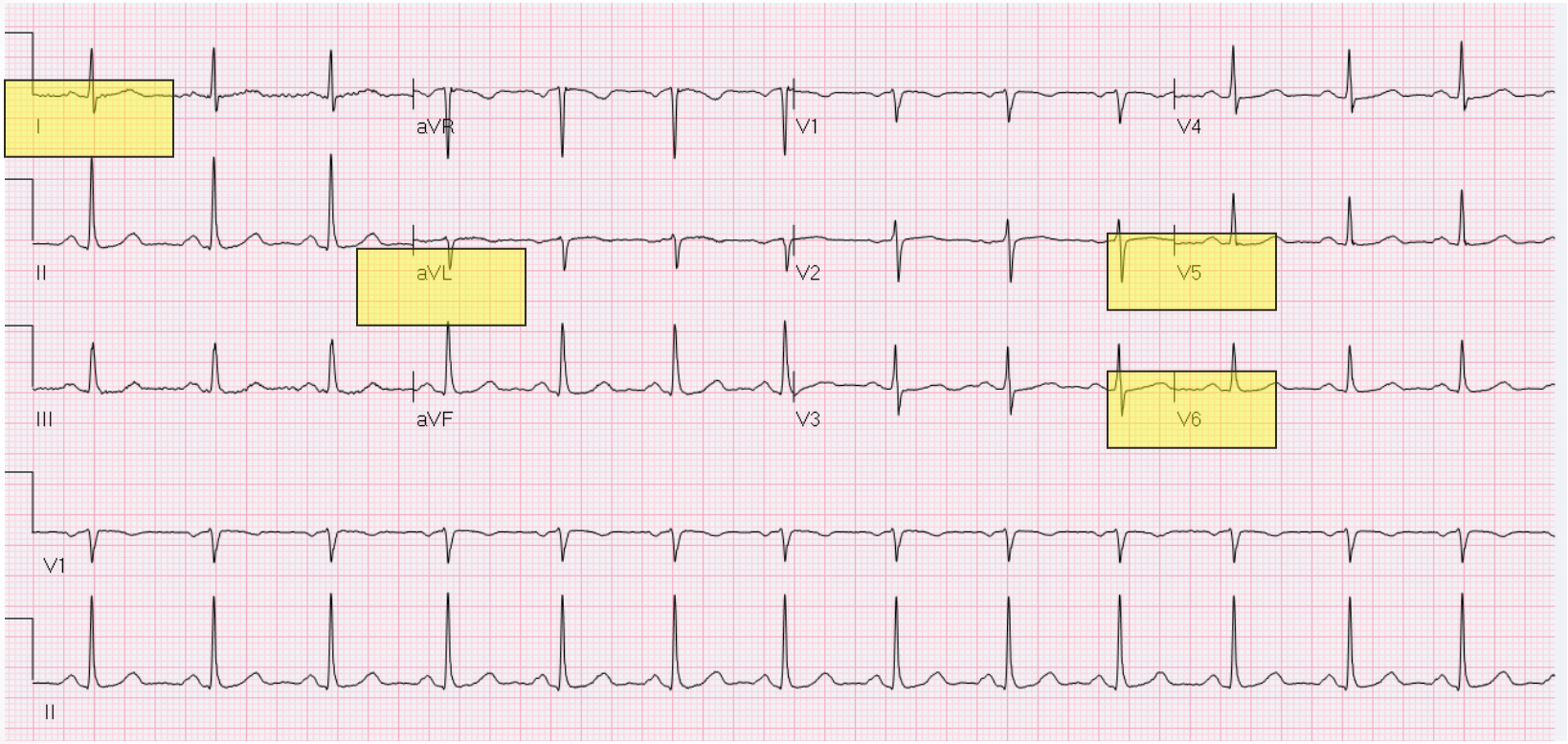
# Leads go together

## ST Elevations - Anterior



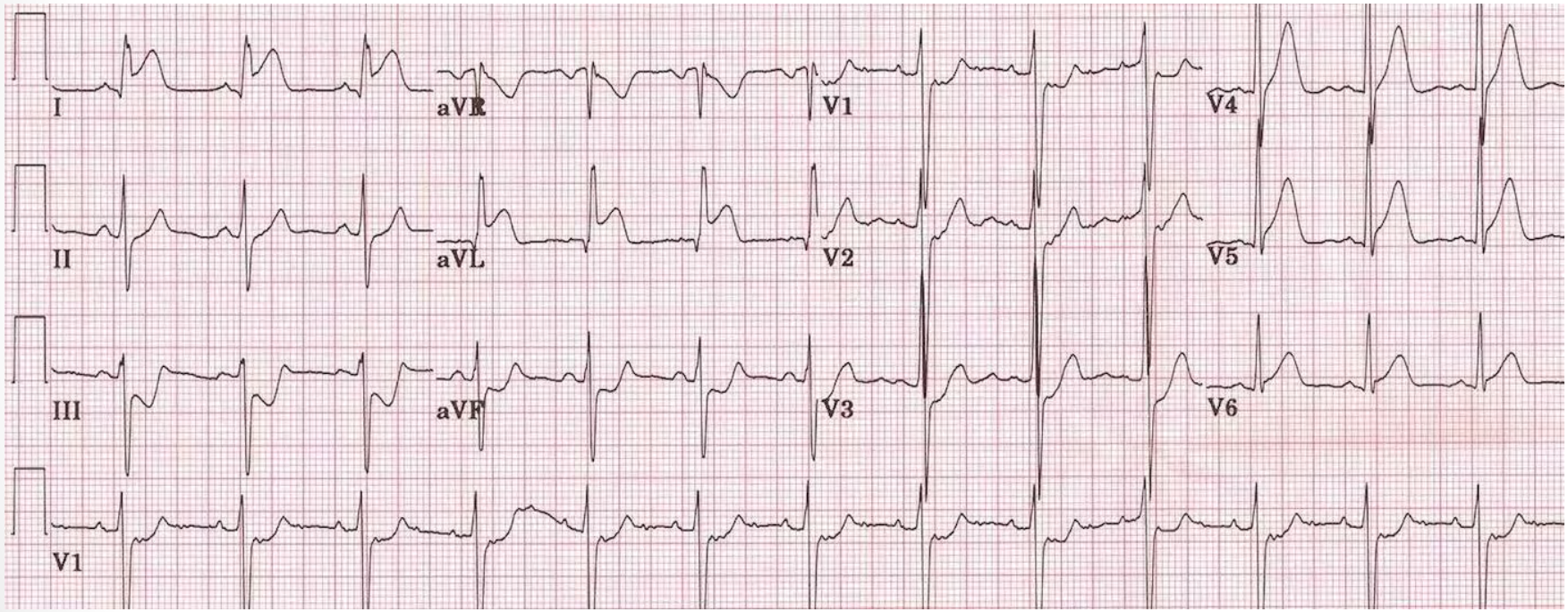
# Leads go together

## ST Elevations - Lateral



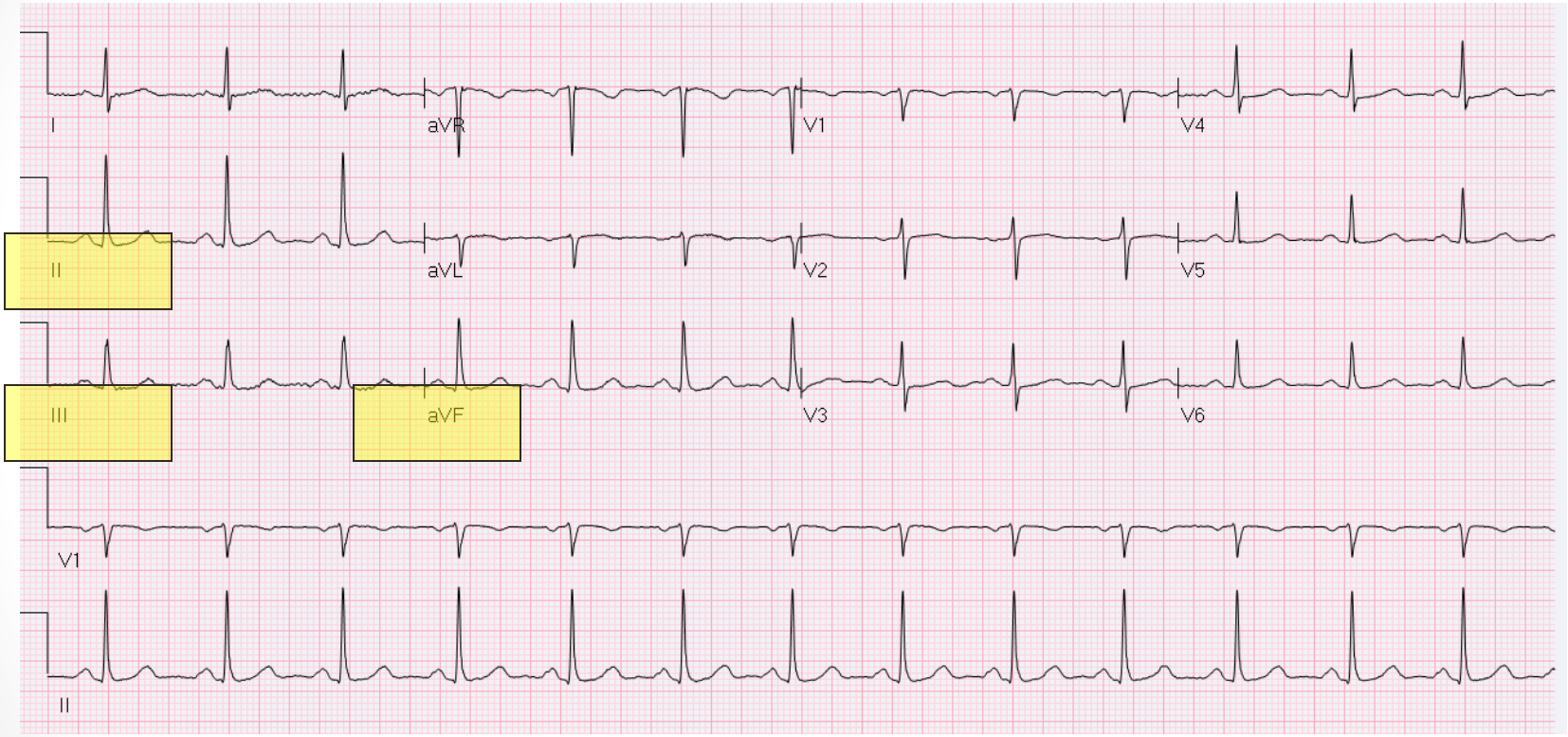
# Leads go together

## ST Elevations - Lateral



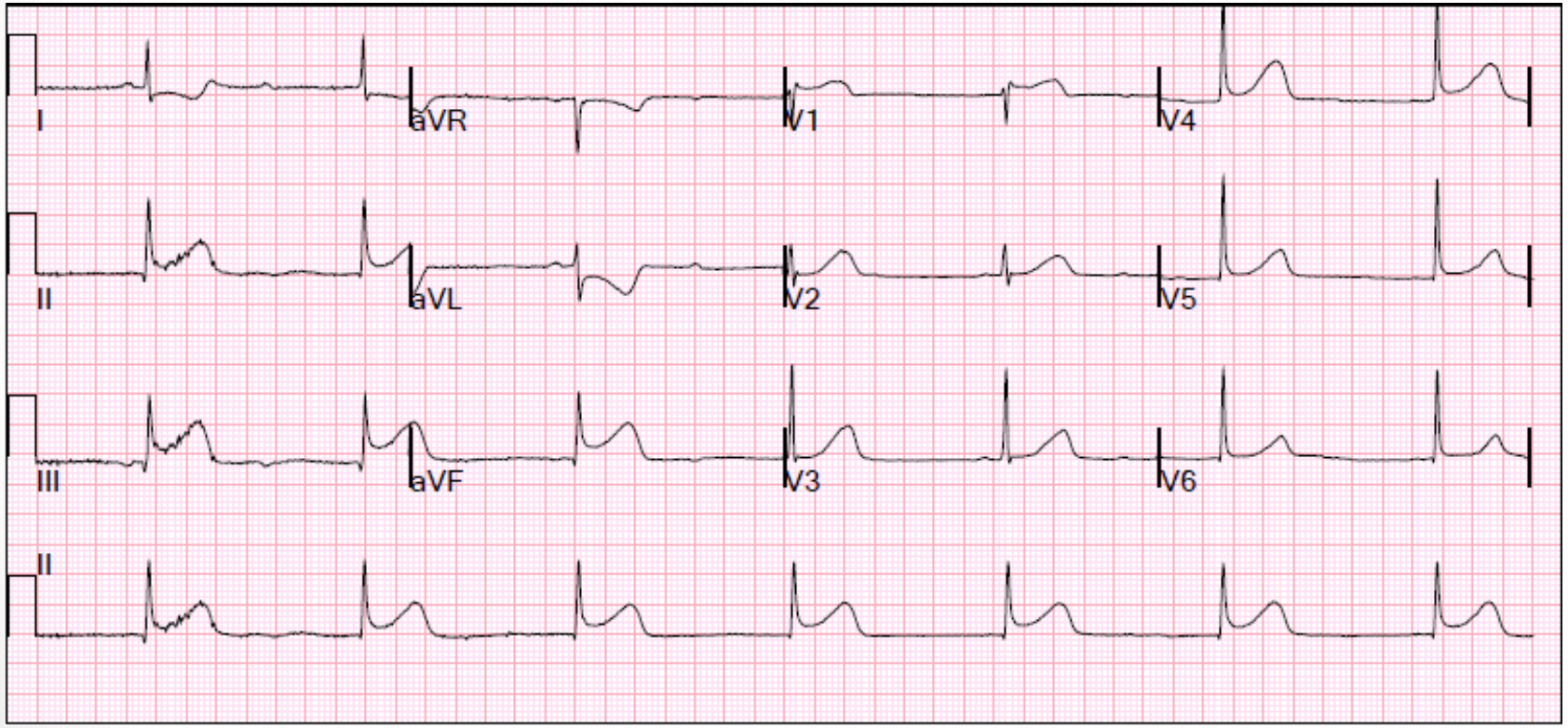
# Leads go together

## ST Elevations - Inferior



# Leads go together

## ST Elevations - Inferior



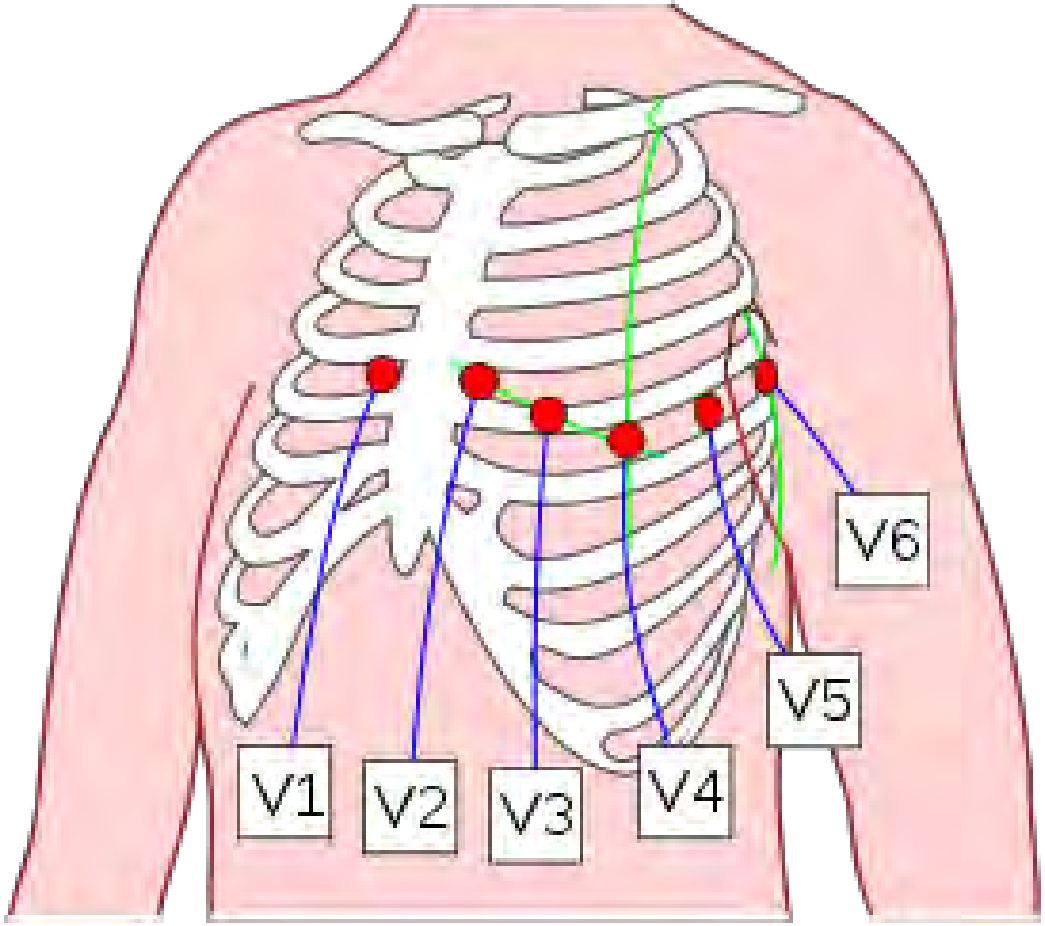
# Coronary Artery Territories

- Left anterior descending artery
  - Anterior → V1-V4
- Left circumflex artery
  - Lateral → I, L, V5, V6
- Posterior descending artery
  - Inferior → II, III, F
  - Branch of **right coronary artery 90%**
  - LCX 10%

# Special Complications

## Inferior MI

- Right ventricular infarction
  - Loss of right ventricular contractility
  - **Elevated jugular venous pressure**
  - Decreased preload to left ventricle → **hypotension**
  - Diagnosis: Right sided chest leads

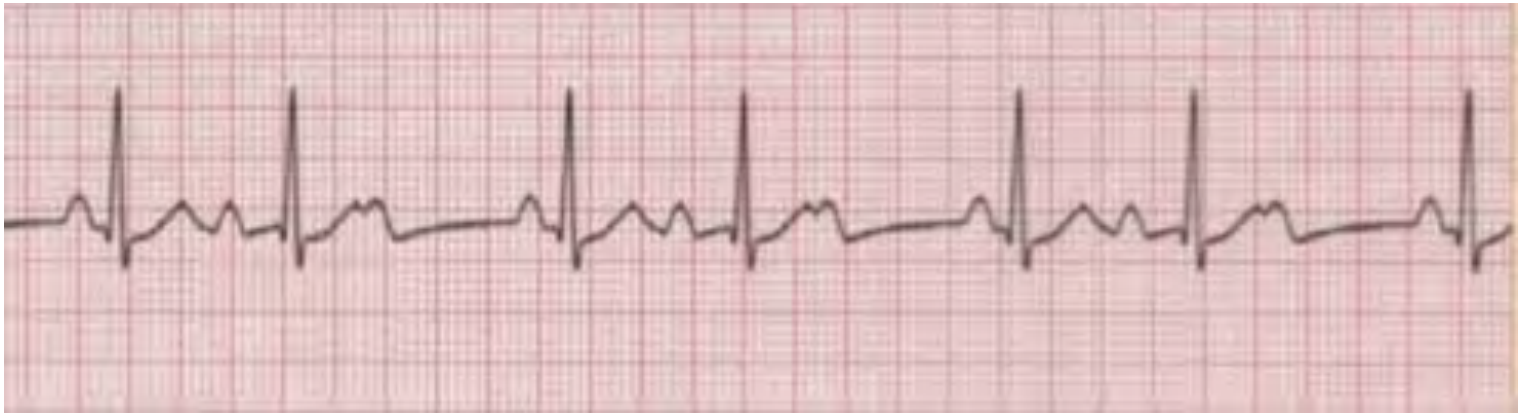



Jmarchn/Wikipedia

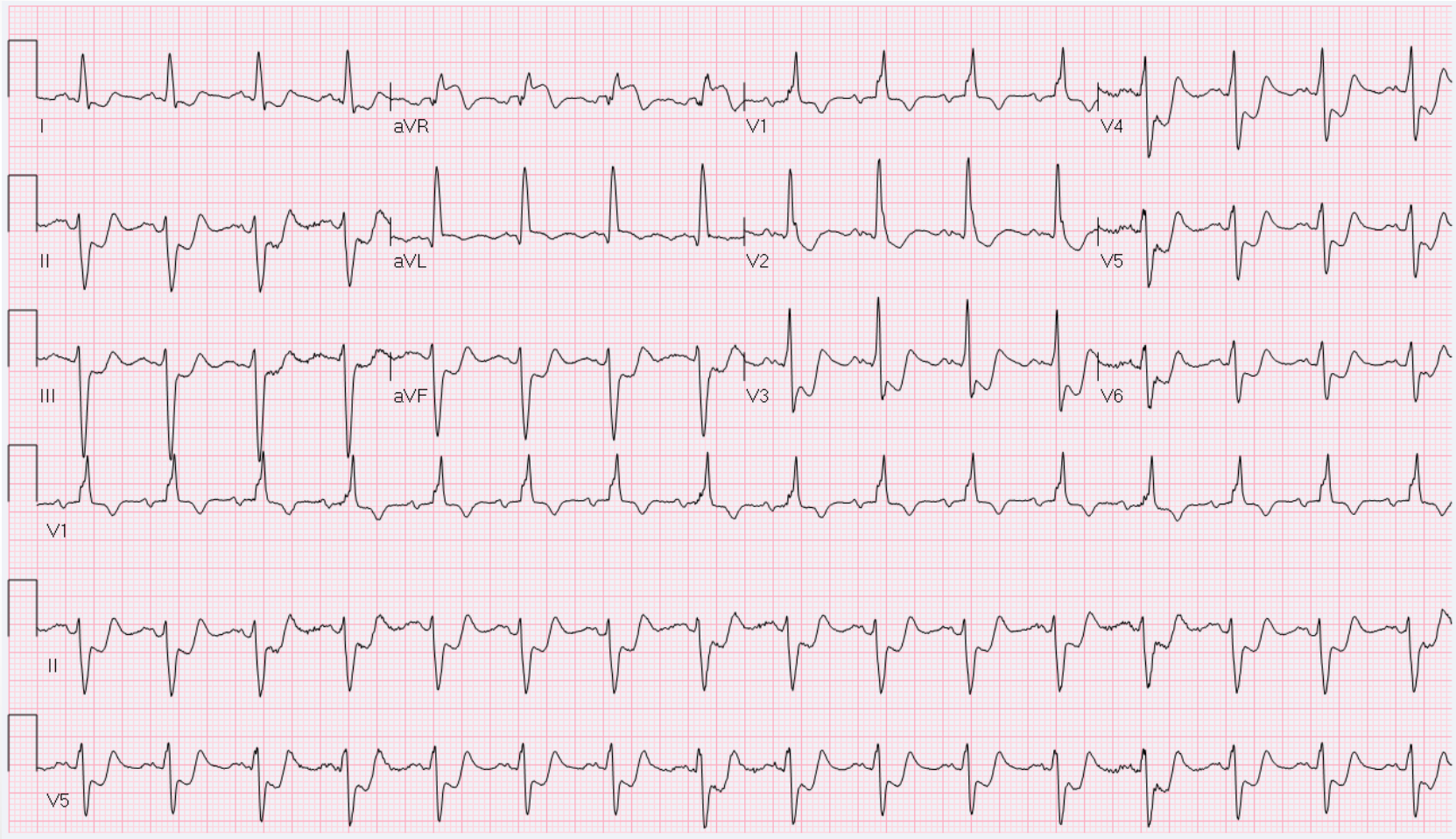
# Special Complications

## Inferior MI

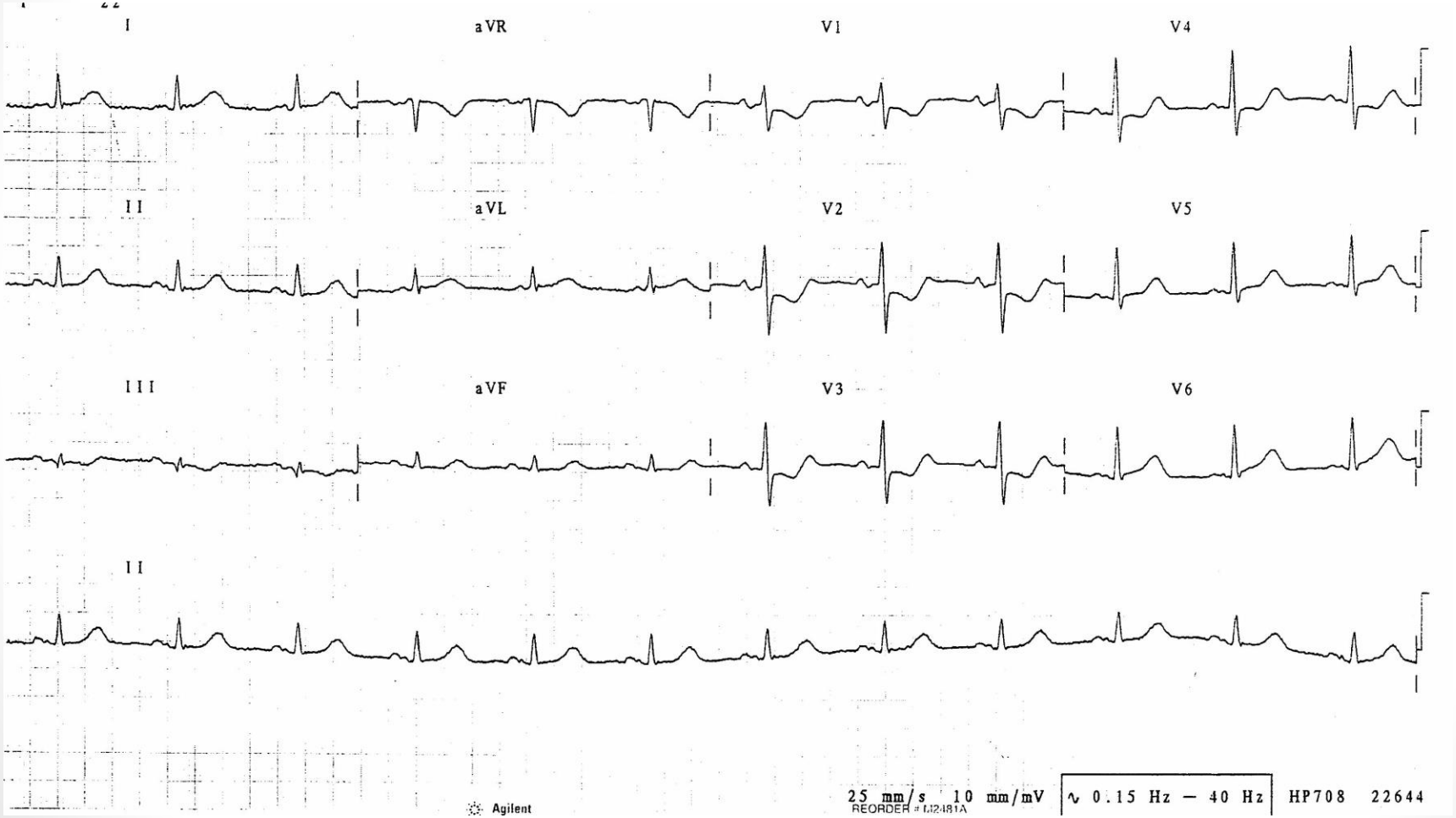
- Sinus bradycardia and heart block
  - **Vagal stimulation** from inferior wall ischemia



# Left Main Occlusion



# Posterior Myocardial Infarction



# STEMI

## Special Subtypes

- Left main
  - **ST-elevation aVR**
  - Diffuse ST depressions
- Posterior
  - Anterior ST depressions with standard leads
  - ST-elevation in **posterior leads (V7-V9)**

# Treatment of STEMI

- "Time is muscle"
- Coronary artery occluded by thrombus
- Longer occlusion → more muscle dies
  - More likely the patient may die
  - More heart failure symptoms
  - More future hospitalization for heart disease
- **Medical emergency**

# Treatment of STEMI

- Main objective is to open the artery
  - "Revascularization"
- Option 1: Emergency angioplasty
  - Mechanical opening of artery
  - Should be done <90min
- Option 2: Thrombolysis
  - Lysis of thrombus with drug
  - Should be done <30min
- "Door to balloon" or "door to needle"

# Treatment of STEMI

- Time matters
  - Medical therapy is supportive
  - Given while working to open artery
- Remember: this is a **thrombotic** problem
  - Aspirin to inhibit platelet aggregation
  - Heparin to inhibit clot formation
- This is also an **ischemic** problem
  - Beta blockers to reduce O2 demand
  - Nitrates to reduce O2 demand

# Cautions

- Beta blockers
  - Inferior MI stimulates vagal nerve
  - **Bradycardia and AV block** can develop
- Nitrates
  - Occlusion of RCA can cause **RV infarct**
  - RV infarction → ↓ preload
  - Nitrates ↓ preload → **hypotension**

# Other STEMI Treatments

- Clopidogrel
  - ADP receptor blocker
  - Inhibits platelets
- Eptifibatide
  - IIB/IIIA receptor blocker
  - Inhibits platelets
- Bivalirudin
  - Direct thrombin inhibitor
  - Inhibits clot formation

# Typical STEMI Course

- Arrival in ER with chest pain 5:42pm
- EKG done 5:50pm
  - STEMI identified
- Cardiac cath lab activated for emergent angioplasty
- Meds given in ER
  - Aspirin
  - Metoprolol
  - Nitro drip
  - Heparin bolus
  - Transport to cath lab 6:15pm
- Artery opened with balloon 6:42pm
  - DTB time 60 minutes (ideal <90min)

# Typical STEMI Course

- Arrival in ER with chest pain 5:42pm
- EKG done 5:54pm
  - STEMI identified
- Meds given in ER
  - Aspirin
  - Metoprolol
  - Nitro drip
  - Heparin bolus
- tPA given based on weight 6:07pm
  - IV push
  - Door to needle time 25min (ideal <30)

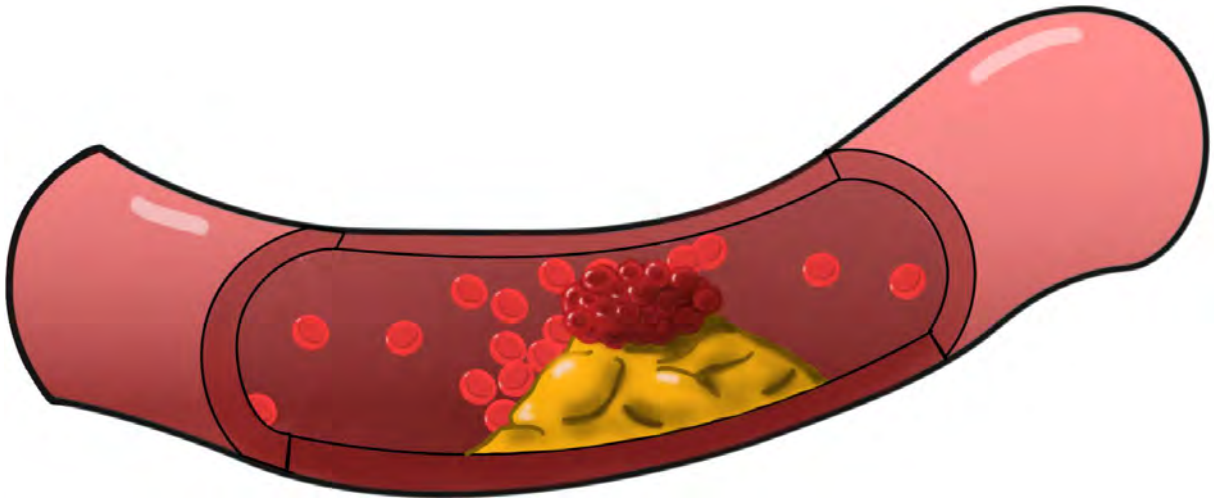
# NSTEMI and Unstable Angina

Jason Ryan, MD, MPH

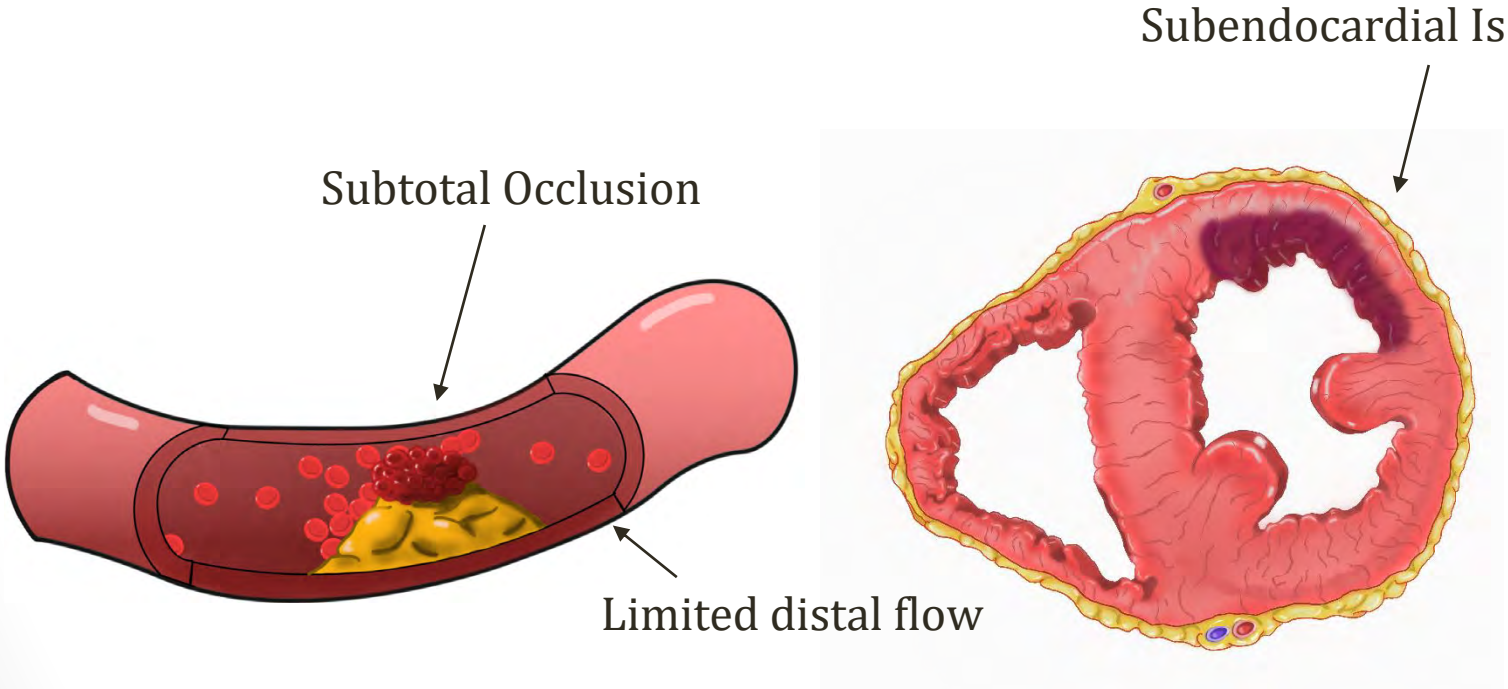
# NSTEMI

## Non-ST-Elevation Myocardial Infarction

- Atherosclerotic plaque rupture
- Thrombus formation
- Subtotal (<100%) vessel occlusion
- Ischemic chest pain



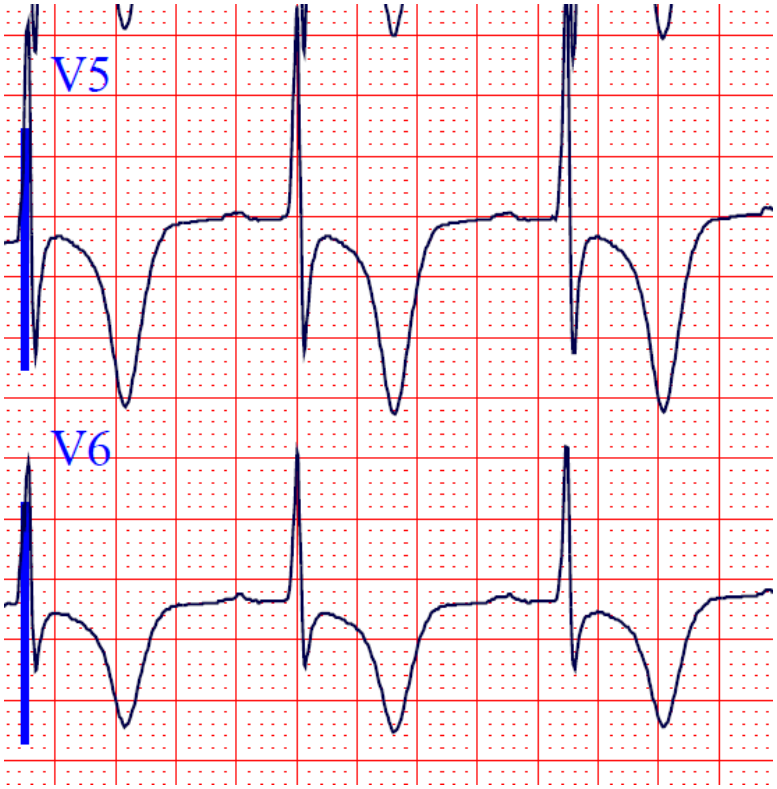
# Subendocardial Ischemia



# NSTEMI

## ECG Changes

- ST depressions
- T-wave inversions



# Cardiac Biomarkers

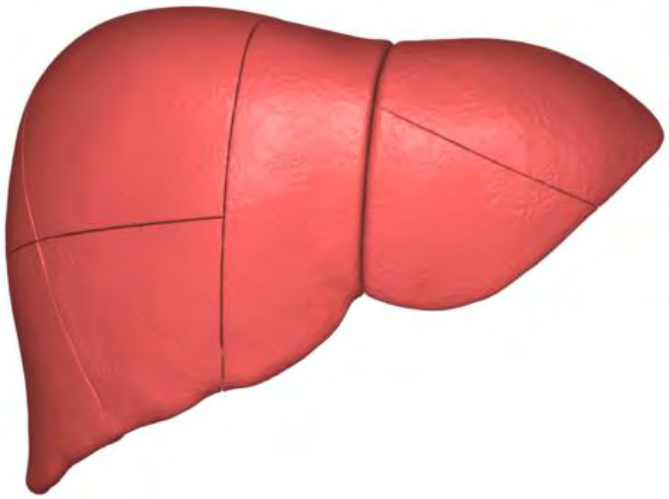
- Biomarkers spill into blood with cardiac injury
- Most common marker used: **Troponin I or T**
  - Increase 2-4 hours after MI
  - Stay elevated for weeks
- **CK-MB also used**
  - Increase 4-6 hours after MI
  - Normalize within 2-3 days

# Cardiac Biomarkers

- Several types of CK
  - MM – Skeletal muscle
  - MB – Cardiac
  - BB – Brain
- Most tissues have some of all three
- Ratio of MB to total CK can be used in ischemia
  - Helpful when total CK also up due to muscle damage

# Cardiac Biomarkers

- Some AST found in cardiac cells
  - Abdominal pain with isolated ↑ AST could be MI



Bodyparts3D/Wikimedia Commons

# Treatment of NSTEMI

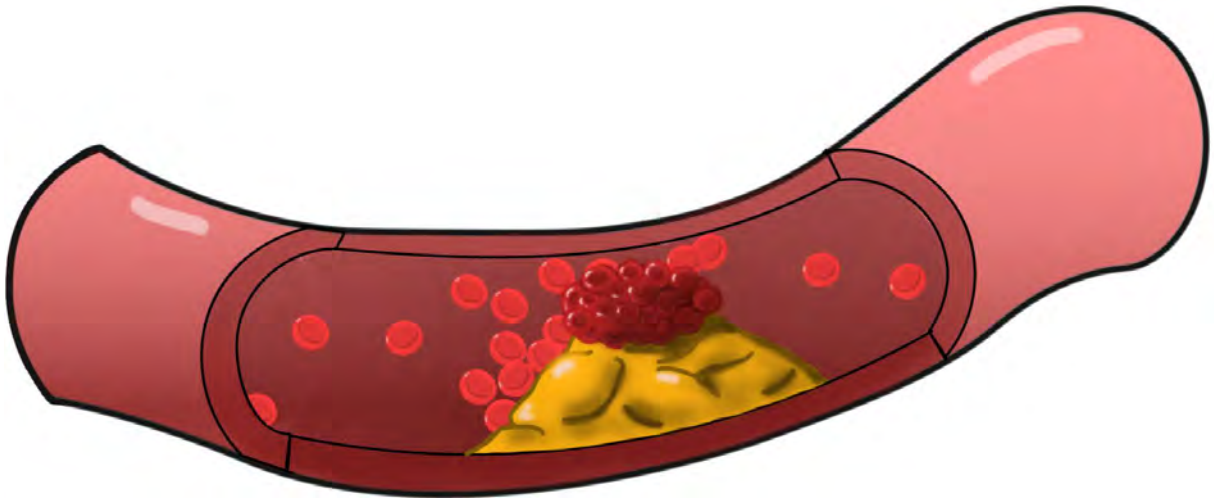
- Thrombotic and ischemic syndrome (like STEMI)
- Unlike STEMI:  No “ticking clock”
  - Subtotal occlusion
  - Some blood flow to distal myocardium
  - No emergency angioplasty
  - No benefit to thrombolysis
- Aspirin
- Beta blocker
- Heparin
- Angioplasty (non-emergent)

# Typical NSTEMI Course

- Presents to ER with chest pain
- Biomarkers elevated
- Medical Therapy
  - Aspirin
  - Metoprolol
  - Heparin drip
- Admitted to cardiac floor
- Hospital day 2 → angiography
- 90% blockage of LAD → Stent

# Unstable Angina

- Atherosclerotic plaque rupture
- Thrombus formation
- Subtotal (<100%) vessel occlusion
- Ischemic chest pain
- **Normal biomarkers**



# Unstable Angina

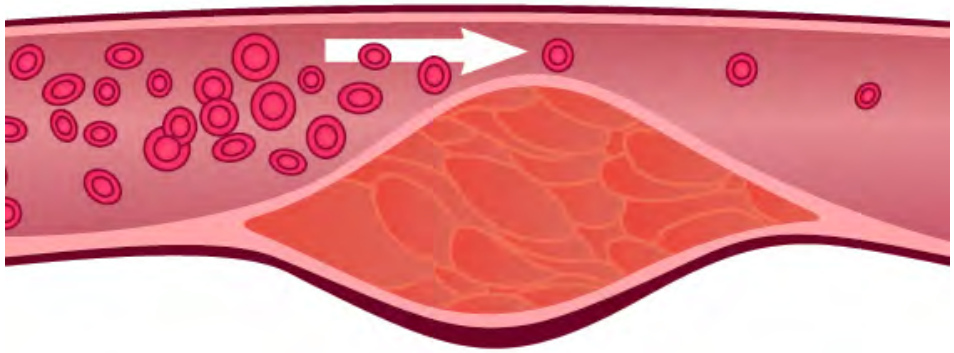
- Diagnosis largely based on **patient history**
  - Chest pain increasing in frequency/intensity
  - Chest pain at rest
- ECG may show ST depressions or T wave inversions
- Treatment is same as for NSTEMI
- Condition often called “UA/NSTEMI”

# Stable Angina

Jason Ryan, MD, MPH

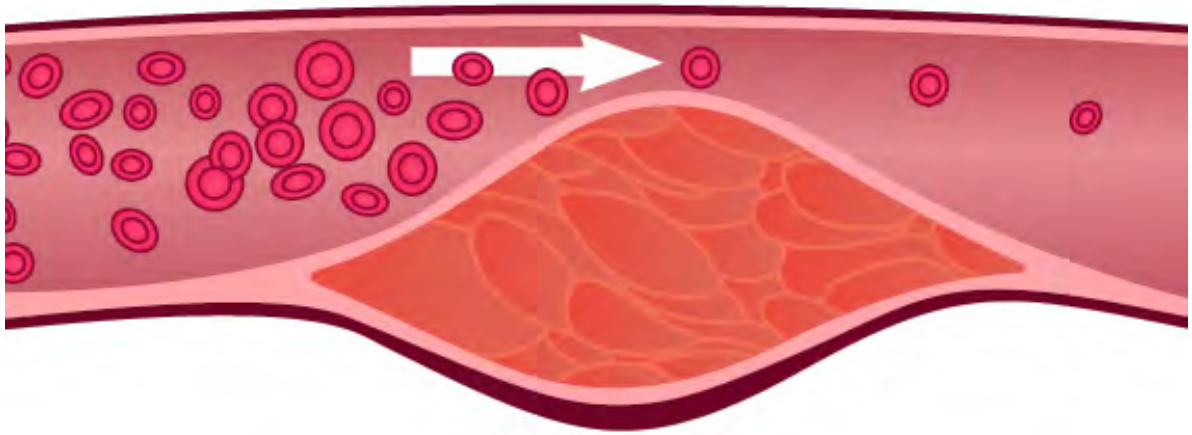
# Stable Angina

- Ischemic chest pain with exertion
- Relieved by rest
- Stable pattern over time
- **Stable coronary atherosclerotic plaque**
- No plaque rupture/thrombus



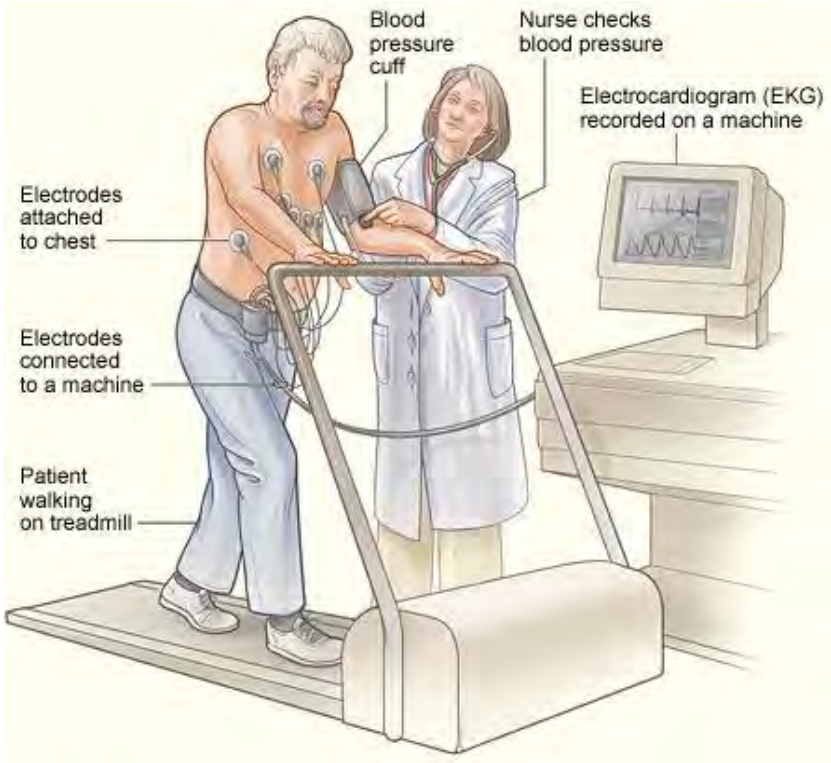
# Stable Angina

- Symptoms generally absent until ~75% occlusion
- Distal arteriolar dilation → normal flow if <75%



# Stable Angina

- Diagnosis: cardiac stress test
- Increases demand for O2




Wikipedia/Public Domain

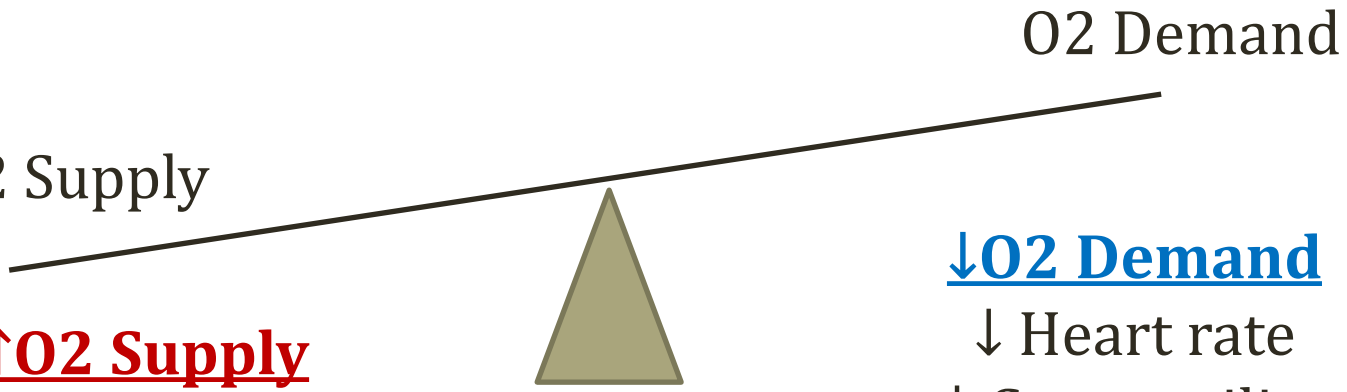
# Stable Angina

- NOT a thrombotic problem
- No role for heparin or antithrombotic drugs
- In US usually treated with revascularization
  - Most common indication PCI, CABG is stable angina
  - Recent clinical trials suggest medical therapy may work just as well as PCI/CABG in some patients

# Stable Angina: Typical Case

- 65-year old man with chest pain while walking
- Relieved with rest
- Presents to ED
  - EKG normal
  - Biomarkers normal
- Stress test
  - Walks on treadmill→ chest pain, EKG changes
- Cardiac catheterization performed
- 90% LAD artery blockage
- Stent placed → angina resolved

# Medical Therapy for Ischemia




**↑O2 Supply**

Dilate coronary arteries

Increase diastole

**↓O2 Demand**

↓ Heart rate

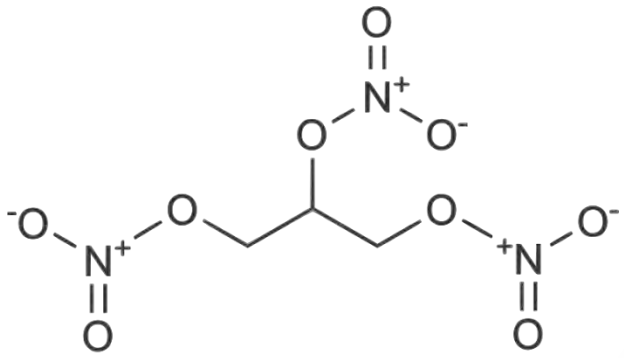
↓ Contractility

↓ Afterload

↓ Preload

# Nitrates

- Converted to nitric oxide → vasodilation
- Predominant mechanism is **venous dilation**
  - Bigger veins hold more blood
  - Takes blood away from left ventricle
  - **Lowers preload (LVEDV)**
- Also arterial vasodilation (art<< veins)
  - Increase coronary perfusion
  - Some peripheral vasodilation



Nitroglycerine

# Nitrates

- ↓ preload → ↓ cardiac output
- **Sympathetic nervous system activation**
- Increased heart rate/contractility
  - Increases O2 demand
  - Opposite of what we want to do for angina

# Nitrates

- Rare patients with complex CAD → angina
- In most patients, preload reducing effects dominate
  - Nitrates alone often improve angina
- **Co-administer beta-blocker or Ca channel blocker**
  - Blunts "reflex" effect

# Nitrates

## Forms

- Nitroglycerin Tablets/Spray
  - Rapid action ~5 minutes
  - Take during angina attack, before exercise
- Isosorbide Dinitrate
  - Effects last ~6hrs
- Isosorbide Mononitrate
  - Once daily drug
- Topical Nitroglycerin
  - Topical cream, patches

# Nitrates

## Adverse Effects

- Headache (meningeal vasodilation)
- Flushing
- Hypotension
- Angina
  - Reflex sympathetic activation

phee/Pixabay/Public Domain

# Nitrate Tolerance

- Drug stops working after frequent use
- Avoid continuous us for more than 24 hours
- Does not occur with daily isosorbide mononitrate


Jpeterson101/Wikipedia

# Nitrate Withdrawal

- Nitrate withdrawal (rebound) after discontinuation
- Occurs when using large doses of long-acting nitrates
- Angina frequency will increase

Freestocks.org

# Monday Disease

- Workers in nitroglycerin manufacturing facilities
- Regular exposure to NTG in the workplace
- Leads to the development of **tolerance**
- Over the weekend workers lose the tolerance
- "Monday morning headache" phenomenon
  - Re-exposed on Monday
  - **Prominent vasodilation**
  - Tachycardia, dizziness, and a headache

# Beta Blockers

- **Slow heart rate and decrease contractility**
- Increase preload (LVEDV)
  - Slower heart rate = more filling time
  - Increase O2 demand
  - Blunts some beneficial effect
- Reduced blood pressure (↓ afterload)
- **Net effect = less O2 demand**

# Beta Blockers

- For angina, generally use cardioselective (β1) drugs
  - Metoprolol, atenolol
- Some beta blockers are partial agonists
  - Pindolol, Acebutolol
  - Don’t use in angina

# Calcium Channel Blockers

- Three major classes of calcium antagonists
  - dihydropyridines (nifedipine)
  - phenylalkylamines (verapamil)
  - benzothiazepines (diltiazem)
- Vasodilators and negative inotropes

# Calcium Channel Blockers

- **Nifedipine: vasodilator**
  - Lower blood pressure
  - Reduce afterload
  - Dilate coronary arteries
  - May cause reflex tachycardia
- **Verapamil/diltiazem: negative inotropes**
  - Similar to beta blockers
  - Reduced heart rate/contractility
  - Can precipitate **acute heart failure if LVEF very low**

# Antianginal Therapy

## Nitrates/Beta Blockers

| | Nitrates | Beta blockers | Nitrates + Beta blockers |
|---|---|---|---|
| **Supply** | | | |
| Coronary vasodilation | **Increase** | -- | **Increase** |
| Duration diastole | **↓ reflex** | **Increase** | -- |
| | | | |
| **Demand** | | | |
| Preload | **Decrease** | **Increase** | **Decrease** |
| Afterload | **Decrease** | **Decrease** | **Decrease** |
| Contractility | **↑ reflex** | **Decrease** | **--/↓** |
| Heart Rate | **↑ reflex** | **Decrease** | **--/↓** |

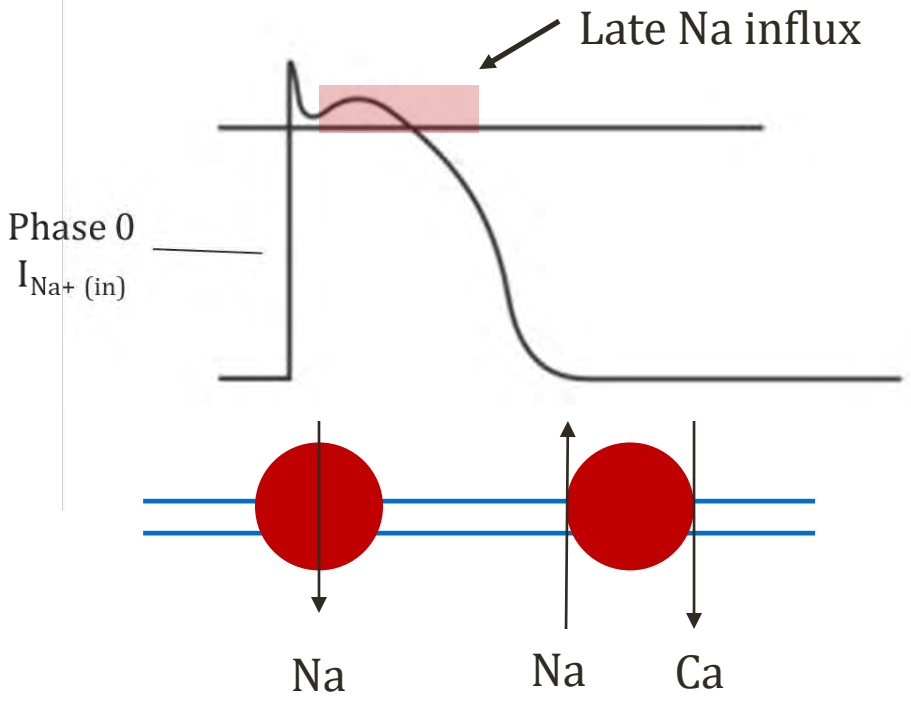
# Antianginal Therapy

## Calcium Channel Blockers

| | Verapamil | Diltiazem | Nifedipine |
|---|---|---|---|
| **Supply** | | | |
| Coronary vasodilation | -- | -- | **Increase** |
| Duration diastole | **Increase** | **Increase** | **↓ reflex** |
| | | | |
| **Demand** | | | |
| Preload | **Increase** | **Increase** | **--** |
| Afterload | **Decrease** | **Decrease** | **Decrease** |
| Contractility | **Decrease** | **Decrease** | **↑ reflex** |
| Heart Rate | **Decrease** | **Decrease** | **↑ reflex** |

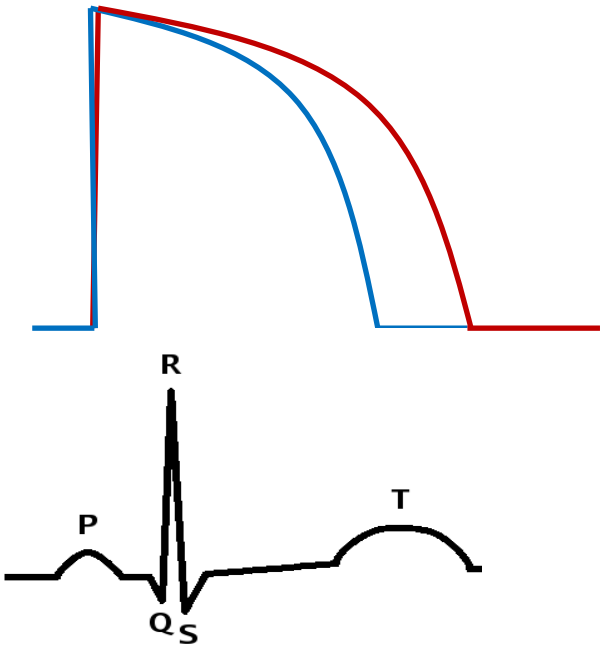
# Ranolazine

- Inhibits **late sodium current**
- Reduces **calcium overload** → high wall tension
- Reduces **wall tension** and O2 demand



# Ranolazine

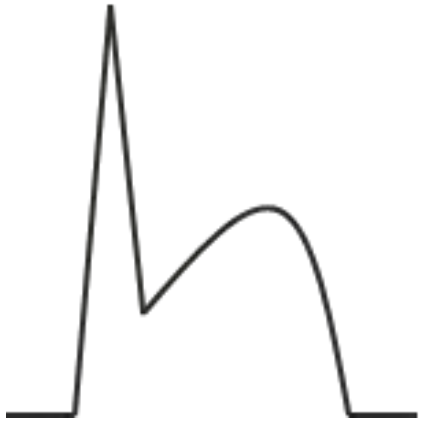
- Constipation, dizziness, headache
- QT prolongation (blockade of K channels)




Prolong QT

# Variant (Prinzmetal) Angina

- Ischemia from **vasospasm**
  - Not caused by atherosclerotic narrowing
  - Often artery is “clean” with no stenosis
  - May also occur near sites of mild atherosclerosis
- **Spontaneous** episodes of angina
- Transient myocardial ischemia
- **ST-segment elevation on ECG**



# Variant (Prinzmetal) Angina

- Episodes usually **at rest**
- Midnight to **early morning**
- Sometimes symptoms improve with exertion
- Associated with smoking

# Variant (Prinzmetal) Angina

## Diagnosis

- Usually based on history
- Intracoronary **ergonovine**
  - Acts on smooth muscle serotonergic (5-HT2) receptors
  - Can be administered during angiography
  - Vasospasm visualized on angiogram
- Intracoronary **acetylcholine**
  - Acts on endothelial muscarinic receptors
  - Healthy endothelium → vasodilation via nitric oxide
  - Endothelial dysfunction → vasoconstriction
  - Vasospasm visualized on angiogram

# Variant (Prinzmetal) Angina

## Treatment

- Quit smoking
- Calcium channel blockers, nitrates
  - Vasodilators
  - Dilate coronary arteries, oppose spasm
- **Avoid propranolol**
  - Non selective blocker
  - Can cause unopposed alpha stimulation
  - Symptoms may worsen

Pixabay/Public Domain

# Coronary Steal

- Mechanism of angina
- Induced by drugs
- Blood flow increased to healthy vessels
- Blood flow decreased in stenotic vessels
- Blood “stolen” from diseased coronary vessels

# Coronary Steal

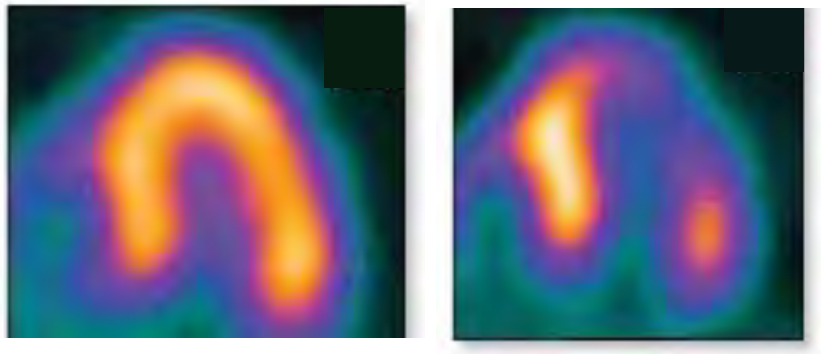
- Stenotic vessels
  - Significant (>75%) narrowing
  - **Arterioles maximally dilated** to maintain flow
- Normal vessels
  - No or minimal narrowing
  - **Arterioles NOT maximally dilated**

# Coronary Steal

- **Vasodilator** administered
- Stenotic vessels → no response
  - Arterioles already maximally dilated
- Normal vessels → vasodilation
- Flow increases to normal vessels
- Flow decreases to abnormal vessels
- Results: ischemia due to coronary steal

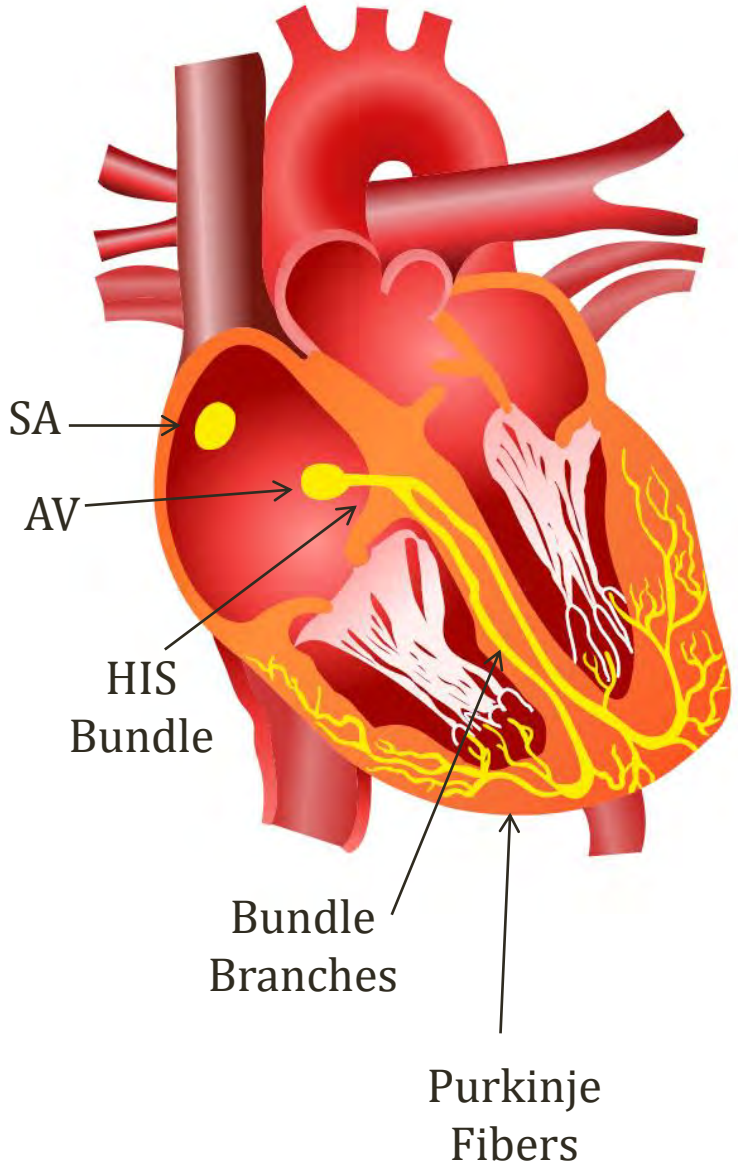
# Coronary Steal

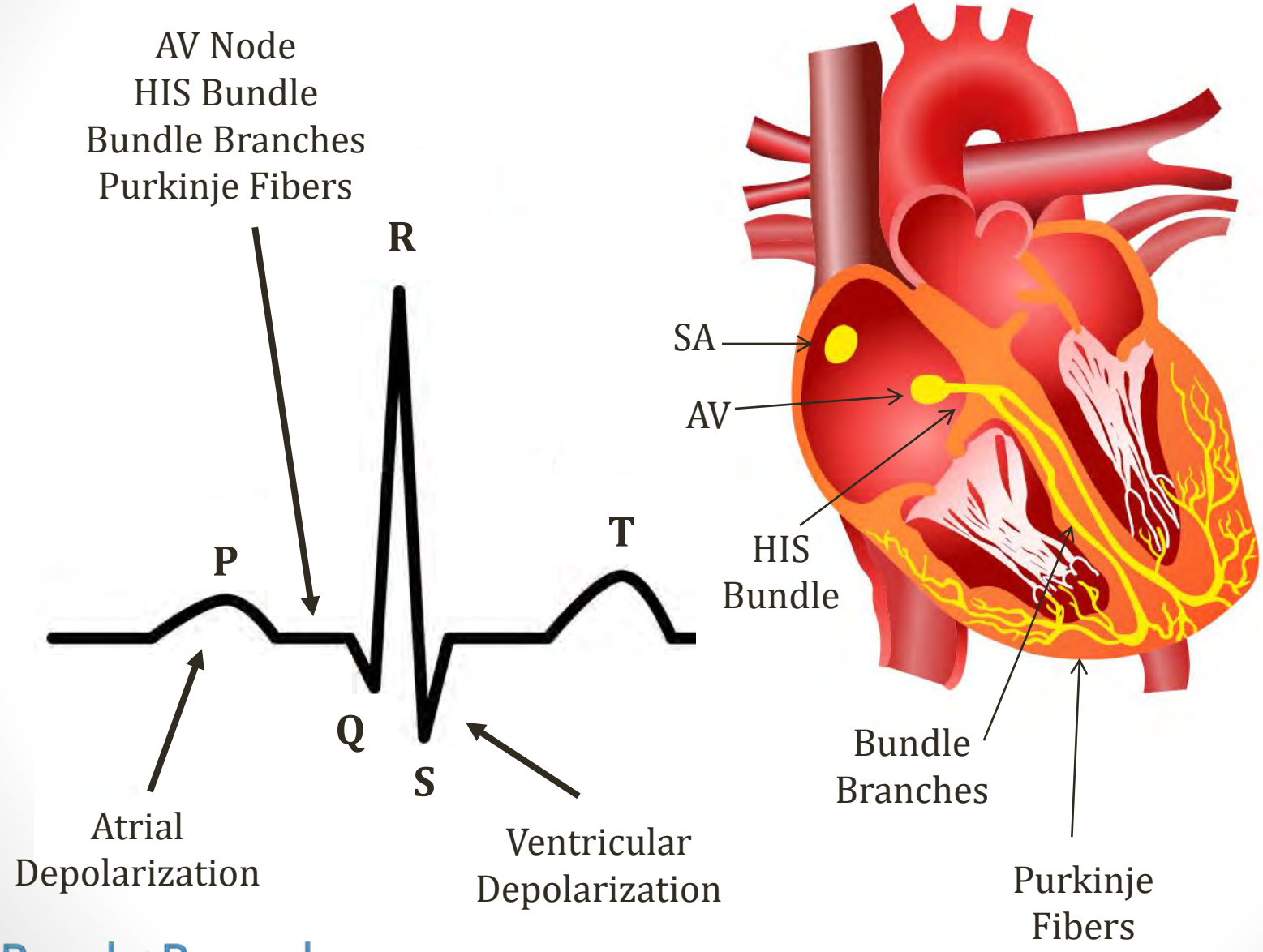
- Rarely seen with nitrates, nifedipine
- Key principle for **chemical stress tests**
  - **Adenosine, persantine, regadenoson**
  - **Potent, short-acting vasodilators**
  - Brief ↓ in blood flow to stenotic vessels → ischemia
  - Nuclear tracers can detect ↓ blood flow



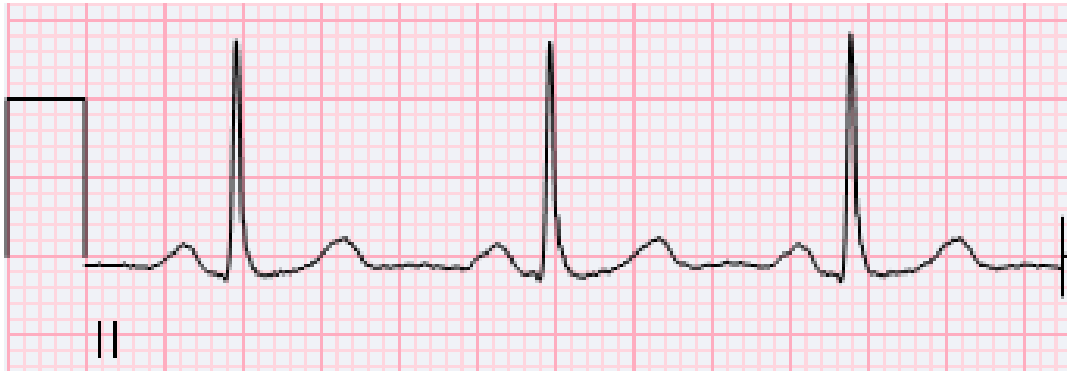
# EKG Basics

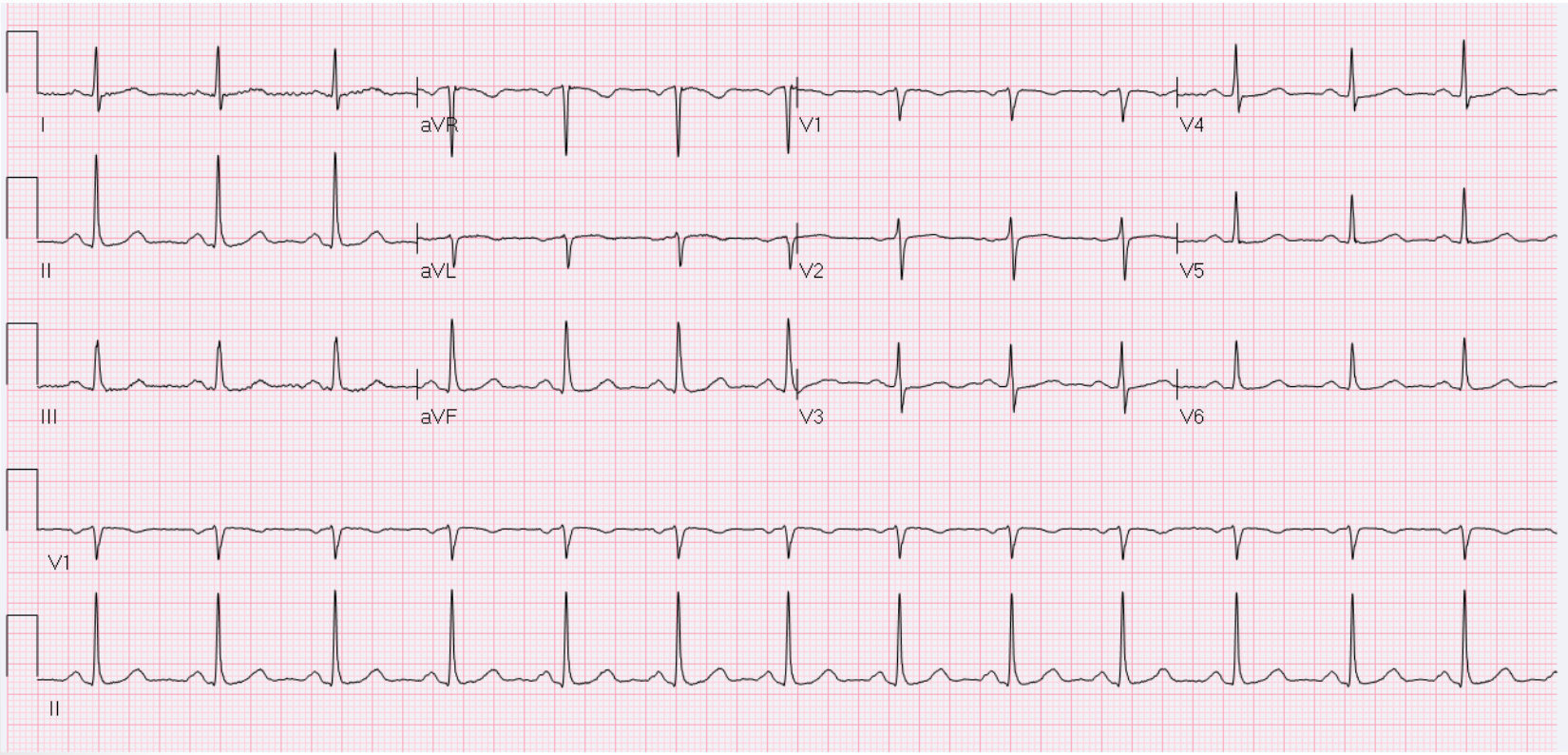
Jason Ryan, MD, MPH



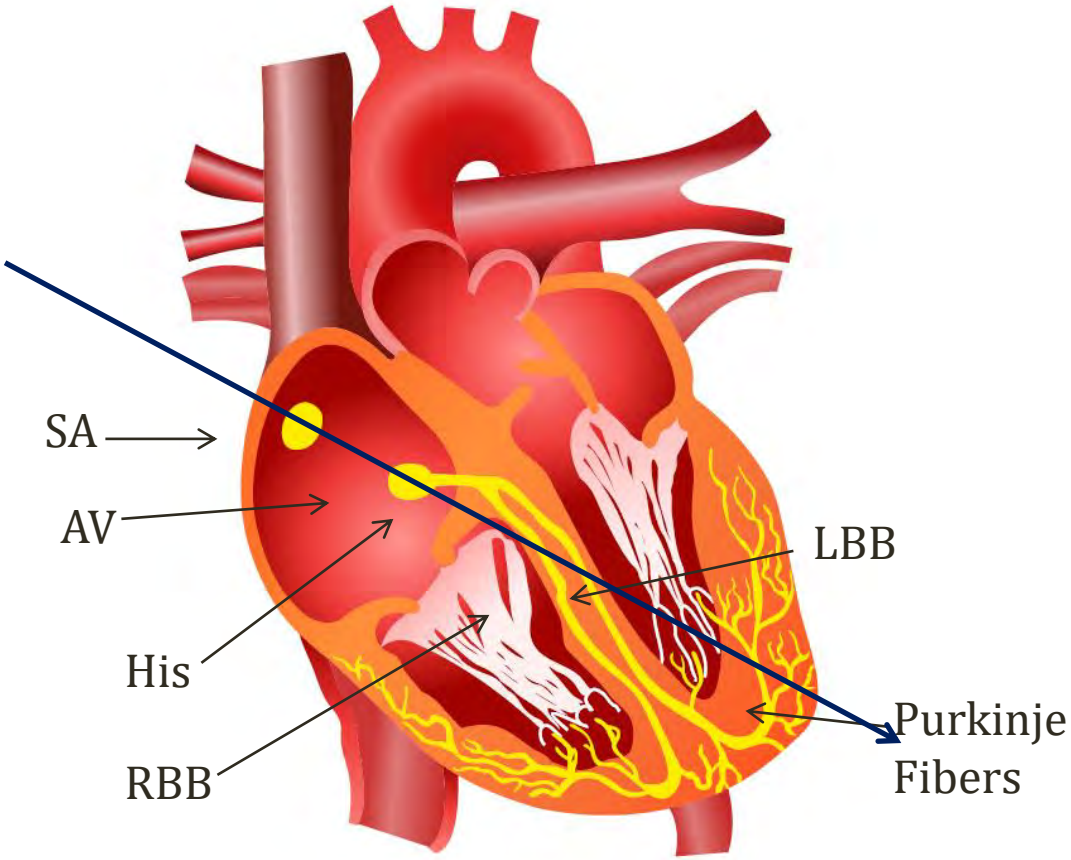


# EKG

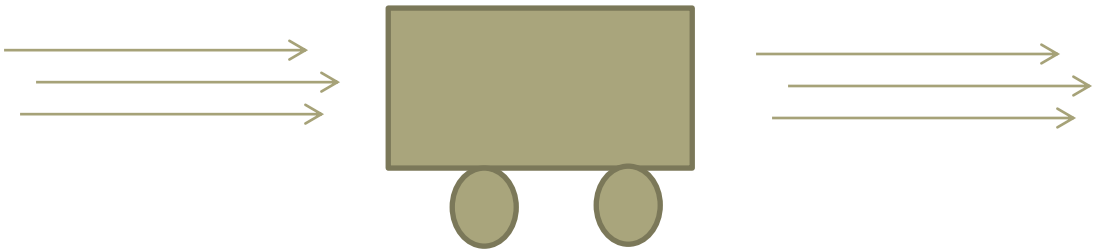


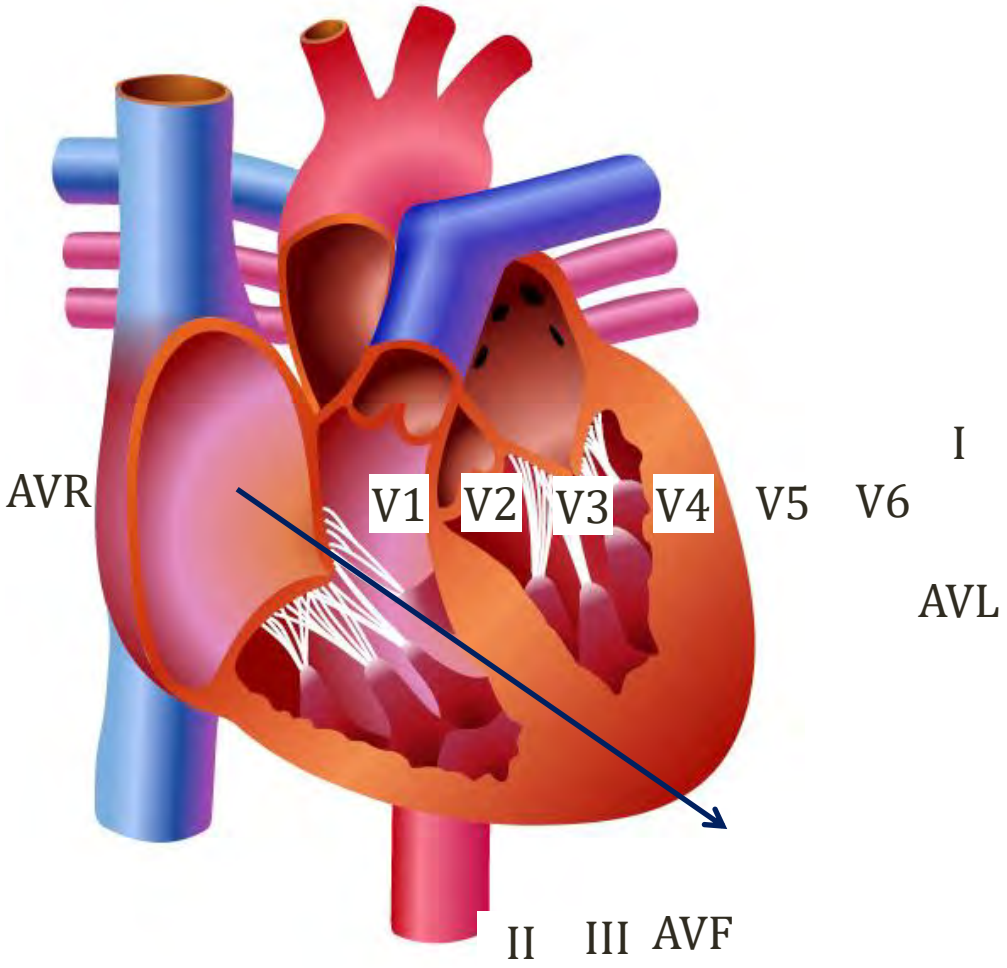
# EKG Electrical Activity



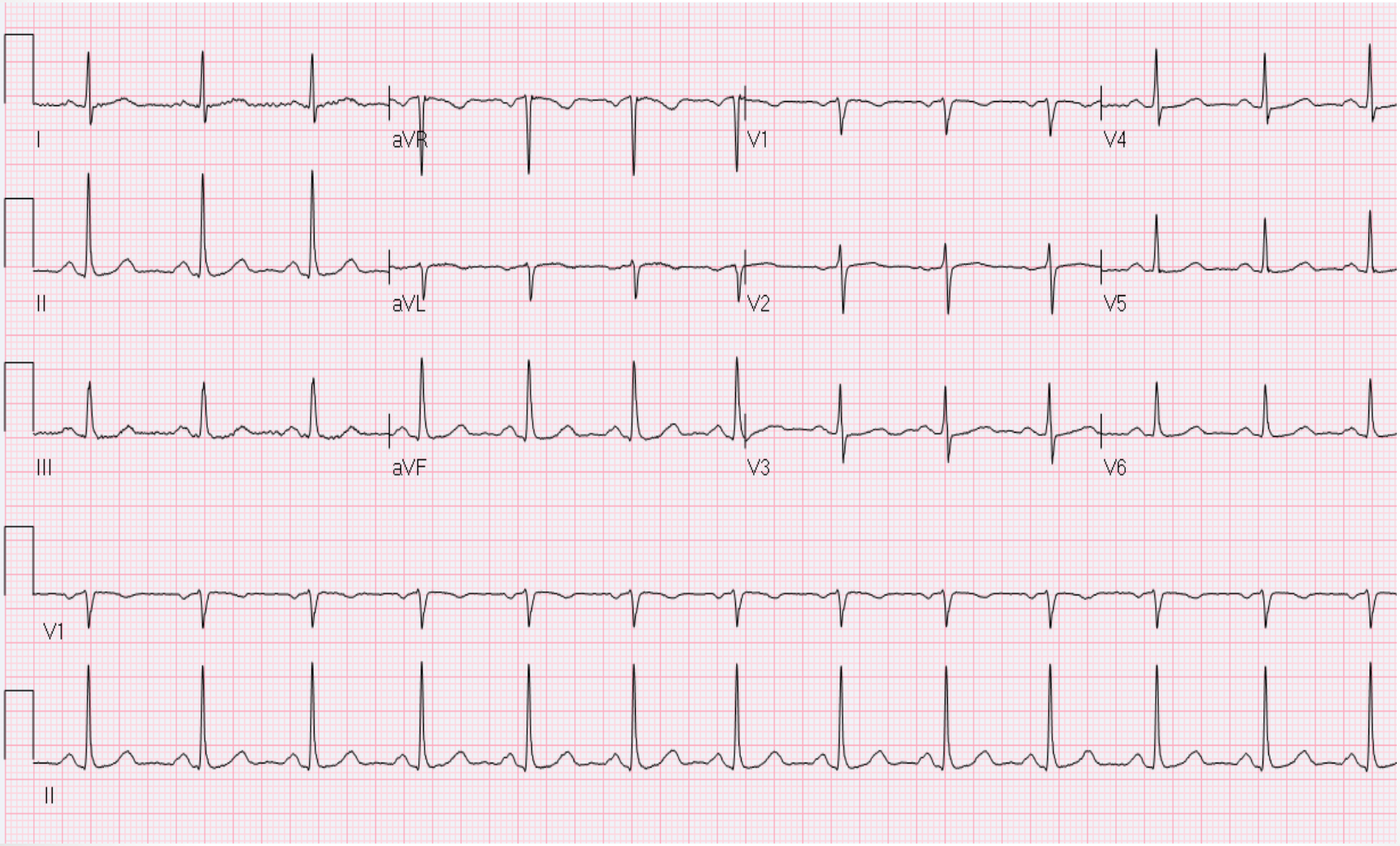
# EKG Electrical Activity



# EKG Electrical Activity



# EKG



# EKGs

## Key Principles

- #1: Waves represent repolarization/depolarization
- #2: EKGs have 12 leads
  - Each lead watches the same thing
  - Each lead watches from different vantage point
  - Electrical activity toward lead = upward deflection
  - Electrical activity away from lead = negative deflection

# Pacemakers

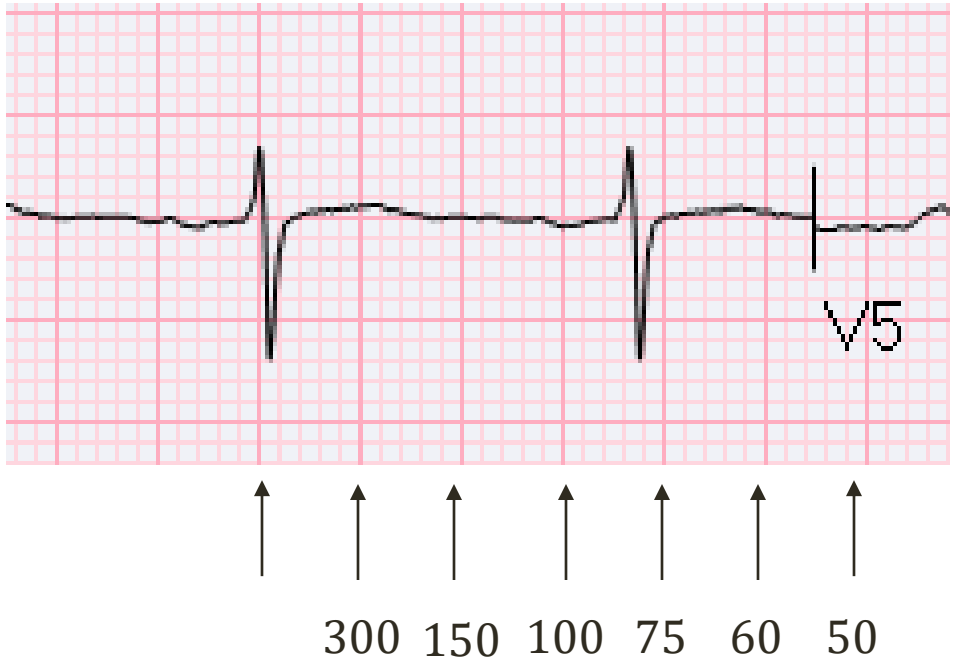
- SA node is dominant pacemaker of the heart
- Other pacemakers exist but are *slower*
- If SA node fails, others takeover
  - SA node (60-100 bpm)
  - AV node (40-60 bpm)
  - HIS (25-40 bpm)
  - Bundle branches (25-40 bpm)
  - Purkinje fibers (25–40 bpm)

# Conduction Velocities

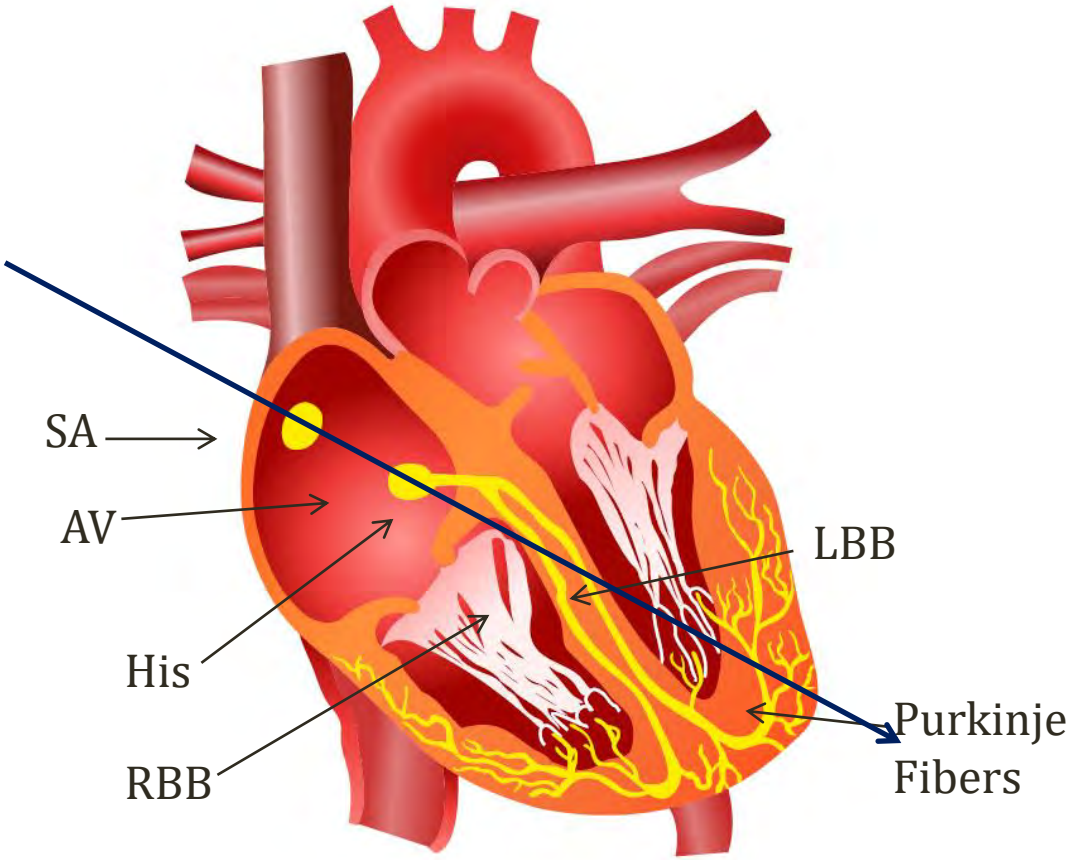
- SLOWEST conduction is through AV node
  - Very important so ventricle has time to fill
- Purkinje fibers → fastest conduction
- Purkinje > Atria > Vent > AV node

# Determining Heart Rate

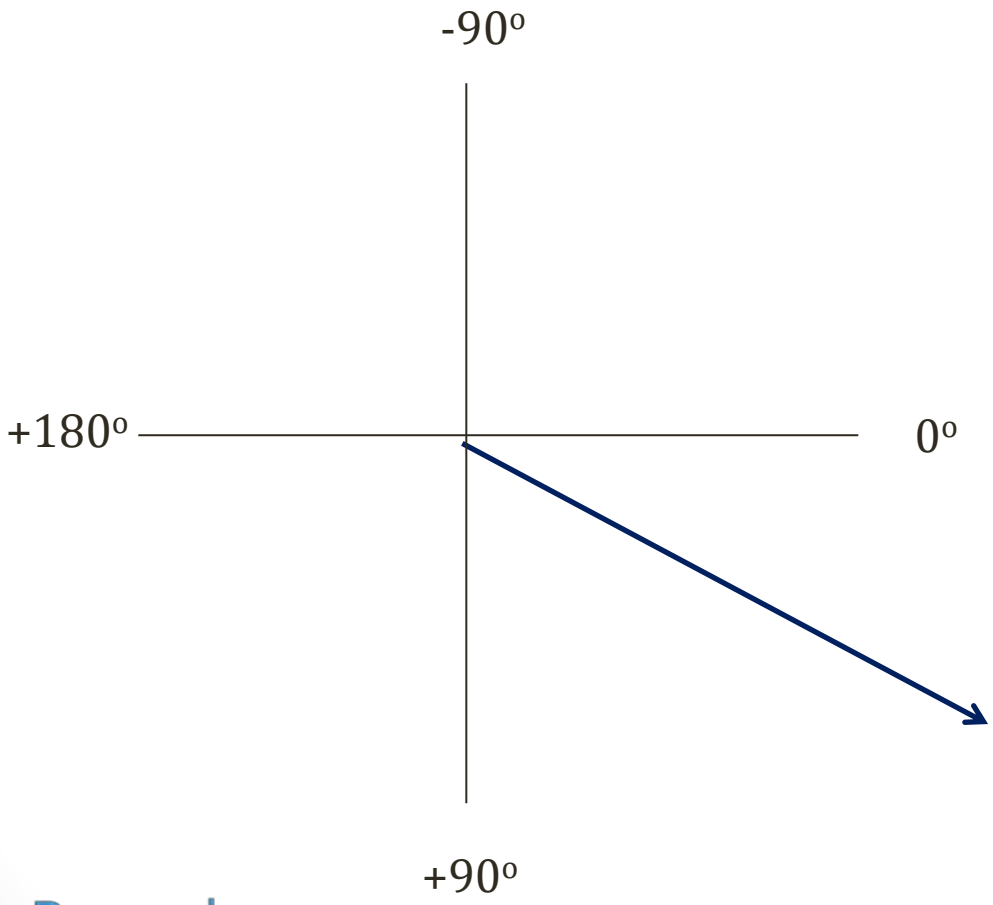
- 3 – 5 big boxes between QRS complex



# QRS Axis

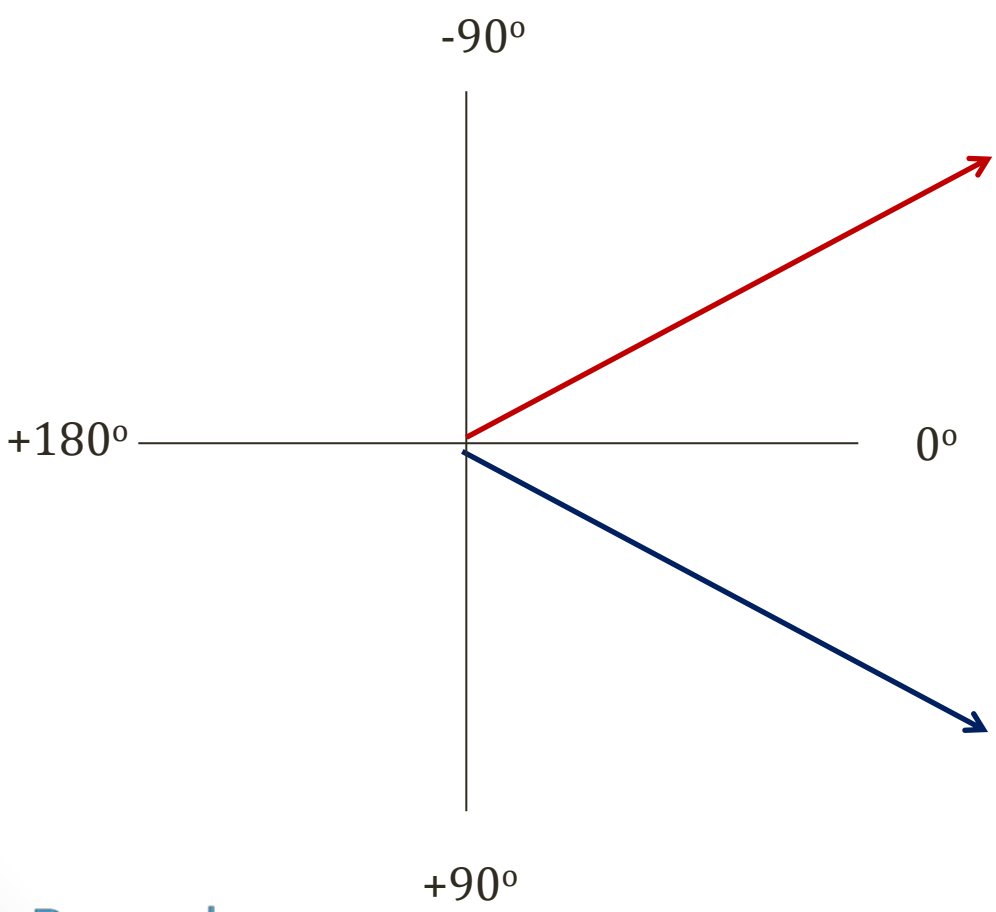


# QRS Axis




<u>Normal QRS Axis</u>
-30 and +90 degrees

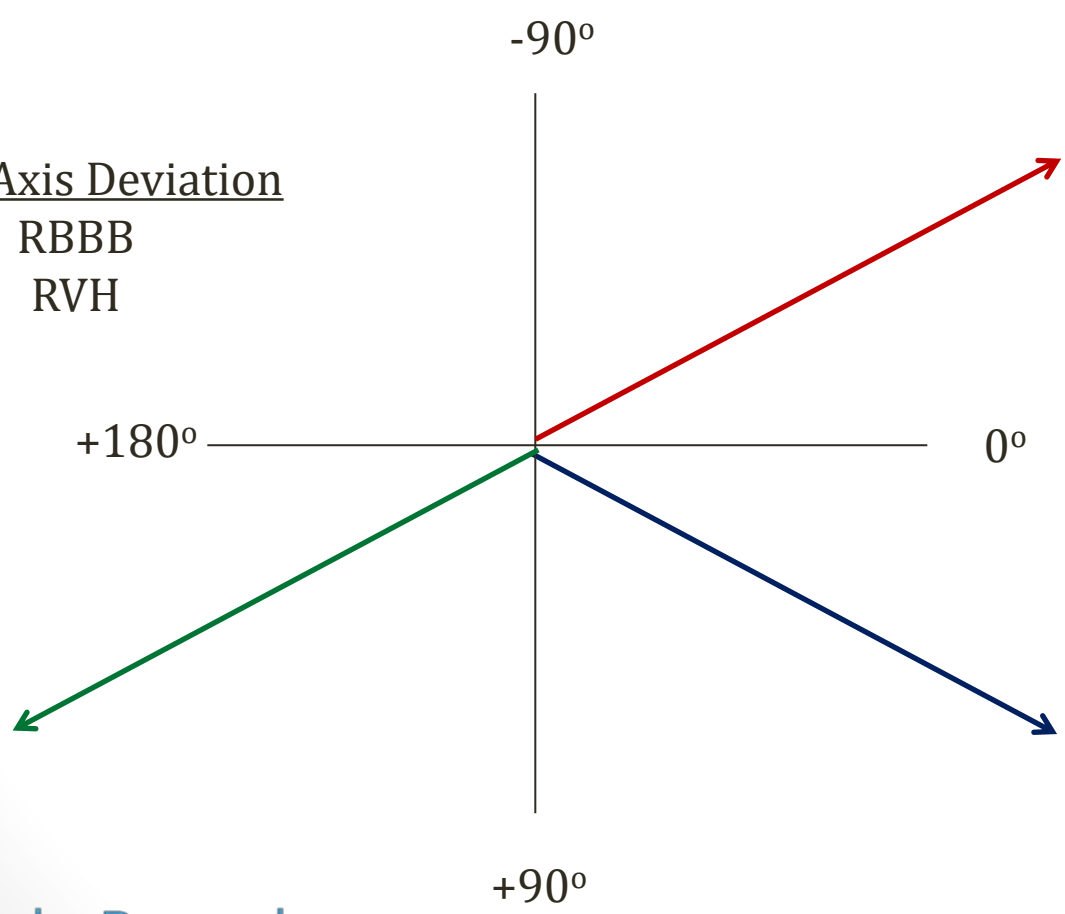
# QRS Axis




<u>Left Axis Deviation</u>
LBBB
Ventricular Rhythm

<u>Normal QRS Axis</u>
-30 and +90 degrees

# QRS Axis

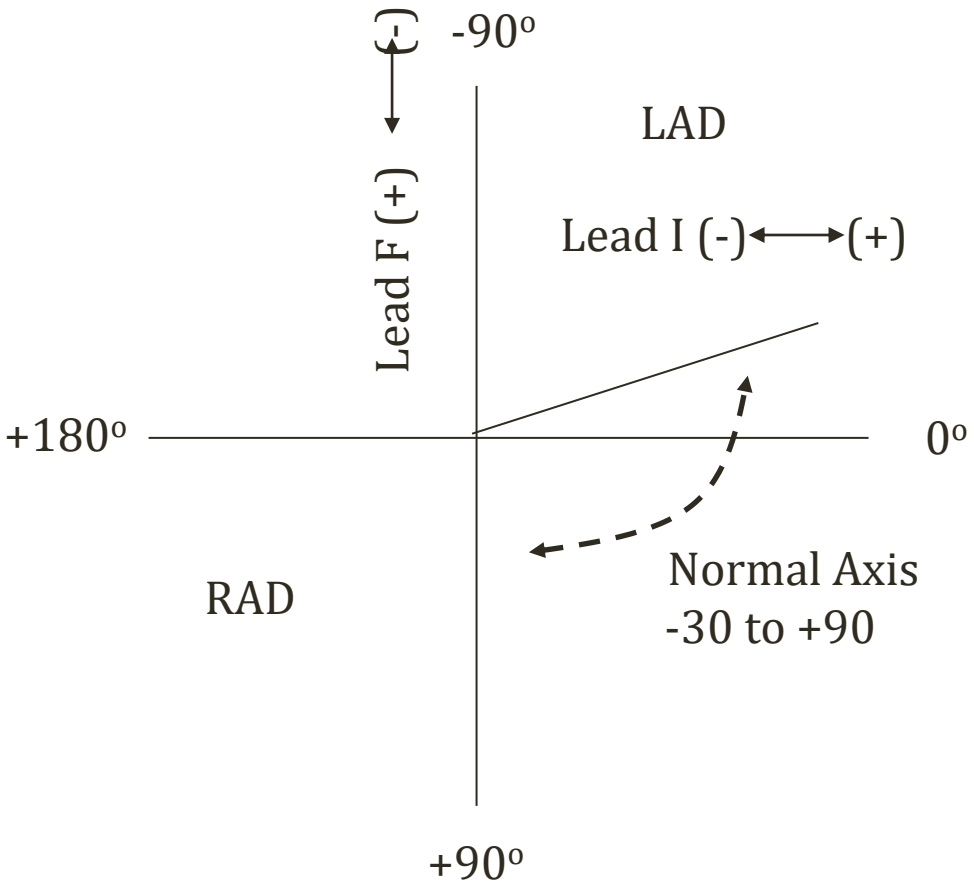



Left Axis Deviation
LBBB
Ventricular Rhythm

Right Axis Deviation
RBBB
RVH

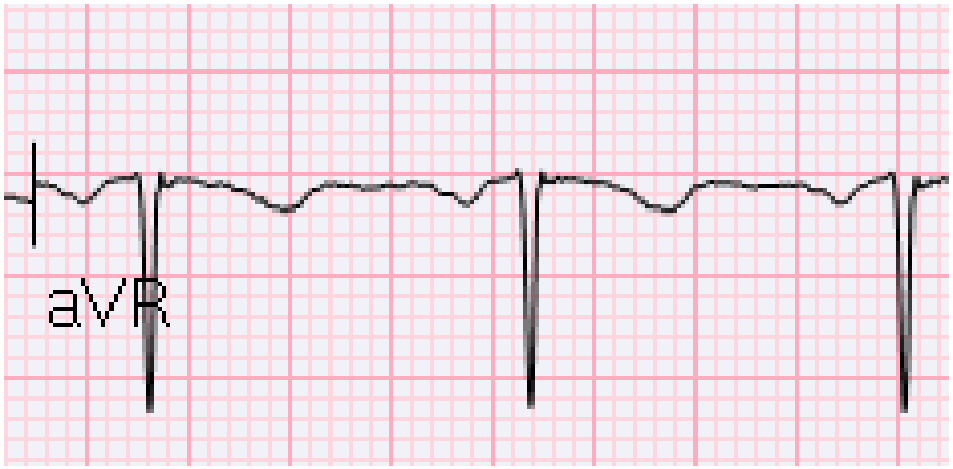
Normal QRS Axis
-30 and +90 degrees

# Determining Axis



# Axis Quick Method

- First, glance at aVr.
- It should be negative
- If upright, suspect limb lead reversal

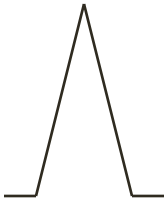



**Normal**

# Axis Quick Method

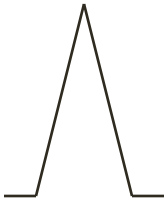
- If leads I and II are both positive, axis is normal

Lead I



Axis 0 to 90°

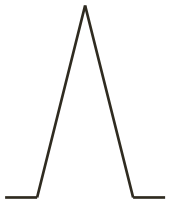
Lead II



# Axis Quick Method

- For left axis deviation:
  - All you need is lead II

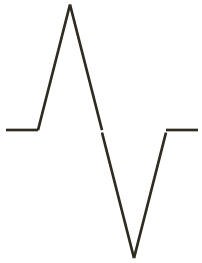
Lead I



Lead II

Axis -30 to -90°

Lead II



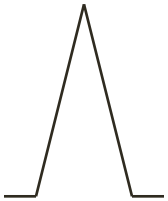
Axis 0 to -30°
Physiologic
Left Axis

# Axis Quick Method

- For right axis deviation:
  - All you need is lead I
  - Negative = RAD

Lead I

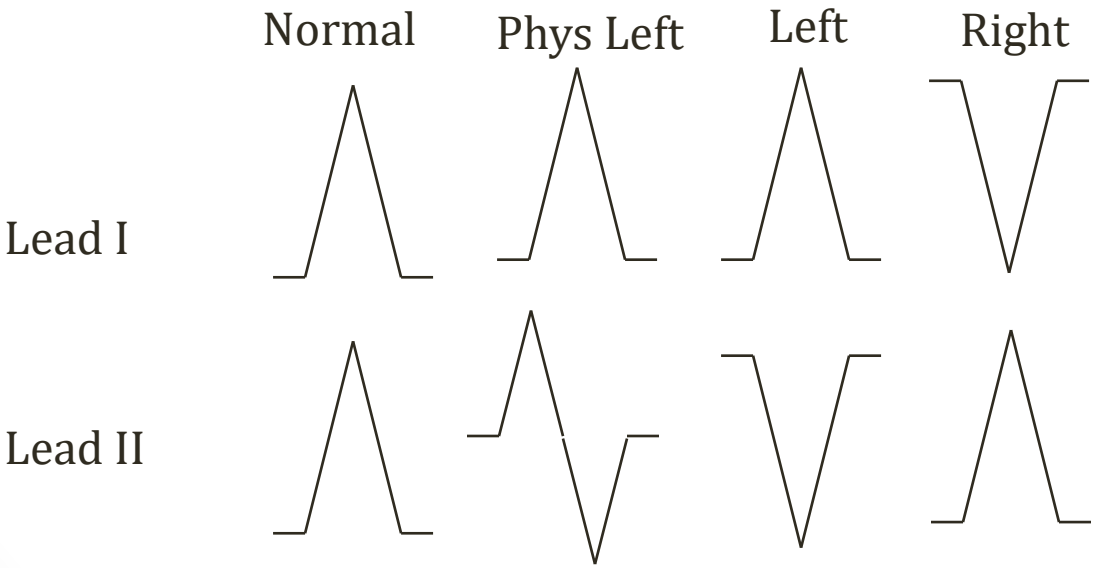
Lead II



Axis 90 to 180°

# Axis Quick Method

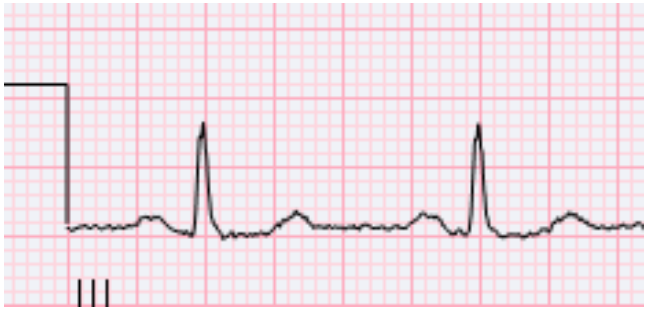
- Look at aVr: Make sure its negative
- Look at I, II: If both positive, axis is normal
- If II is negative: LAD
- If I is negative: RAD

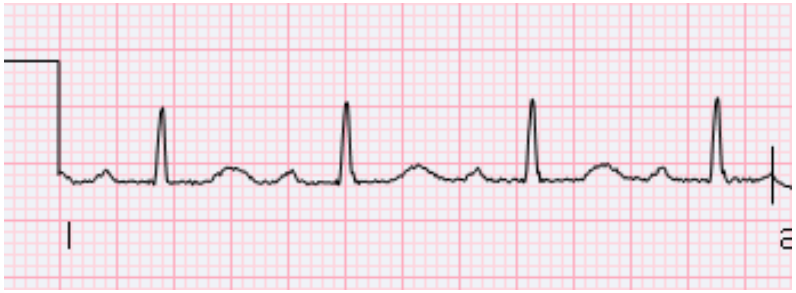


# PR Interval

Normal PR

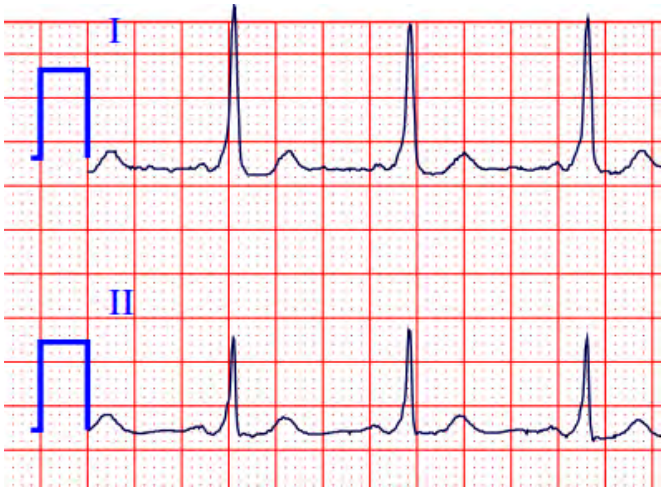
120-200ms




Prolonged PR

1° AV block

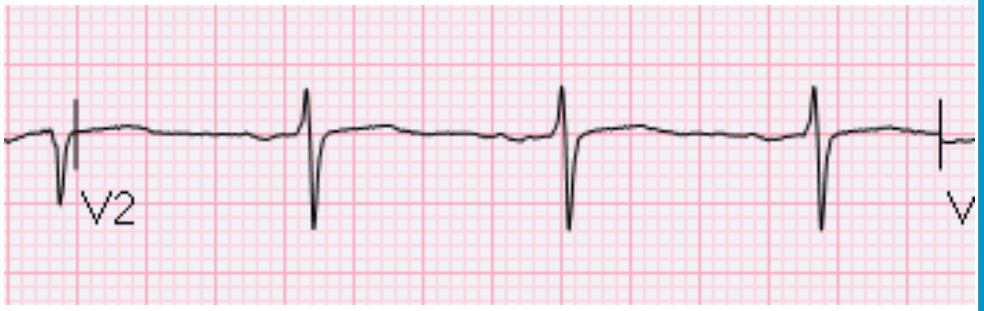


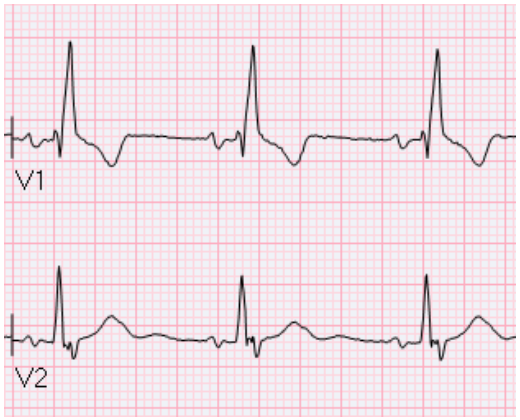

Short PR - WPW

# QRS Interval

Normal QRS

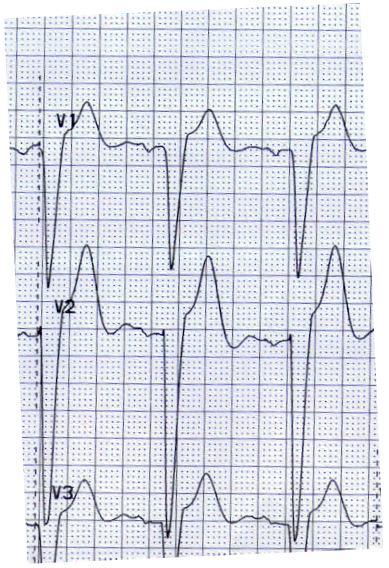
<120ms



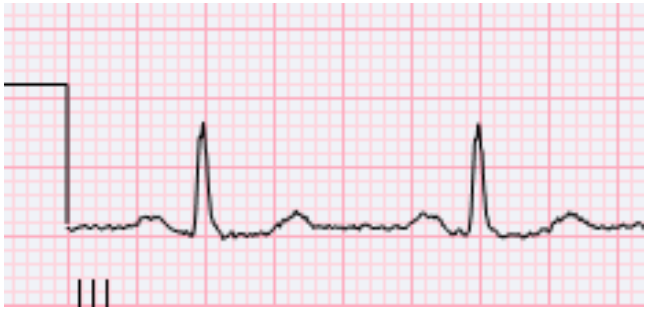

Right Bundle Branch Block

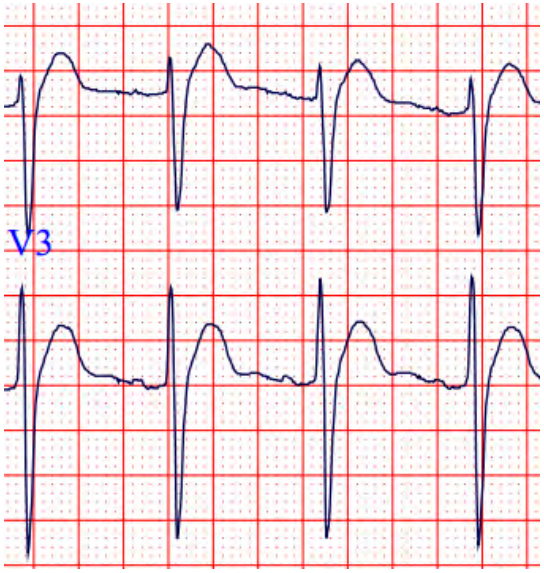
Left Bundle Branch Block



# Qt Interval

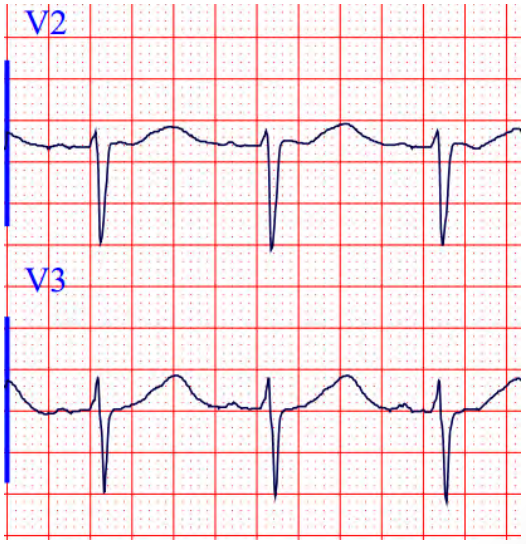
Normal Qt



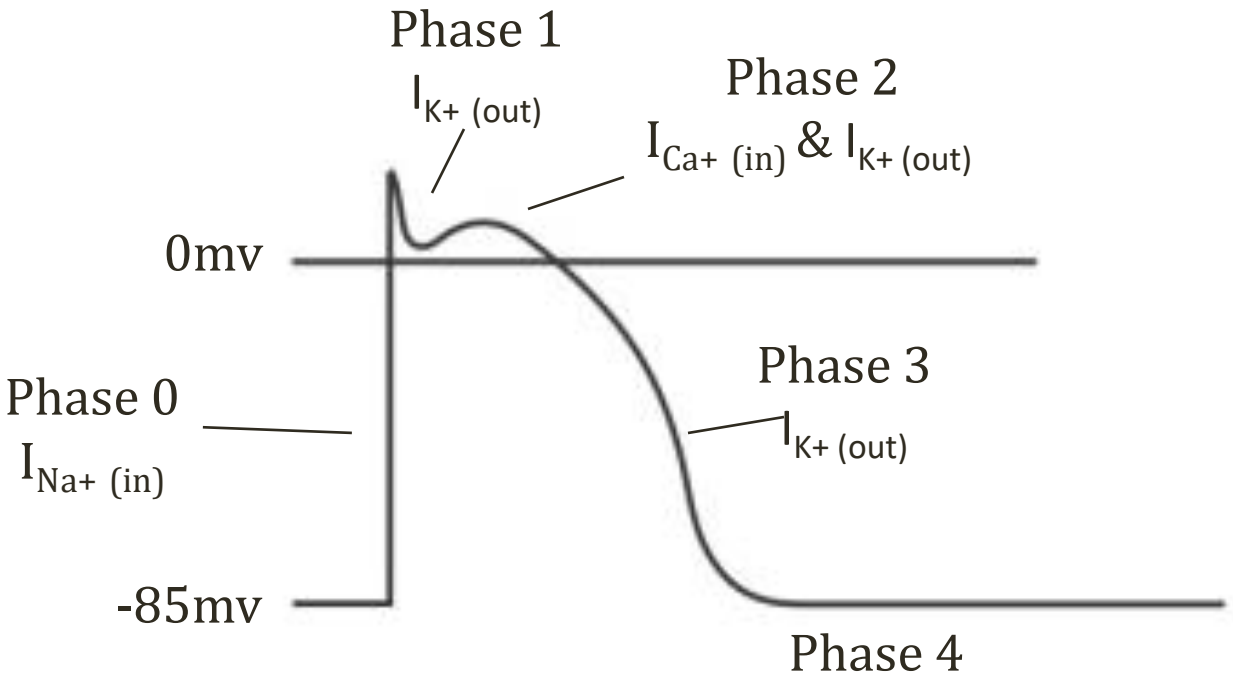

Short Qt: <u>Hypercalcemia</u>

**<u>Prolonged Qt</u>**
Hypocalcemia
Drugs
LQTS



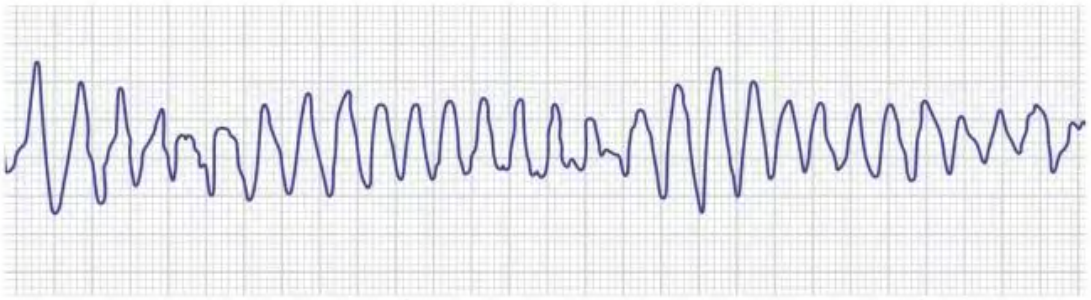
# Calcium

## Myocyte Action Potential



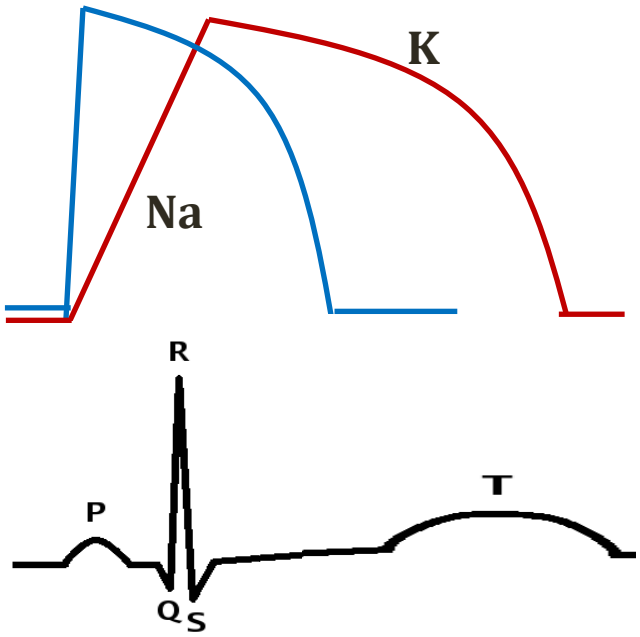
# Torsade de Pointes

- Feared outcome of Qt prolongation
- Results in cardiac arrest
- **Antiarrhythmic drugs**
- **Hypokalemia, hypomagnesemia**
- Rarely from hypocalcemia



# Congenital Long Qt Syndrome

- Rare genetic disorder
  - Abnormal K/Na channels




Prolonged QT

# Congenital Long Qt Syndrome

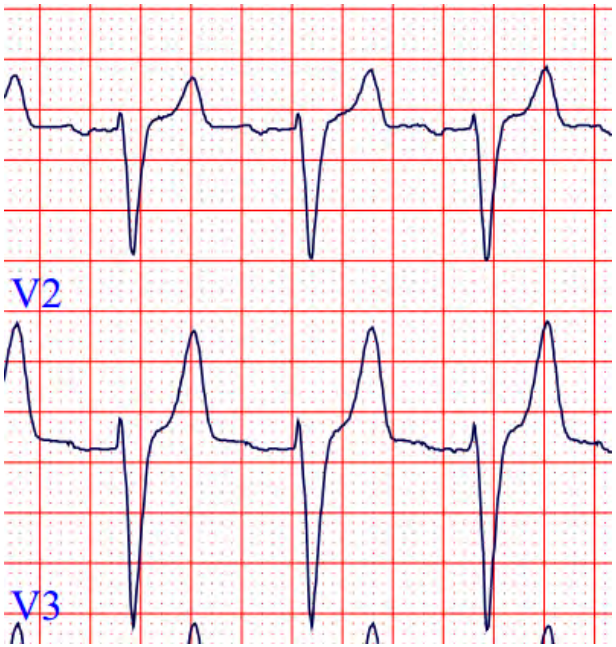
- Family history of sudden death (torsades)
- Classic scenario: Young patient recurrent “seizures”
  - EKG shows long Qt interval
- Jervell and Lange-Nielsen Syndrome
    - Norway and Sweden
    - Congenital deafness

# Acquired Long Qt Syndrome

- Antiarrhythmic drugs
- Levofloxacin (antibiotic)
- Haldol (antipsychotic)
- Many other drugs
- Congenital LQTS: need to avoid these drugs

# T waves

Peaked T waves
↑K
Early ischemia
(hyperacute)

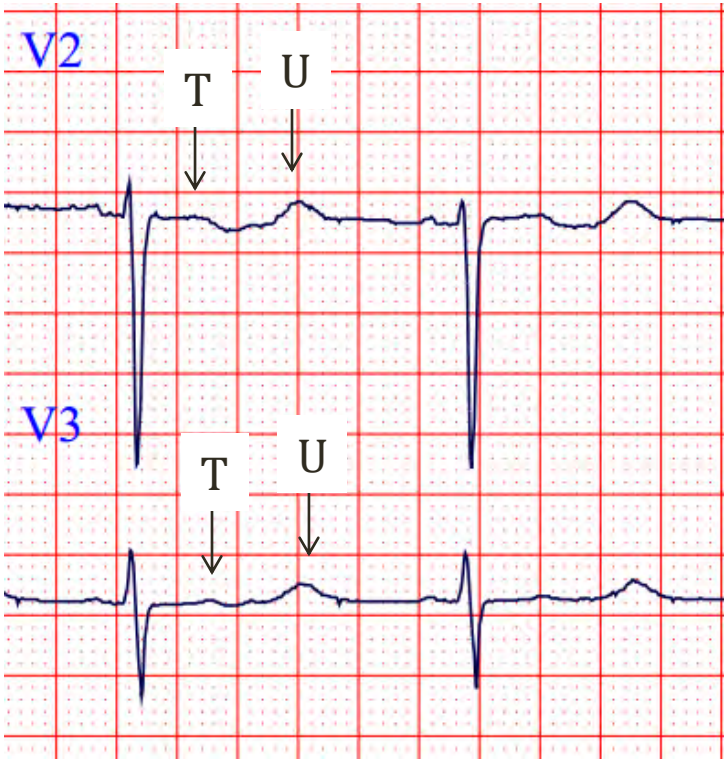


# U waves

Origin unclear

May represent repolarization of Purkinje fibers

Can be normal but also seen in *hypokalemia*



# High Yield EKGs

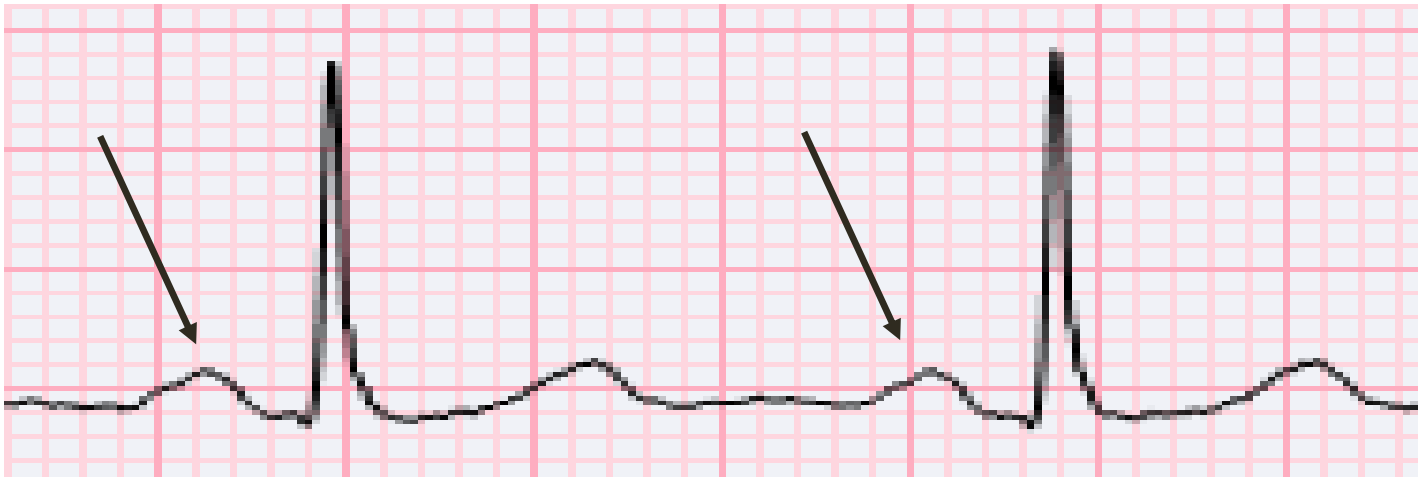
Jason Ryan, MD, MPH

# EKGs You Should Know

1. Sinus rhythm
2. Atrial Fibrillation/Flutter
3. Ischemia: ST elevations, ST depressions
4. Left bundle branch block
5. Right bundle branch block
6. PAC/PVC
7. $1^{st}$, $2^{nd}$, $3^{rd}$ degree AV block
8. Ventricular tachycardia
9. Ventricular fibrillation/Torsades

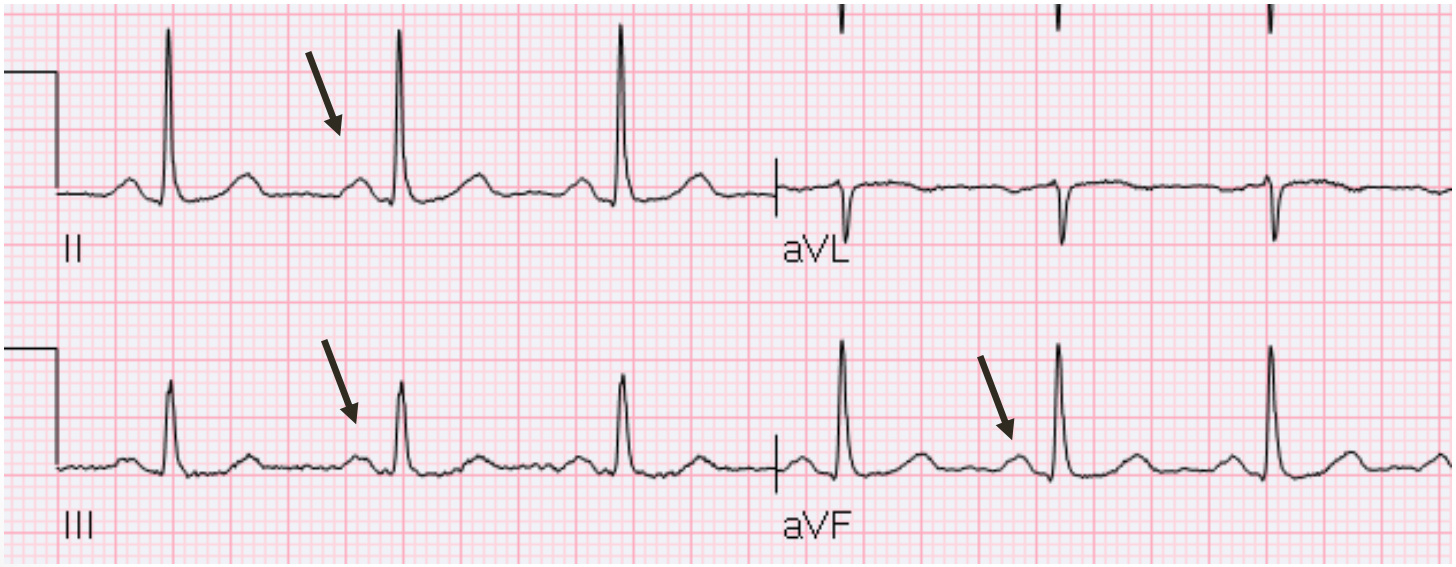
# Step 1: Find the p waves

- Are p waves present?



# Sinus p waves

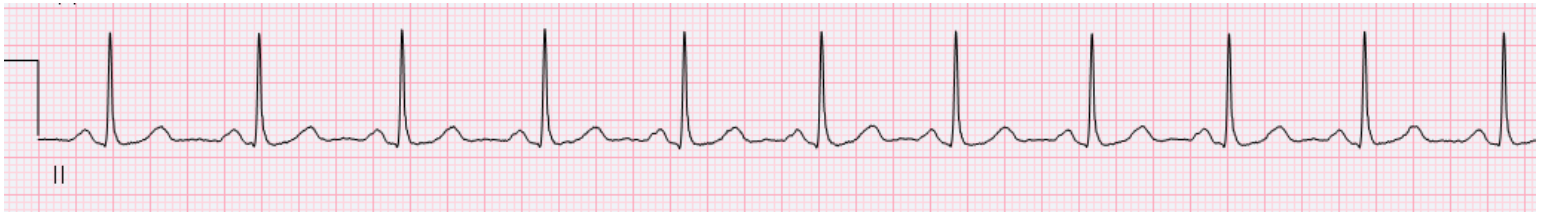
- Originate in sinus node
- Upright in leads II, III, F



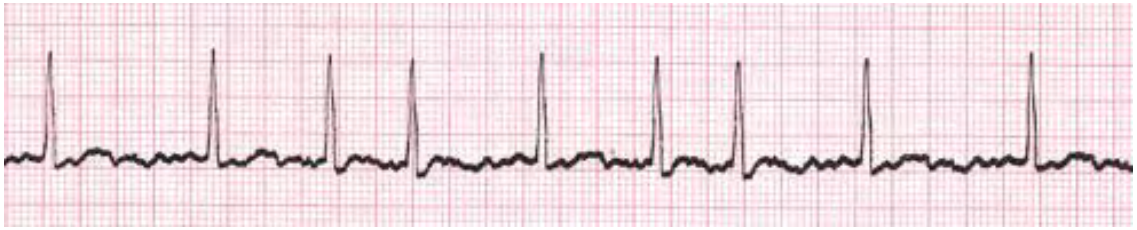
# Step 2: Regular or Irregular

- Distance between QRS complexes (R-R intervals)

Regular




Irregular



# Steps 1 & 2

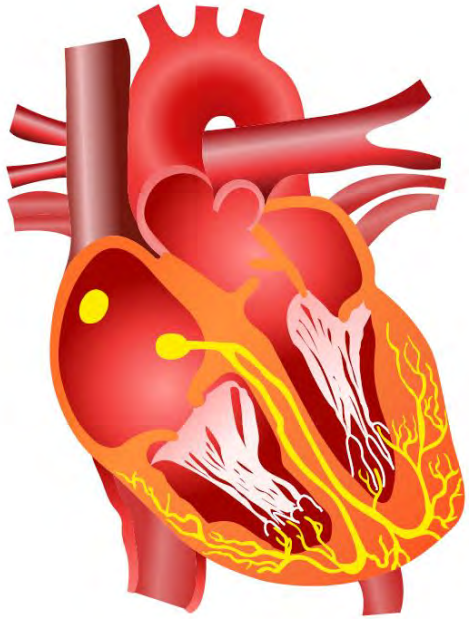
- P waves present, regular rhythm
  - **Sinus rhythm**
  - Rare: atrial tachycardia, atrial rhythm
- No p waves, irregular rhythm
  - **Atrial fibrillation – irregularly irregular**
  - Atrial flutter with variable block

# Steps 1 & 2

- P waves present, irregular rhythm
  - Sinus rhythm with PACs
  - Multifocal atrial tachycardia
  - Sinus with AV block
- No p waves, regular rhythm
  - Hidden p waves: retrograde
  - Supraventricular tachycardias (SVTs)
  - Ventricular tachycardia

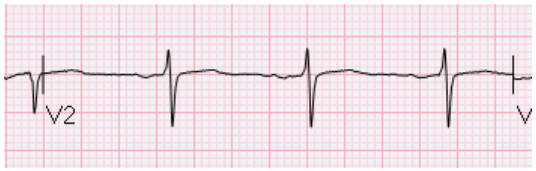
# Step 3: Wide or narrow

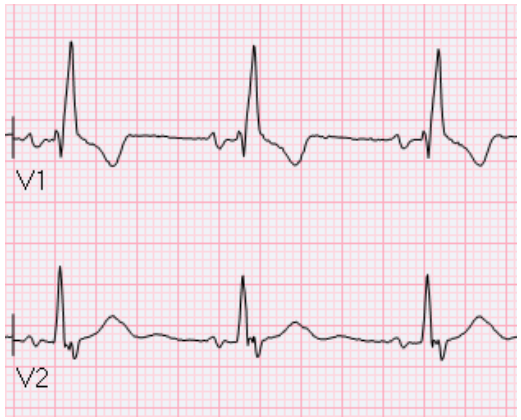
- Narrow QRS (<120ms; 3 small boxes)
  - His-Purkinje system works
  - No bundle branch blocks present
- Wide QRS
  - Most likely a **bundle branch block**
  - Ventricular rhythm (i.e. tachycardia)



# QRS Interval

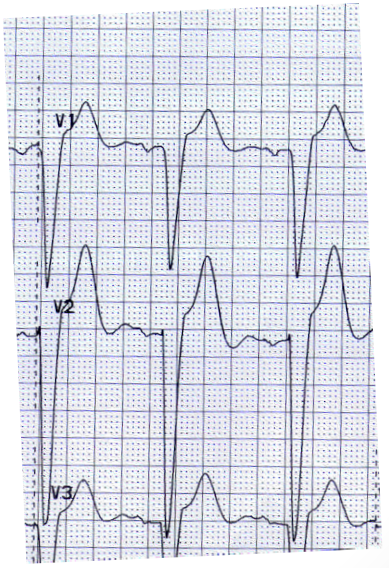
Normal QRS




Right Bundle Branch Block

Left Bundle Branch Block

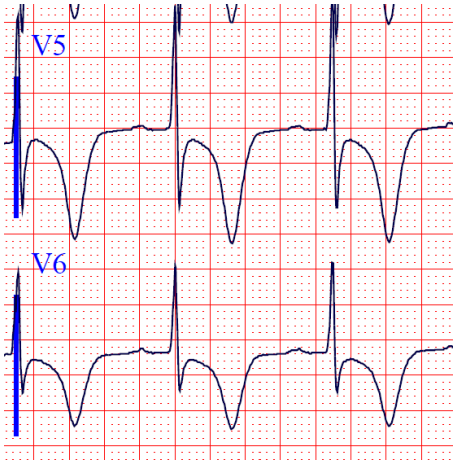


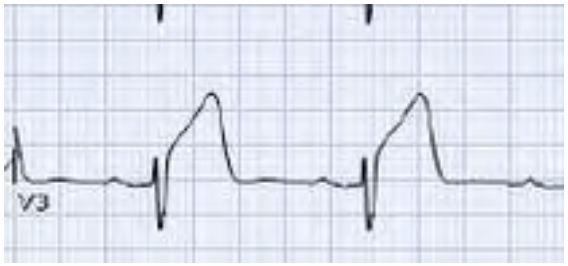
# Step 4: Check the intervals

- PR (normal <210ms; ~5 small boxes; ~1 big box)
  - Prolonged in AV block
  - Lengthens with vagal tone, drugs
  - Shortens with sympathetic tone
- QT (normal <1/2 R-R interval)
  - Prolonged with ↓ Ca (tetany; numbness; spasms)
  - Prolonged by antiarrhythmic drugs
  - Shortened with ↑ Ca (confusion, constipation)

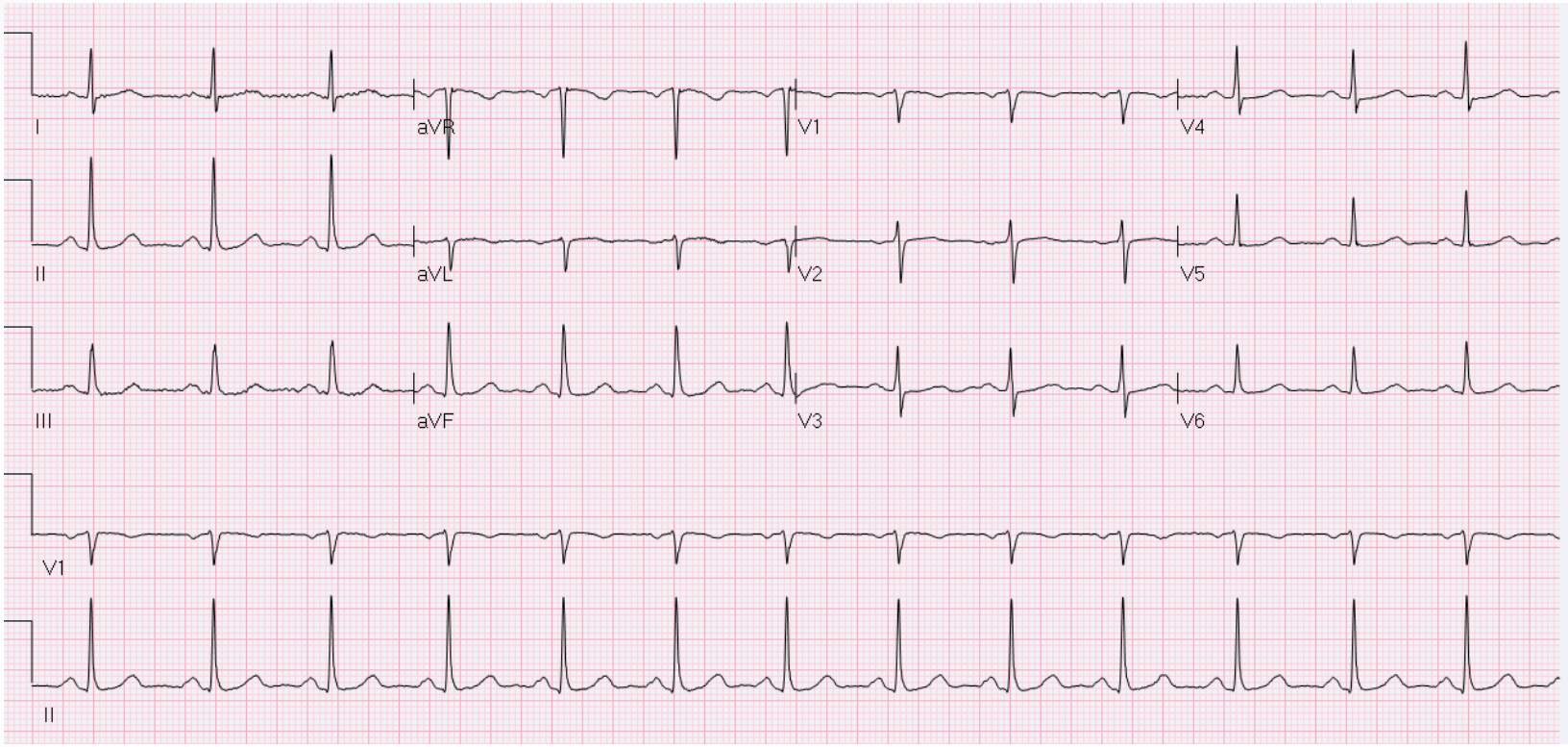
# Step 5: ST segments

- T wave abnormalities
  - Inverted: ischemia
  - Peaked: Early ischemia, hyperkalemia (↑K)
  - Flat/U waves: Hypokalemia (↓K)
- ST Depression
  - Subendocardial ischemia
- ST Elevation
  - Transmural ischemia

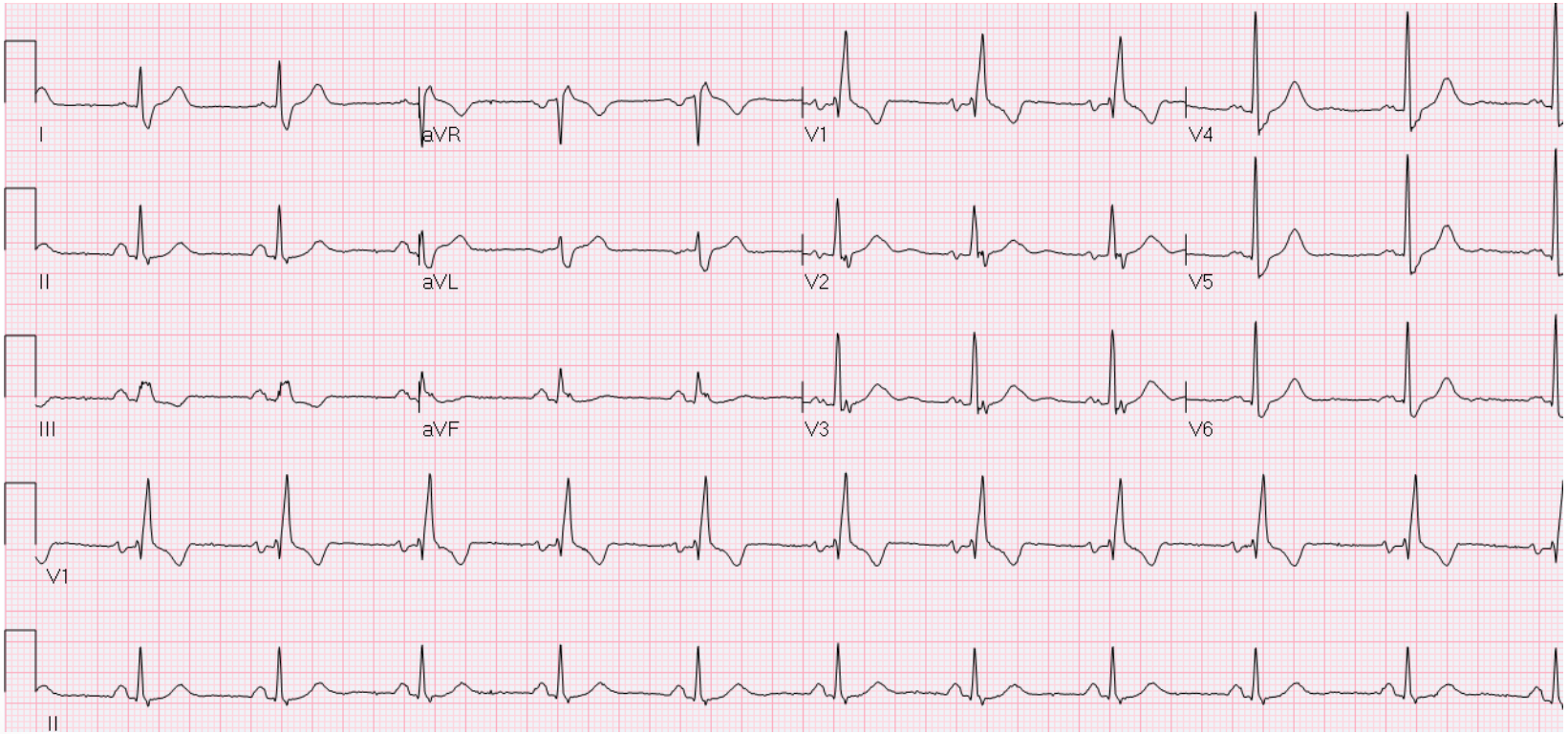


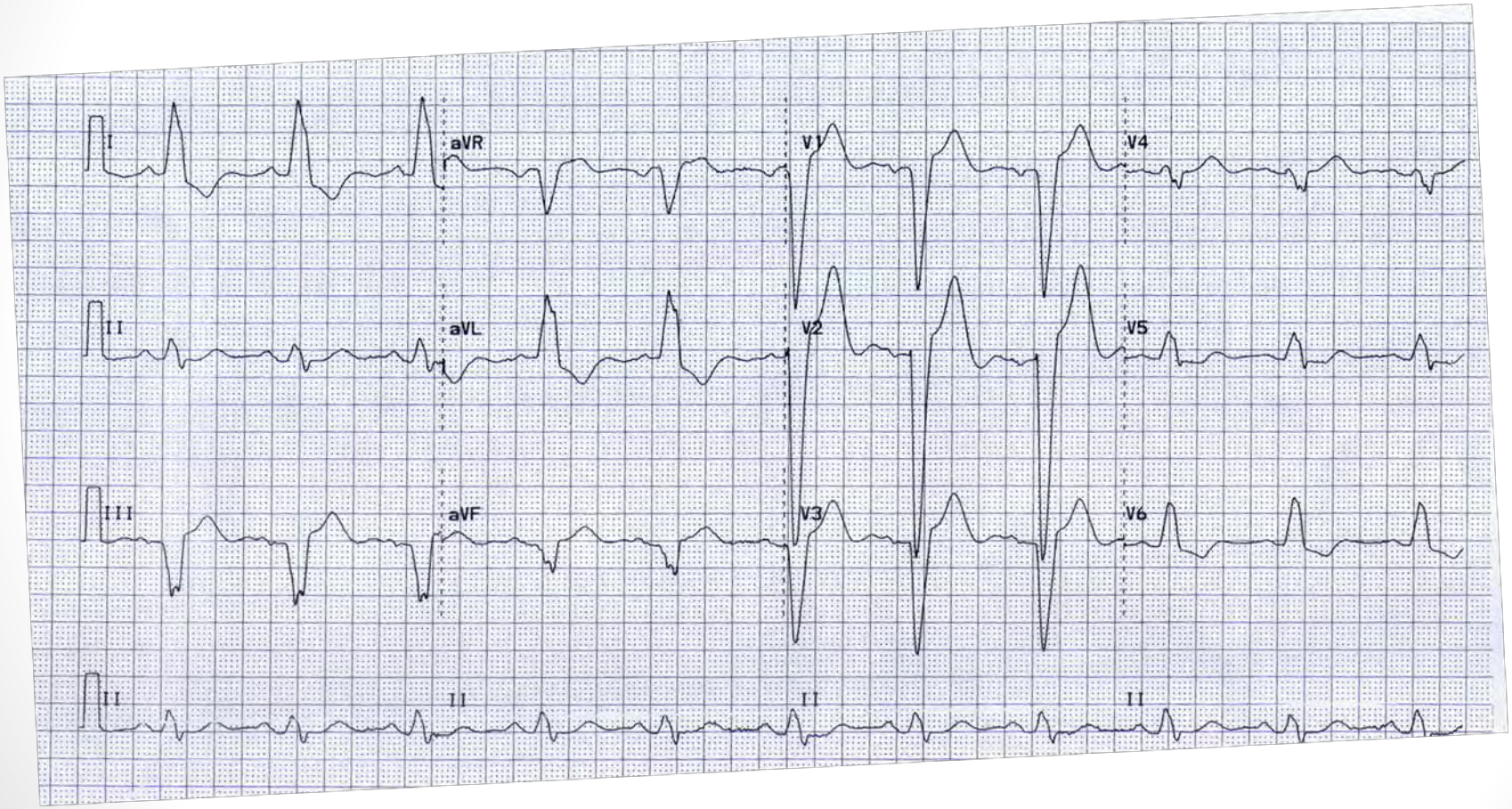
# Normal Sinus Rhythm



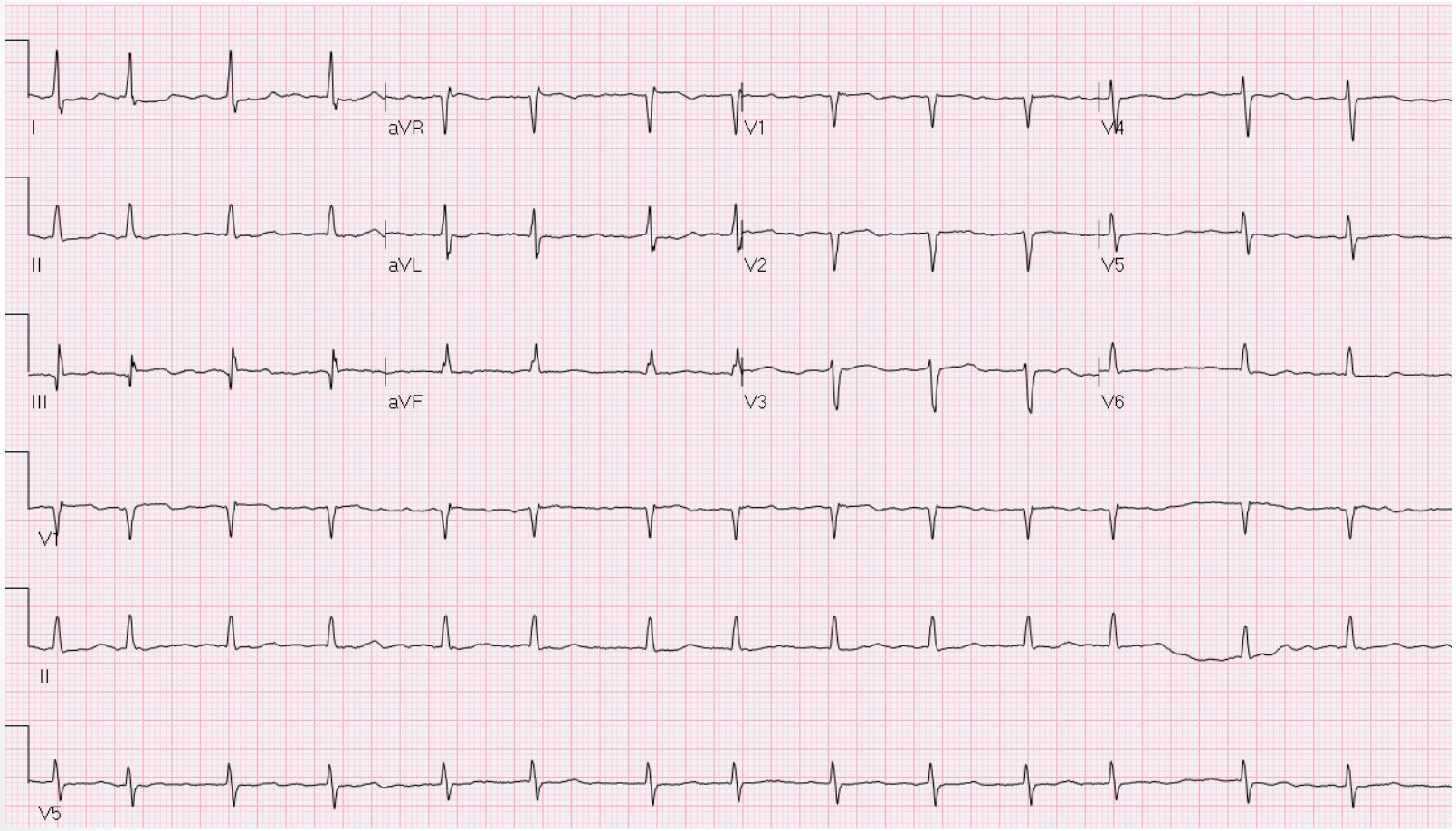
# Right Bundle Branch Block



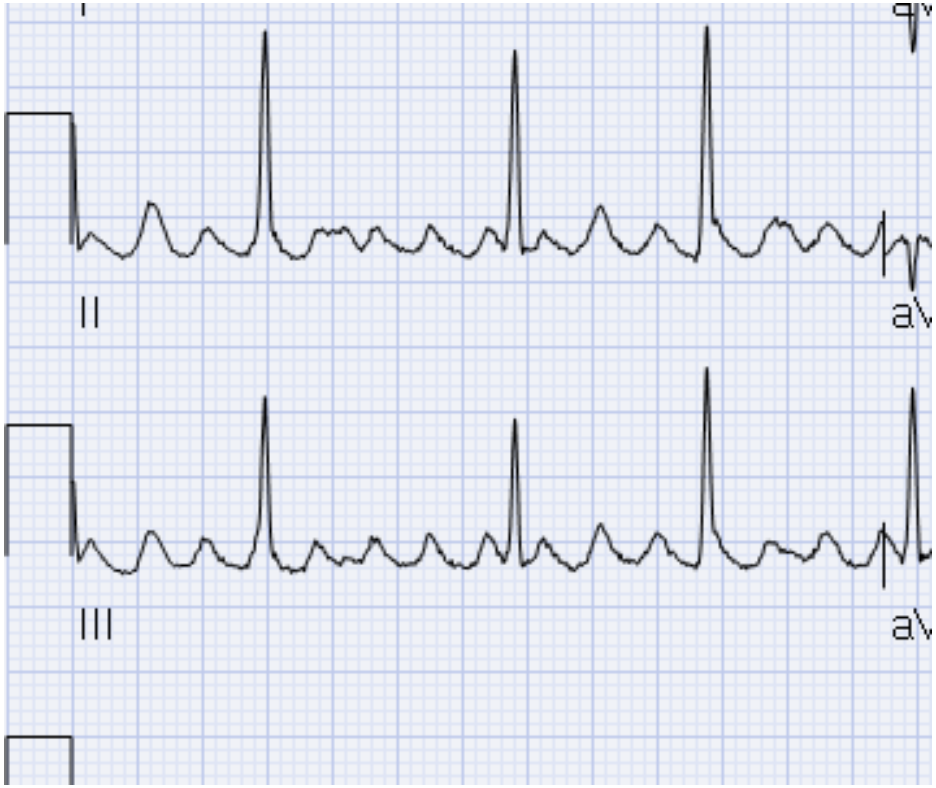
# Left Bundle Branch Block



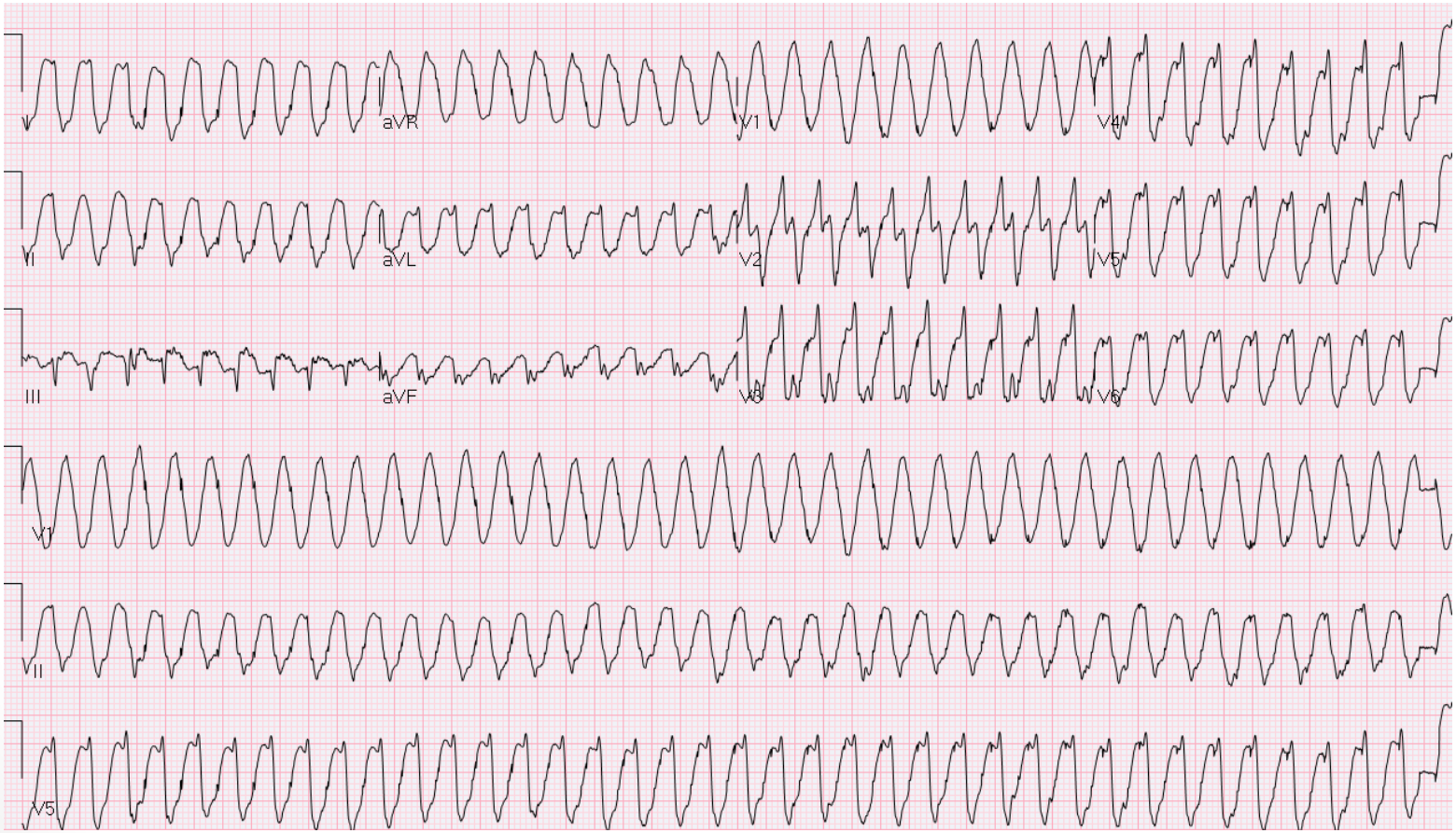
# Atrial Fibrillation



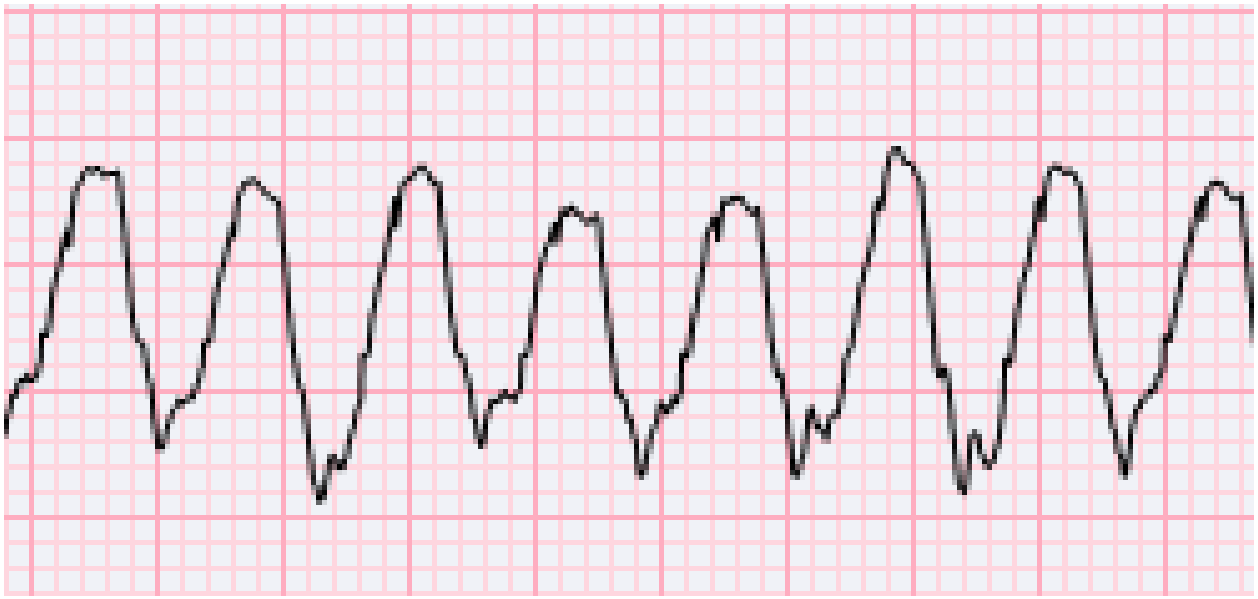
# Atrial Flutter



# Ventricular Tachycardia

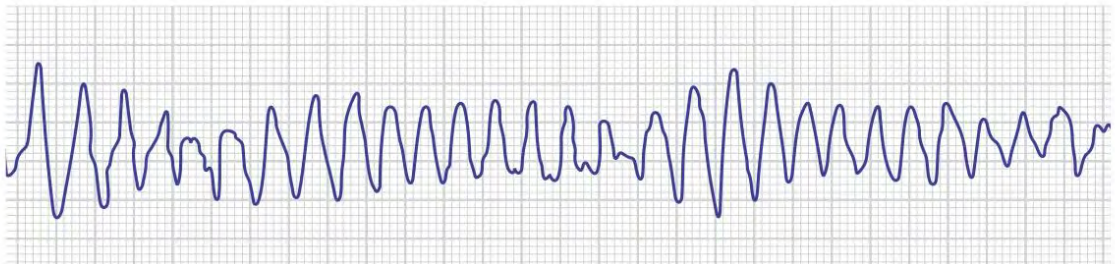


# Ventricular Tachycardia

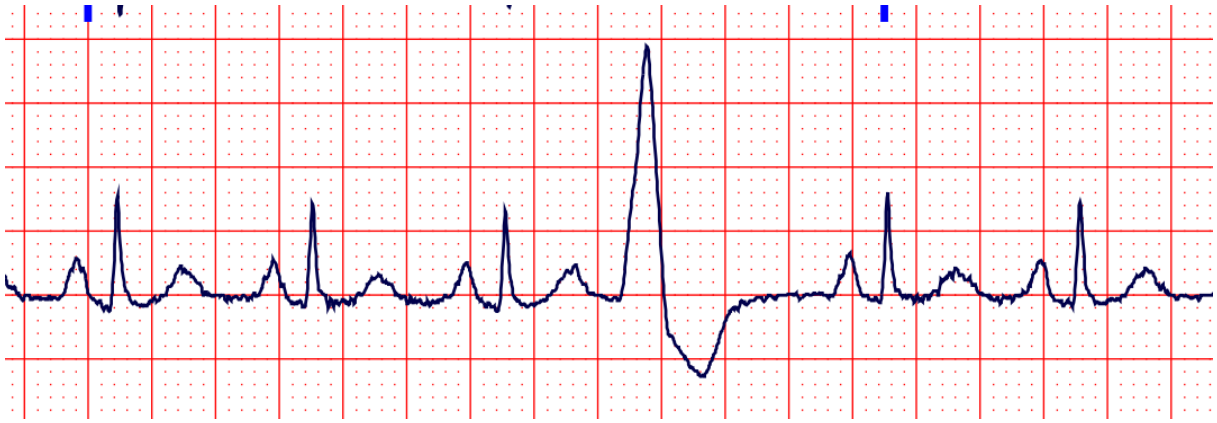


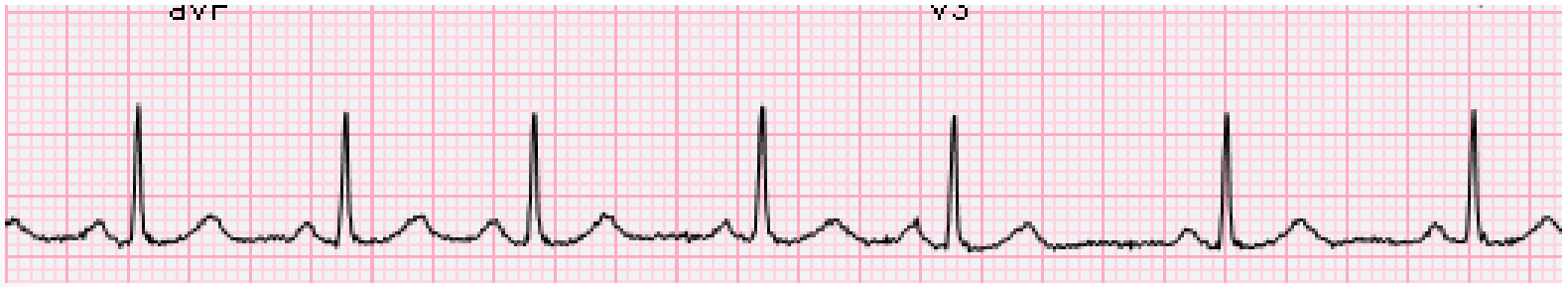
# Torsades de pointes

- ↑ risk with **prolonged Qt interval**
  - Antiarrhythmic drugs
  - Congenital long Qt syndrome
  - Antibiotics (erythromycin, quiniolones)
- Hypokalemia
- Hypomagnesemia
- Rarely hypocalcemia



# PAC and PVC





# Cardiac Action Potentials

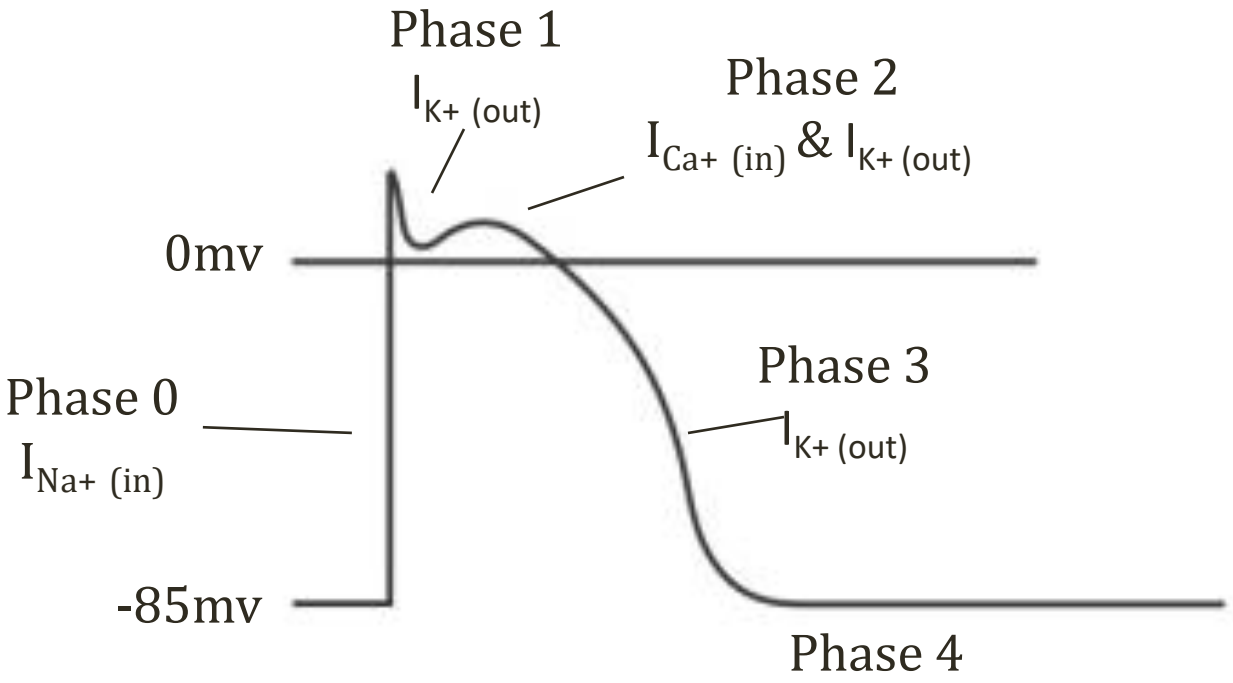
Jason Ryan, MD, MPH

# Cardiac Action Potential

- Changes in membrane voltage of cell
- Transmit electrical signals through heart
- Triggers contraction of myocytes

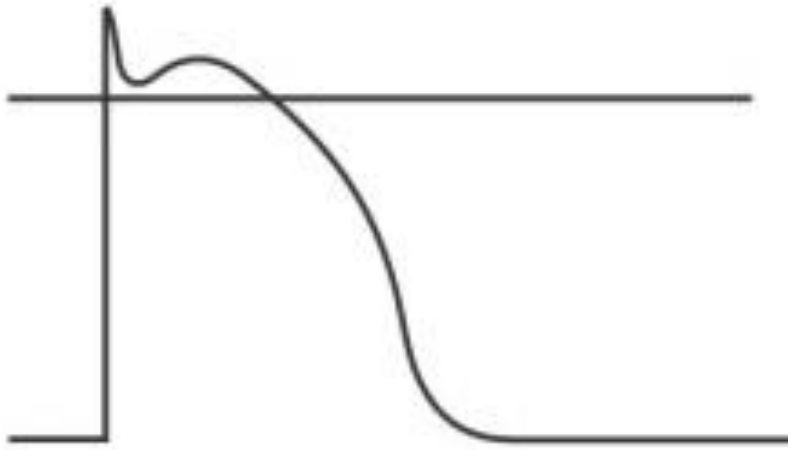
# Myocyte Action Potential

## Atrial/ventricular myocytes



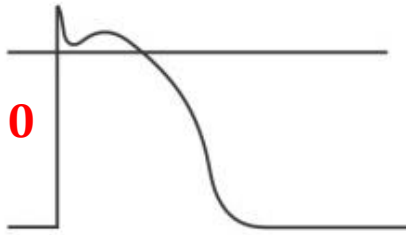
# Phase 4

- Resting potential: about −85mV
- Constant outward leak of $K^+$
- "Inward rectifier channels"
- $Na^+$ and $Ca^{2+}$ channels are closed



**Phase 4** **Phase 4**

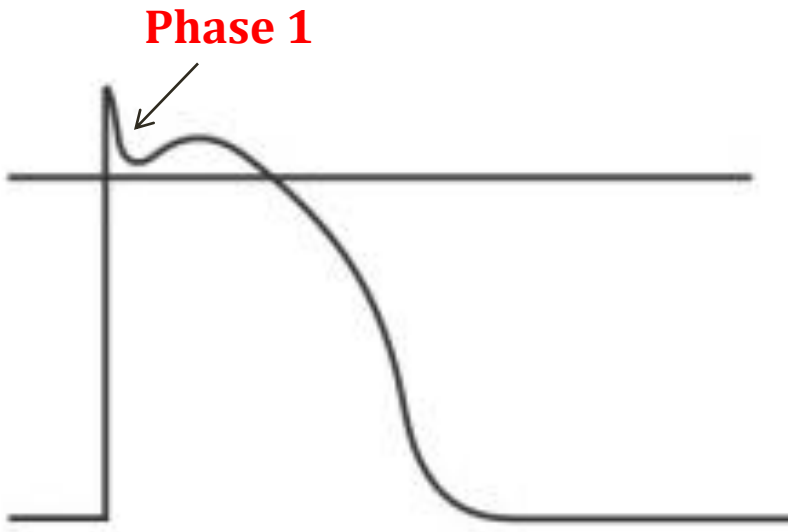
# Phase 0




- Nearby myocyte raise membrane potential
- **Gap junctions**
- Rising potential opens **"Fast" $Na^+$ channels**
- Threshold potential reached (about -70mV)
- Large $Na^+$ current → rapid depolarization
- Membrane potential overshoots (>0mV)
- Fast $Na^+$ channels close
- **Class I antiarrhythmic drugs**: block Na channels

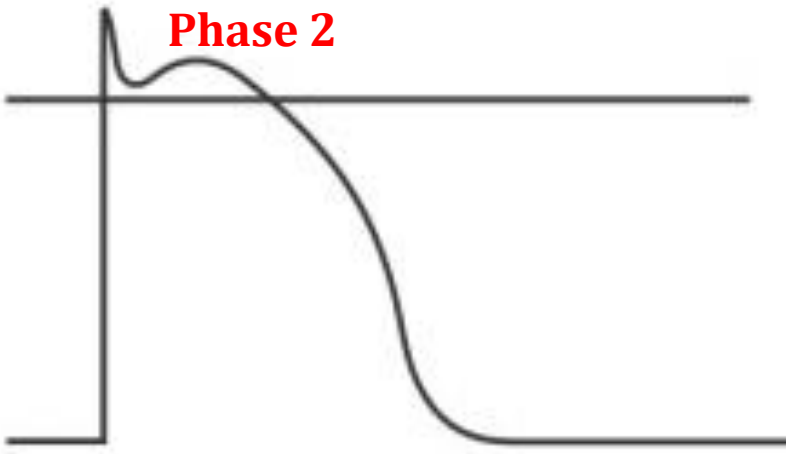
# Phase 1

- Membrane potential is positive
- **$K^+$ channels open**
- Outward flow of $K^+$ returns membrane to ~0 mV



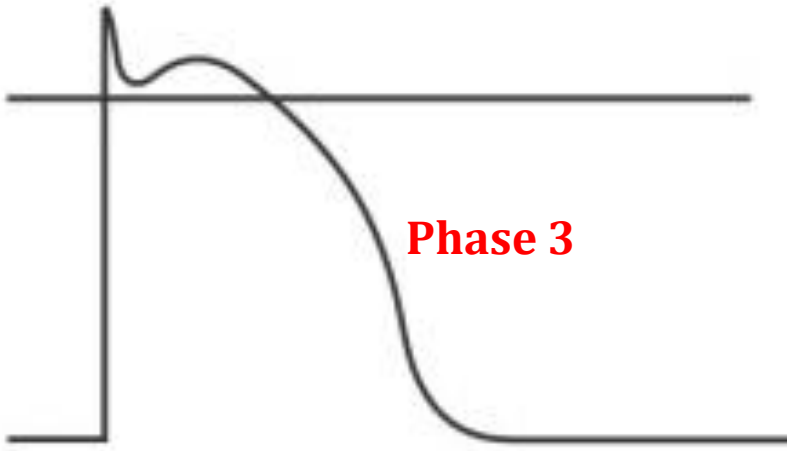
# Phase 2

- L-type $Ca^{2+}$ channels open → inward $Ca^{2+}$ current
- Contraction trigger: **excitation-contraction coupling**
- $K^+$ leaks out (down concentration gradient)
- Delayed rectifier $K^+$ channels
- **Balanced flow in/out** = plateau of membrane charge
- **Verapamil/Diltiazem** = block L-type Ca channels



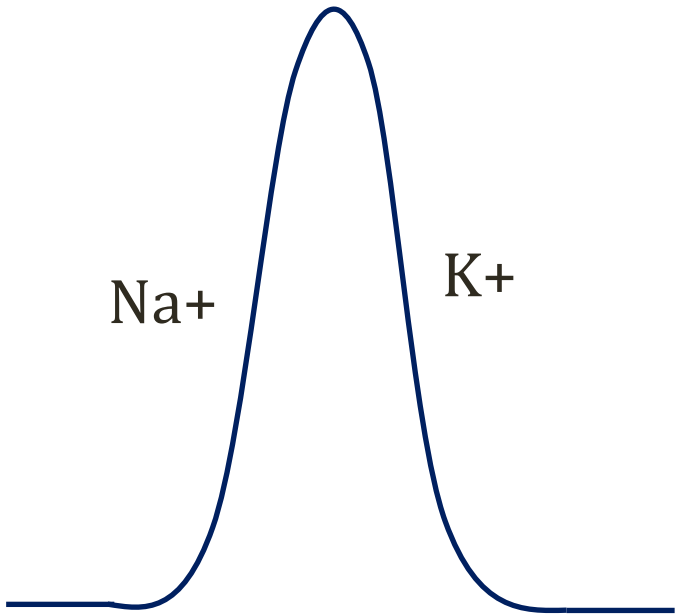
# Phase 3

- $Ca^{2+}$ channels inactivated
- **Persistent outflow of $K^+$**
- Resting potential back to −85 mV
- **Class III antiarrhythmic drugs**: block K channels



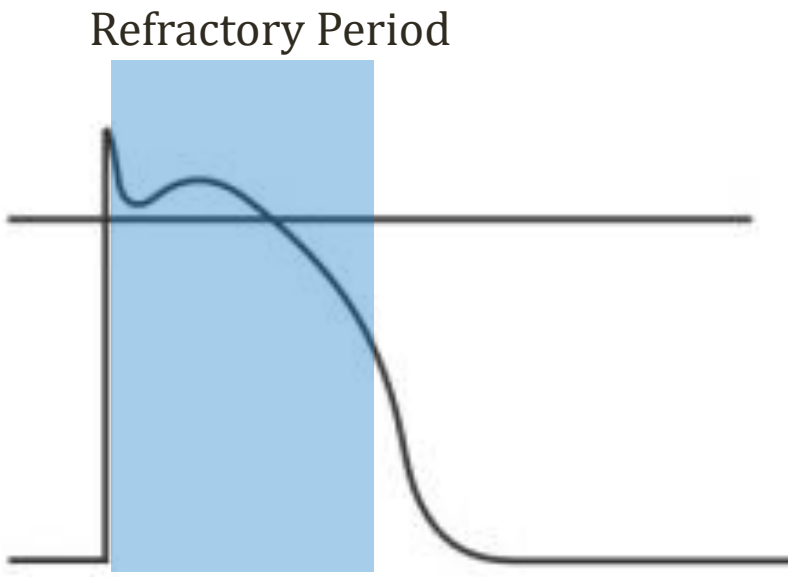
# Skeletal Muscle

- No plateau (phase 2)
- No gap junctions
- Each cell has its own NMJ



# Refractory Period

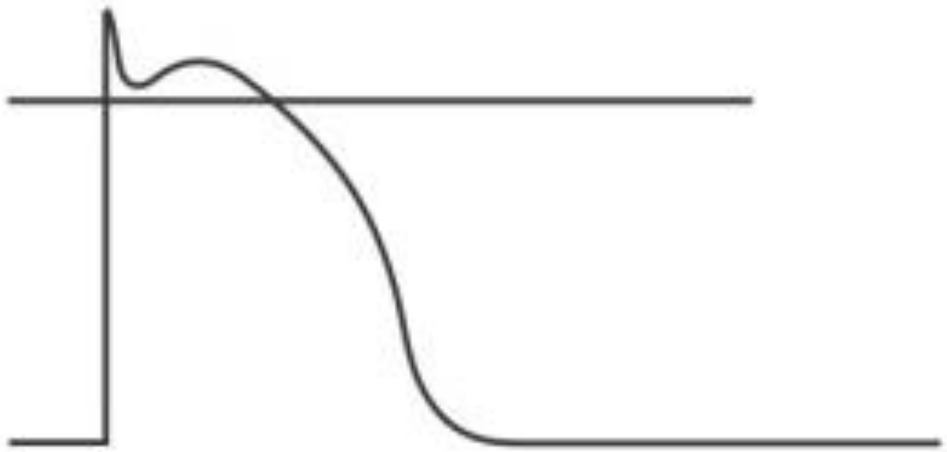
- Phase 0 until next possible depolarization
- Determines how fast myocyte can conduct
- Many antiarrhythmic drugs prolong refractory period



# Myocyte Action Potential

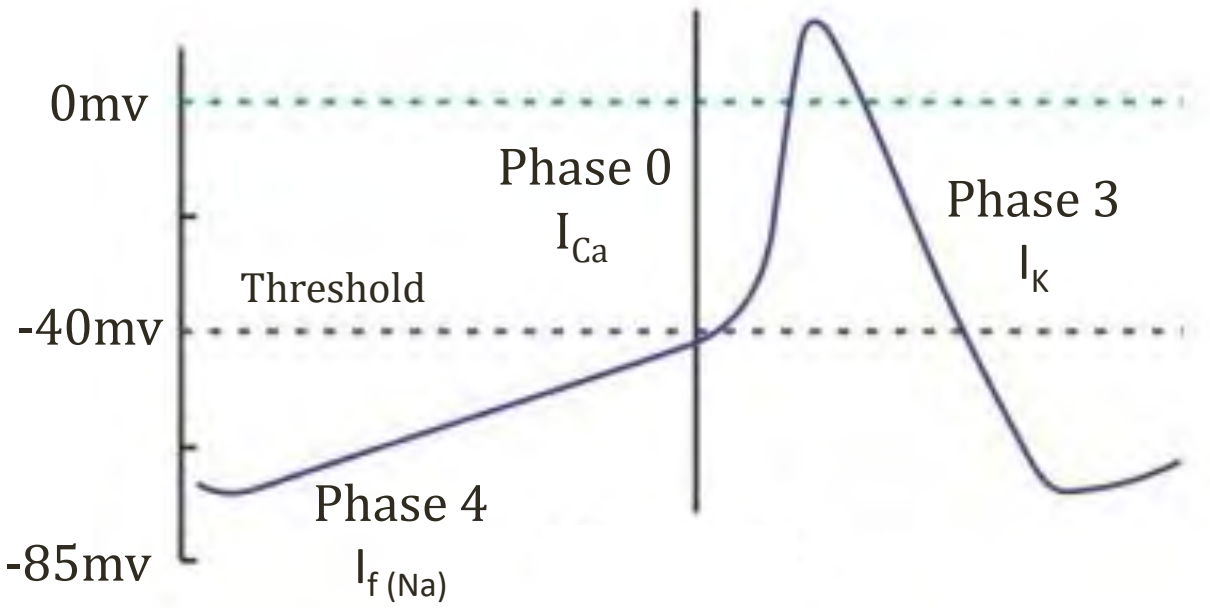
## Atrial/ventricular myocytes

- Similar AP in HIS, bundle branches, Purkinje fibers



# Pacemaker Action Potential

## SA node, AV node



# Pacemaker Action Potential

## SA node, AV node

- **Funny current** (pacemaker current)
  - Spontaneous flow of $Na^+$
- About −40 mV: threshold potential
- L-type $Ca^{2+}$ channels open → depolarize cell
- Delayed rectifier $K^+$ channels open
- Return cell to −60 mV

# Pacemaker Action Potential

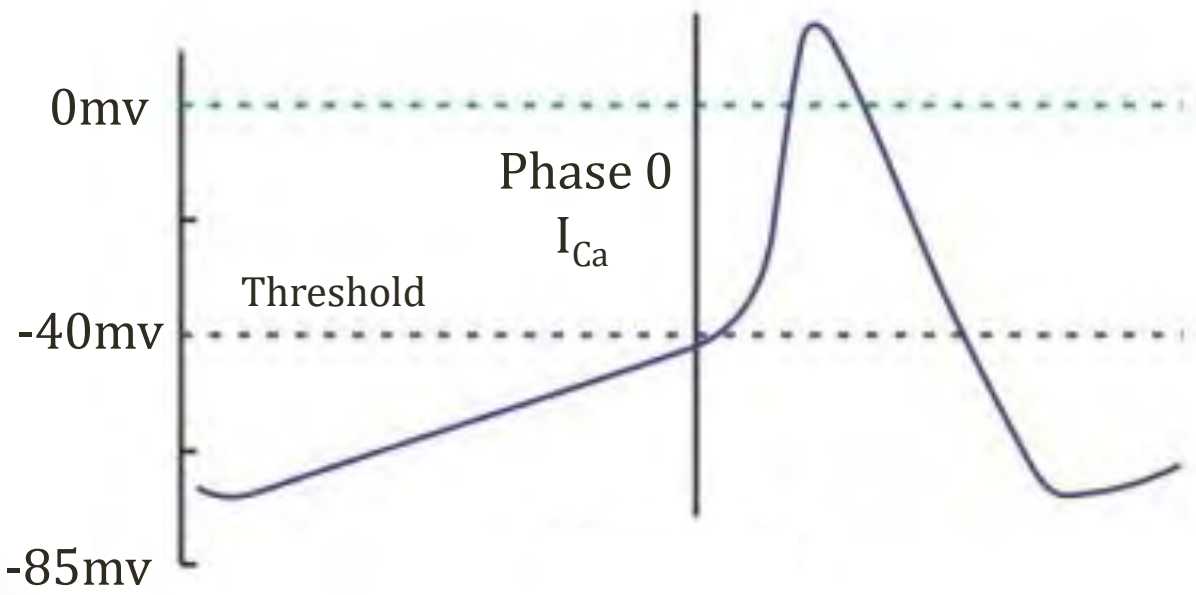
## SA node, AV node

- Automaticity
  - Do not require stimulation to initiate action potential
  - Capable of self-initiated depolarization
- No fast $Na^+$ channel activity
  - Fewer inward rectifier $K^+$ channels
  - Membrane potential never lower than −60 mV
  - Fast $Na^+$ channels need −85 mV to function

# Pacemaker Action Potential

## SA node, AV node

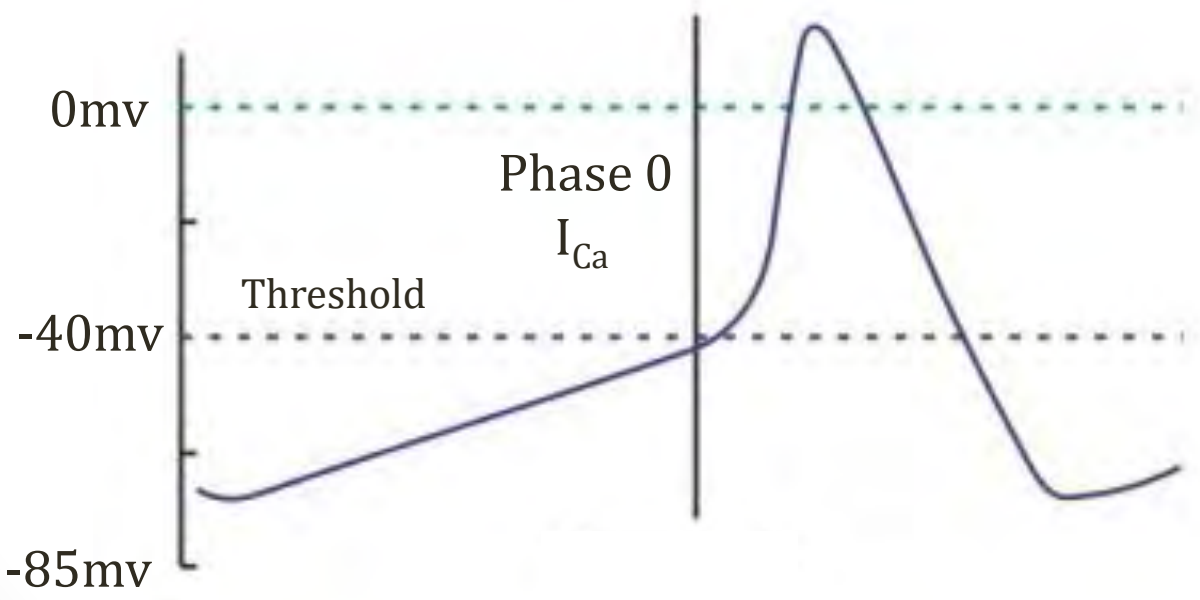
- Any drug that slows this AP may cause two effects:
  - **Slower heart rate** (sinus node)
  - **Slower AV conduction** (AV node)



# Pacemaker Action Potential

## SA node, AV node

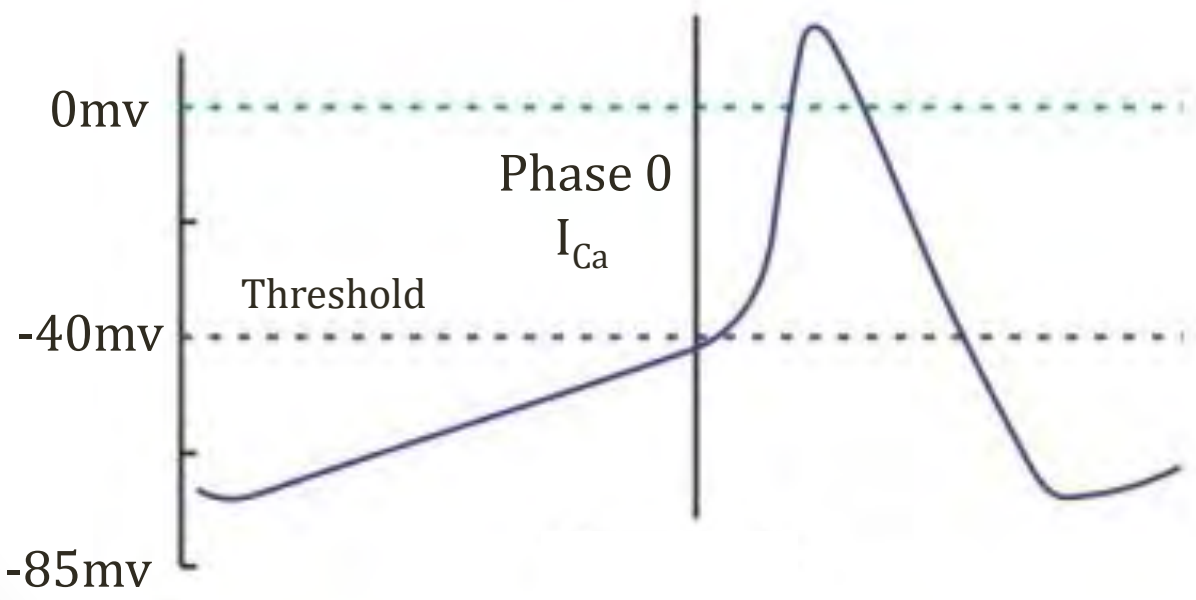
- Two key drug classes that affect pacemaker AP
  - **Calcium channel blockers** (Verapamil/Diltiazem)
  - **Beta blockers**



# Pacemaker Action Potential

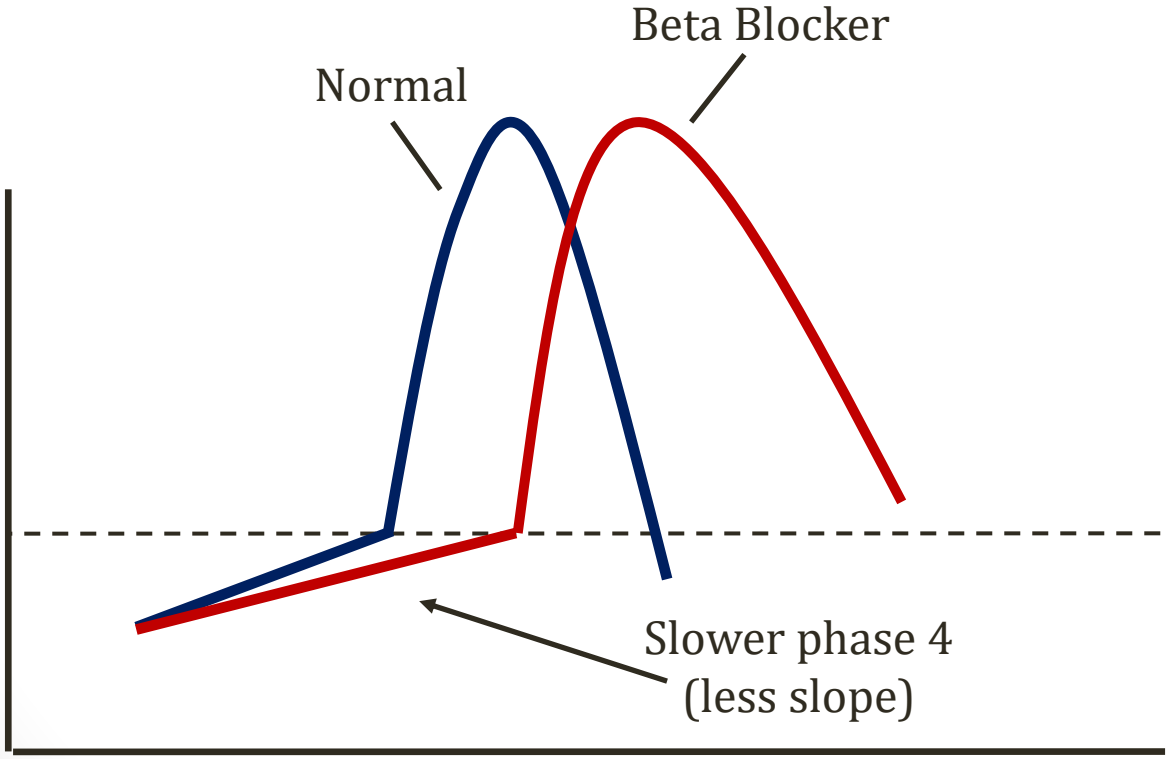
## SA node, AV node

- **Verapamil/Diltiazem** = block L-type Ca channels
  - Slow rate of sinus depolarization (slow heart rate)
  - Slow AV node conduction



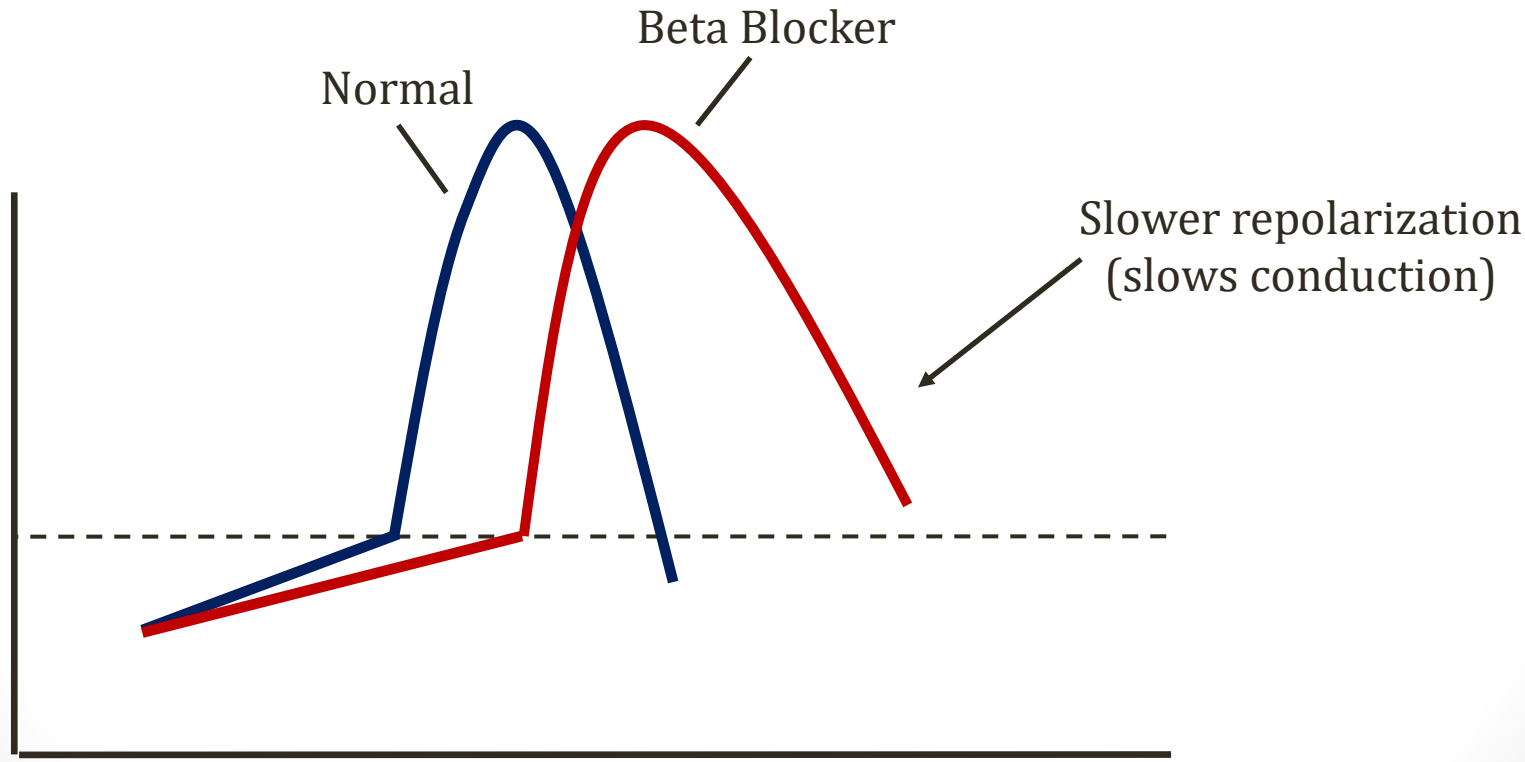
# Beta Blockers

- Modify slope of phase 4
- Less slope → longer to reach threshold → ↓ HR



# Beta Blockers

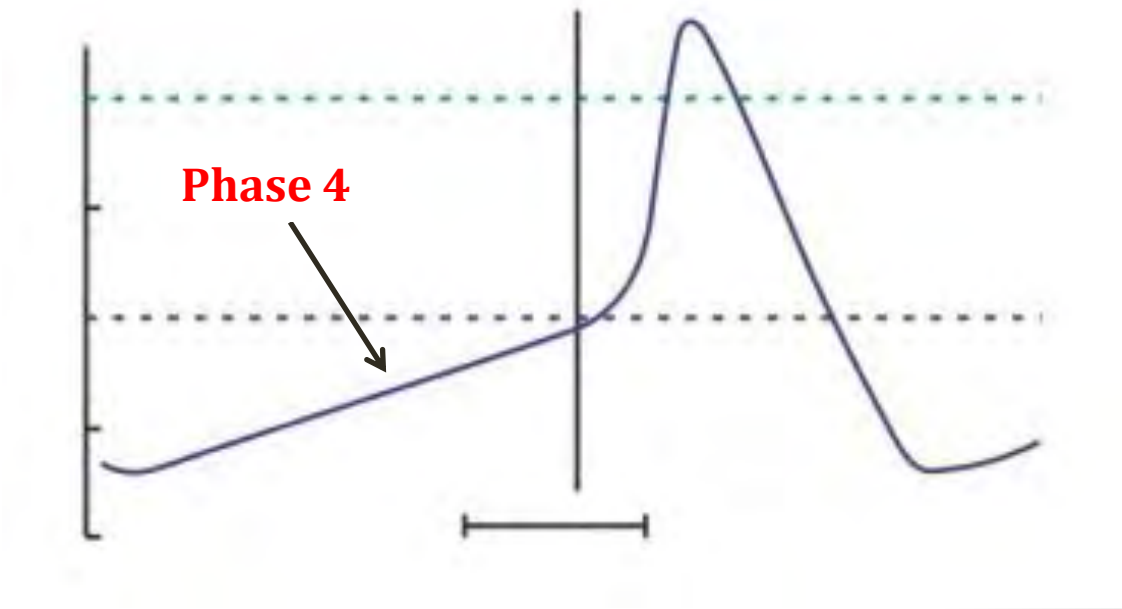
- Also prolong repolarization
- Slow AV node conduction



# Slope of Phase 4

## Sinus Node

- Changes in slope modify heart rate
- Decrease slope (slower rise)
  - Parasympathetic NS, beta blockers, adenosine
- Increased slope (faster rise)
  - Sympathetic NS, sympathomimetic drugs

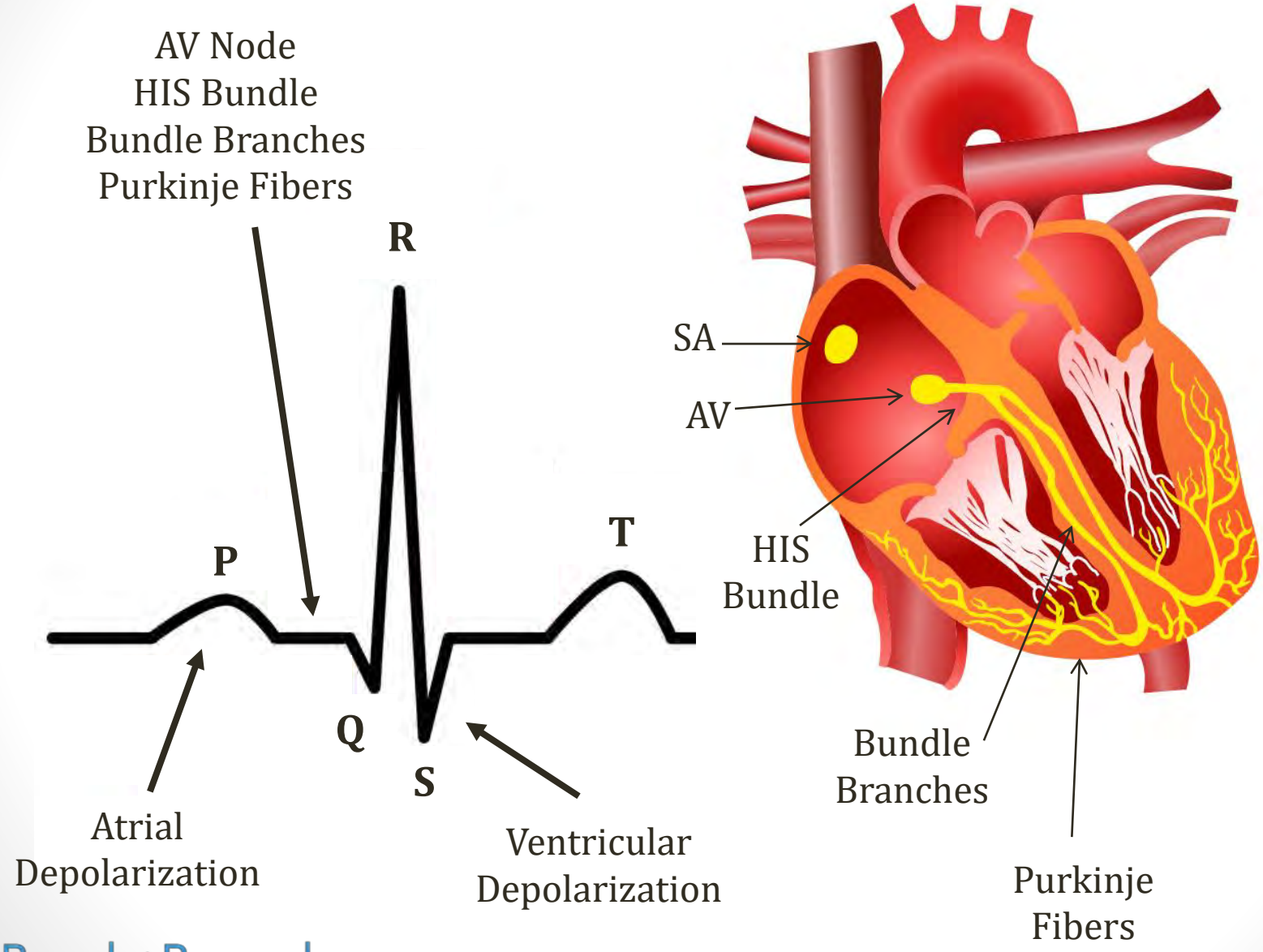


# Pacemakers

- Many cardiac cells capable of automaticity
- SA node normally dominates
  - Fastest rise in phase 4
  - Controls other pacemaker cells
- Pacemakers: SA Node > AV Node > Bundle of HIS
  - SA node (60-100 bpm)
  - AV node (40-60 bpm)
  - HIS (25-40 bpm)

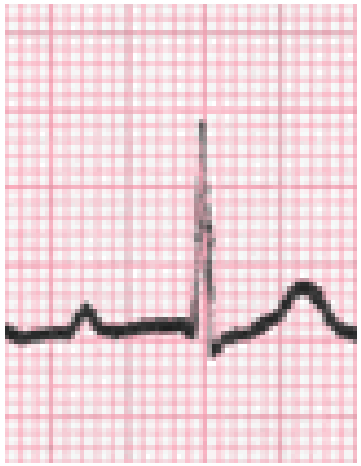
# AV and Bundle Branch Blocks

Jason Ryan, MD, MPH

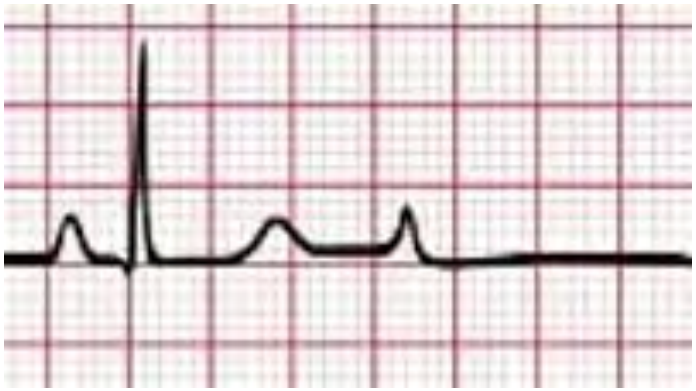


# AV Blocks

- Slowed or blocked conduction atria → ventricles
- Can cause prolonged PR interval
- Can cause non-conducted p wave



Prolonged PR Interval



Non-conducted P wave

# AV Blocks

## Symptoms

- Often incidentally noted on EKG
  - Especially milder forms with few/no non-conducted p waves
- Can cause bradycardia
  - Occurs when many or all p waves not conducted
  - Fatigue, dizziness, syncope
  - Symptomatic AV block often treated with a pacemaker

# AV Blocks

## Anatomy

- Caused by disease in AV conduction system
  - AV node → HIS → Bundle Branches → Purkinje fibers
- Divided into two causes
  - **AV node disease**
  - **HIS-Purkinje disease**

# AV Blocks

## Anatomy

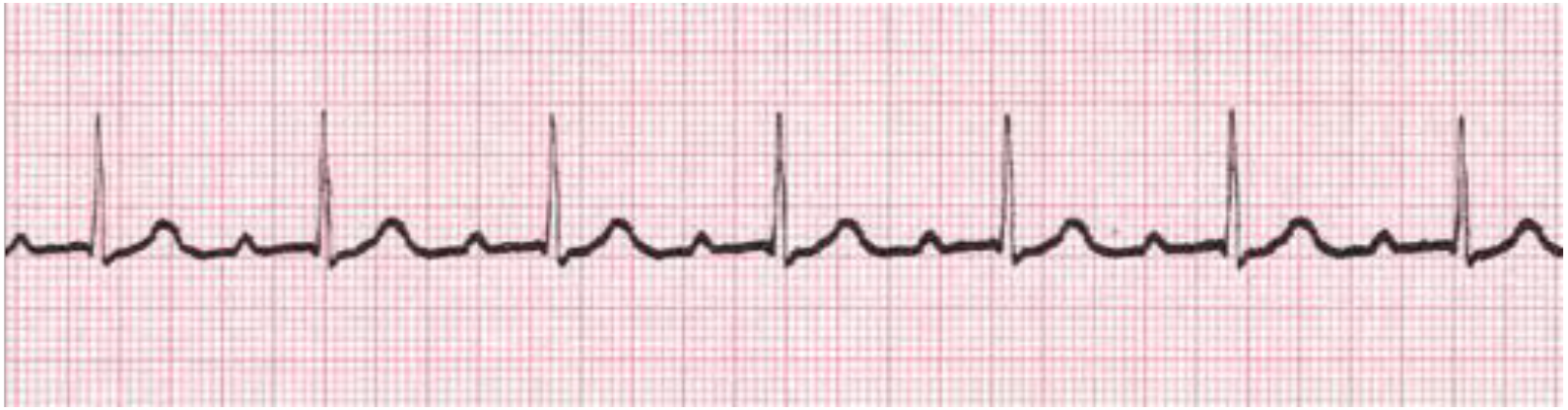
- AV node disease
  - Usually less dangerous
  - Conduction improves with exertion (sympathetic activity)
- HIS-Purkinje disease
  - **More dangerous**
  - Usually does not improve with exertion
  - Often progresses to complete heart block
  - Often requires a pacemaker

# AV Blocks

## Four Types

- Type 1
  - **Prolongation of PR interval only**
  - All p waves conducted
- Type II
  - **Some p waves conducted**
  - **Some p waves NOT conducted**
  - Two sub-types: Mobitz I and Mobitz II
- Type III
  - **No impulse conduction** from atria to ventricles

# 1st degree AV Block



Prolonged PR (normal <200ms)

**Block usually in AV Node**

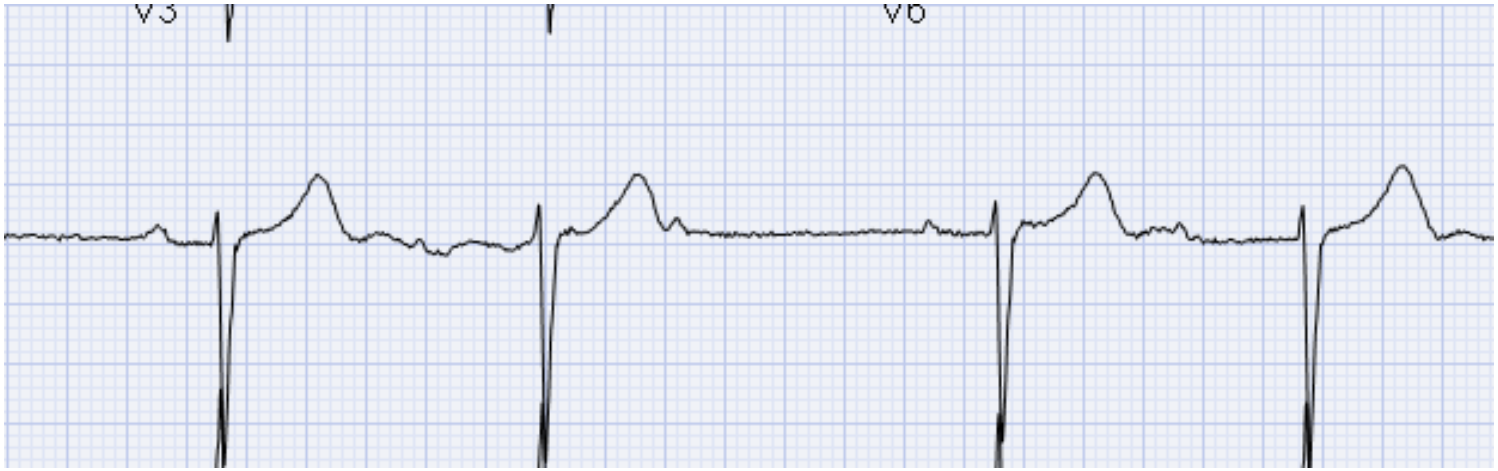
Beta blockers

Calcium channel blockers

Well-trained athletes

# 2nd degree AVB

## Mobitz I/Wenckebach




**Block usually in AV Node**

Progressive PR prolongation

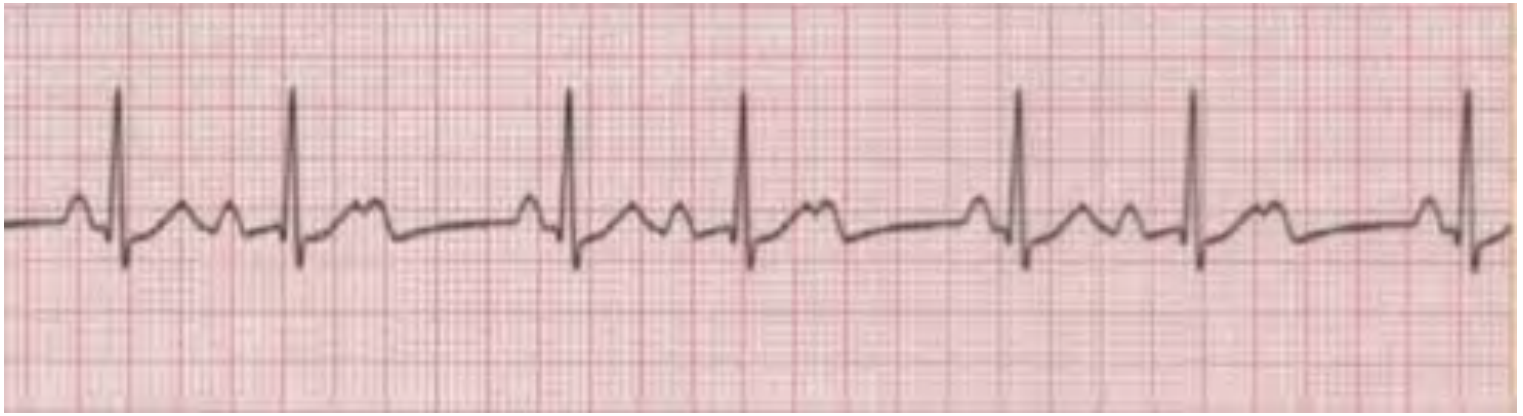
Grouped Beating

RR intervals NOT regular

Similar causes as 1st degree AV block

# 2nd degree AVB

## Mobitz I/Wenckebach



**Block usually in AV Node**

Progressive PR prolongation

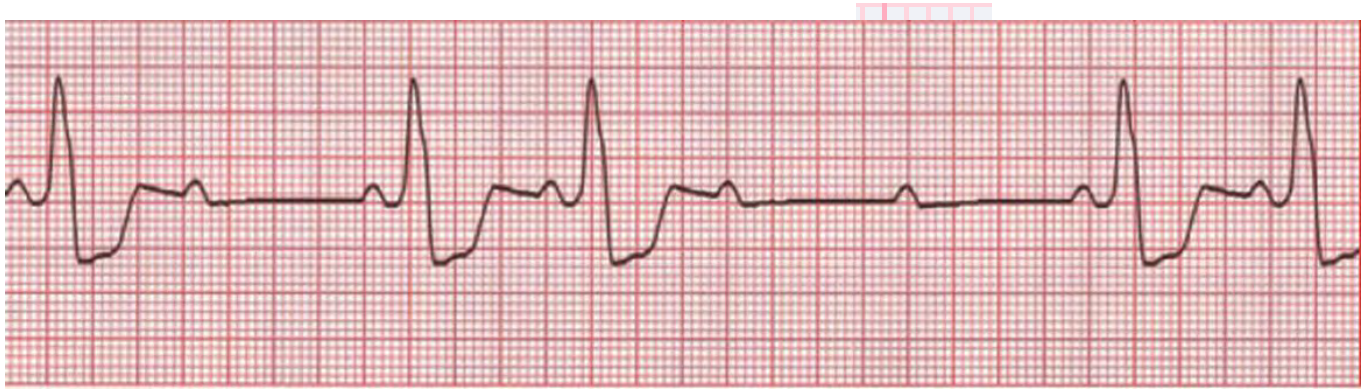
Grouped Beating

RR intervals NOT regular

Similar causes as 1st degree AV block

# 2nd degree AVB

## Mobitz II



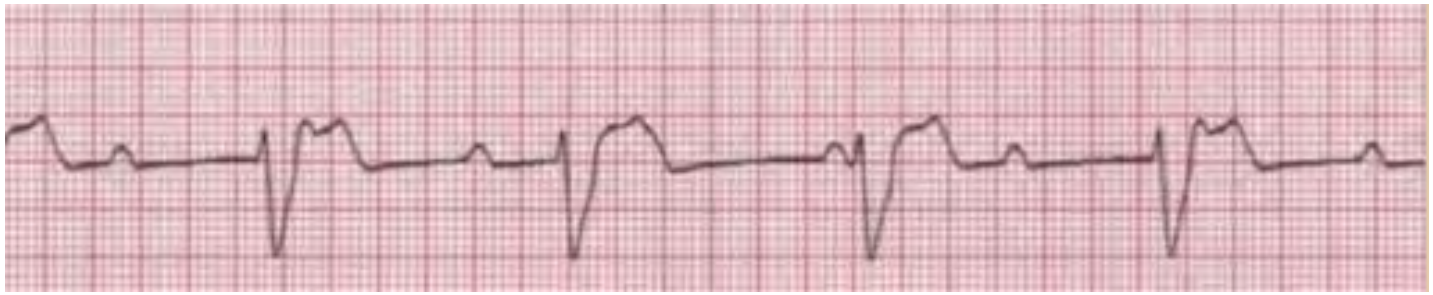
**Block usually in the HIS-Purkinje System**

Often seen with bundle branch block

Usually symptomatic

Dizziness, syncope

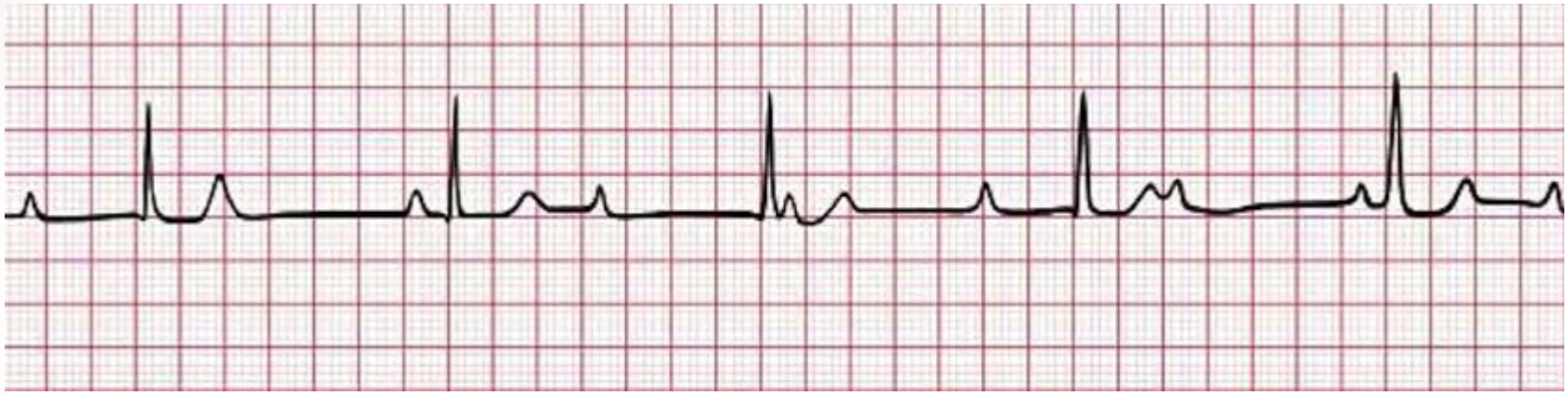
# 3rd degree AVB



**Block usually in the HIS-Purkinje System**

Regular RR intervals excludes Wenckebach

# 3rd degree AVB



**Block usually in the HIS-Purkinje System**

Regular RR intervals excludes Wenckebach

# Lyme Disease

- Spirochete infection with **Borrelia burgdorferi**
- Stage 2: Lyme carditis
- Varying degrees of AV block
  - 1st, 2nd, 3rd
- AV block improves with antibiotics

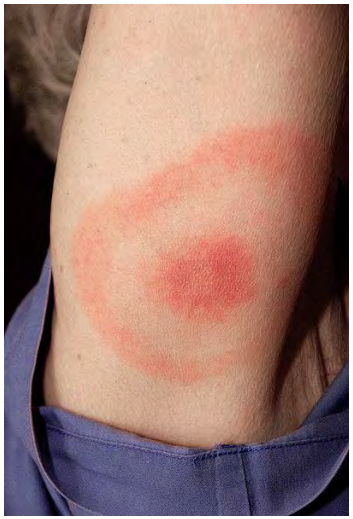
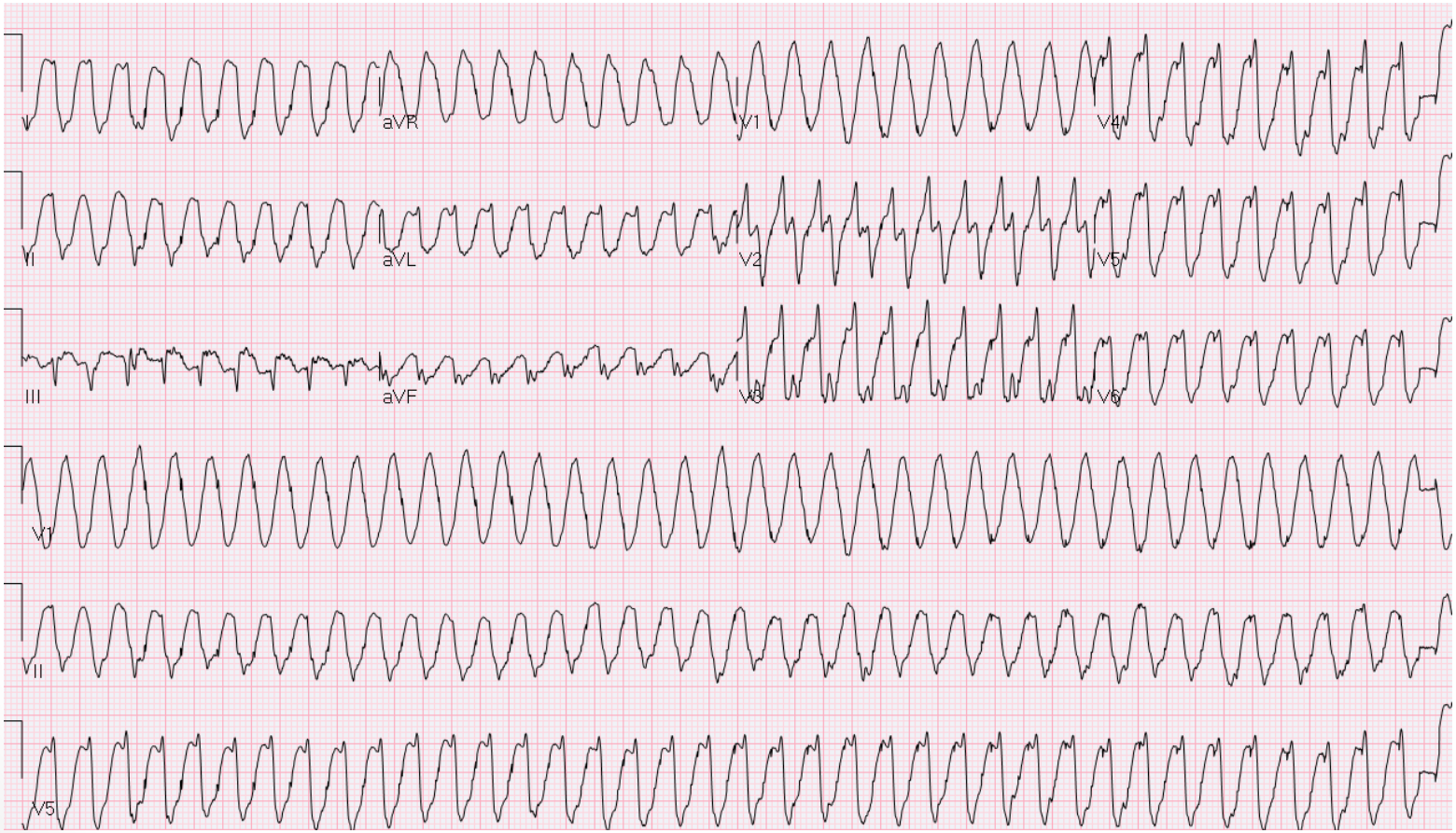


Image courtesy of Wikipedia/Public Domain

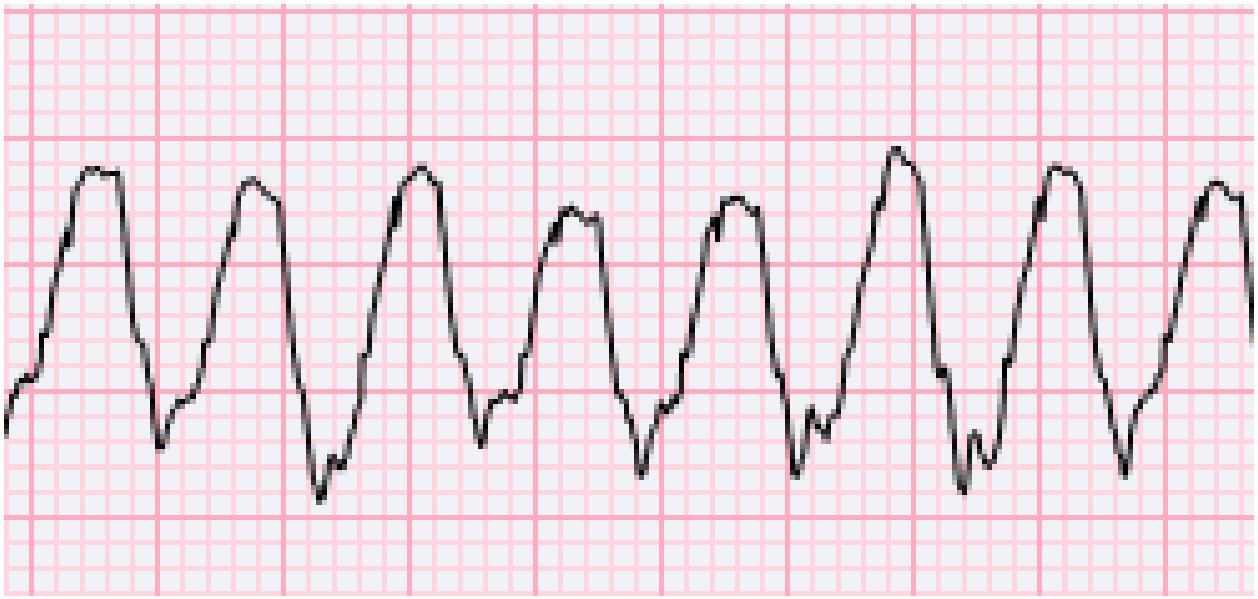
# Vocabulary

- **Complete heart block**
  - Impulses cannot be transmitted from atria to ventricle
- **AV dissociation**
  - Atria and ventricular depolarization uncoupled ("dissociated")
  - Can be cased by complete heart block
  - Also occurs if ventricular rate > sinus rate (no heart block)
  - Seen in ventricular tachycardia and other rhythms

# Ventricular Tachycardia



# Ventricular Tachycardia



# Escape Rhythm

- SA node: Dominant (fastest) pacemaker
- Heart block: SA cannot send impulses to ventricles
- Other pacemakers exist but are slower
  - SA node (60-100 bpm)
  - AV node (40-60 bpm)
  - HIS (25-40 bpm)
  - Bundle branches (25-40 bpm)
  - Purkinje fibers (25–40 bpm)

# Escape Rhythm

- Heart block: lower pacemaker depolarizes ventricles
  - "Escape rhythm"
- Rate of lower pacemaker determines symptoms
  - Very slow: dizziness, syncope, hypotension
  - Less slow: fatigue, exercise intolerance

# Sites of AV Block

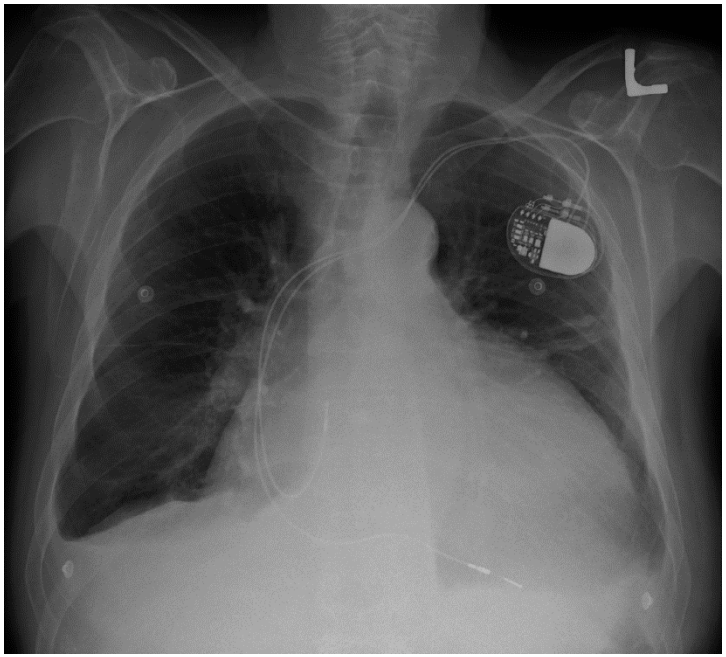
| Disorder | Common Site of Block |
|---|---|
| 1st Degree | AV node |
| Mobitz I | AV Node |
| Mobitz II | His-Purkinje System |
| 3rd degree (Complete) | His-Purkinje System |

# Causes of Heart Block

- Drugs
  - Beta blockers, calcium channel blockers
  - Digoxin
- High vagal tone
  - Athletes
- Fibrosis and sclerosis of conduction system

# Pacemaker

- Treatment for “high grade” AV block
- Usually 3rd degree or Mobitz II
- Often in patients with symptoms (syncope, dizziness)

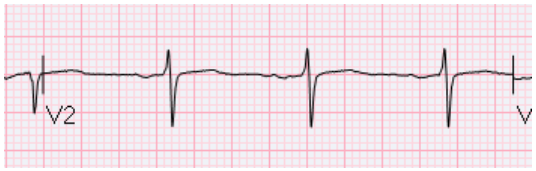


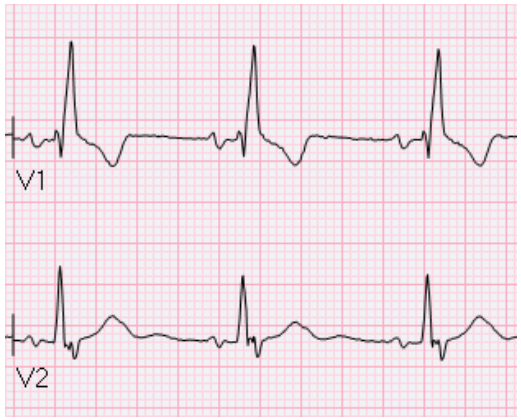
# Bundle Branch Blocks

- Both bundle branches blocked
  - Results in AV block
  - Form of HIS-Purkinje system disease
- **ONE** bundle branch blocked
  - Does not cause AV block
  - Normal PR interval
  - **QRS will be prolonged**

# Bundle Branch Blocks

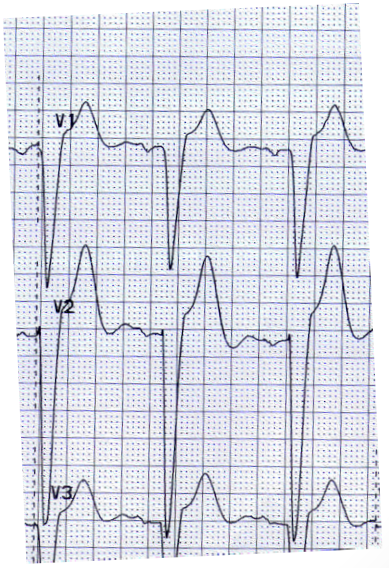
Normal QRS



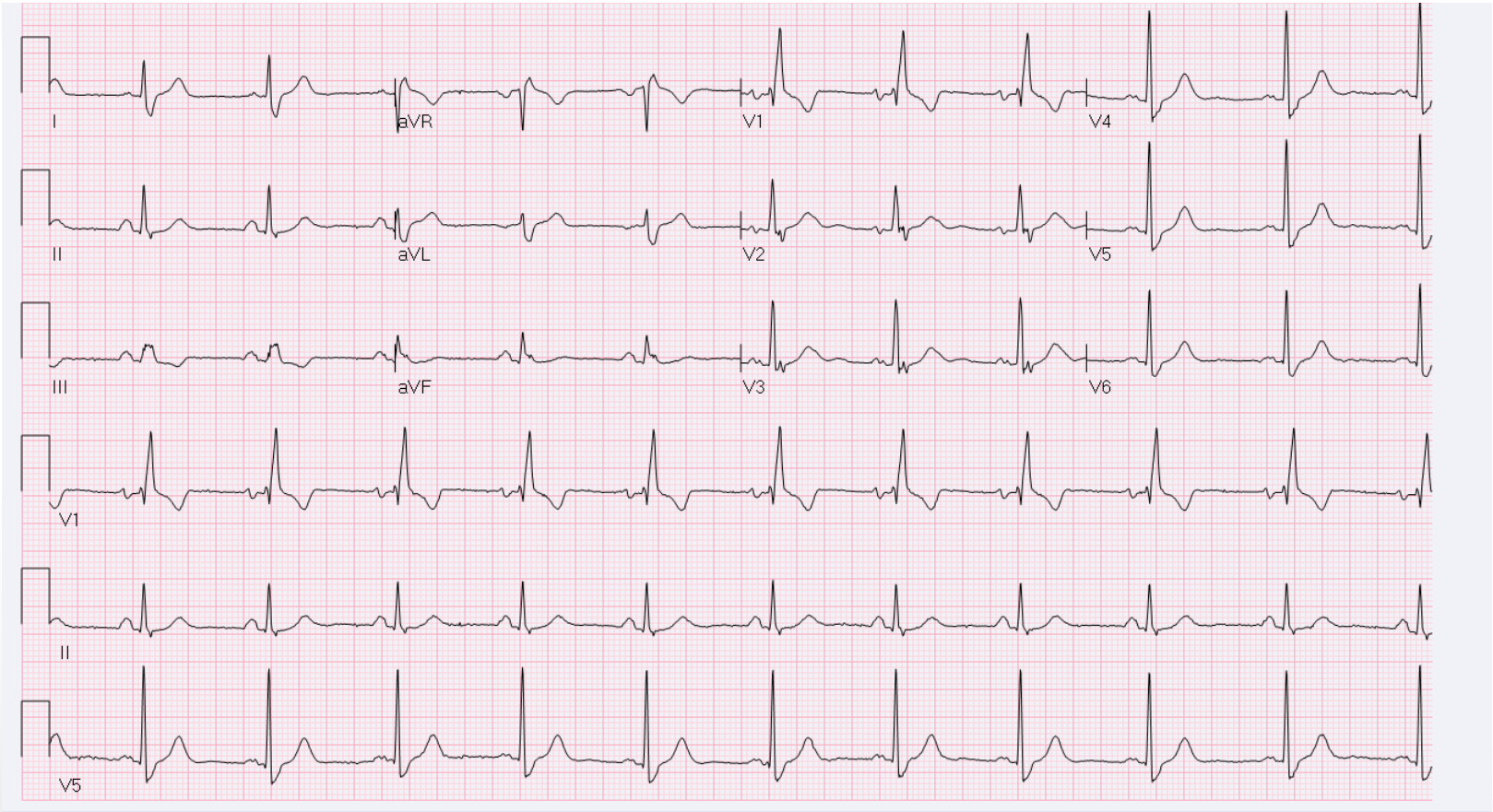




Right Bundle Branch Block

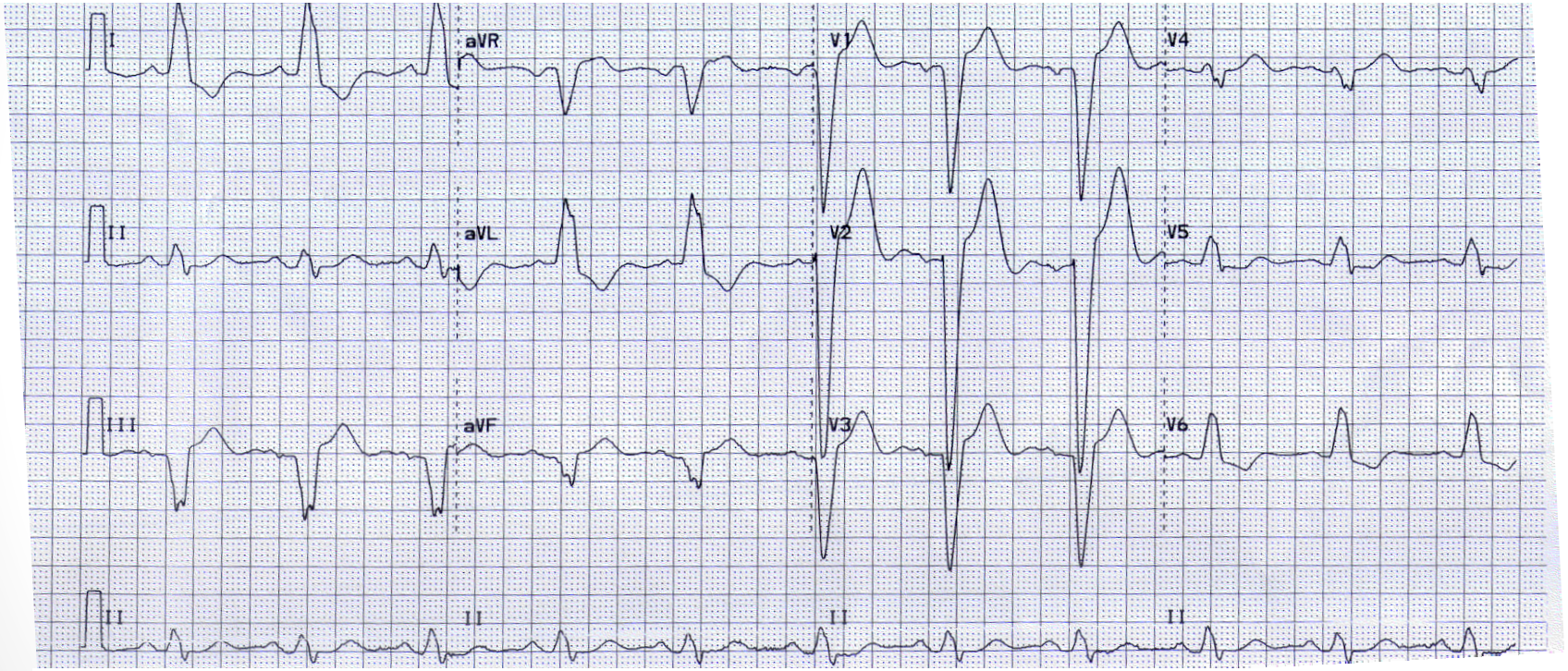
Left Bundle Branch Block



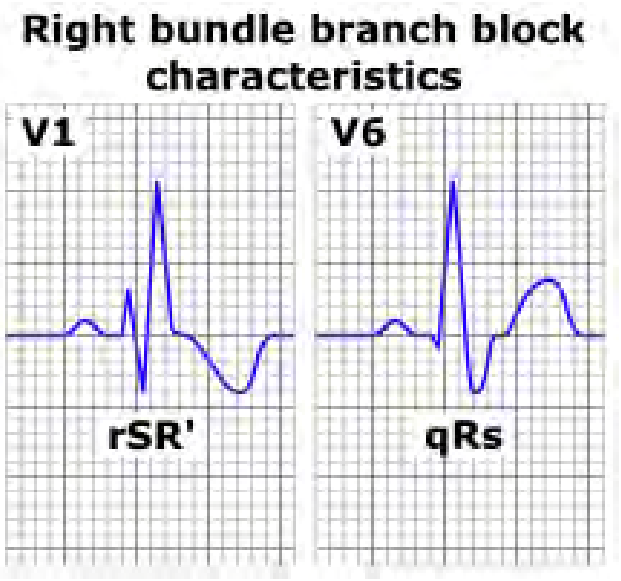
# Right Bundle Branch Block

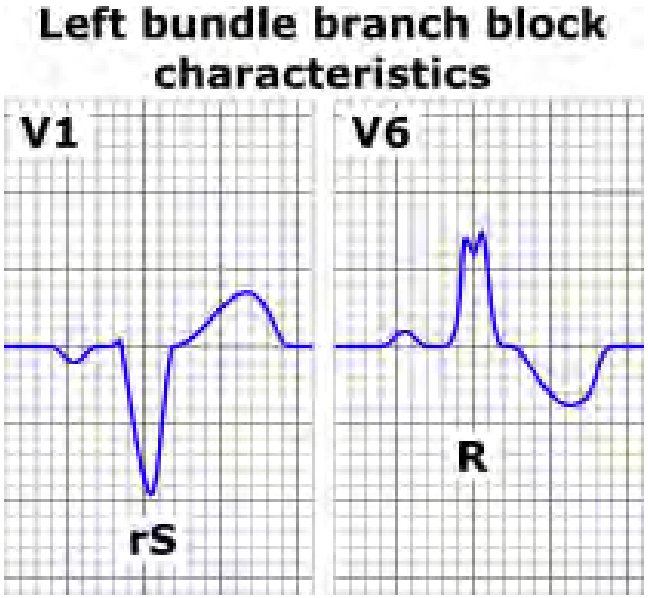


# Left Bundle Branch Block



# Bundle Branch Blocks






A. Rad/Wikipedia

# Bundle Branch Blocks

- Symptoms: **None**
  - Identified incidentally on ECG
- May progress to AV block (need for pacemaker)
- Interfere with detection of ischemia
  - ST elevations, T-wave inversions can be normal

# Bundle Branch Blocks

## Causes

- Often caused by slowly progressive fibrosis/sclerosis
- More common in older patients
- Can result from “structural heart disease”
- LBBB: Prior MI, cardiomyopathy
- RBBB: Right heart failure

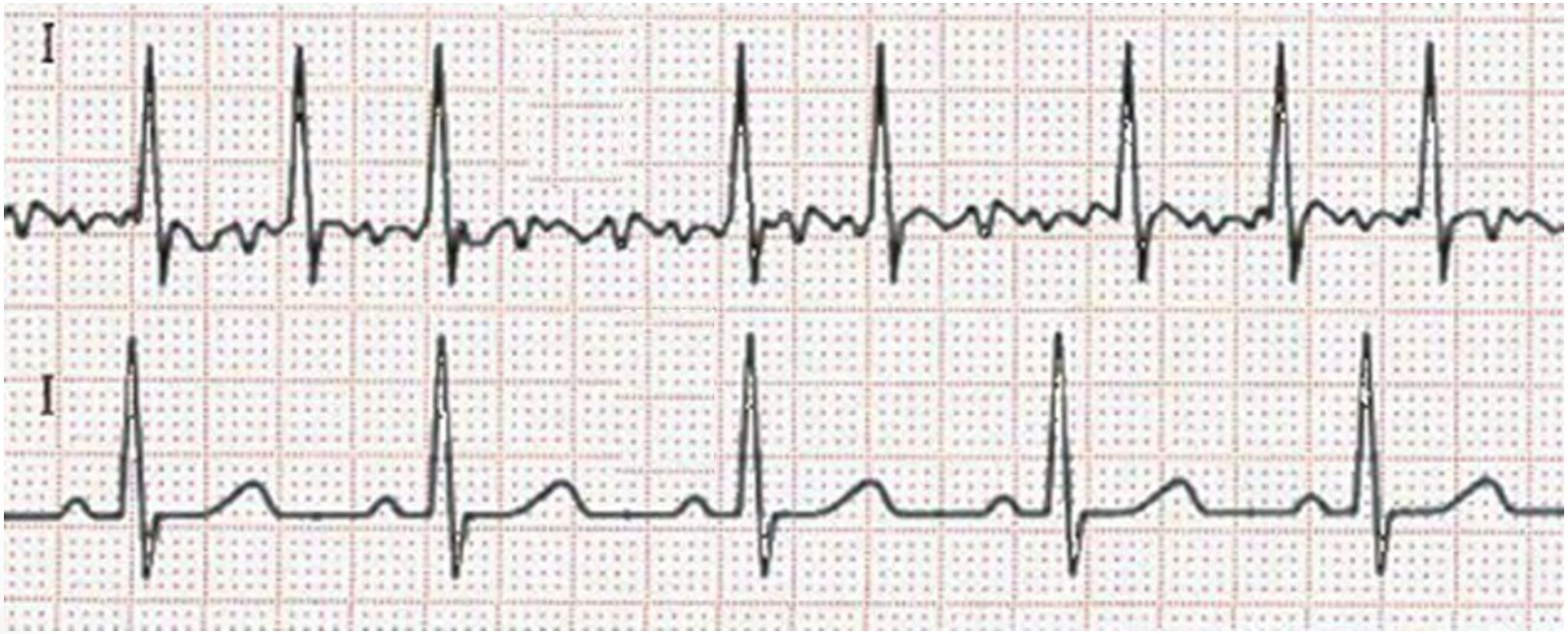
# Atrial Fibrillation and Flutter

Jason Ryan, MD, MPH

# Atrial Fibrillation

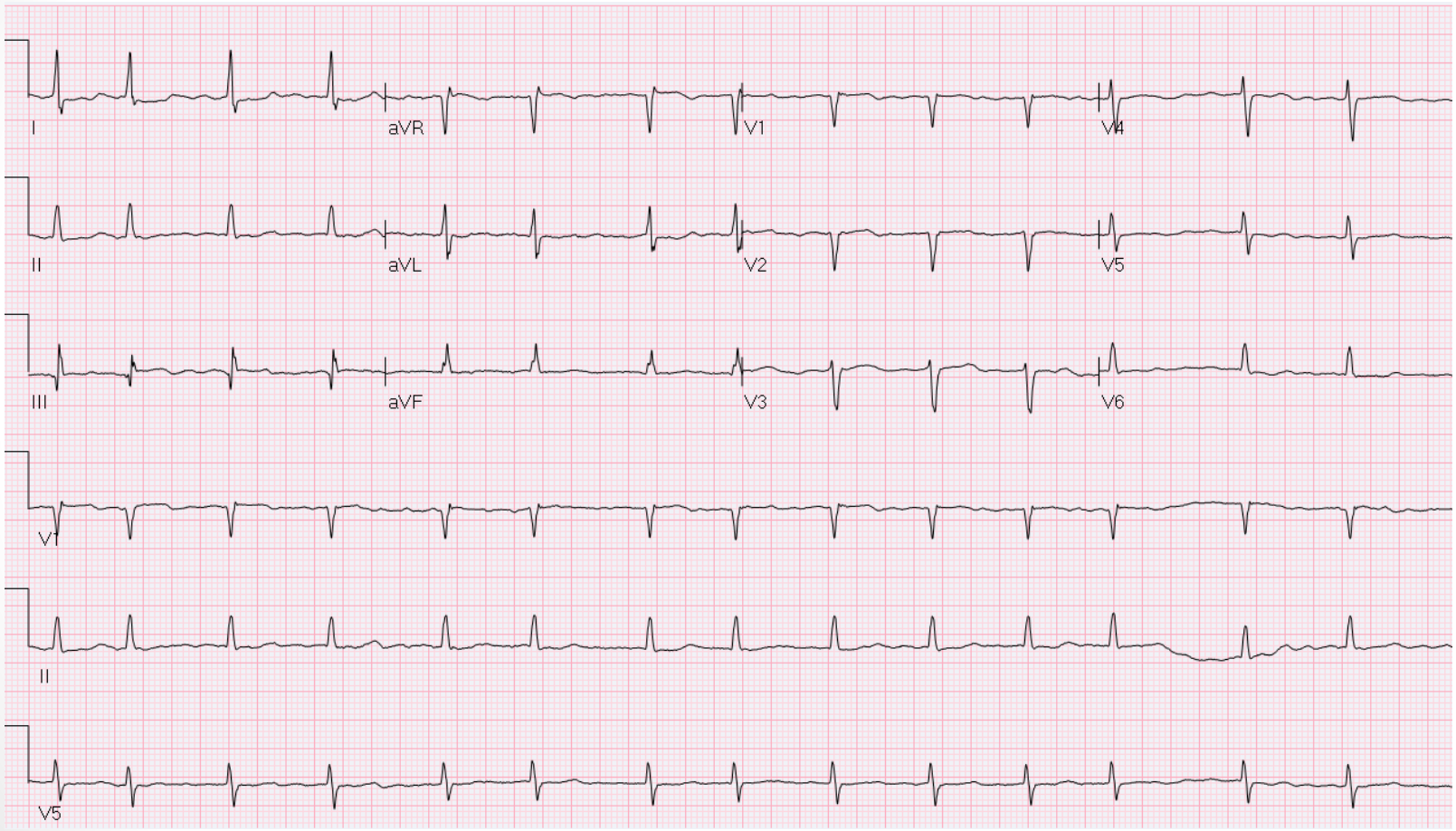
- Cardiac arrhythmia
- Results in an **irregularly, irregular** pulse
- Can cause palpitations, fatigue, dyspnea
- Diagnosis: EKG

# Atrial Fibrillation

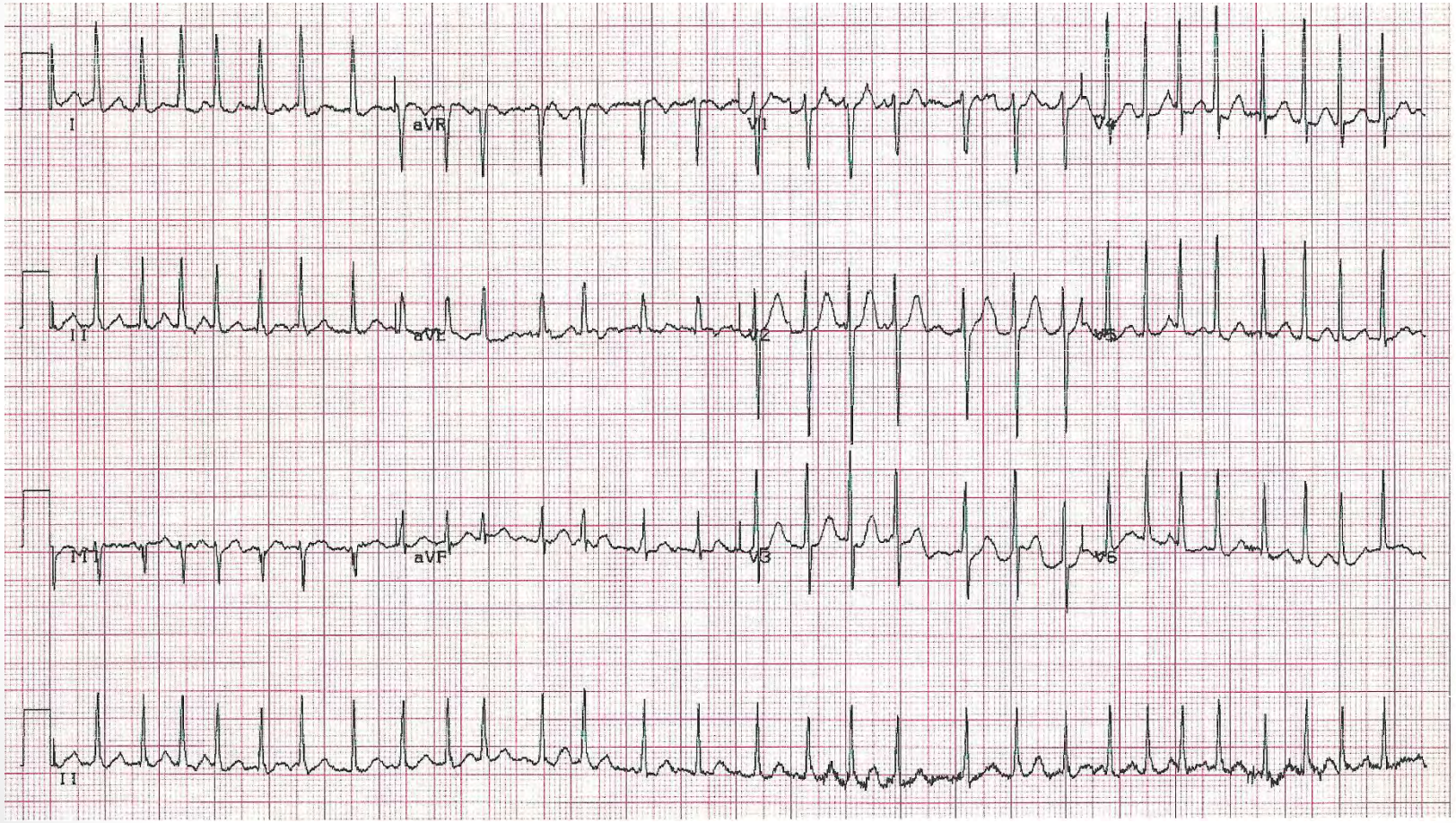



J. Heuser/Wikipedia

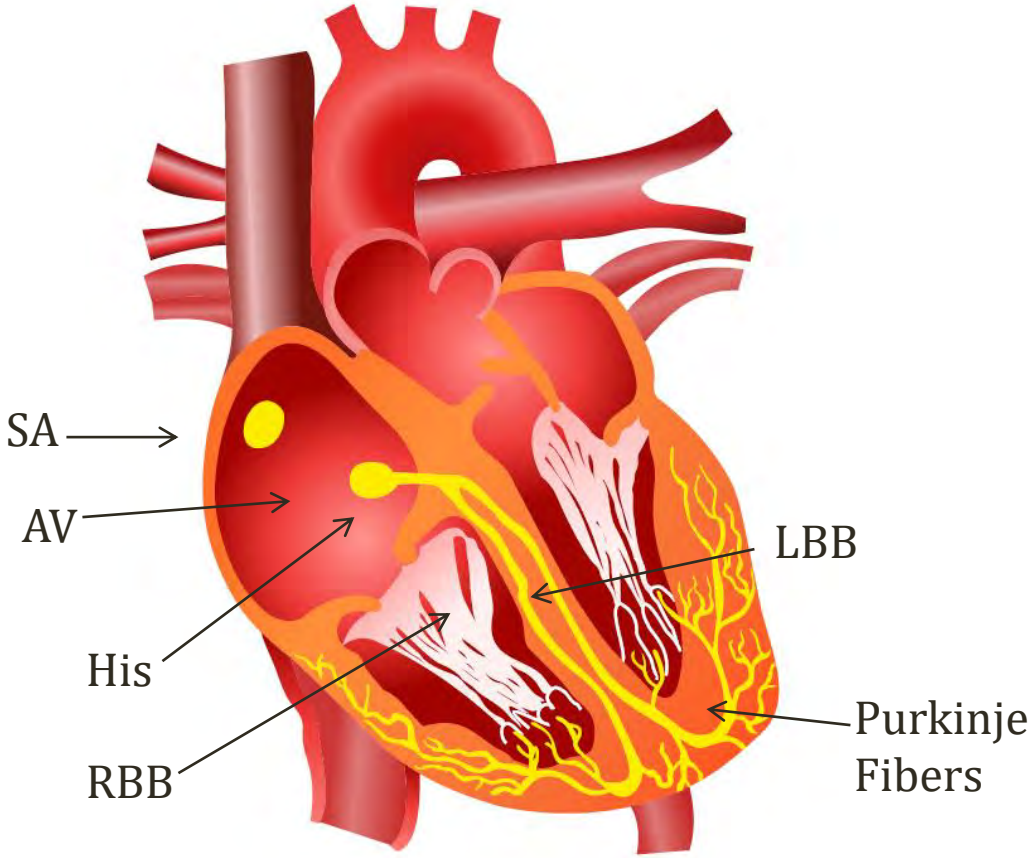
# Atrial Fibrillation



# Atrial Fibrillation



# Atrial Fibrillation



# Atrial Fibrillation

## Terminology

- Paroxysmal
  - Comes and goes; spontaneous conversion to sinus rhythm
- Persistent
  - Lasts days/weeks; often requires cardioversion
- Permanent

# Atrial Fibrillation

## Symptoms

- Wide spectrum of symptoms

**Asymptomatic**
Heart Rate <100bpm

**Palpitations, Dyspnea, Fatigue**
Heart Rate >100bpm

# Cardiomyopathy

- Caused by untreated, **rapid** atrial fibrillation
- "Tachycardia-induced cardiomyopathy"
- ↓ LVEF
- Systolic heart failure

# Heart Rate

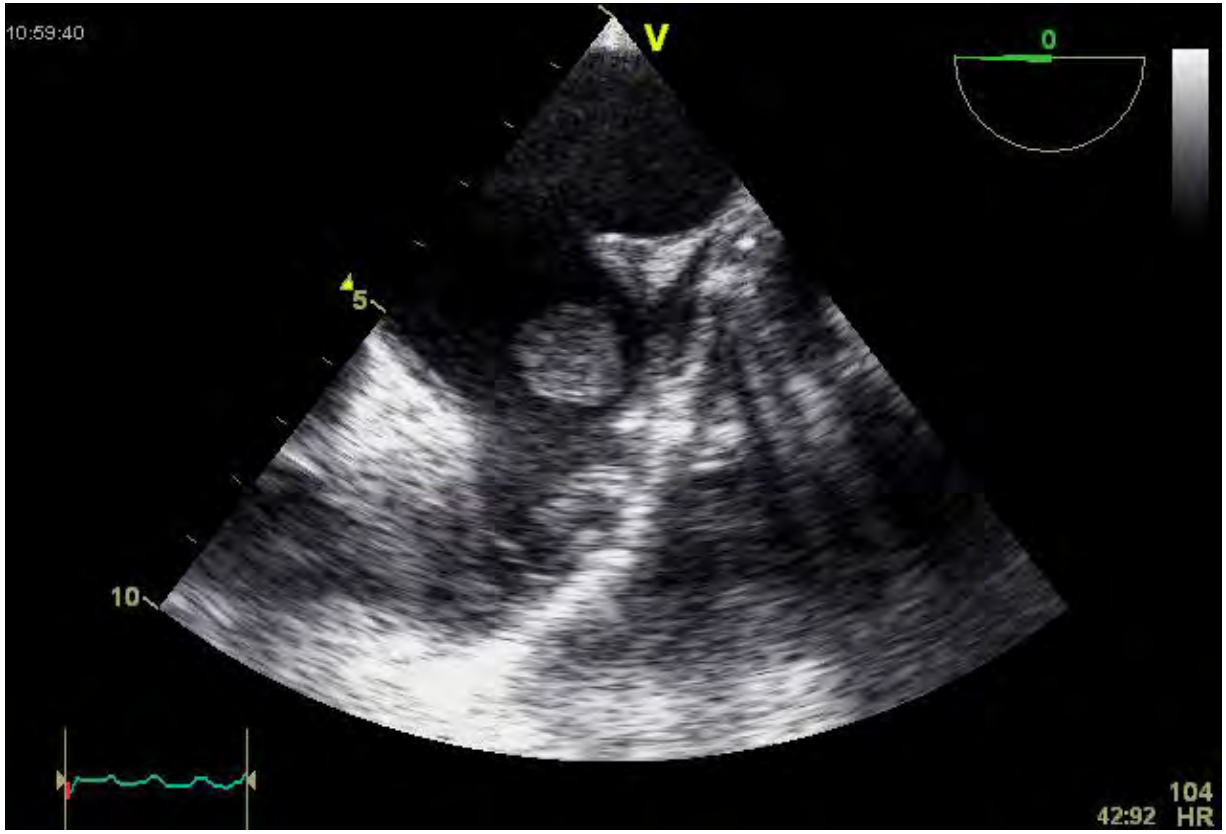
- **AV node refractory period** determines heart rate
- Young, healthy patients → rapid heart rate
- Older patients → slower heart rate
- Atrial rate in fibrillation: 300-500bpm
- Ventricular rate: 70-180bpm

# Preload

- Atrial fibrillation eliminates ventricular pre-filling
- “Loss of atrial kick”
- **Decreases preload**
- Can lead to low cardiac output and hypotension
- Especially in “preload dependent” patients
  - Aortic stenosis
  - LVH or diastolic heart failure (stiff ventricle)

# Atrial Fibrillation

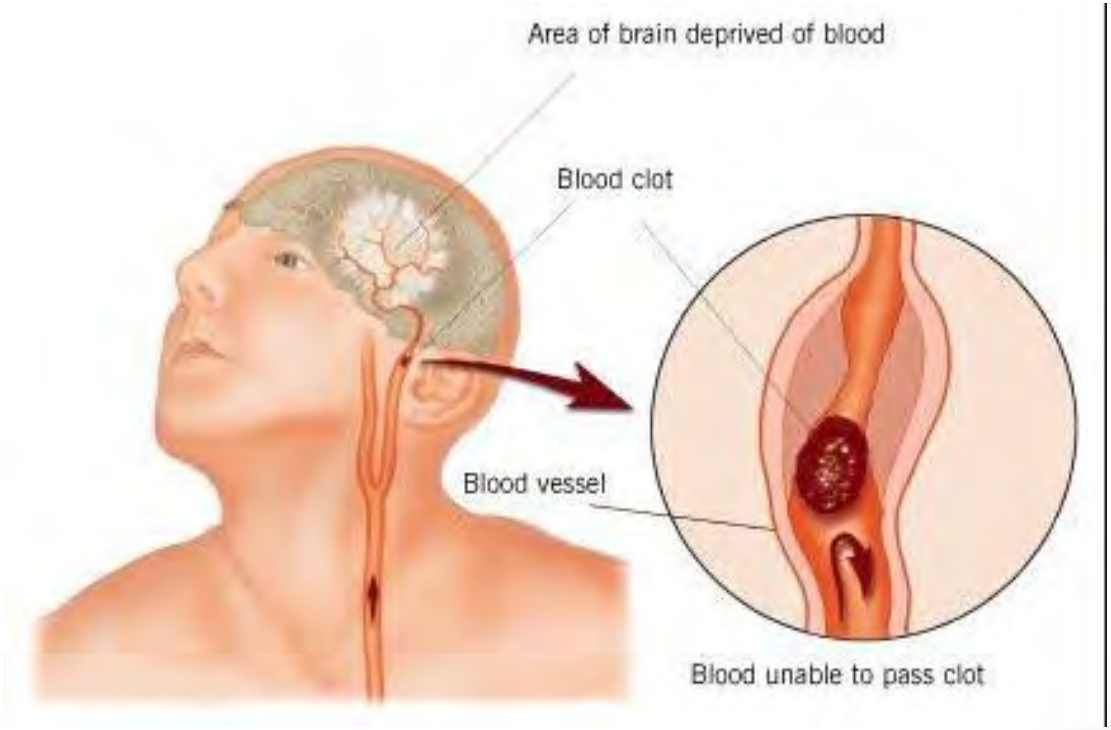
## Thrombus in Left Atrial Appendage



# Atrial Fibrillation

## Cardiac Embolism

- Brain (stroke)
- Gut (mesenteric ischemia)
- Spleen



# Valvular Atrial Fibrillation

- Associated with rheumatic heart disease
- Usually **mitral stenosis**
- Often refractory to treatment
- VERY high risk of thrombus
- Non-valvular: not associated with rheumatic disease

# Atrial Fibrillation

## Risk Factors

- **Age**
  - ~10% of patients >80
  - <1% of patients <55
- More common in women
- Most common associated disorders: **HTN, CAD**
- Anything that dilates the atria → atrial fibrillation
  - Heart failure
  - Valvular disease
- Key diagnostic test: Echocardiogram

# Hyperthyroidism

- Commonly leads to atrial fibrillation
- Reversible with therapy for thyroid disease
- Atrial fibrillation therapies less effective
- Key diagnostic test: **TSH**

# Atrial Fibrillation

## Triggers

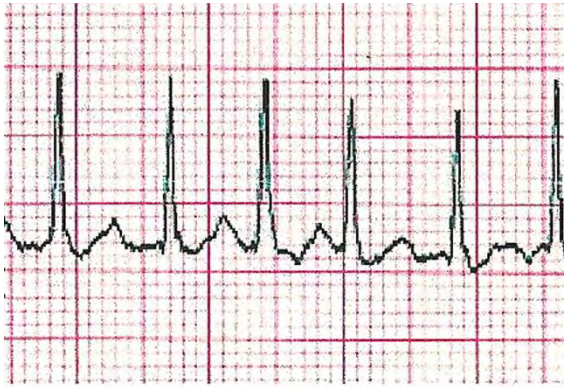
- Often no trigger identified
- Binge drinking ("holiday heart")
- Increased catecholamines
  - Infection
  - Surgery
  - Pain

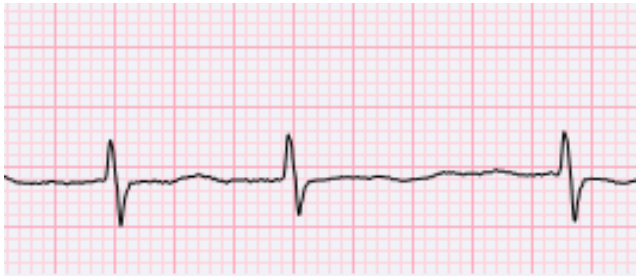
# Atrial Fibrillation

## Treatment

- Heart Rate
  - “Rate control”
  - Ideally <110bpm
- Heart Rhythm
  - “Rhythm control”
  - Restoration of sinus rhythm
- Anticoagulation

# Rate Control





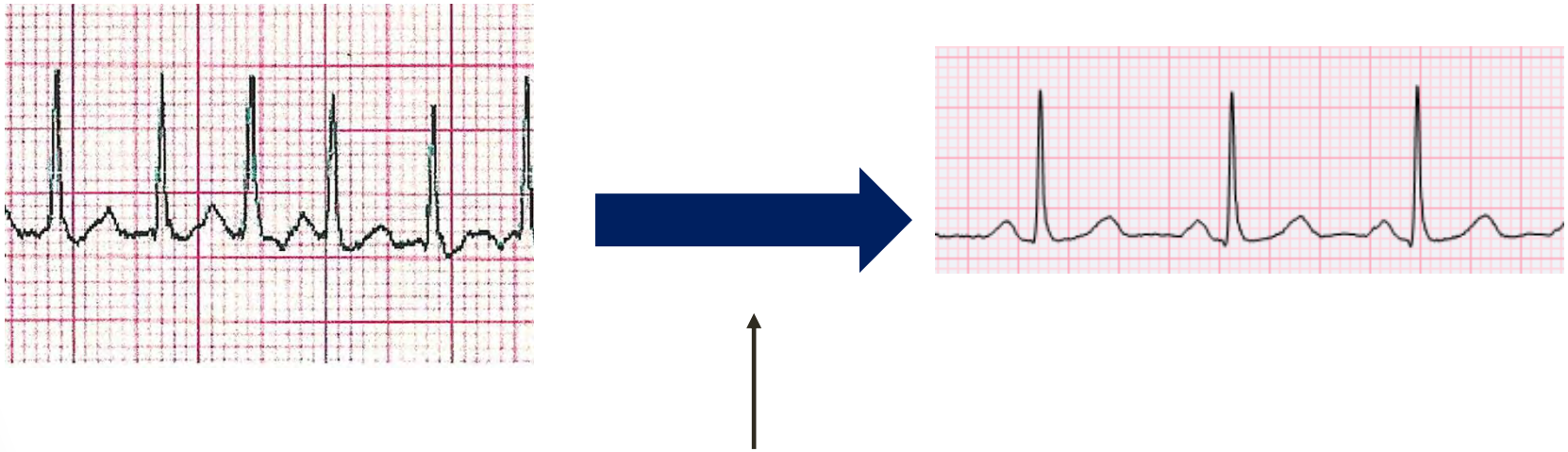
Beta Blockers
Calcium Channel Blockers
Digoxin

# Rate Control

- Use drugs that **slow AV node conduction**
- Beta blockers
  - Usually β1 selective agents
  - Metoprolol, Atenolol
- Calcium channel blockers
  - Verapamil, Diltiazem
- Digoxin
  - Increases parasympathetic tone to heart

# Rhythm Control

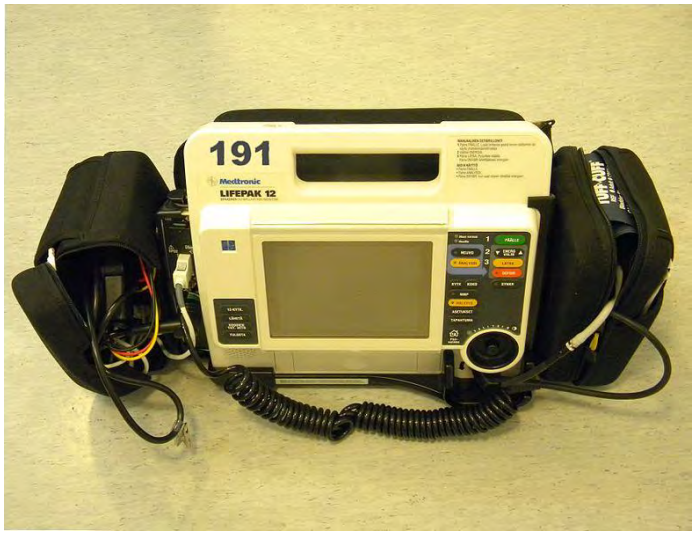
- Goal: restore sinus rhythm



**Cardioversion**

# Cardioversion

- **Electrical**
  - Deliver “synchronized” shock at time of QRS
  - Administer anesthesia
  - Deliver electrical shock to chest
  - All myocytes depolarize
  - Usually sinus node first to repolarize/depolarize




Pollo/Wikipedia

# Cardioversion

- **Chemical**
  - Administration of antiarrhythmic medication
  - Often Ibutilide (class III antiarrhythmic)
  - Less commonly used due to drug toxicity

# Cardioversion

- **Spontaneous**
  - Often occurs after hours/days

# Cardioversion

## Risk of Stroke

- Chemical/electrical cardioversion may cause stroke
- 48hours required for thrombus formation
- Symptoms <48hours: cardioversion safe
- Symptoms >48hours (or unsure)
  - Anti-coagulation 3 weeks → cardioversion
  - Transesophageal echocardiogram to exclude thrombus
- Exception: Hypotension/shock
  - Emergent cardioversion performed

# Rhythm Control

- **Antiarrhythmic medications**
- Administered before/after cardioversion
- Class I drugs
  - Flecainide, propafenone
- Class III drugs
  - Amiodarone, sotalol, dofetilide

# Anticoagulation

- Warfarin
  - Requires regular INR monitoring
  - Goal INR usually 2-3
- Rivaroxaban, Apixaban
  - Factor X inhibitors
- Dabigatran
  - Direct thrombin inhibitor
- Aspirin
  - Less effective
  - Only used if risk of stroke is very low
  - Less risk of bleeding

# Anticoagulation

- Whether atrial fibrillation persists or sinus rhythm restored anticoagulation MUST be administered
- Studies show similar stroke risk for rate control versus rhythm control

# Stroke Risk

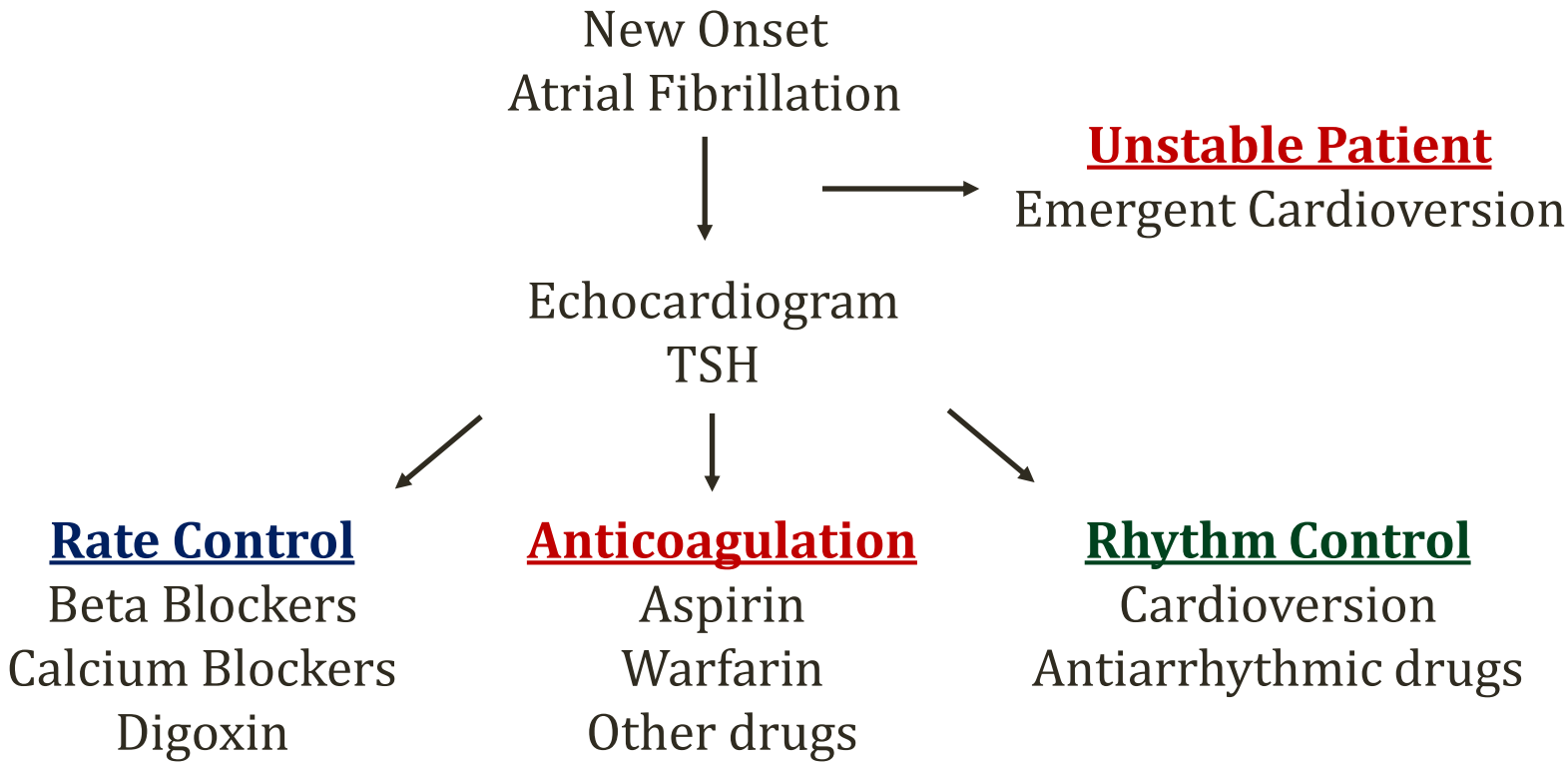
- **CHADS Score**
  - CHF (1 point)
  - HTN (1 point)
  - Age >75yrs (1 point)
  - Diabetes (1 point)
  - Stroke (2 points)
- Score $\geq$2 = Warfarin or other anticoagulant
- Score 0 -1 = Aspirin

# Stroke Risk

- **CHADS VASC Score**
  - CHF (1point)
  - HTN (1pont)
  - Diabetes (1point)
  - Stroke (2points)
  - Female (1point)
  - Age 65-75 (1point)
  - Age >75yrs (2points)
  - Vascular disease (1point)
- Score $\geq$2 = Warfarin or other anticoagulant
- Score 0 -1 = Aspirin

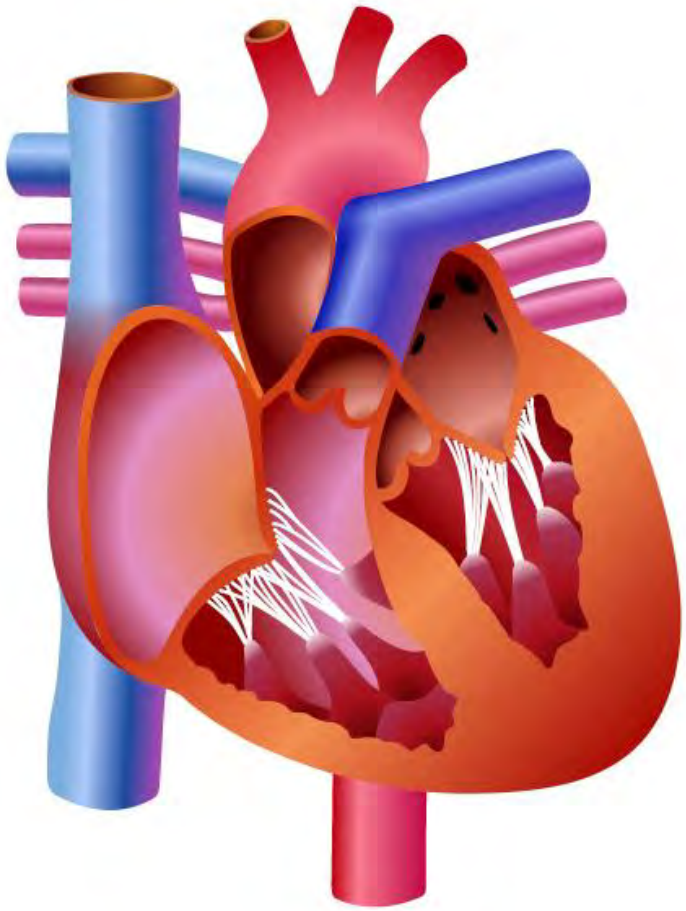
# Atrial Fibrillation

## Summary



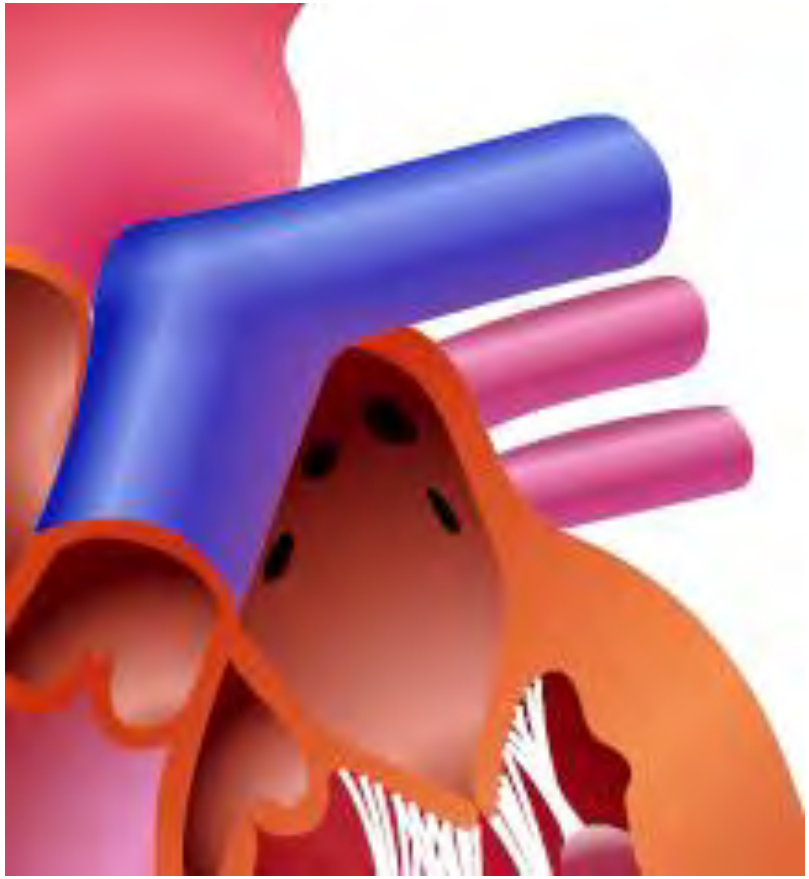
# Pulmonary Vein Isolation

## Surgical Therapy for Atrial Fibrillation

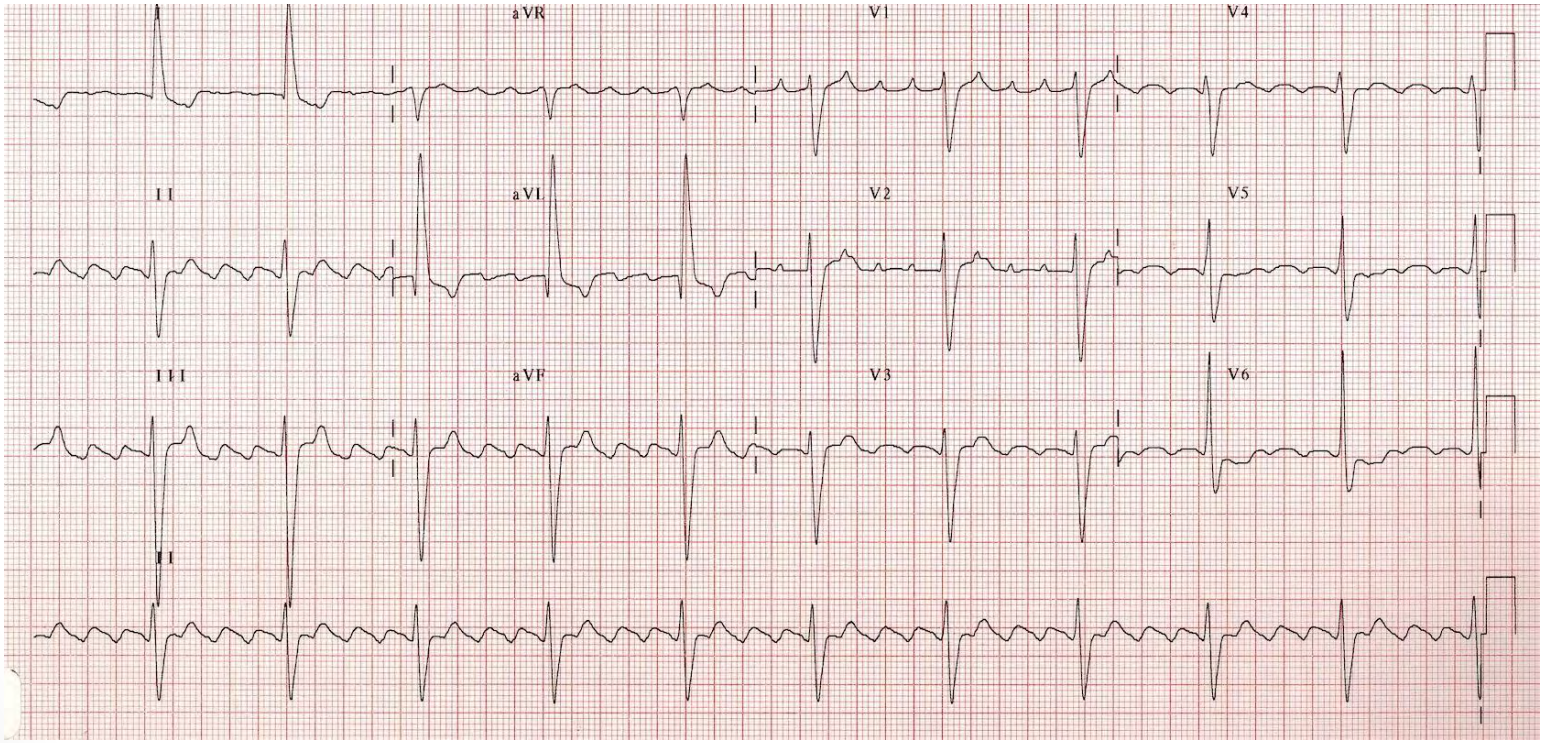


# Pulmonary Vein Isolation

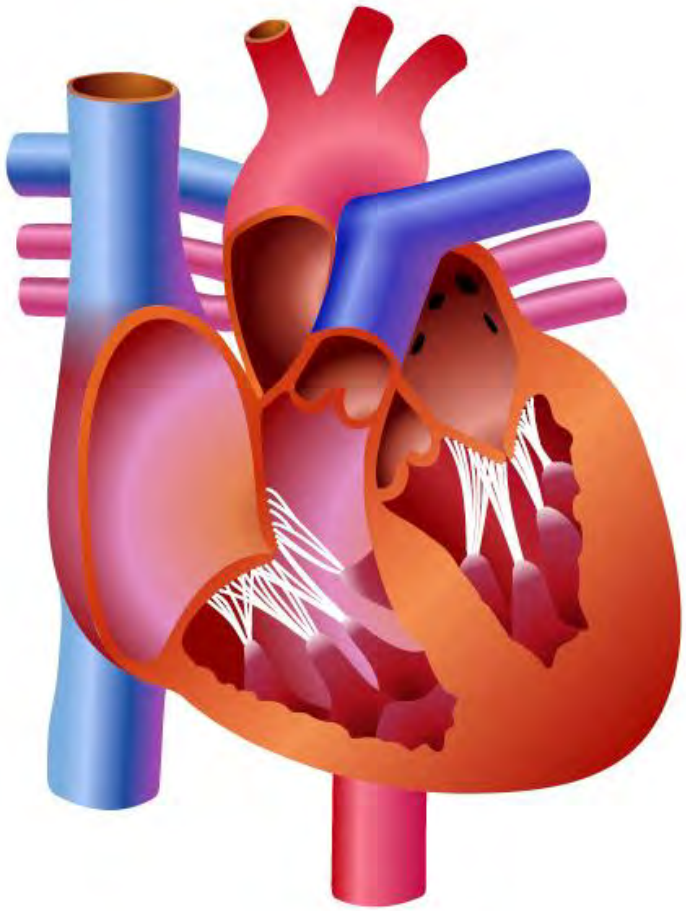
## Surgical Therapy for Atrial Fibrillation



# Atrial Flutter



# Atrial Flutter



# Atrial Flutter

## Symptoms

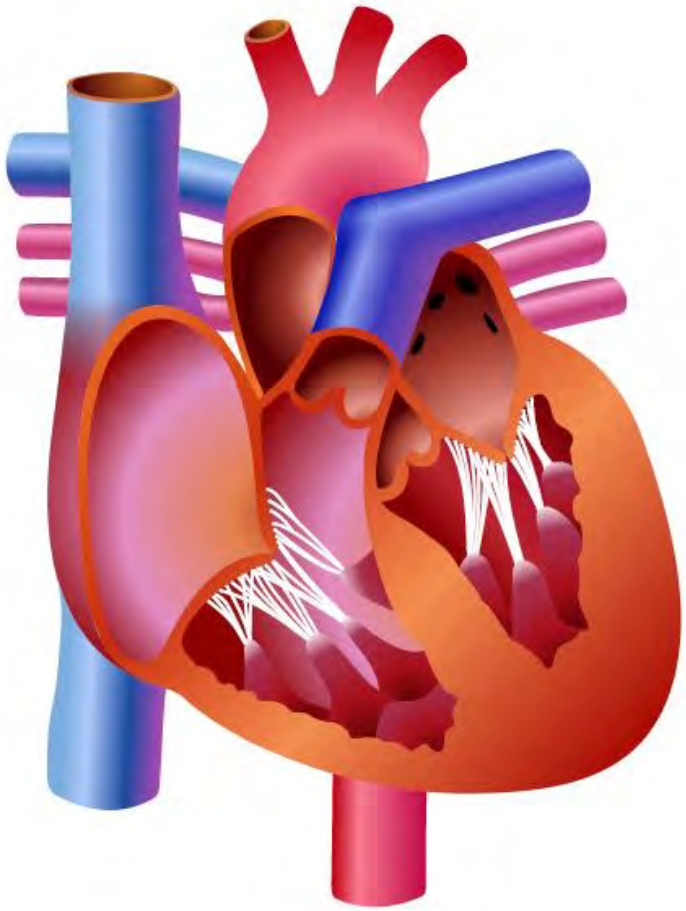
- Generally the same as atrial fibrillation
- May be asymptomatic
- Palpitations, dyspnea, fatigue

# Atrial Flutter

## Treatment

- Generally the same as atrial fibrillation
- Rate or rhythm control
- Rate-slowing drugs
- Cardioversion
- Anticoagulation based on stroke risk

# Atrial Flutter Ablation



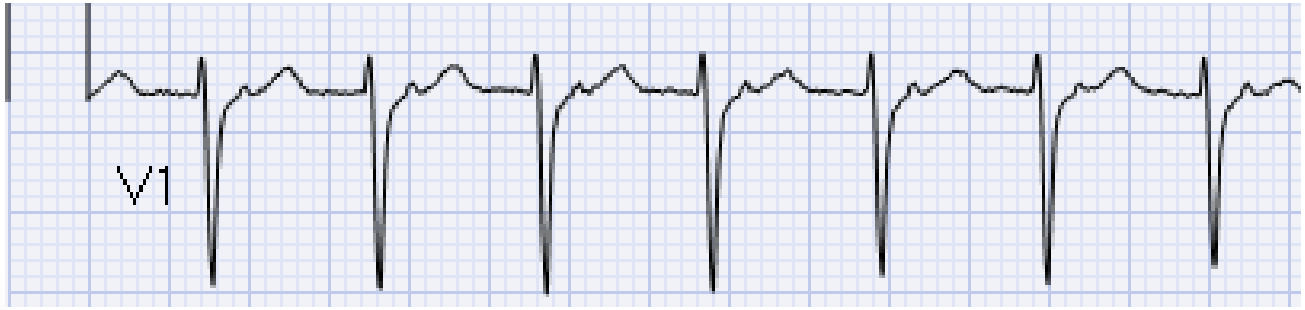
# AVNRT

Jason Ryan, MD, MPH

# PSVT

## Paroxysmal Supraventricular Tachycardia

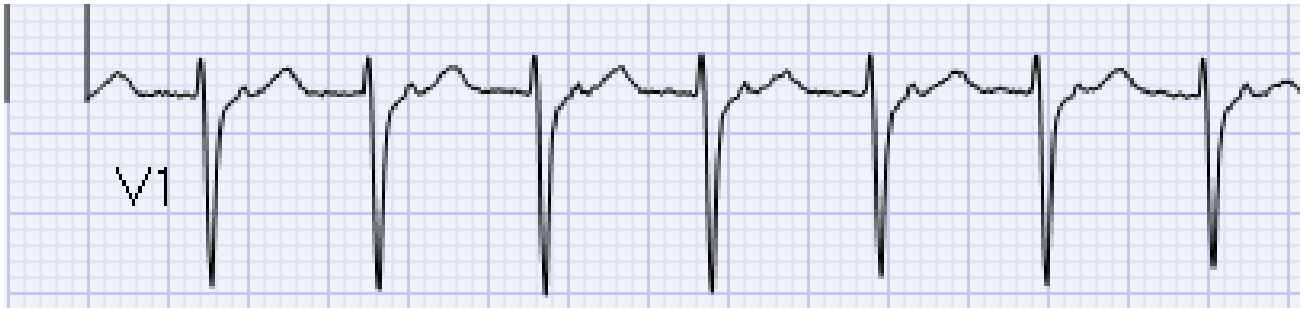
- Intermittent tachycardia (HR > 100bpm)
- **Sudden onset/offset**
  - Contrast with sinus tachycardia
- Electrical activity originates above ventricle
  - "Supraventricular"
  - Contrast with ventricular tachycardia
  - Produces narrow QRS complex (<120ms)



# PSVT

## Paroxysmal Supraventricular Tachycardia

- Often causes **sudden-onset palpitations**
- Chest discomfort
- Rarely syncope

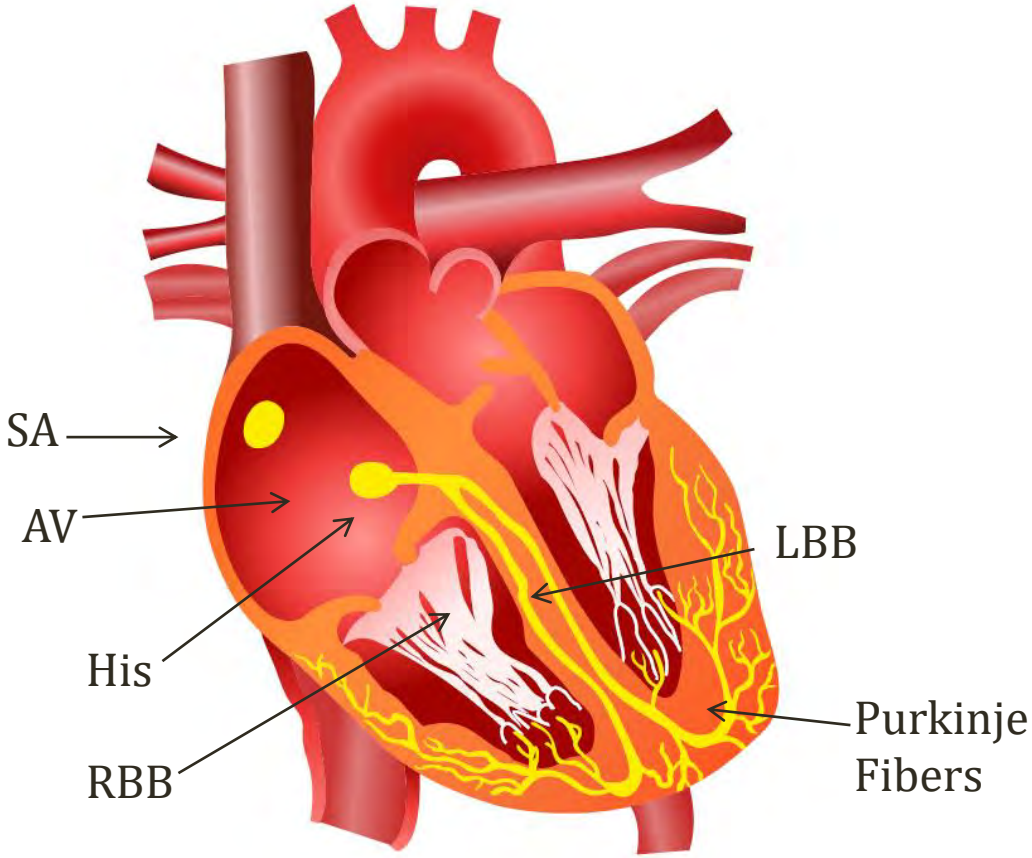


# AVNRT

## Atrioventricular nodal reentrant tachycardia

- **Most common cause of PSVT**
- More common in young women
- Mean age onset: 32 years old
- Requires **dual AV nodal pathways**

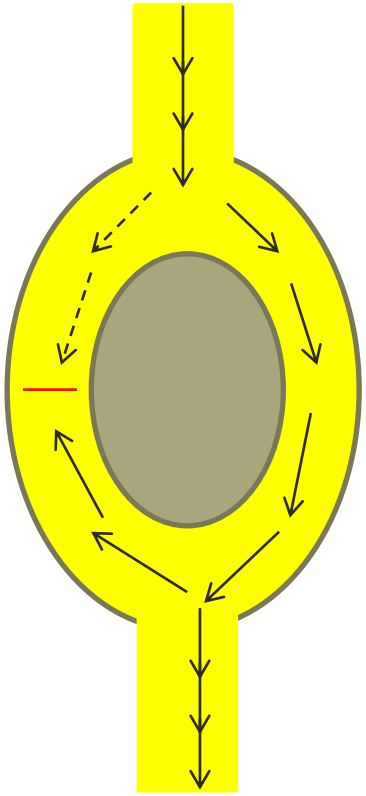
# Normal Conduction



# Dual Pathways

## Sinus Rhythm

**Slow**
Conduction
Short RP



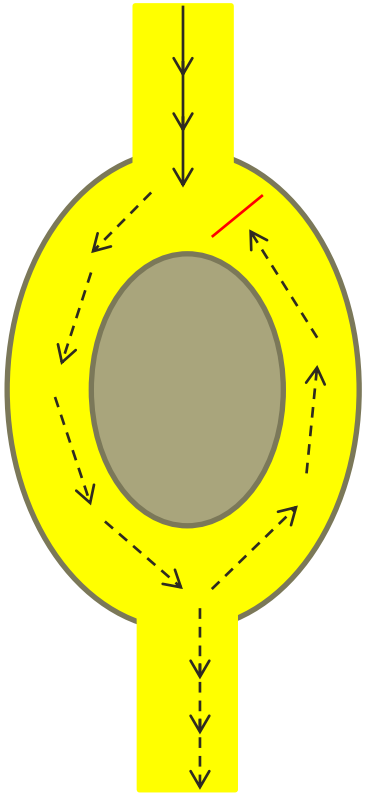
**Fast**
Conduction
Long RP

HIS

# Dual Pathways

PAC

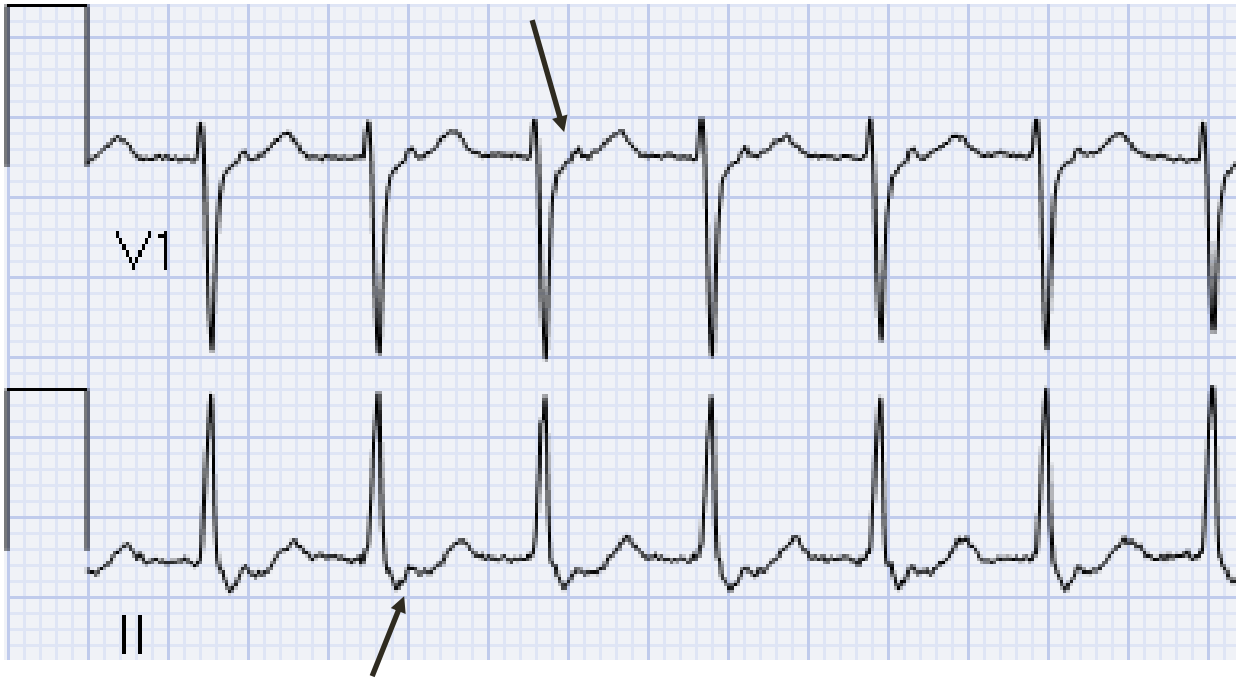
**Slow**
Conduction
Short RP



**Fast**
Conduction
Long RP

HIS

# Retrograde P Waves



# AVNRT

- Recurrent episodes of palpitations
- Many episodes spontaneously resolve
- ↓ conduction in AV node breaks arrhythmia
  - Will halt conduction is slow pathway
- Carotid massage
- Vagal maneuvers
- Adenosine

# Carotid Massage

- Examiner presses on neck near carotid sinus
- **Stretch of baroreceptors**
- CNS response as if **high blood pressure**
- Increased vagal tone
- ↓ AV node conduction

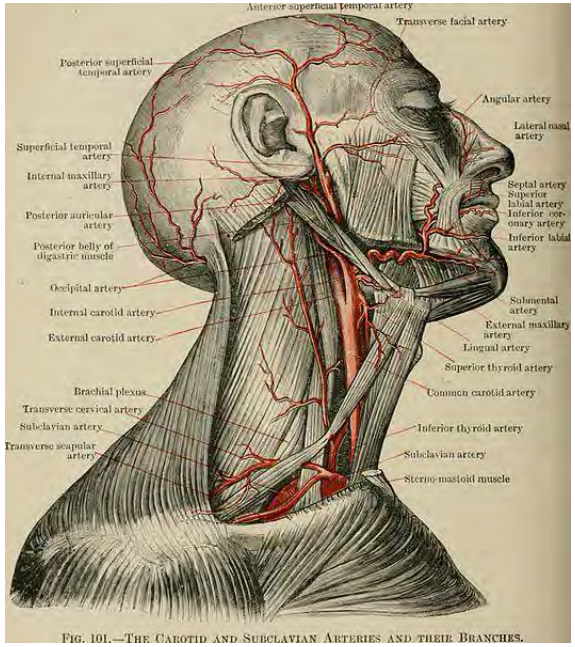


FIG. 101.—THE CAROTID AND SUBCLAVIAN ARTERIES AND THEIR BRANCHES.

Wikipedia/Public Domain

# Vagal Maneuvers

- **Valsalva**
  - Patient bears down as if moving bowels
  - Increased thoracic pressure
  - Aortic pressure rises → ↓ heart rate and AV conduction
- Breath holding
- Coughing
- Deep respirations
- Gagging
- Swallowing

# AVNRT

## Chronic Treatment

- Many patients need no therapy
- Beta blockers, Verapamil/Diltiazem
  - Slow conduction in slow pathway
- Surgical ablation of slow pathway

# Wolff-Parkinson White

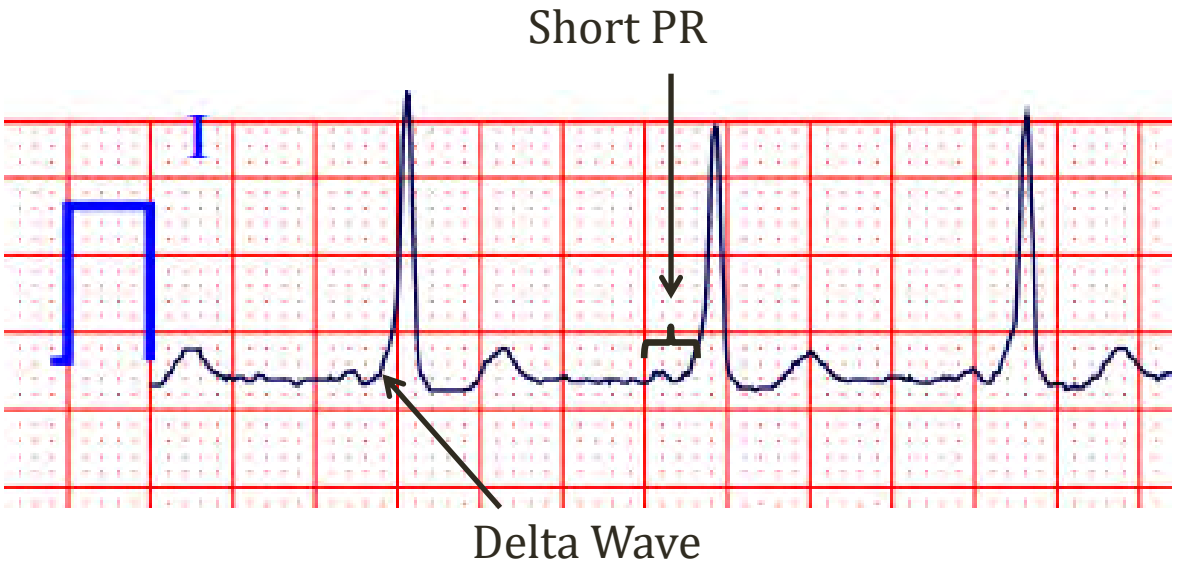
Jason Ryan, MD, MPH

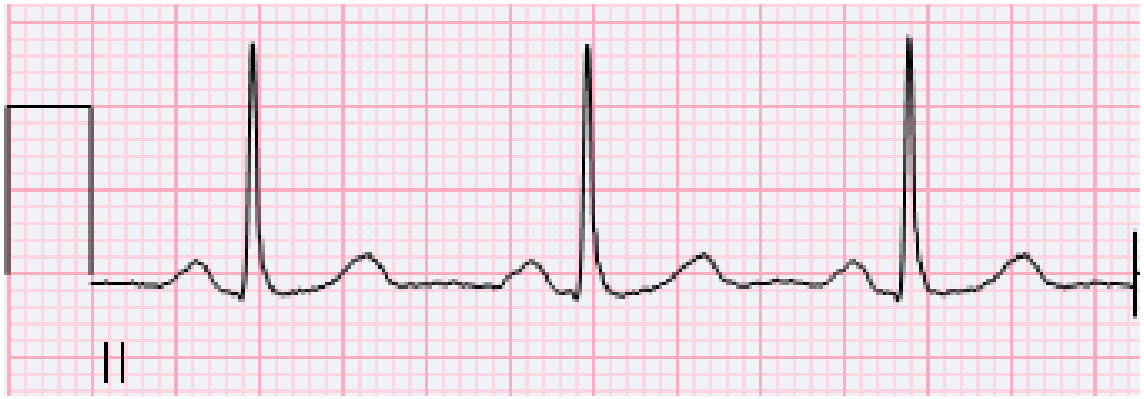
# WPW Syndrome

## Wolff-Parkinson White Syndrome

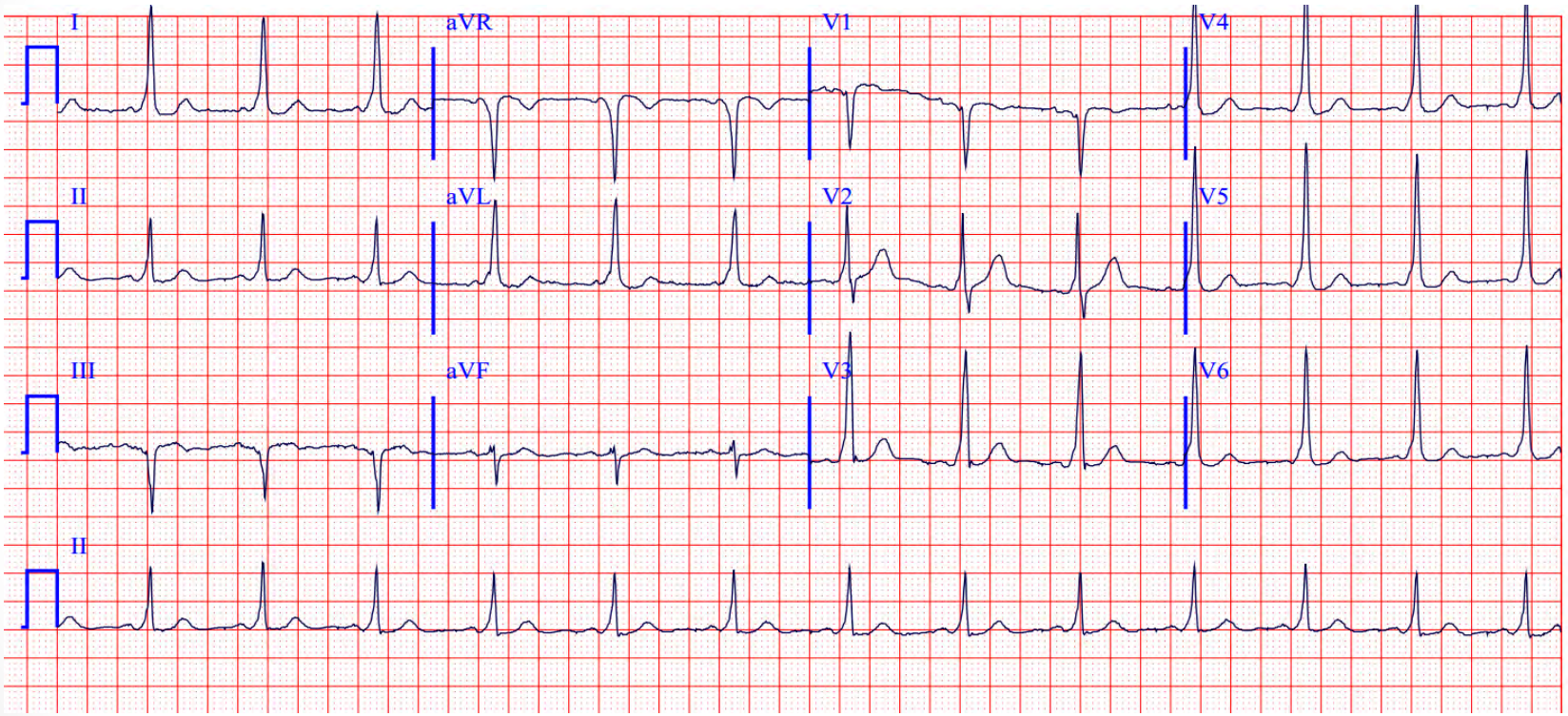
- Cardiac electrical disorder
- **"Accessory atrioventricular pathway"**
  - Conducts impulses from atria to ventricles
  - Bypasses AV node
  - "Bundle of Kent"
- Causes **"pre-excitation"**
  - Ventricular depolarization before AV nodal impulse
- May lead to **arrhythmias**

# EKG in WPW

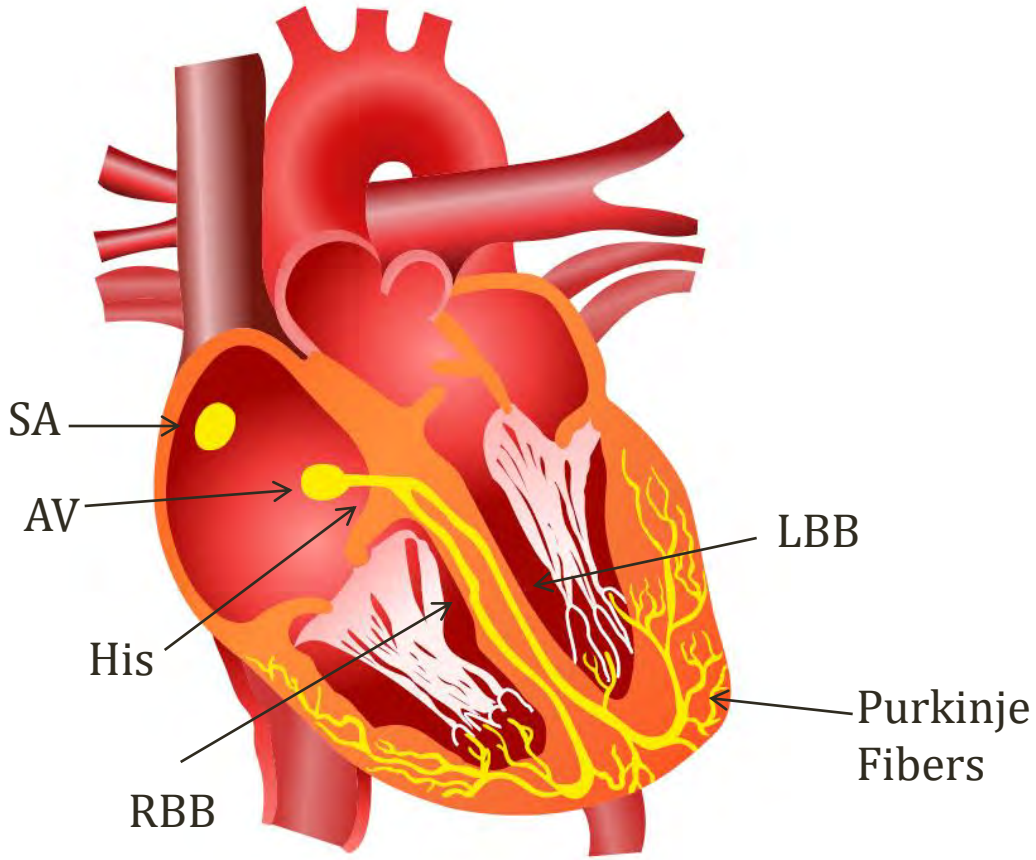


# WPW EKG

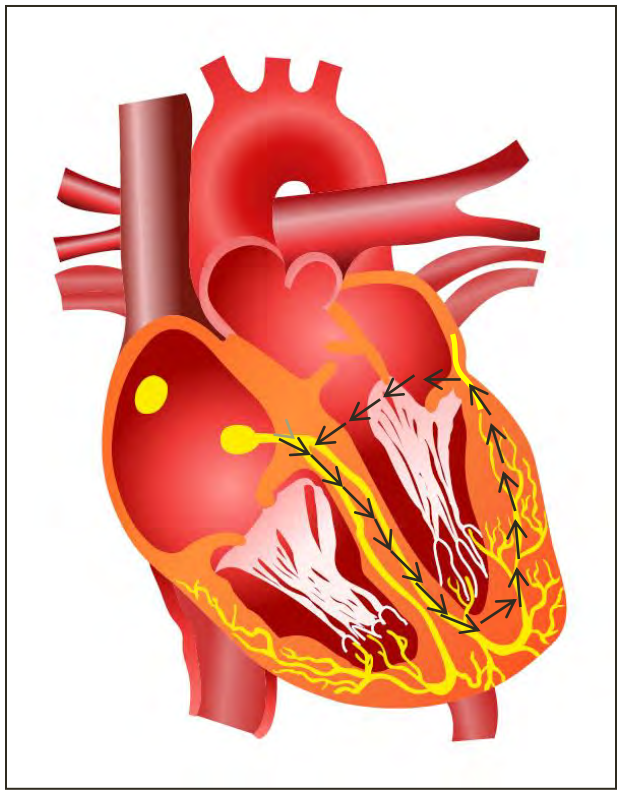


# Cardiac Electrical System

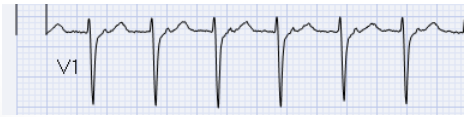


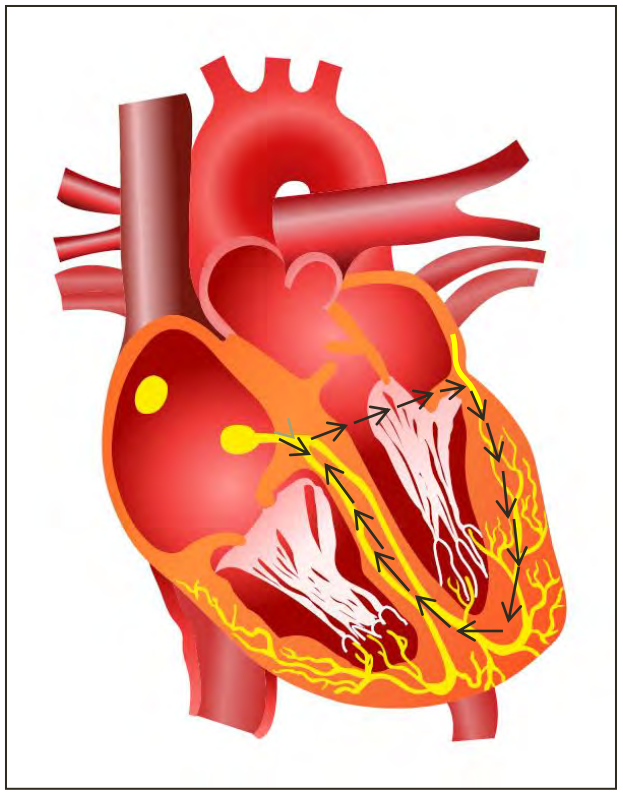
# AVRT

## AV Re-entrant Tachycardia

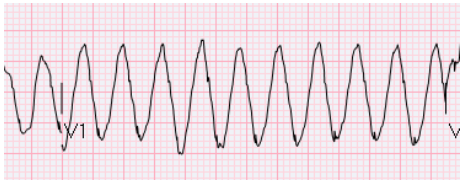


Orthodromic



Antidromic



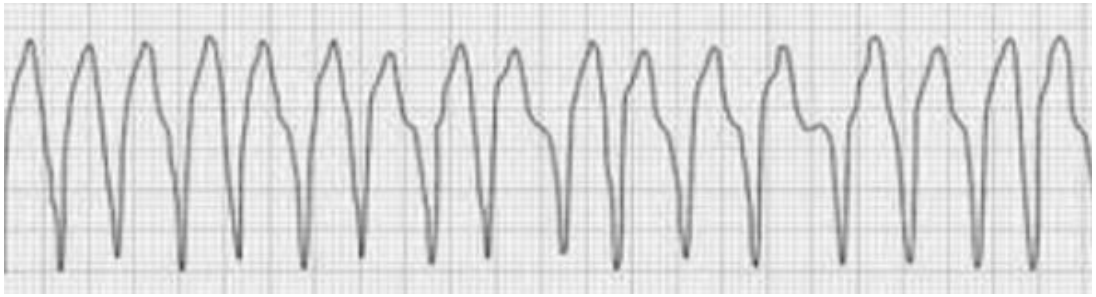
# Bypass Tract Consequences

- Most patients **asymptomatic**
  - EKG with delta wave only
  - Called **WPW "pattern"**
- Some have tachycardias
  - Presents as **palpitations**
  - Called **WPW syndrome**
  - AVRT (anti or orthodromic)
- Rarely causes syncope or sudden death
- Treatment: Ablation of accessory pathway

# Atrial Fibrillation in WPW

- Atrial fibrillation can be **life threatening**
- Atrial depolarization rate 300-500/min
- AV node conducts <200/min
- Impulses may conduct rapidly over bypass tract

Wide complex, irregular, tachycardic



# Atrial Fibrillation in WPW

- Slowing AV node conduction is dangerous
- Allows more impulses over bypass tract
- **Usual atrial fibrillation therapies contraindicated**
  - Beta blockers
  - Calcium channel blockers
  - Digoxin
  - Adenosine
- Acute treatment: Cardioversion or antiarrhythmics
  - Ibutilide, procainamide
  - Slow conduction in bypass tract

# Antiarrhythmic Drugs

Jason Ryan, MD, MPH

# Vaughan Williams

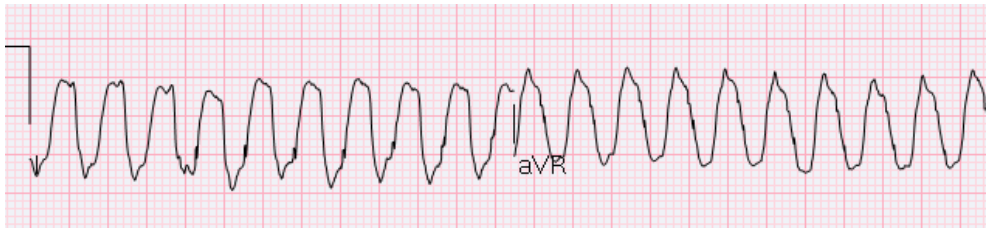
| Class I | Class II |
| --- | --- |
| Quinidine, Procainamide } Ia<br>Lidocaine, Mexiletine } Ib<br>Flecainide, Propafenone } Ic | Beta Blockers |
| **Class III**<br>Amiodarone<br>Sotalol<br>Dofetilide<br>Ibutilide | **Class IV**<br>Ca-channel Blockers<br>(Verapamil/Diltiazem) |

# Use of Antiarrhythmic Drugs

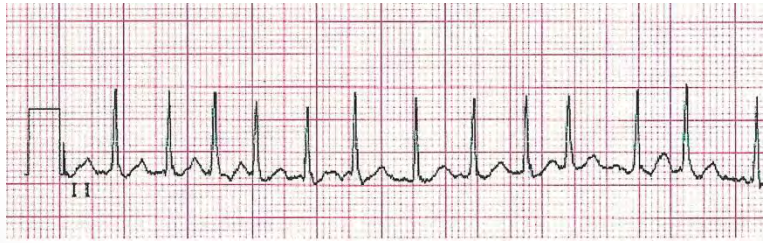
- Drugs used to “suppress” arrhythmias
- Prevent formation of aberrant impulses
- Most also ***cause*** arrhythmias
- Can lead to cardiac arrest and death
- Used in dangerous arrhythmias
- Also used in recurrent symptomatic arrhythmias

# Use of Antiarrhythmic Drugs

- Persistent/recurrent ventricular tachycardia
- Recurrent atrial fibrillation




Ventricular Tachycardia

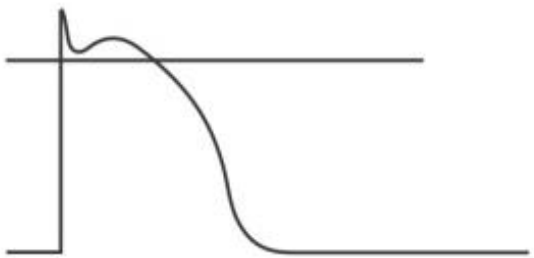



Rapid Atrial Fibrillation

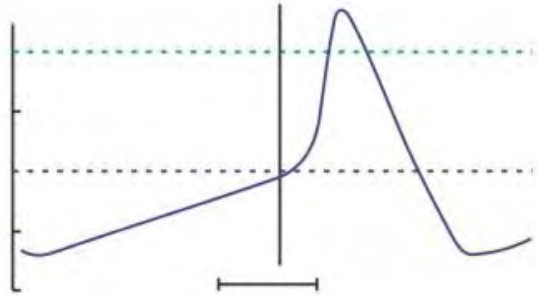
# Mechanisms

- All drugs slow cardiac electrical activity
- Class I drugs → Block Na channel
- Class III drugs → Block K channels
- Class II, IV: Slow sinus and AV node conduction

Class I, III

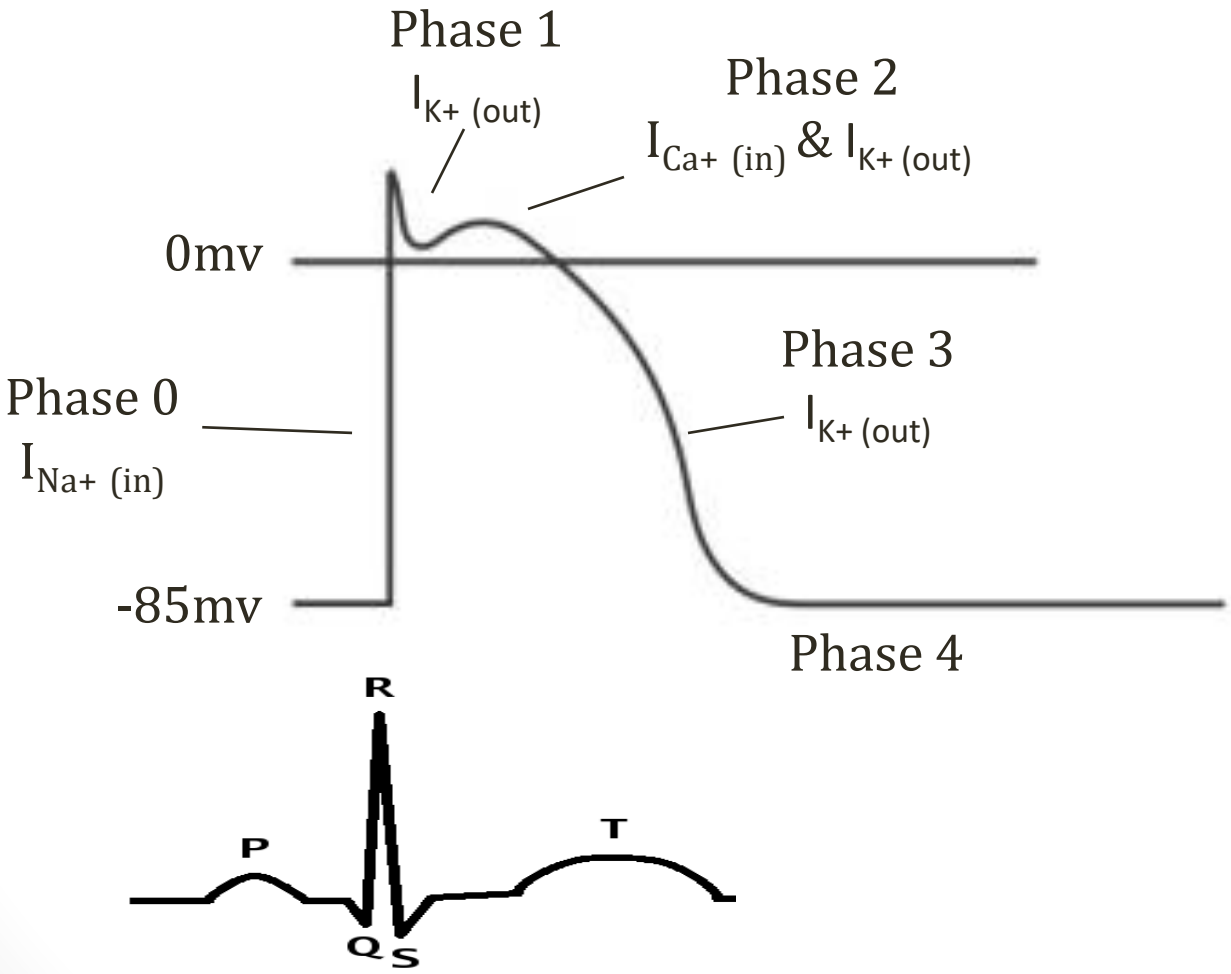


BB, CCB
(Class II, IV)

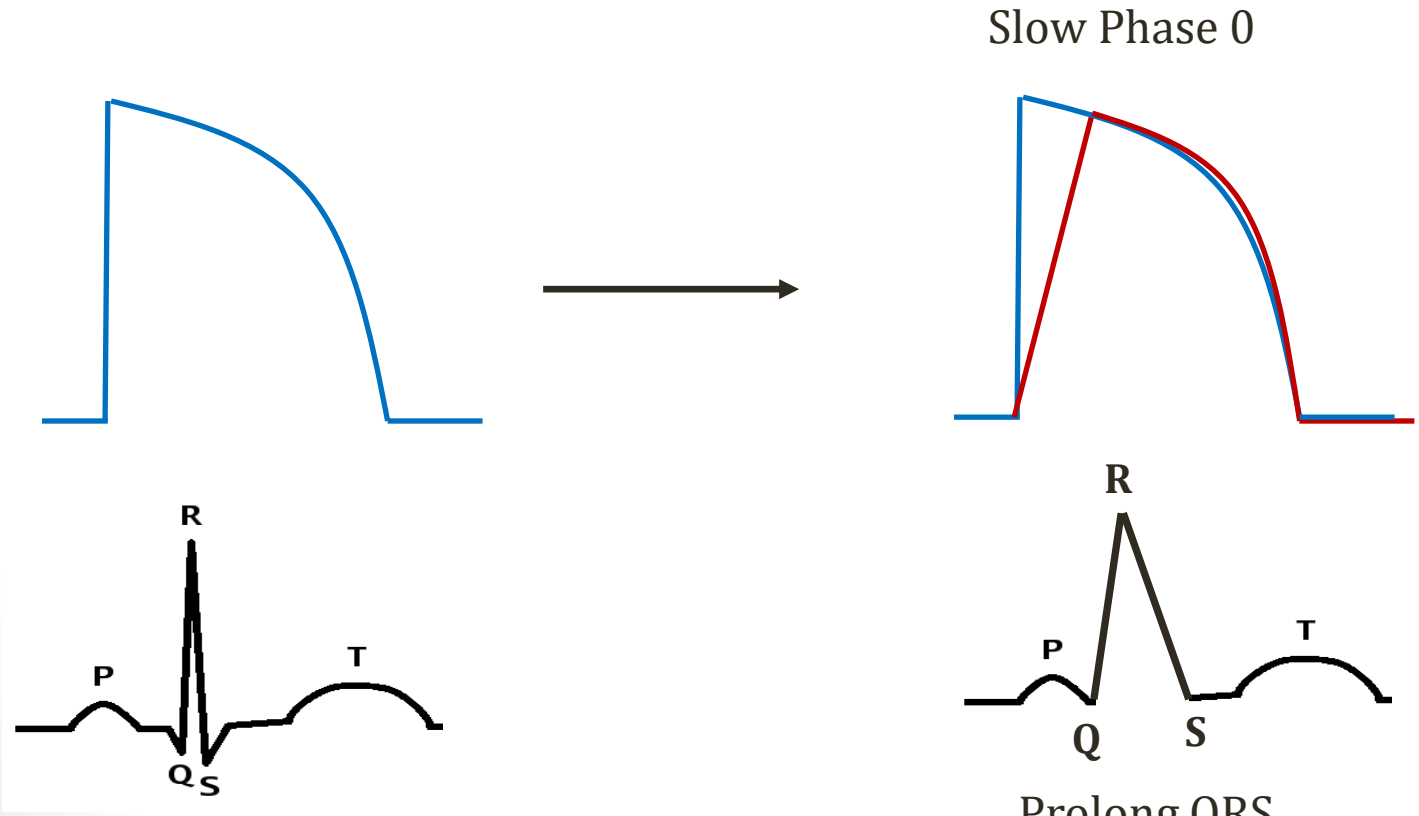


# Myocyte Action Potential

## Atrial/ventricular myocytes

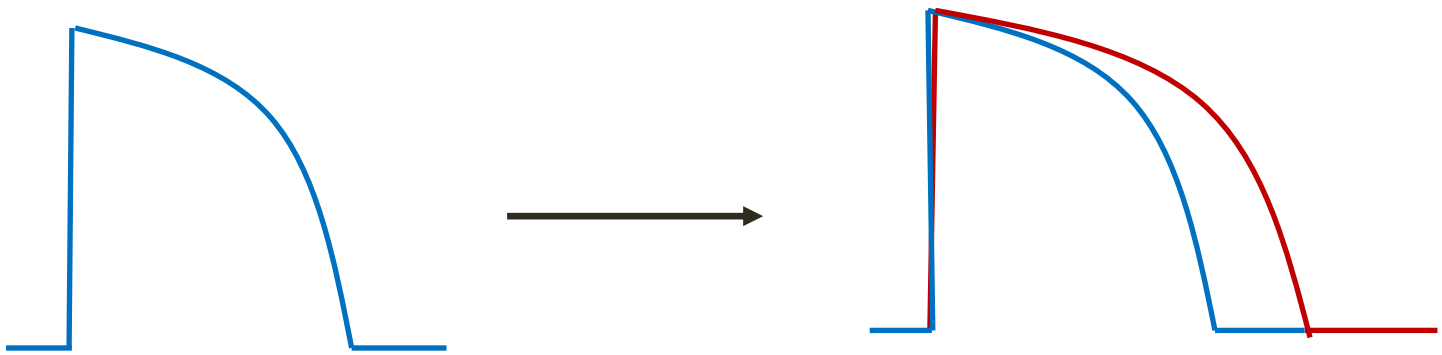


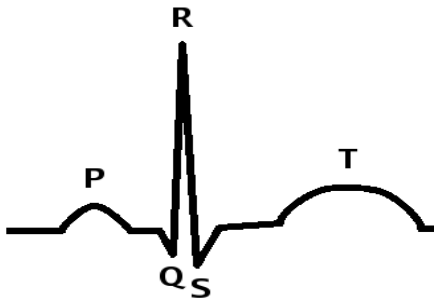
# Na Channel Blockade

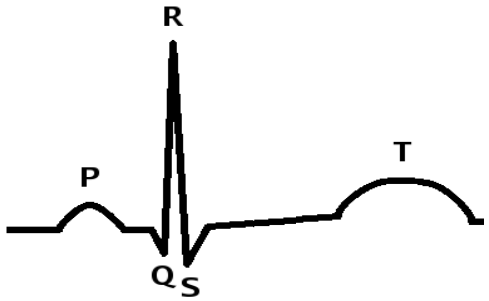


# K Channel Blockade

Prolonged Repolarization



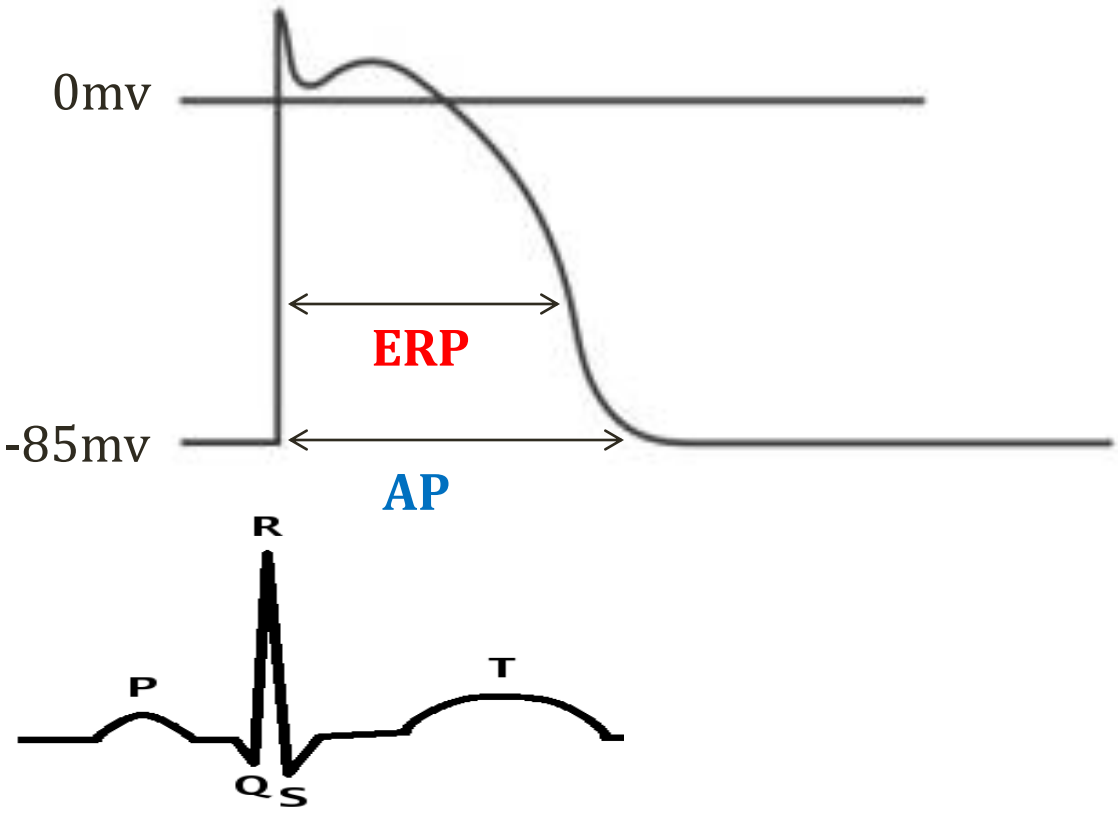



Prolong QT

# Myocyte Action Potential

## Atrial/ventricular myocytes

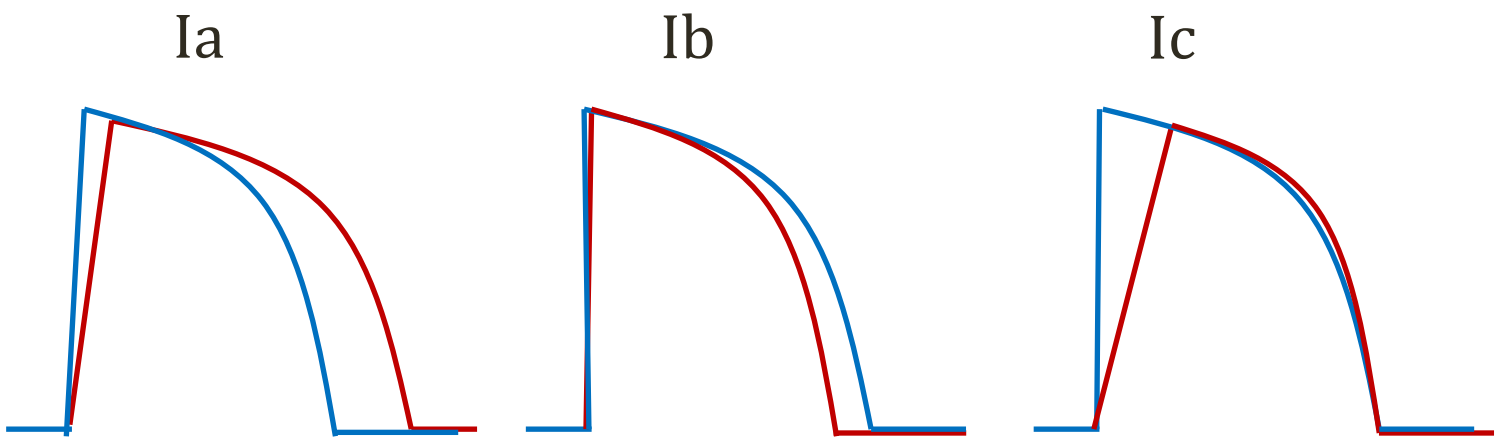


# Class I drugs

- Block sodium channels → prolong QRS
- Some also affect K+ channels → prolong Qt
- Can prolong action potential duration
- Can prolong effective refractory period

# Class I drugs

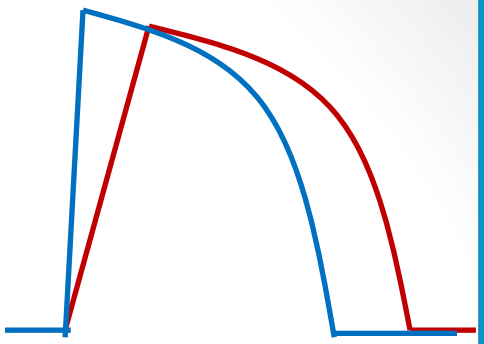
## Effects on Resting Action Potential




| Ia | Ib | Ic |
|---|---|---|
| ↑QRS ↑QT | +/-QRS ↓ QT | ↑ QRS +/-QT |
| ↑AP ↑ERP | ↓AP ↓ ERP | +/-AP |

# Class Ia Drugs

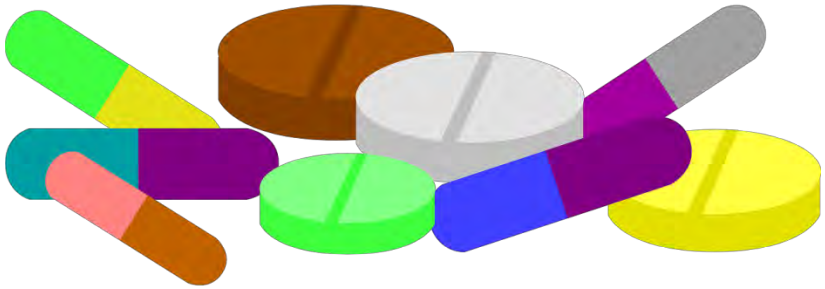
## Quinidine, procainamide



- **Prolong QRS**
- **Can also prolong Qt** ($\downarrow K^+$ outflow)
- Quinidine
  - Oral drug
  - Can decrease recurrence rate of atrial fibrillation
  - Associated with increased mortality
- Procainamide
  - Intravenous drug
  - Slows conduction in accessory pathways (WPW)
  - Used in arrhythmias associated with bypass tracts

# Procainamide

- Associated with **drug-induced lupus**
  - Classic drugs: **INH, hydralazine, procainamide**
- Often rash, arthritis, anemia
- Antinuclear antibody (ANA) can be positive
- Key features: **anti-histone antibodies**
- Resolves on stopping the drug



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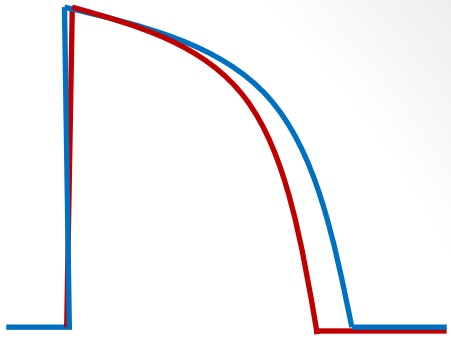
# Class Ib Drugs

## Lidocaine, Mexiletine

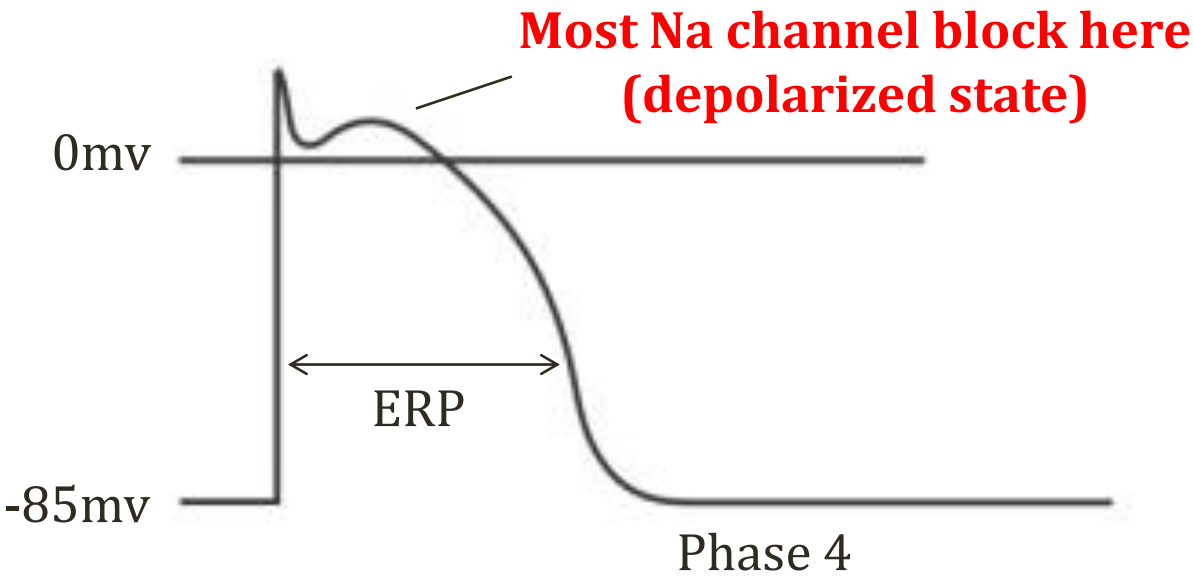


- Little/no effect on QRS at normal HR
- Slight decrease in Qt interval (minimal)
- **Least effect on action potential of class 1 drugs**

# Class Ib Drugs

## Lidocaine, Mexiletine

- Most Na channel binding in **depolarized state**
- Ischemia → more depolarized myocytes
- Effective drugs in ischemic arrhythmias



# Class Ib Drugs

## Lidocaine, Mexiletine

- Drug **rapidly unbinds**
- Slow heart rates: little drug effect by next heart beat
- More effective in fast heart rates
- Less time to unbind before Na channels open again
- Main use: ischemic ventricular tachycardia
  - Fast heart rates
  - Depolarized Na channels

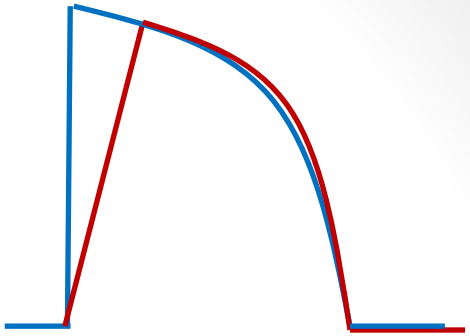
# Class Ib Drugs

## Lidocaine, Mexiletine

- Lidocaine also a local anesthetic
  - Na channel nerve block
- May cause **CNS stimulation**
  - Tremor, agitation
  - Tremor in patient on Mexiletine = toxicity
- Cardiovascular side effects
  - From excessive block of Na channels
  - Bradycardia, heart block, hypotension

# Class Ic Drugs

## Flecainide, Propafenone



- Block open Na channels
- Very slow unbinding
- Result: **QRS can markedly prolong**
- Limited use due to concern of toxicity
- Especially proarrhythmic effects

# CAST Trial

## The Cardiac Arrhythmia Suppression Trial

- Landmark clinical trial of antiarrhythmic drugs
- Tested the suppression hypothesis
  - Suppression of arrhythmias with drugs is a good thing
- Patients with asymptomatic arrhythmias after MI
- Encainide and flecainide administered
- Patients taking drugs had less arrhythmias
- Also: **3.6-fold increased risk of arrhythmic death**
- Result: Major ↓ antiarrhythmic drugs
- Now used only with compelling indication

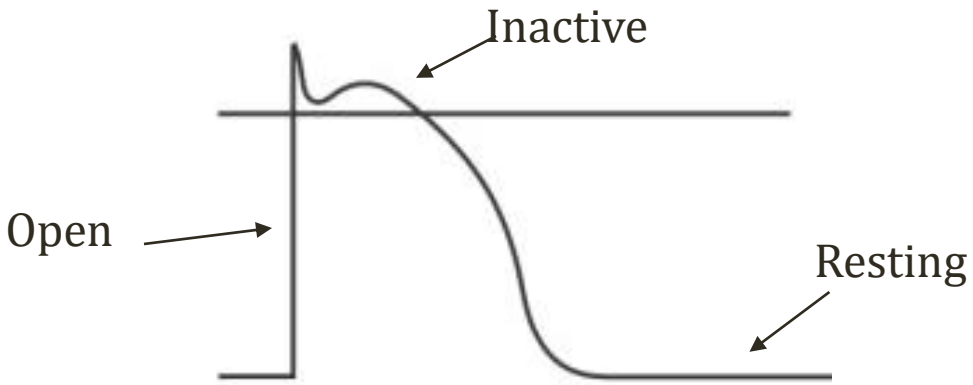
# Class Ic Drugs

## Flecainide, Propafenone

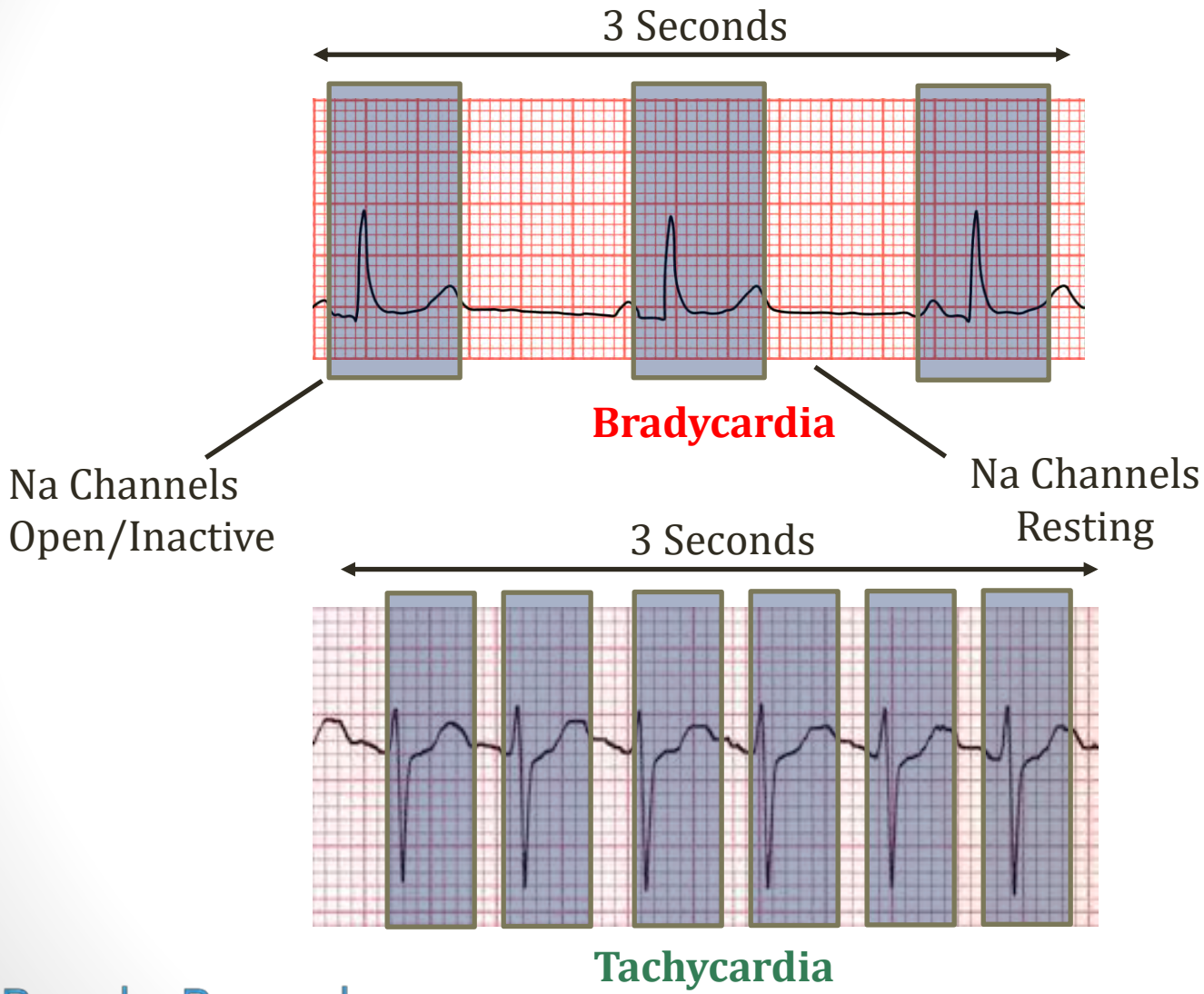
- Only used in patients with structurally normal hearts
- Effective in reducing recurrence of atrial fibrillation
- Must monitor for **QRS prolongation**
- Prolonged QRS → Risk of cardiac arrest

# Use Dependence

- Na channels fluctuate between 3 different states
- Resting, Open and Inactivated
- Drugs bind more in certain states
- Class I drugs bind best in **open/inactivate states**
  - States when Na channel is in "use"
- These drug exhibit "use dependence"



# Use Dependence

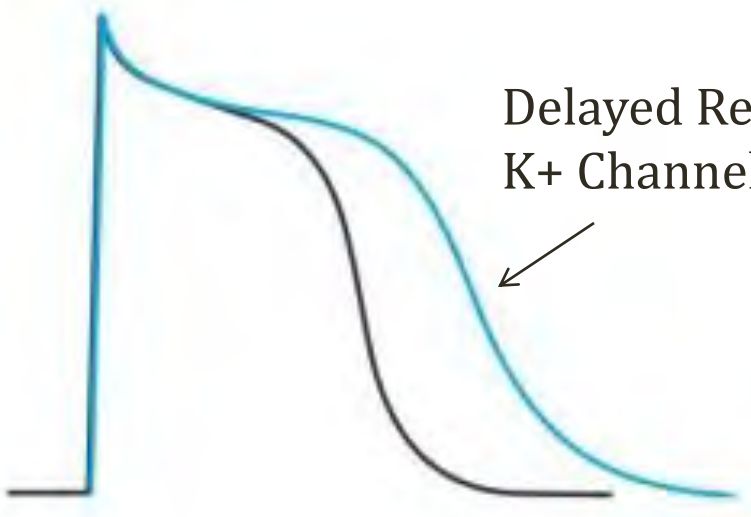


# Use Dependence

- Use dependent drugs: **more binding fast heart rates**
- All class I drugs have some use dependence
- Seen most frequently IC drugs
- Practical implication:
  - Flecainide and propafenone (IC drugs)
  - Marked use dependence
  - Toxicity (QRS prolongation) at high heart rates
  - Stress testing often done to screen for toxicity

# Class III drugs

## Amiodarone, Sotalol, Dofetilide, Ibutilide

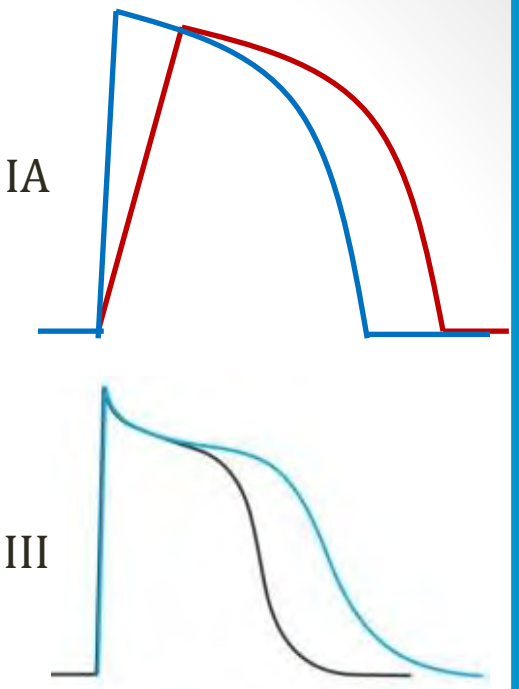


Delayed Repolarization
K+ Channel Blockade

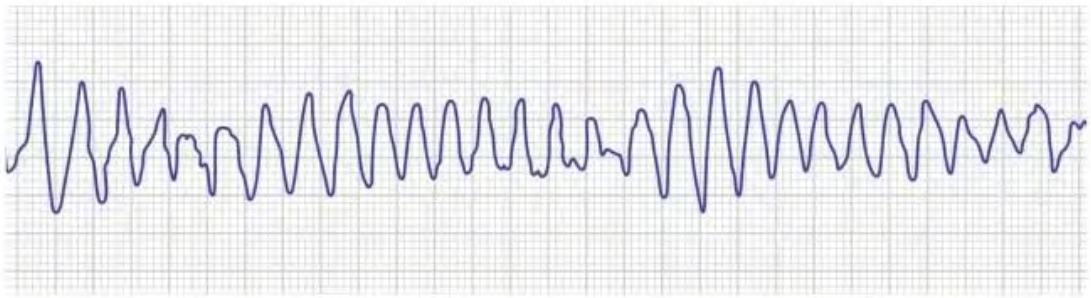
+/-QRS ↑QT

↑AP ↑ERP

# Torsade de Pointes




- Feared outcome of Qt prolongation
- Results in cardiac arrest
- **Class IA, III drugs** prolong Qt



# Amiodarone

- Class III drug
  - K channel blocker: Prolongs Qt interval
  - Lowest incidence TDP of all class IIIs
- **Also has class I, II, and IV effects**
  - Class I: Prolongs QRS
  - Class II, IV: Slow HR, delay AV conduction
- Very effective drug
- Suppresses atrial fibrillation
- Suppresses ventricular tachycardia

# Amiodarone

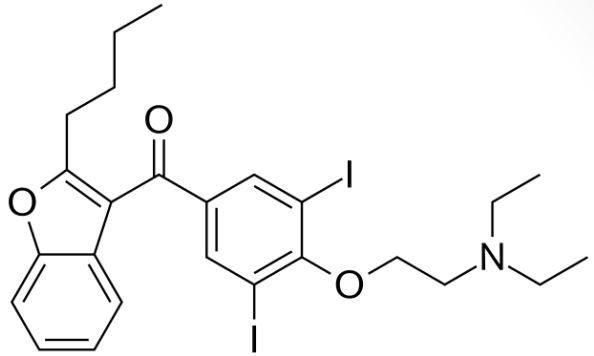
- Highly **lipid soluble**
- Accumulates in liver, lungs, skin, other tissues
- Half-life **about 58 days**
- Once steady state reached, very long washout
- Safe in renal disease (biliary excretion)

# Amiodarone

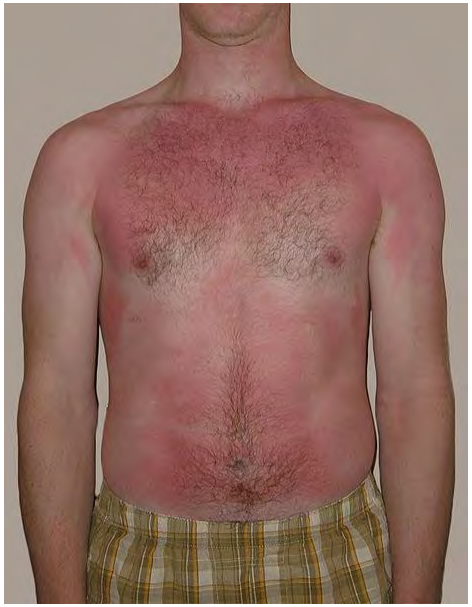
- Many potential side effects related to accumulation
- Less likely at lower dosages
- Risk accumulates over time
- Young patients on indefinite therapy at greatest risk
- Often used in older patients

# Amiodarone

## Side Effects




- **Hyper and hypothyroidism**
  - Contains iodine
- **Increased LFTs**
  - Usually asymptomatic and mild
  - Drug stopped if elevation is marked
- **Skin sensitivity to sun**
  - Patients easily sunburn



Wikipedia/Public Domain

# Amiodarone

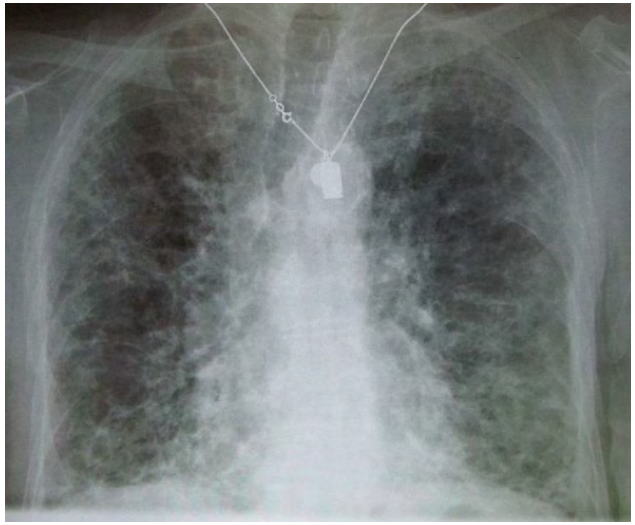
## Side Effects

- **Blue-gray discoloration**
  - Less common skin reaction
  - “Blue man syndrome”
  - Most prominent on face
- **Corneal deposits**
  - Secretion of amiodarone by lacrimal glands
  - Accumulation on corneal surface
  - Appearance of “cat whiskers” on cornea
  - Does not usually cause vision problems
  - See in many patients on chronic therapy

# Amiodarone

## Side Effects

- Pulmonary fibrosis
- Most common cause of death from amiodarone
- Foamy macrophages seen in air spaces
- Filled with amiodarone and phospholipids
- “Honeycombing” pattern on chest x-ray



# Amiodarone

## Side Effects

- When starting amiodarone
  - Chest X-ray
  - Pulmonary function tests (PFTs)
  - Thyroid function tests (TFTs)
  - Liver function tests (LFTs)

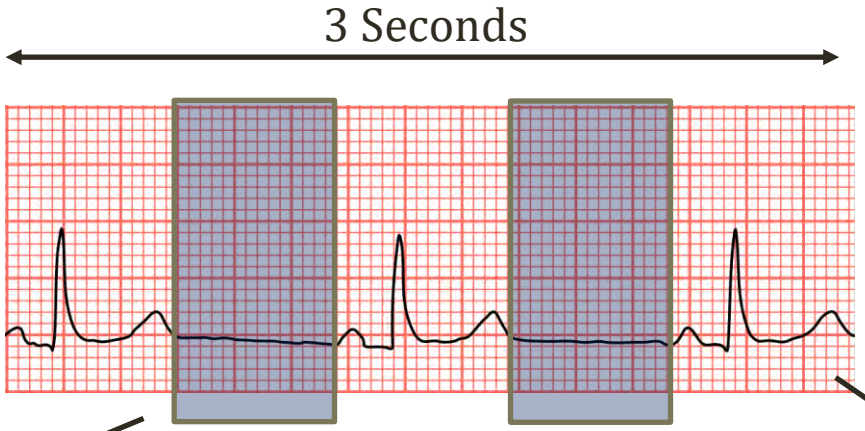
# Sotalol and Dofetilide

- Both drugs block K channels (class III)
- Can prolong Qt interval → **torsade de pointes**
- Practical consideration:
  - Patients often admitted to hospital to start therapy
  - Rhythm monitored on telemetry
  - Qt segment checked by EKG each day
- Sotalol: Also has beta blocking properties
- Can be used in patients with cardiomyopathy
- "Reverse use dependence"

# Reverse Use Dependence

- K channels also fluctuate between 3 different states
- Class III drugs bind best in **resting state**
- These drug exhibit “reverse use dependence”

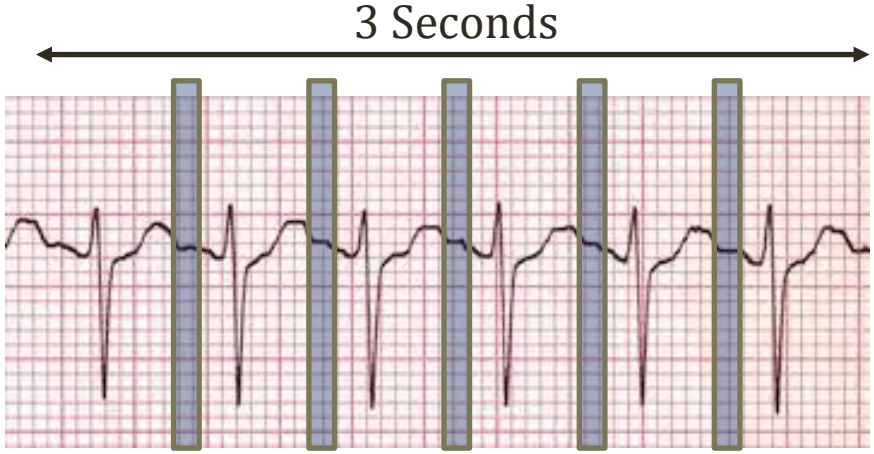
# Reverse Use Dependence




**Bradycardia**

K Channels Resting

K Channels Open/Inactive




**Tachycardia**

# Sotalol and Dofetilide

- Reverse use dependence: **more binding slow rates**
- Practical implication:
  - Bradycardia in patient on sotalol/dofetilide
  - Qt interval may prolong
  - Increased risk of torsade de pointes

# Sotalol and Dofetilide

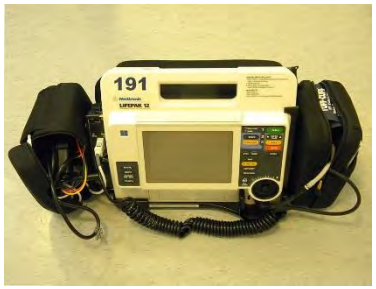
- Commonly used in patients with **atrial fibrillation**
- Typical case
  - Recurrent episodes symptomatic atrial fibrillation
  - Sotalol/Dofetilide started
  - Cardioversion to restore sinus rhythm
  - Sinus rhythm persists on therapy
- Other antiarrhythmic also used in this manner
  - Amiodarone
  - Propafenone
  - Flecainide

# Ibutilide

- Intravenous drug
- Half life of 2 to 12 hours
- Used for “chemical cardioversion”

# Cardioversion

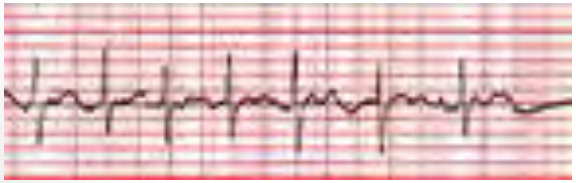
- Termination of arrhythmias
- Often atrial fibrillation or flutter

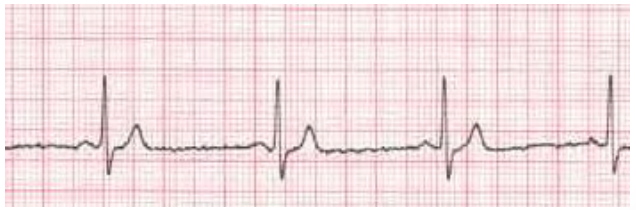



**Ibutilide**

**Electrical Cardioversion**
Requires sedation

**Chemical Cardioversion**
No sedation
May cause Torsade

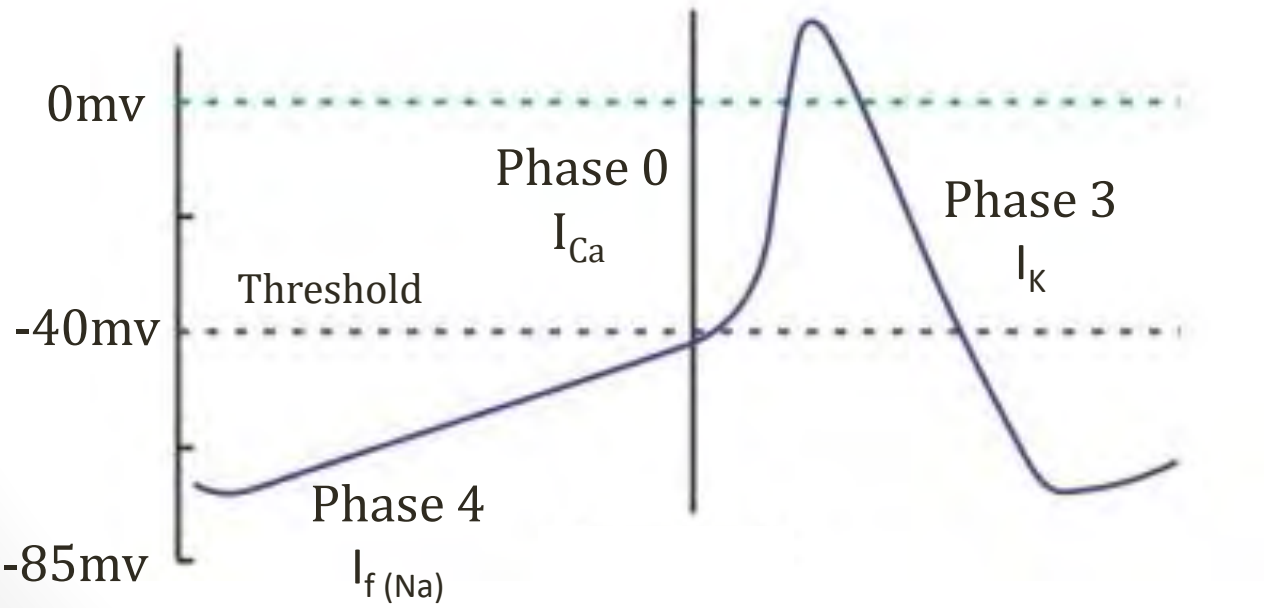




# Beta Blockers

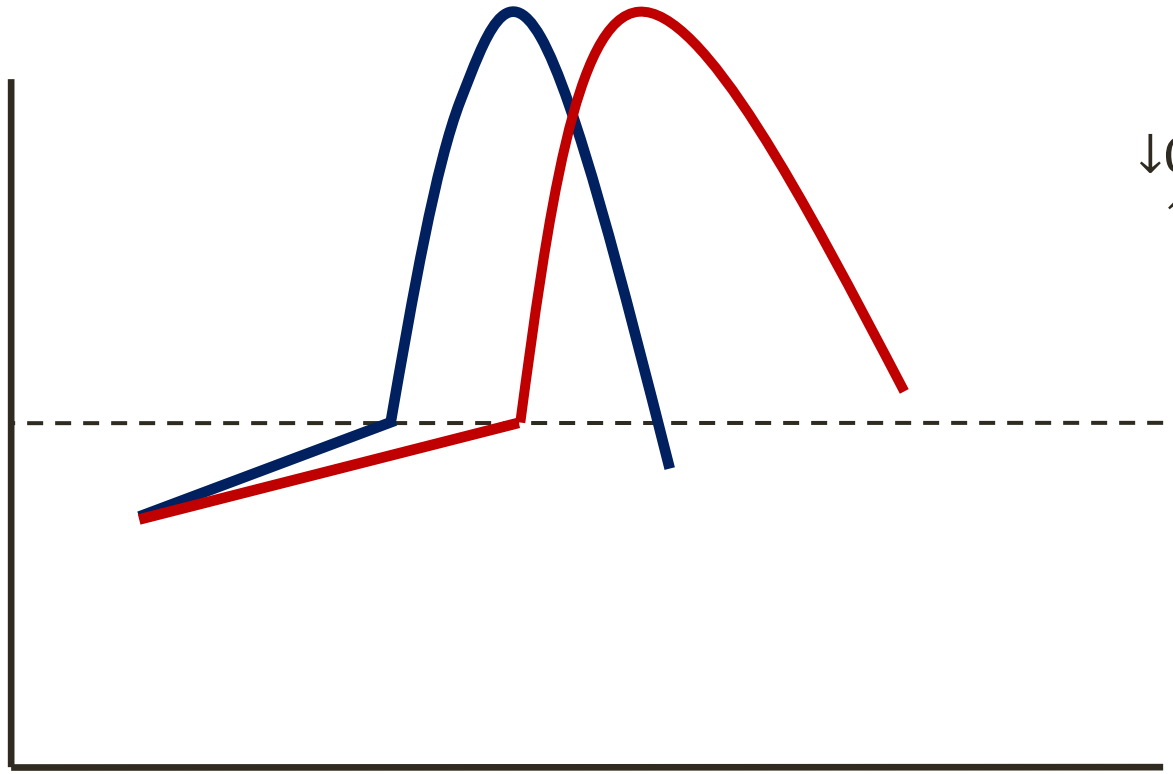
## Class II Antiarrhythmics

- Main effect: **Pacemaker cells** (SA and AV node)
- **Decrease slope of phase 4**
- **Prolong repolarization (phase 3)**



# Beta Blockers

## Class II Antiarrhythmics

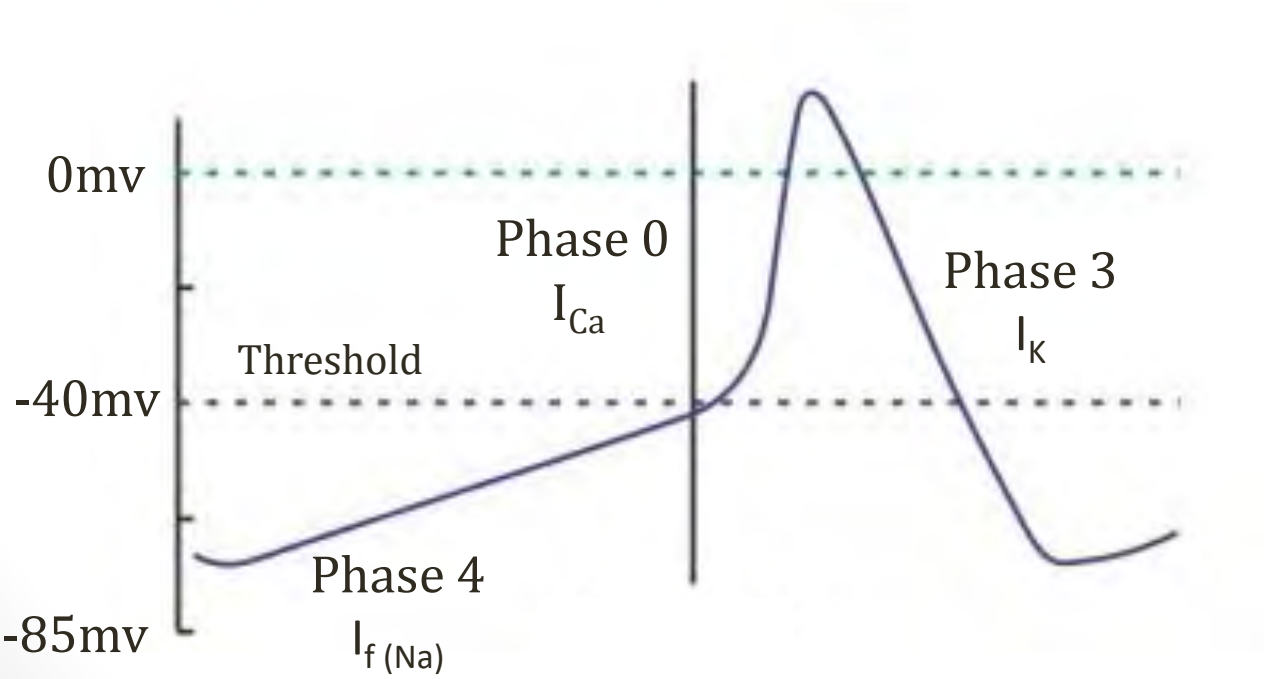


↓HR
↓Cond Velocity
↑PR Interval

# Calcium Channel Blockers

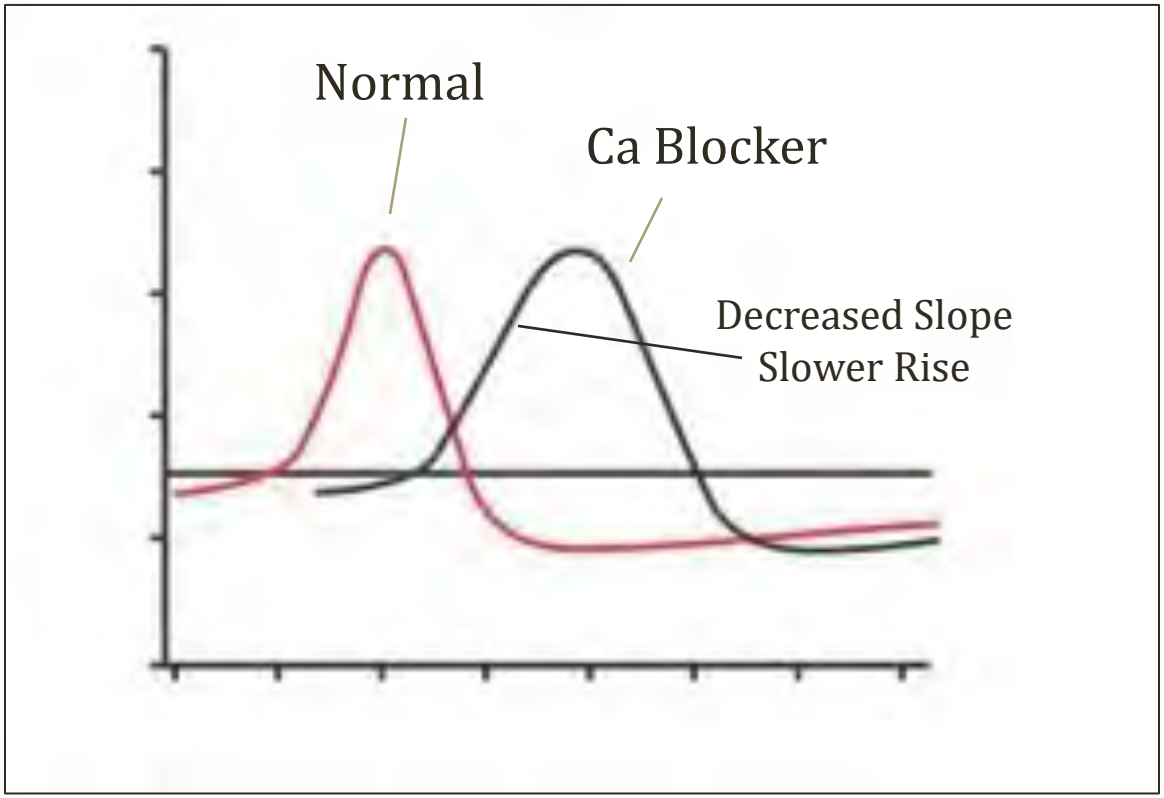
## Verapamil and Diltiazem

- Block **calcium channels**
- Slow heart rate
- Slow AV node conduction



# Calcium Channel Blockers

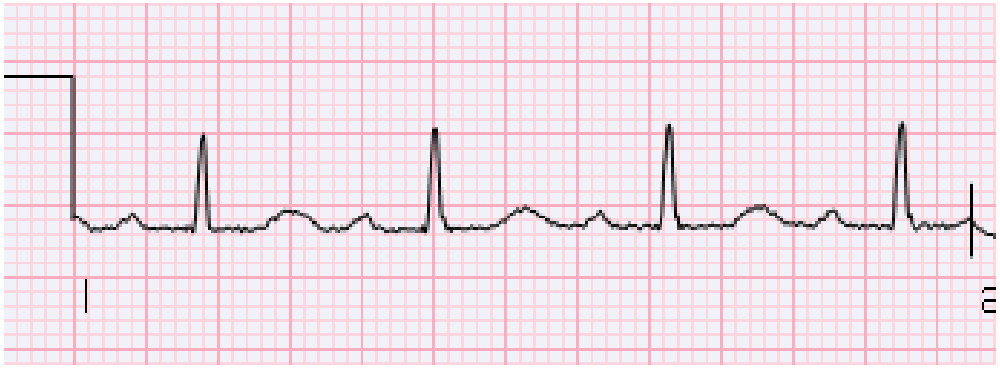
## Verapamil and Diltiazem



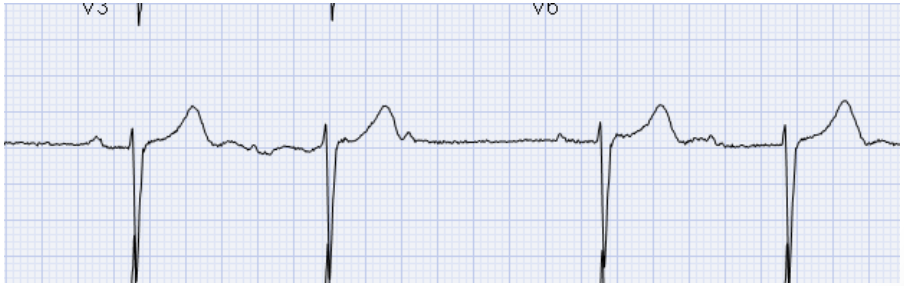

↓HR
↓Cond Velocity
↑PR Interval

# AV Block

- Beta blockers/Ca channel blockers → ↓ AV conduction



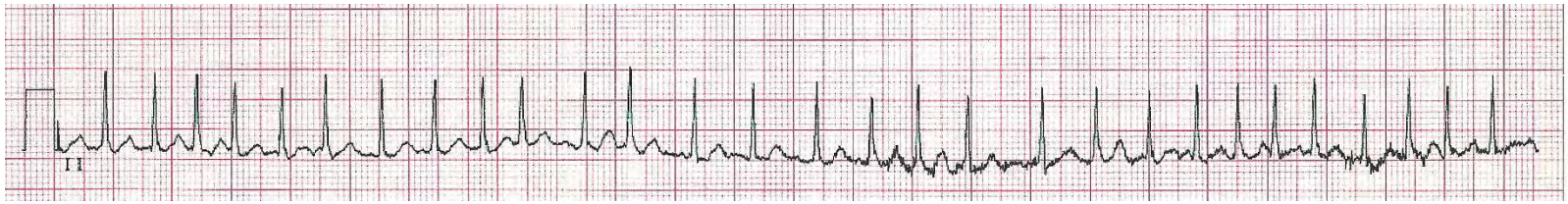
Type 1 AV block



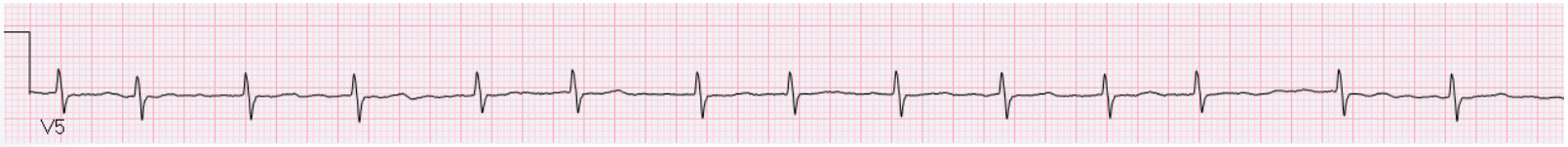

Wenckebach (Mobitz I)

# Atrial Fibrillation

- Beta blockers and CCBs commonly used
- Control ventricular rate



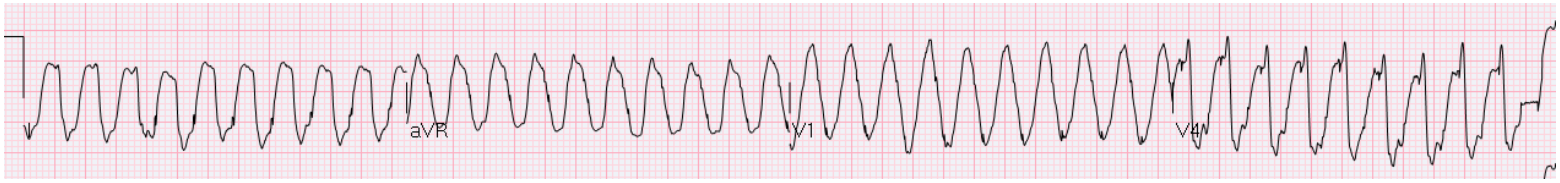

Atrial Fibrillation with rapid ventricular response



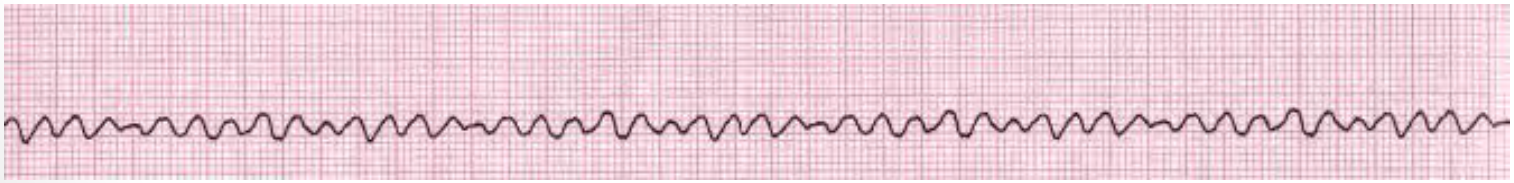

Rate controlled with beta blocker or CCB

# Sudden Cardiac Death

- Increased risk among systolic heart failure patients
- Lower rates among patients on **beta blockers**
- Improved mortality



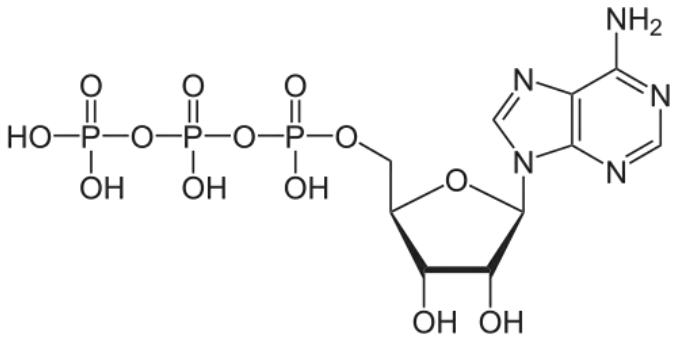

Ventricular Tachycardia



Ventricular Fibrillation

# Adenosine

- Nucleoside base
- Used to make ATP
- Receptors in many locations (purinergic receptors)
  - **AV nodal tissue**
  - **Vascular smooth muscle**



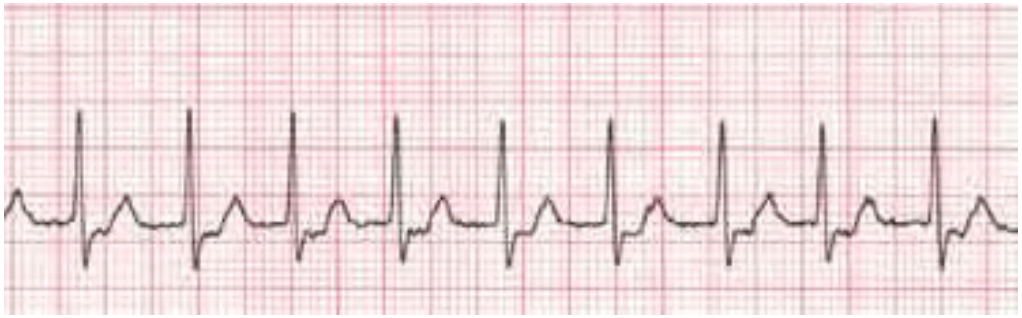

Adenosine Triphosphate

# Adenosine

- AV nodal cells:
  - **Activates K+ channels**
  - Drives K+ out of cells
  - Hyperpolarizes cells: Takes longer to depolarize
  - Also **blocks Ca influx**
- Result: **Slowing** of conduction through AV node

# Adenosine

- Short half life
- Given IV for acute therapy of SVT
- Slows AV node conduction



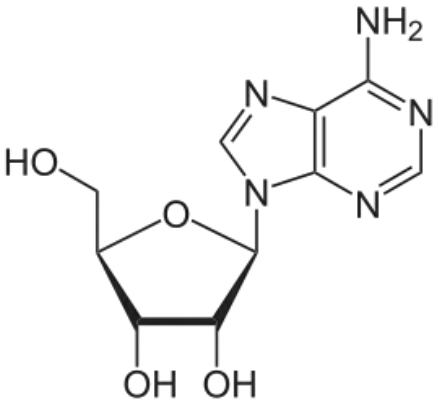
Narrow Complex
Originates above HIS bundle

# Adenosine

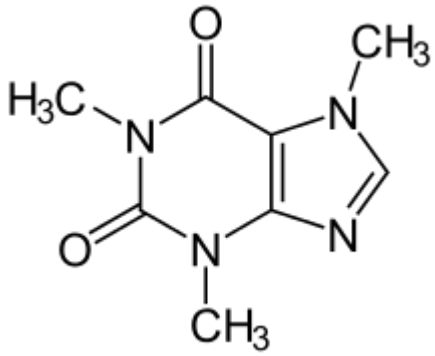
- Most common SVT: **AVNRT**
  - AV node reentrant tachycardia
- Slow and fast circuits in AV node → arrhythmia
- Adenosine slows AV node conduction
- Arrhythmia with terminate

# Adenosine

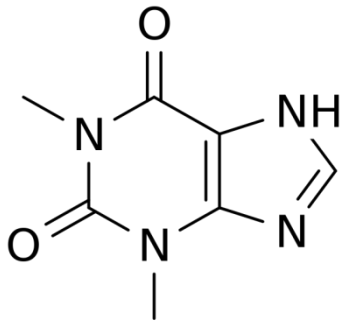
- Effects blocked by **theophylline** and **caffeine**
- Block adenosine receptors



Adenosine



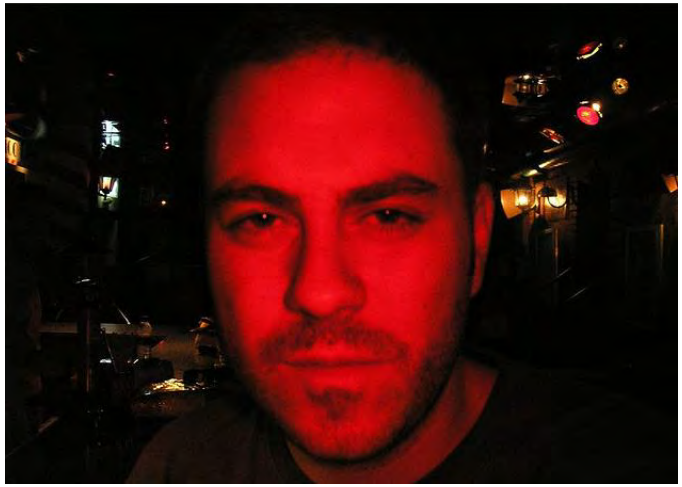
Caffeine



Theophylline

# Adenosine

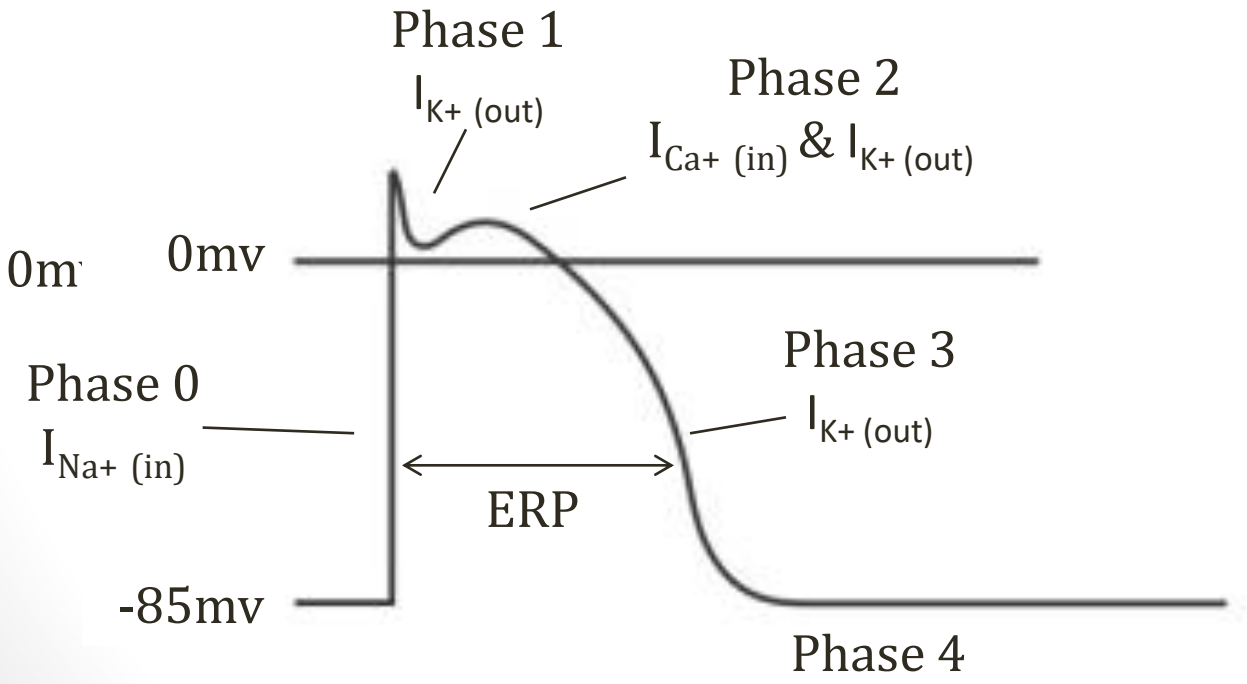
- Also a vasodilator
- Causes skin flushing, hypotension
- Some patients also develop dyspnea, chest pain
- Effects quickly resolve
- Must warn patients before administration for SVT



**Jorge González**/Flikr

# Magnesium

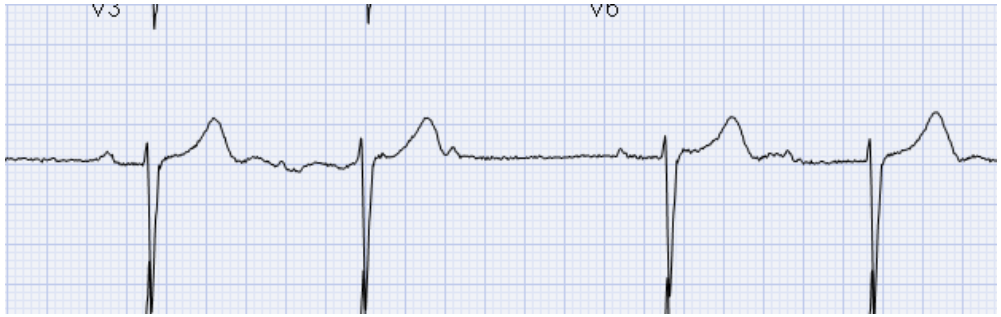
- Acute management of **torsade de pointes**
- Mg **blocks influx of Ca** into cells
- Ca influx leads to early afterdepolarizations



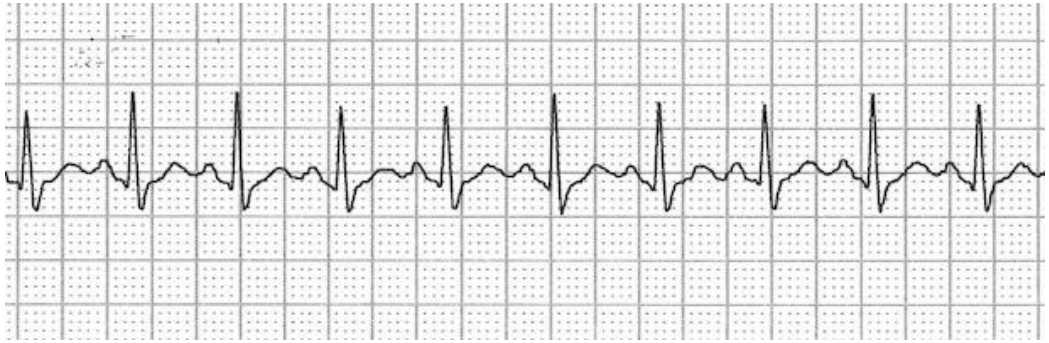
# Atropine

- **Muscarinic receptor antagonist**
  - Parasympathetic block → ↑ HR and AV conduction
- Used in bradycardia → **↑ heart rate**
- Also speeds conduction through AV node
- Useful for bradycardia especially from AV block

# Atropine




Before Atropine



After Atropine

# Atropine

- May **side effects** related to muscarinic block
- Toxicity:
  - Dry mouth
  - Constipation
  - **Urinary retention**
  - Confusion (elderly)

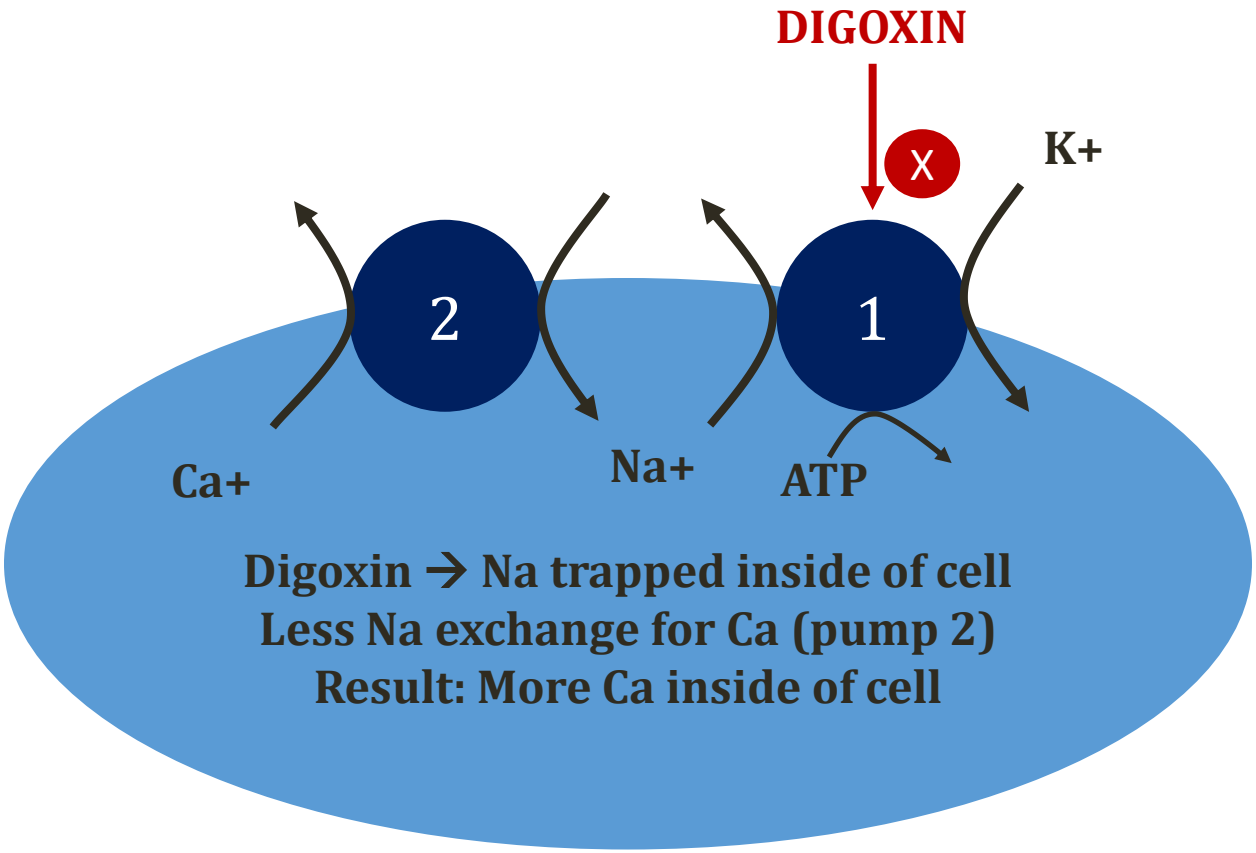
# Digoxin

- Two cardiac effects
- #1: Increases contractility
  - Used in systolic heart failure with ↓ LVEF
- #2: Slows AV node conduction
  - Used in atrial fibrillation to slow ventricular rate

# Digoxin

## Increased Contractility

- Inhibits Na-K-ATPase



# Digoxin

## AV Nodal Slowing

- Suppresses **AV node conduction**
  - Increased **vagal (parasympathetic) tone**
  - Separate effect from blockade of Na-K-ATPase
- Can be used to **↓ heart rate** in rapid atrial fibrillation
  - Continued atrial fibrillation
  - Fewer impulses to ventricle → slower heart rate
- Effects similar to BB and CCB in AV node

# Digoxin Toxicity

- **Renal** clearance
  - Risk of toxicity in patients with chronic kidney disease
- **Hypokalemia** promotes toxicity
  - Caused by many diuretics, especially loop diuretics
  - Digoxin patient on furosemide → toxicity
- Levels often need to be monitored

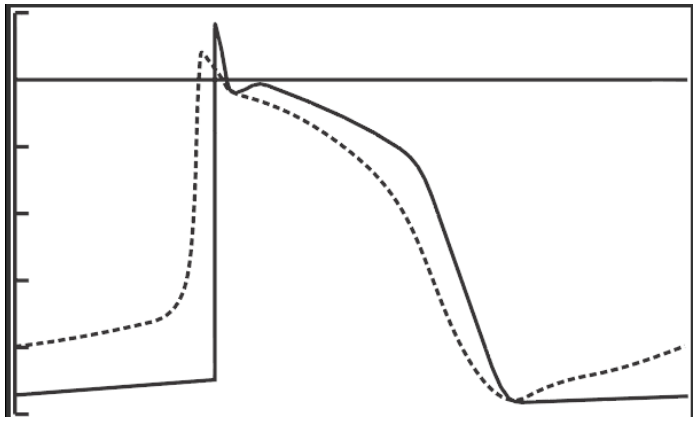
# Digoxin Toxicity

- Gastrointestinal
  - Anorexia, nausea, vomiting, abdominal pain
- Neurologic
  - Lethargy, fatigue
  - Delirium, confusion, disorientation
  - Weakness
- Visual changes
  - Alterations in color vision, scotomas, blindness
- Cardiac arrhythmias

# Digoxin Toxicity

## Cardiac Toxicity

- More Na inside of cell
- ↑ resting potential atrial/ventricular cells
- Increased automaticity
- Dig toxic rhythms:
  - **Extra beats**: atrial, junctional, ventricular
  - Evidence of **AV node block**



# Digoxin Toxicity

## Treatment

- Digibind
  - Digoxin antigen binding fragments (Fab)
  - Produced in animals (sheep)
  - Dig bound to albumin (hapten) → antibodies
  - Antibody converted to fragments
- Corrects hyperkalemia, symptoms

# Heart Murmurs

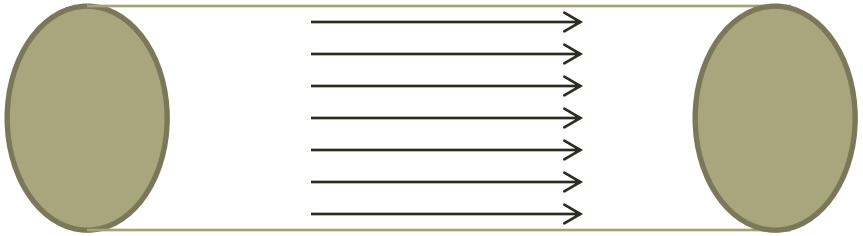
Jason Ryan, MD, MPH

# Heart Murmurs

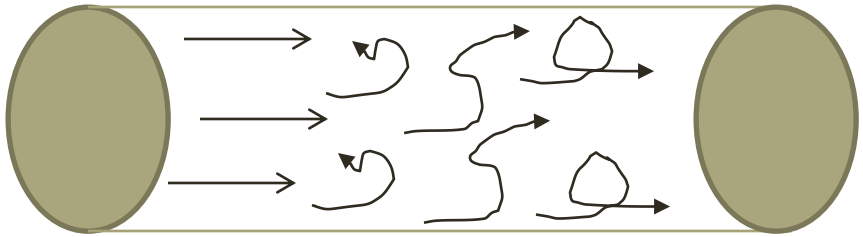
- Cardiac sound heard with stethoscope
- Caused by **turbulent blood flow**
- May be normal or pathologic

Wikipedia/Public Domain

# Laminar vs. Turbulent Flow



Laminar Flow = Quiet(er)



Turbulent Flow = Loud
High Flow Rates
Narrow Flow Areas

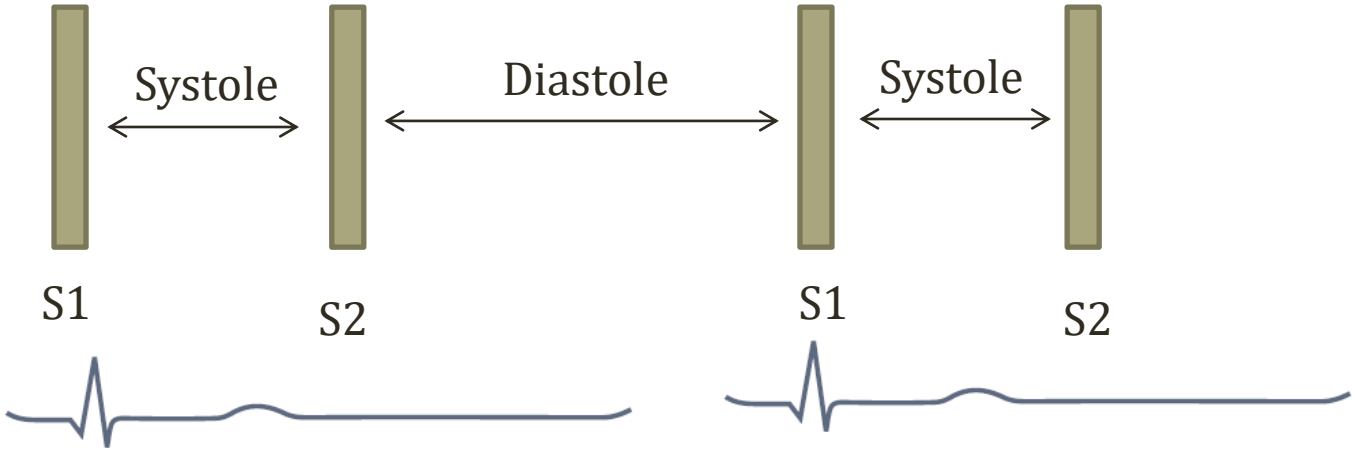
# Murmurs

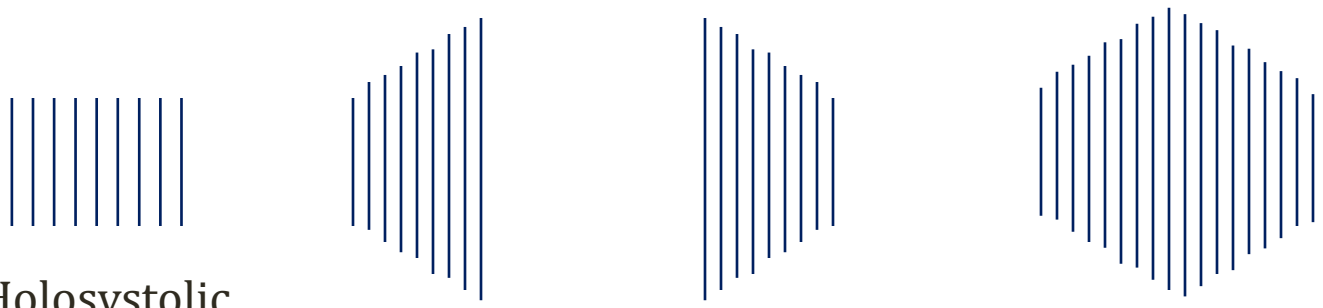
## Grading

- I - barely audible on listening carefully
- II - faint but easily audible
- III - loud and easily audible, no thrill
- IV - loud murmur with a thrill
- V –heard with scope barely touching chest
- VI - audible with scope not touching the chest

# Murmurs

## Other Descriptors



Holosystolic
Pansystolic

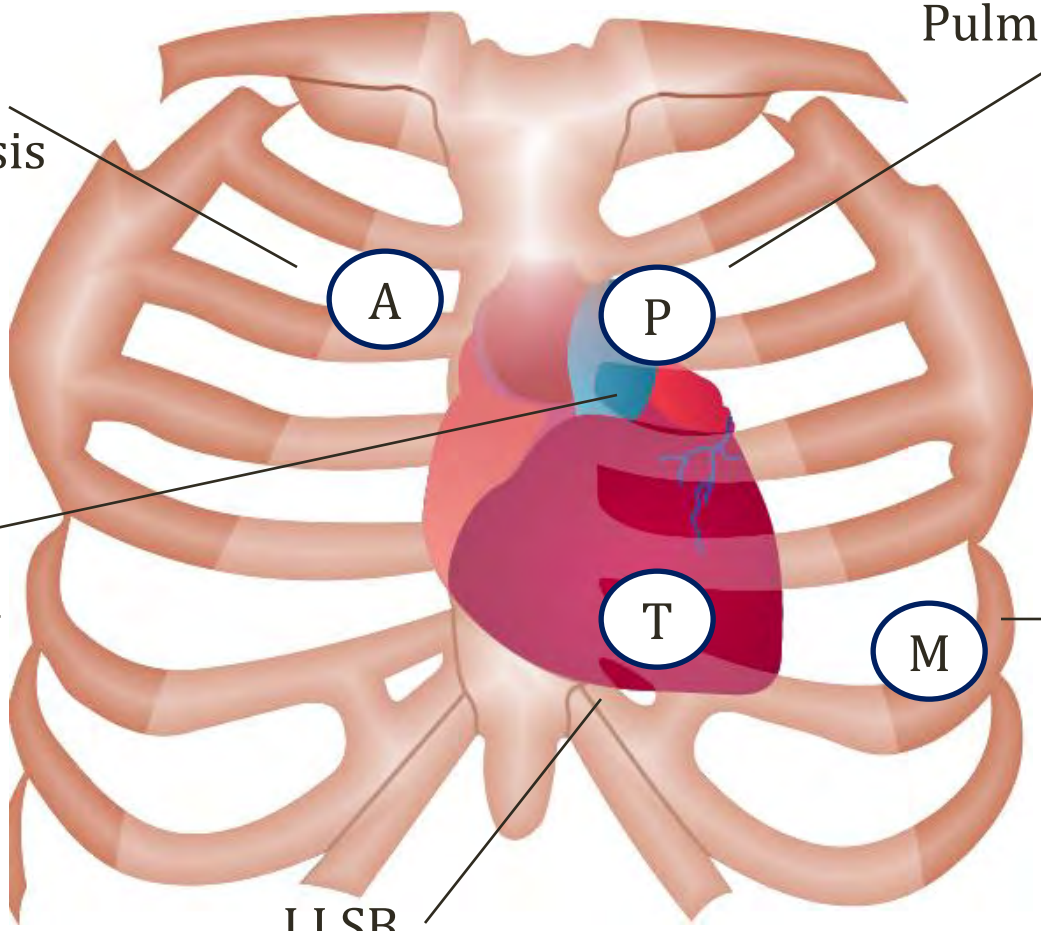
Crescendo

Decrescendo

Crescendo-
decrescendo

# Murmurs

## Location




RUSB
Aortic Stenosis

LUSB
Pulmonic Murmurs
PDA

LSB
Aortic Regurg
HCM

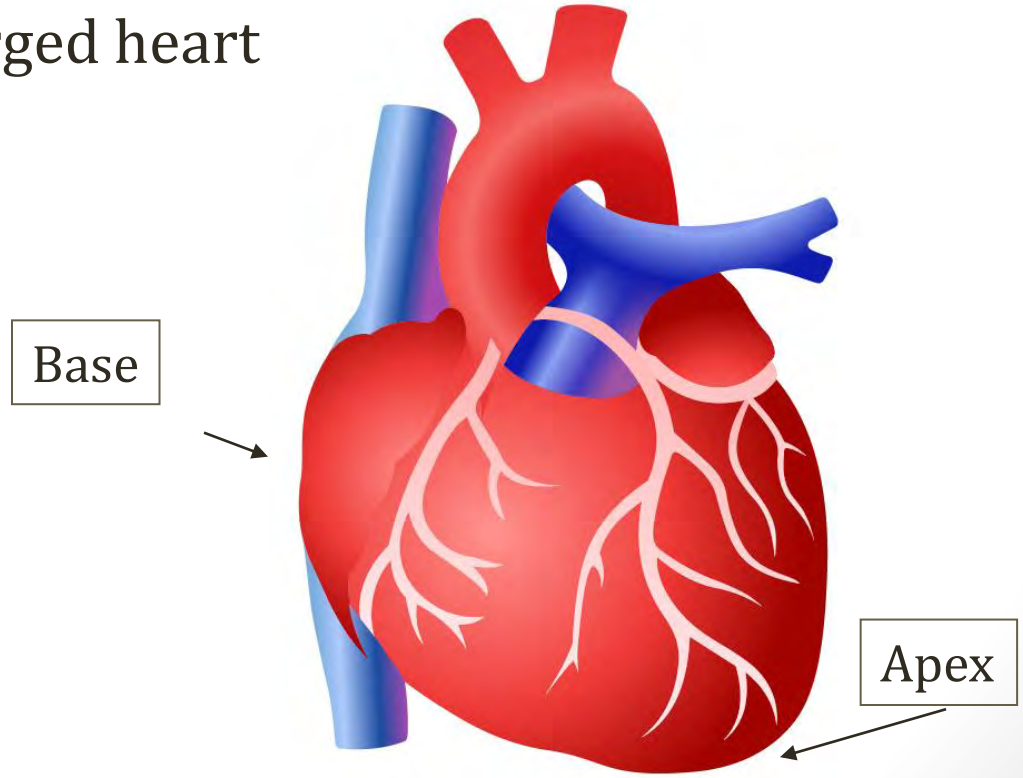
Apex
Mitral Murmurs

LLSB
Tricuspid Murmurs
VSD

# Murmurs

## Location

- Point of maximal impulse (apical impulse)
  - Left 5th intercostal space
  - Mid-clavicular line
- Lateral shift = Enlarged heart
- Hyperdynamic



# Innocent/Functional Murmurs

- Caused by normal flow of blood
- Common in children
- Also young, thin patients
- Generally soft murmurs
- No signs/symptoms of heart disease
- Stills murmur
- Pulmonic flow murmur
- Venous hum

# Systolic Murmurs

- Occur when heart contracts/squeezes
- Between S1-S2
- Aortic stenosis
- Mitral regurgitation
- Pulmonic stenosis
- Tricuspid regurgitation
- Hypertrophic cardiomyopathy
- Ventricular septal defect (VSD)

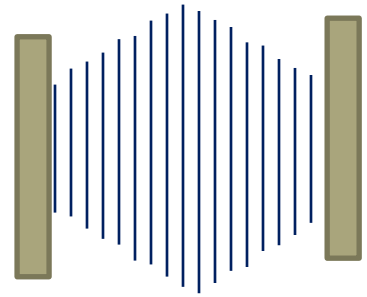
# Diastolic Murmurs

- Occur when heart relaxes/fills
- Between S2-S1
- Aortic regurgitation
- Mitral stenosis
- Pulmonic regurgitation
- Tricuspid stenosis

# Aortic Stenosis

## Murmur

- Systolic crescendo-decrescendo murmur
- Also called an “ejection murmur”




# Aortic Stenosis

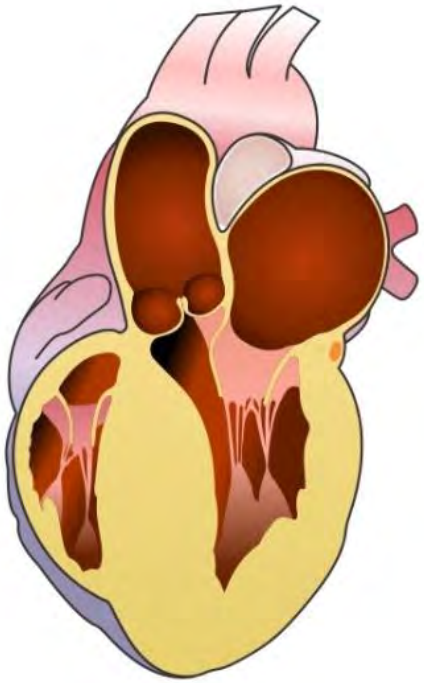
## Severe Disease Findings

- **Late-peaking murmur**
  - Slow flow across stenotic valve
- **Soft/quiet S2**
  - Stiff valve can't slam shut
- **Pulsus parvus et tardus**
  - Weak and small carotid pulses
  - Delayed carotid upstroke

# HCM

## Hypertrophic Cardiomyopathy

- Same murmur as aortic stenosis
- Differentiated by maneuvers
- **Valsalva**
  - Decreases venous return/preload
  - Increase HCM murmur
  - Decrease AS murmur

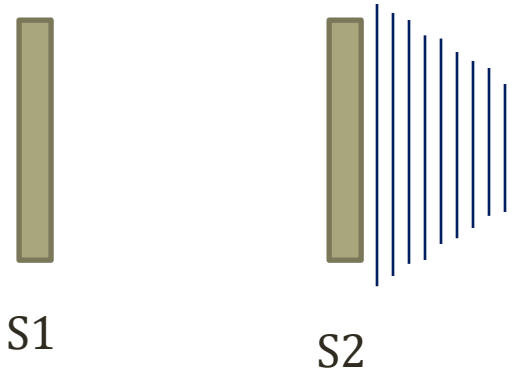


HCM

# Aortic Regurgitation

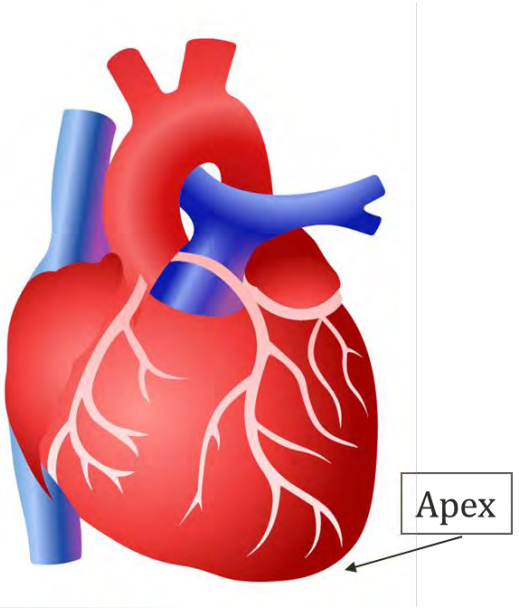
## Murmur

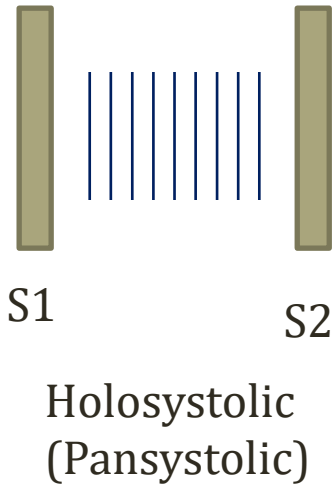
- Decrescendo, **blowing** diastolic murmur



# Mitral Regurgitation

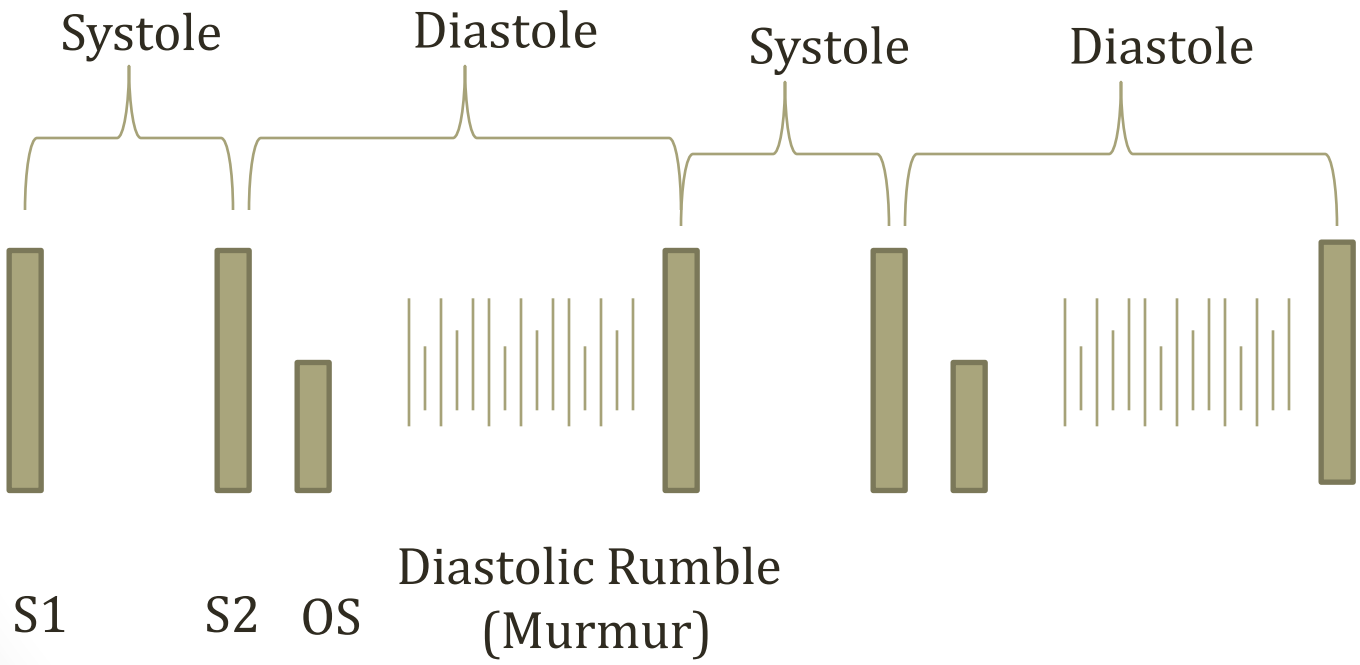
- **Holosystolic murmur heard best at the apex**
  - 5th intercostal space, mid-clavicular line




# Mitral Stenosis

- **Diastolic rumbling murmur**
- Preceded by **opening snap**



# Mitral Stenosis

- No left sided S3, S4 in mitral stenosis
- **Time to opening snap** associated with severity
  - **High left atrial pressure** in severe disease
  - Higher left atrial pressure → ↓ time to opening snap
  - Short time to opening snap seen in severe disease

# Tricuspid/Pulmonic Disease

- Valve lesions sound like left sided-counterparts
- Heard in different locations
- Left upper sternal border
  - Pulmonic stenosis/regurgitation
- Left lower sternal border
  - Tricuspid stenosis/regurgitation

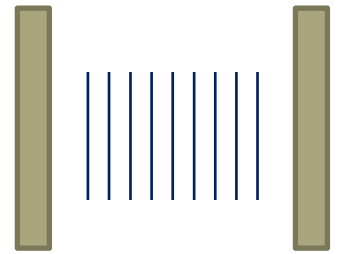
# Carvallo's Sign

- Most right sided murmurs louder with inspiration
- Inspiration draws blood volume to lungs
- Louder right sided murmurs
- Softer left sided murmurs
- **rIght sided** murmurs increase with Inspiration
- **lEft sided** murmurs increase with Exhalation

# VSD

## Ventricular Septal Defect

- Holosystolic murmur similar to MR
- Small VSD → more turbulence → loud murmur




Holosystolic
(Pansystolic)

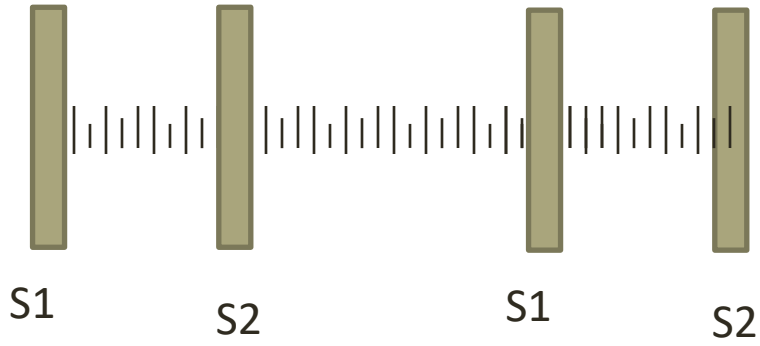
3 Causes Holosytolic Murmurs

Mitral Regurgitation
Tricuspid Regurgitation
VSD

# PDA

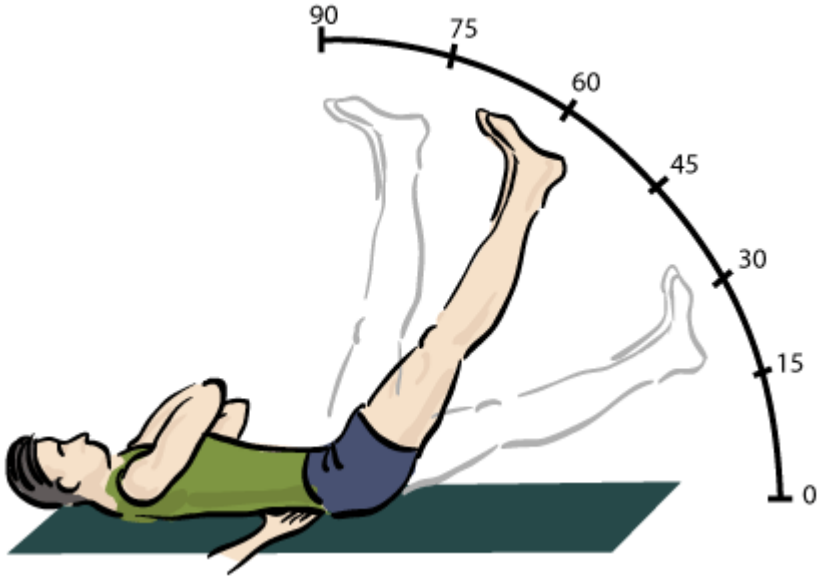
## Patent Ductus Arteriosus

- **Continuous, "machine-like" murmur**



# Maneuvers

- Performed at bedside with patient
- May increase or decrease murmur
- Used to make diagnosis




Davidjr74/Wikipedia

# Maneuvers

## Preload/Venous Return

- Increase preload/venous return
  - **Leg raise** – blood falls back toward heart
  - **Squatting** – blood in legs forced back toward heart
- Decrease preload/venous return
  - **Valsalva**- ↑ intra-thoracic pressure→ vein compression →↓ VR
  - **Standing** – Blood falls toward feet, away from heart
- Most murmurs INCREASE with more preload except:
  - HCM
  - MVP

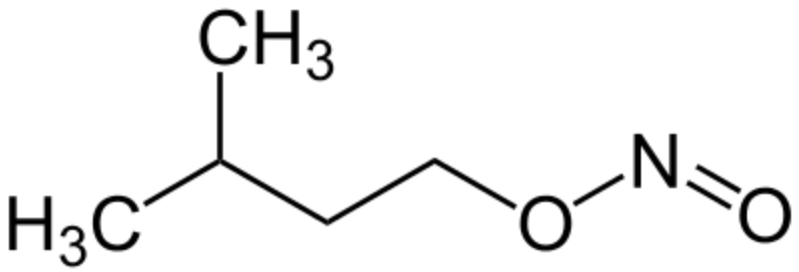
# Valsalva Maneuver

- Bear down as if moving bowels
- Phase I (few seconds)
  - ↑ thoracic pressure
  - ↓ venous return (compression of veins → ↑RA pressure)
  - Transient rise in aortic pressure (compression)
  - ↓ heart rate and AV node conduction (baroreceptors)
- Phase II
  - ↓ preload → ↓ cardiac output
  - ↑ heart rate and AV node conduction (baroreceptors)

# Maneuvers

## Afterload

- Increase Afterload
  - **Hand grip -** clench fist
- Decrease Afterload
  - **Amyl Nitrate** - vasodilator




Amyl Nitrate

# Maneuvers

## Afterload

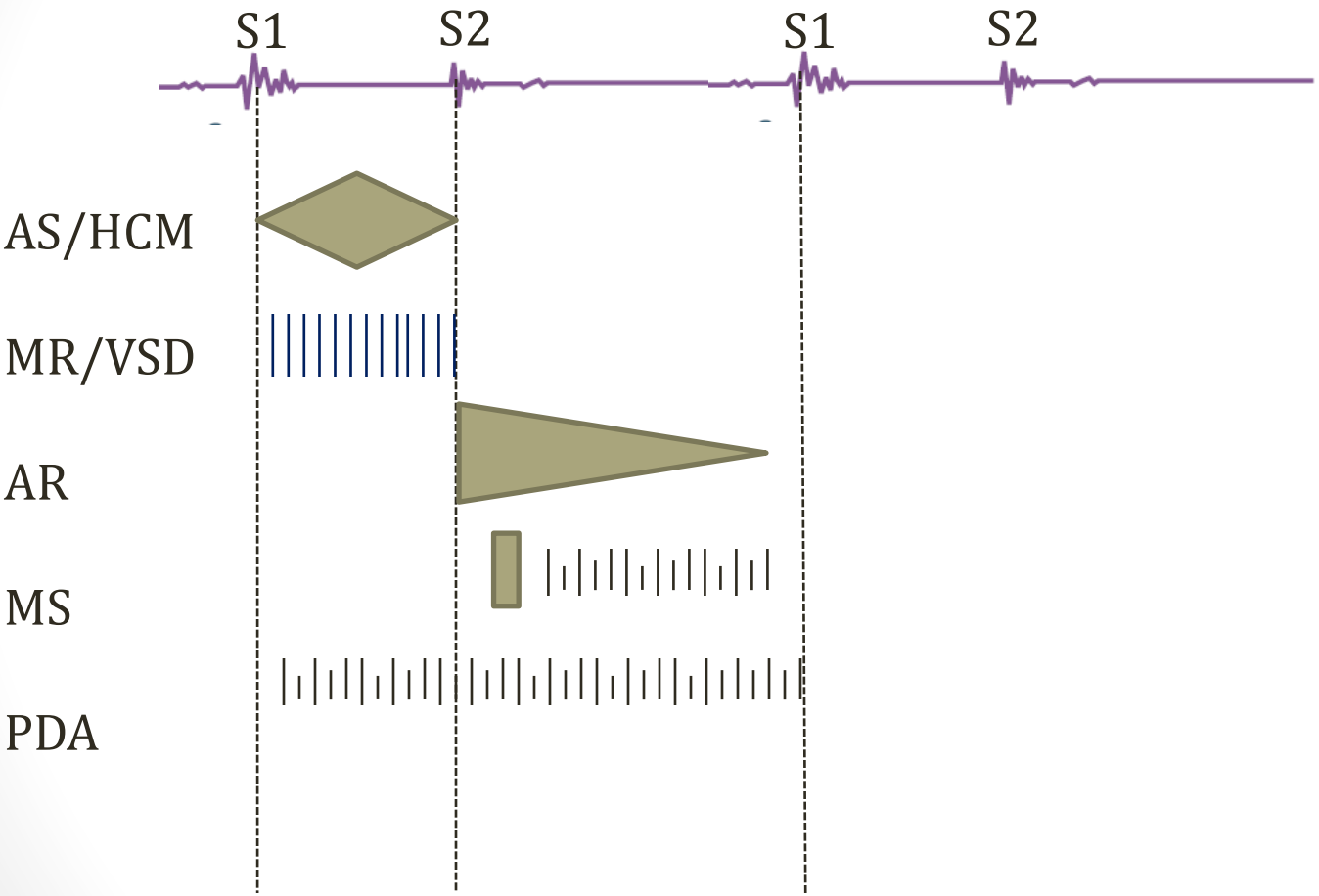
- Backward Valve Disorders
  - AR, MR, VSD
  - Louder with more afterload
  - More force pushing blood backward
- Forward Valve Disorders
  - MS, AS
  - Softer with more afterload
  - Less pressure difference moving blood forward
- MVP, HCM
  - Softer
  - Increased LV cavity size

# Clues to Diagnosis

- Young female, otherwise healthy → MVP
- Healthy, young athlete, syncope → HCM
- Immigrant or pregnant → Mitral stenosis
- IV drug abuser → Tricuspid regurgitation
- Turner Syndrome or Aortic Coarctation
  - Bicuspid AV
  - Early stenosis
  - Aortic regurgitation
- Marfan → MVP

# Summary

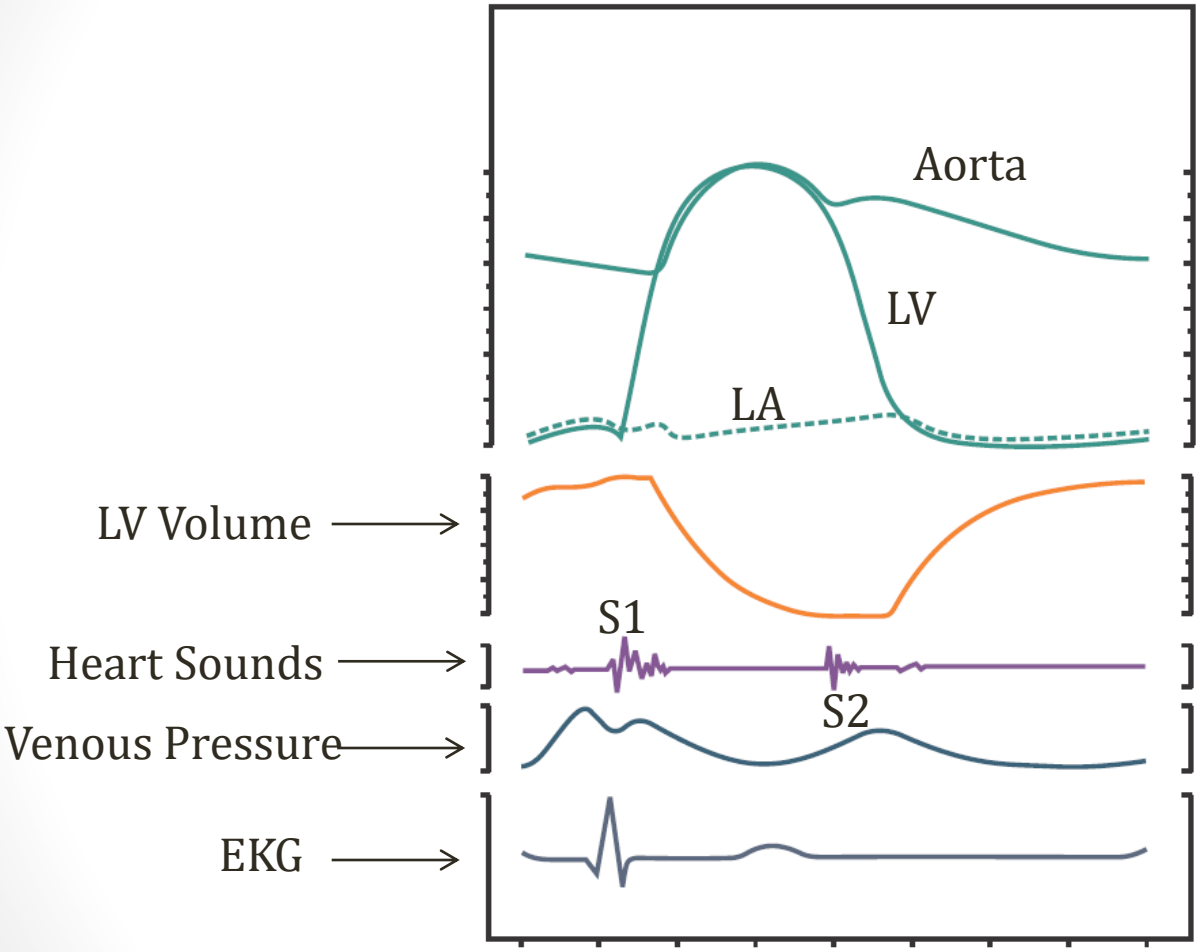
## Commonly Tested Murmurs



# Heart Sounds

Jason Ryan, MD, MPH

# The Cardiac Cycle

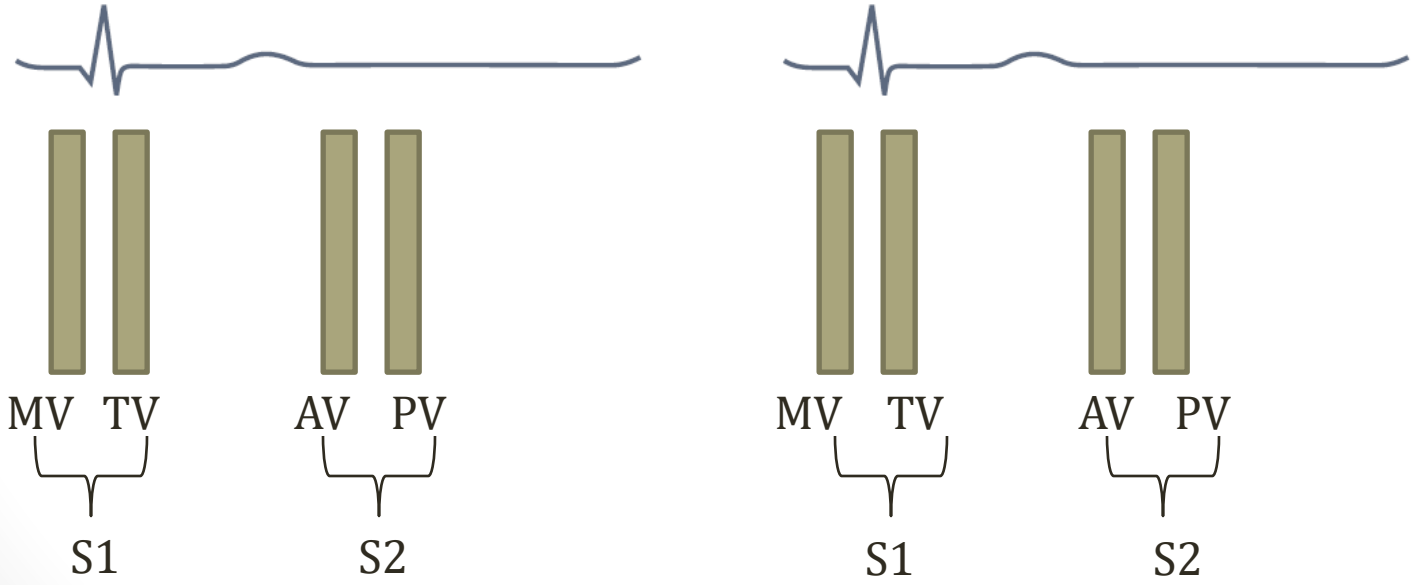


# S1 and S2

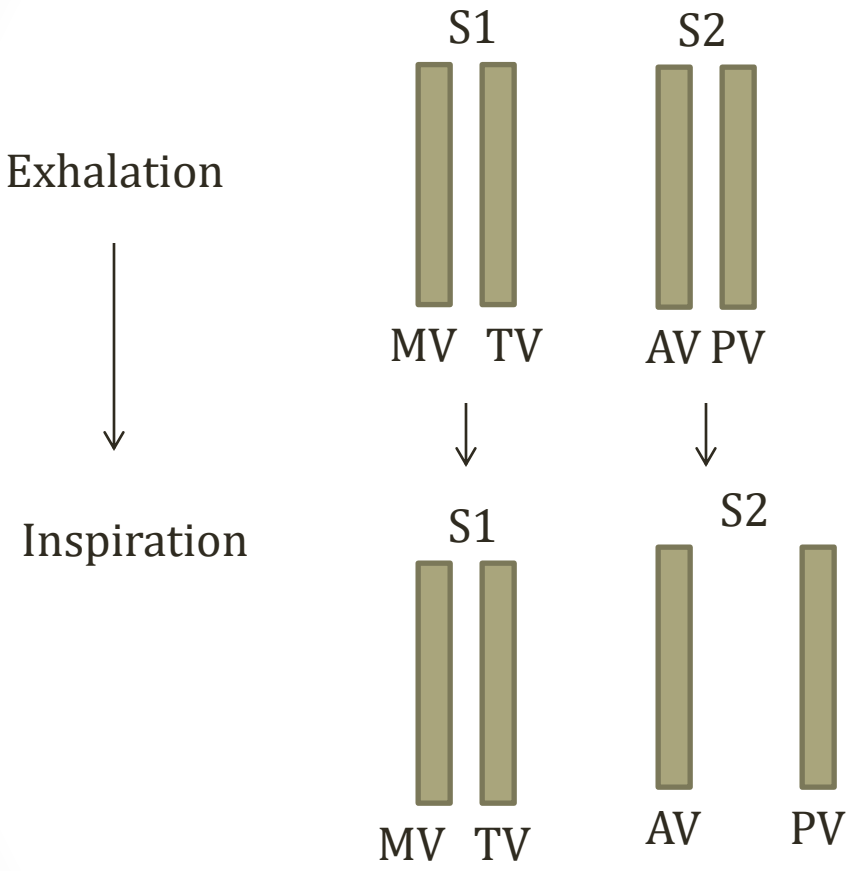
- **Normal** heart sounds
- Each has **two components**
  - One from left sided valves (aortic, mitral)
  - One from right sided valves (tricuspid, pulmonic)
- S1 usually “single”
  - Two components close together
  - Cannot distinguish separate sounds
- S2 can be “split”
  - Two components far enough apart to be audible

# S1 and S2

- S1
  - Mitral and tricuspid valves close
- S2
  - Aortic and pulmonary valves close



# Physiologic S2 splitting

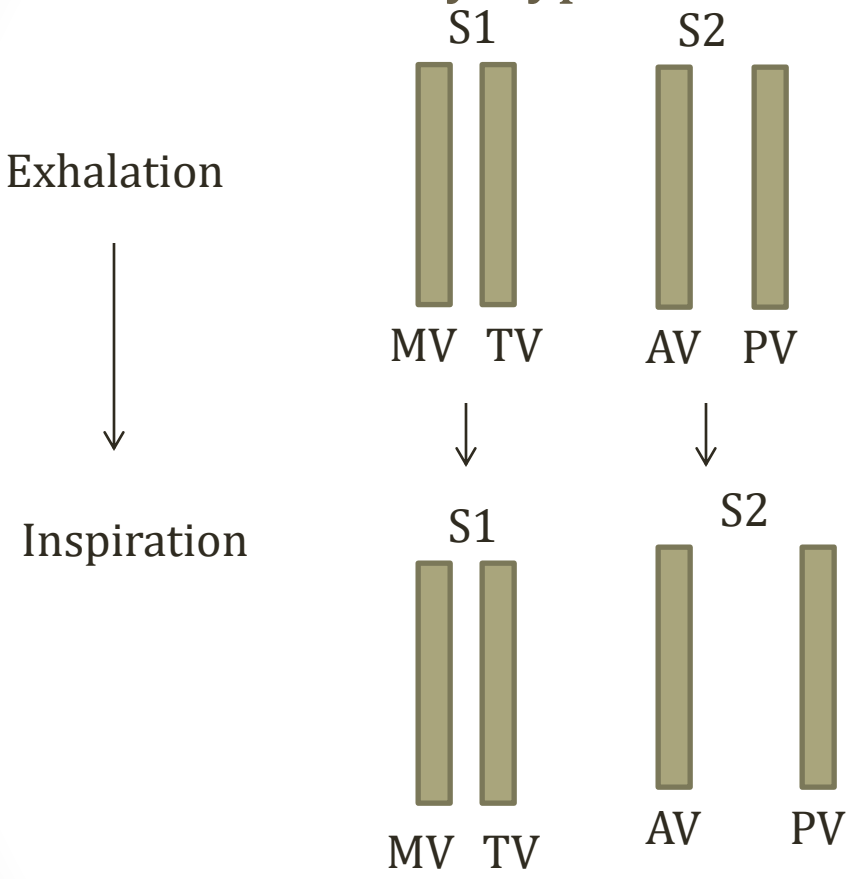



Increased venous return delays P2 by 40-60ms

**Single to split with inspiration**

# Persistent S2 splitting

## RBBB or Pulmonary Hypertension

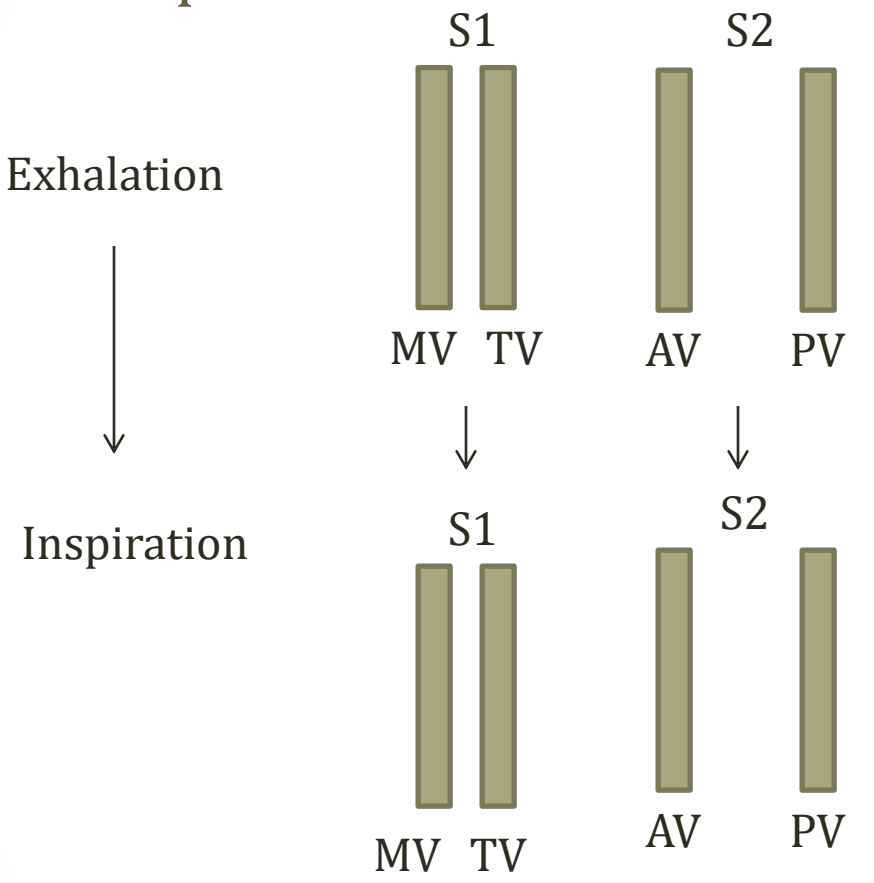



PeRsistent = Right sided delay

Delayed PV closure even during exhalation

# Fixed S2 splitting

## Atrial septal defect

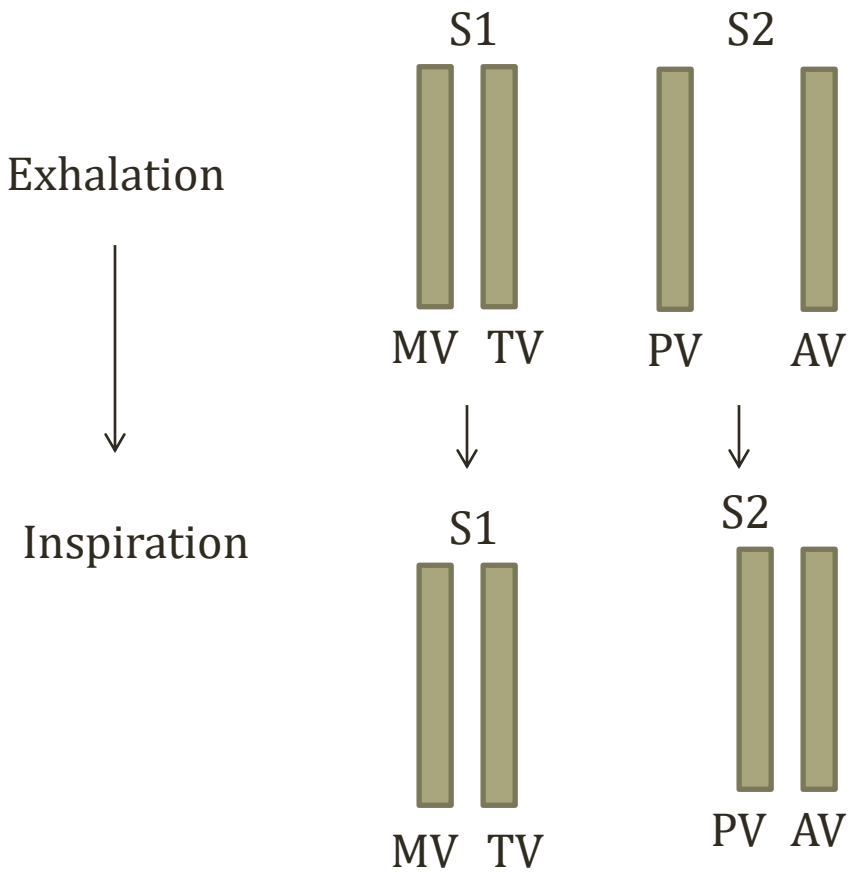



<u>Atrial Septal Defect</u>
Fixed split S2
Systolic Ejection Murmur LSB

Flow across ASD → **increased right sided flow**

# Paradoxical S2 splitting

## Delayed closure of aortic valve



# Paradoxical Splitting

- Electrical causes → delayed LV activation
  - LBBB
  - RV pacing
- Mechanical causes → delayed LV outflow
  - LV systolic failure
  - Aortic stenosis
  - Hypertrophic cardiomyopathy

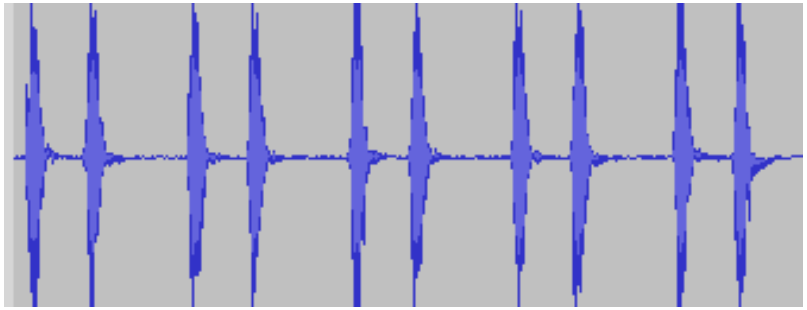
**ParodoxicaL = Left sided delay**

# Summary of S2 Splitting

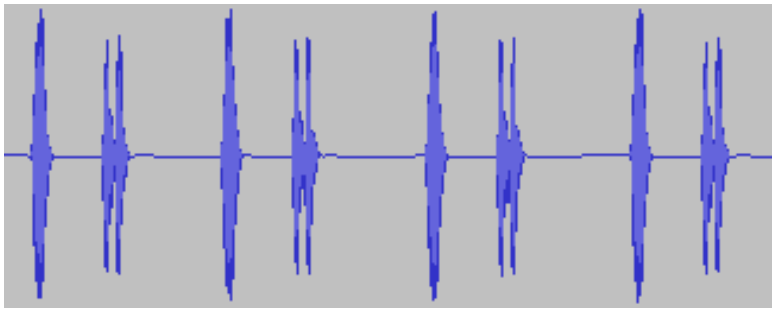
- Physiologic = normal respiratory variation
- PeRsistent = RBBB, pulmonary HTN
- Fixed = Atrial septal defect
- ParadoxicaL = LBBB, cardiomyopathy

# Cardiac Phonography

S1, S2



Fixed Split S2



# Loud P2

- Loud pulmonic component of S2
- **Pulmonary hypertension**
- Forceful closure of pulmonary valve
- Normally P2 not heard at apex
  - If you hear it here, it's "loud"

# S3 and S4

- Pathologic/abnormal heart sounds
- Occur in **diastole** during filling of left ventricle
- **Low-pitched** sounds heard best with bell
- S3: Early filling sound
- S4: Late filling sound


Tama988/Wikipedia

# S3

- Commonly seen in **acute heart failure**
  - High LA pressure → rapid early filling of LV → S3
  - Associated with ↑ LAP & ↑LVEDP
  - "Pushers" → push blood into LV
  - Very specific sign of high left atrial pressure
- **May be heard in normal hearts**
  - Young patients (<30), pregnant women
  - These patients are "suckers"
  - Vigorous LV relaxation lowers pressure rapidly

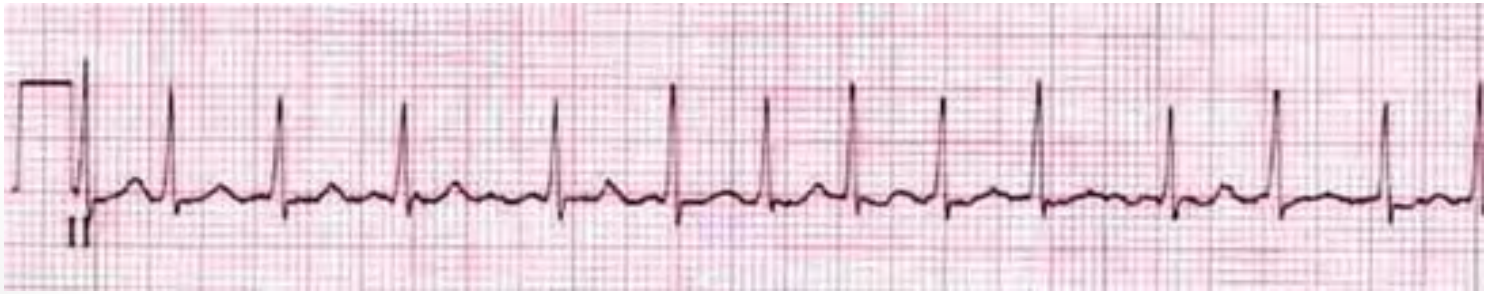
# S3

- Low frequency **best heard with bell**
- Louder in left **lateral decubitus position**
- Loudest at **apex**

Rama/Wikipedia

# S4

- Heard in patients with **stiff left ventricle**
  - Long-standing hypertension
  - Hypertrophic cardiomyopathy
  - Diastolic heart failure
- Rapid late filling of LV due to atrial kick
- Not heard in **atrial fibrillation**

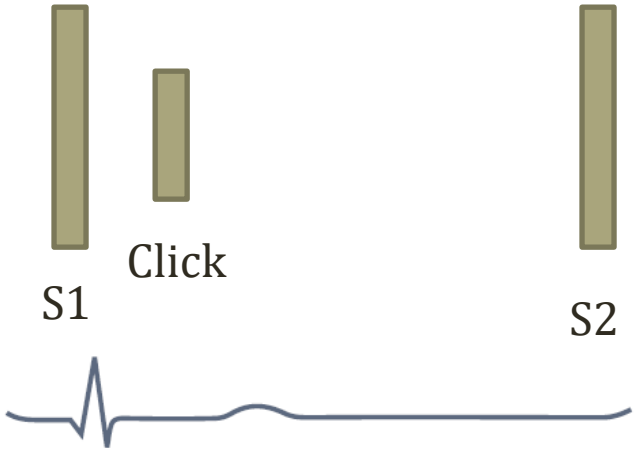


Atrial Fibrillation

# Right Sided S3 & S4

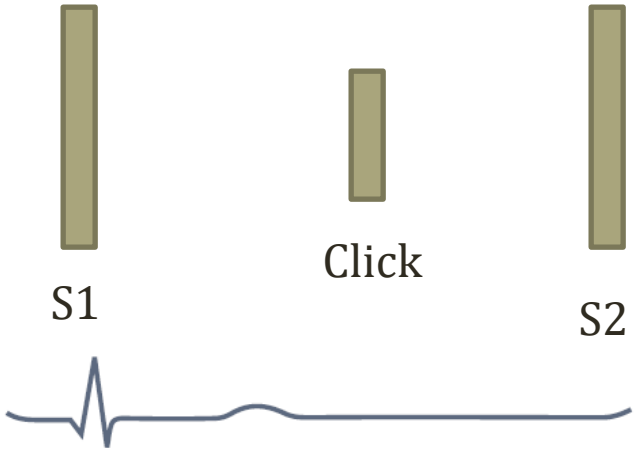
- Both sounds can occur in right ventricle
- Same mechanisms as left sounds
- Right heart failure → right sided S3
- Right ventricular hypertrophy → right sided S4

# Systolic Clicks




## Ejection Click

Early in systole
BEFORE carotid pulse
**Bicuspid Aortic Valve**



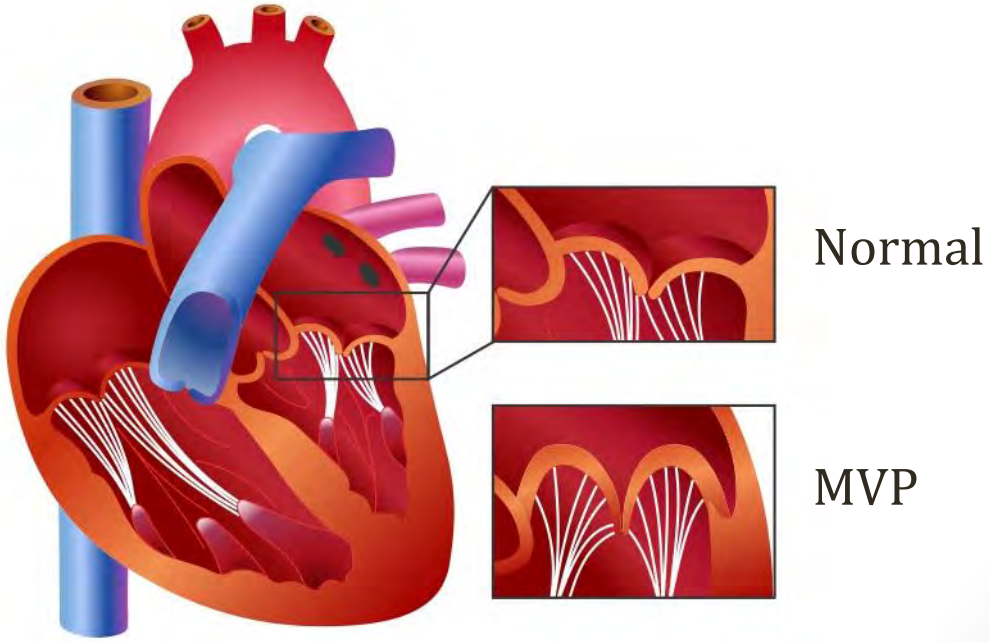

## Non-Ejection Click

Late in systole
AFTER carotid pulse
**Mitral Valve Prolapse**

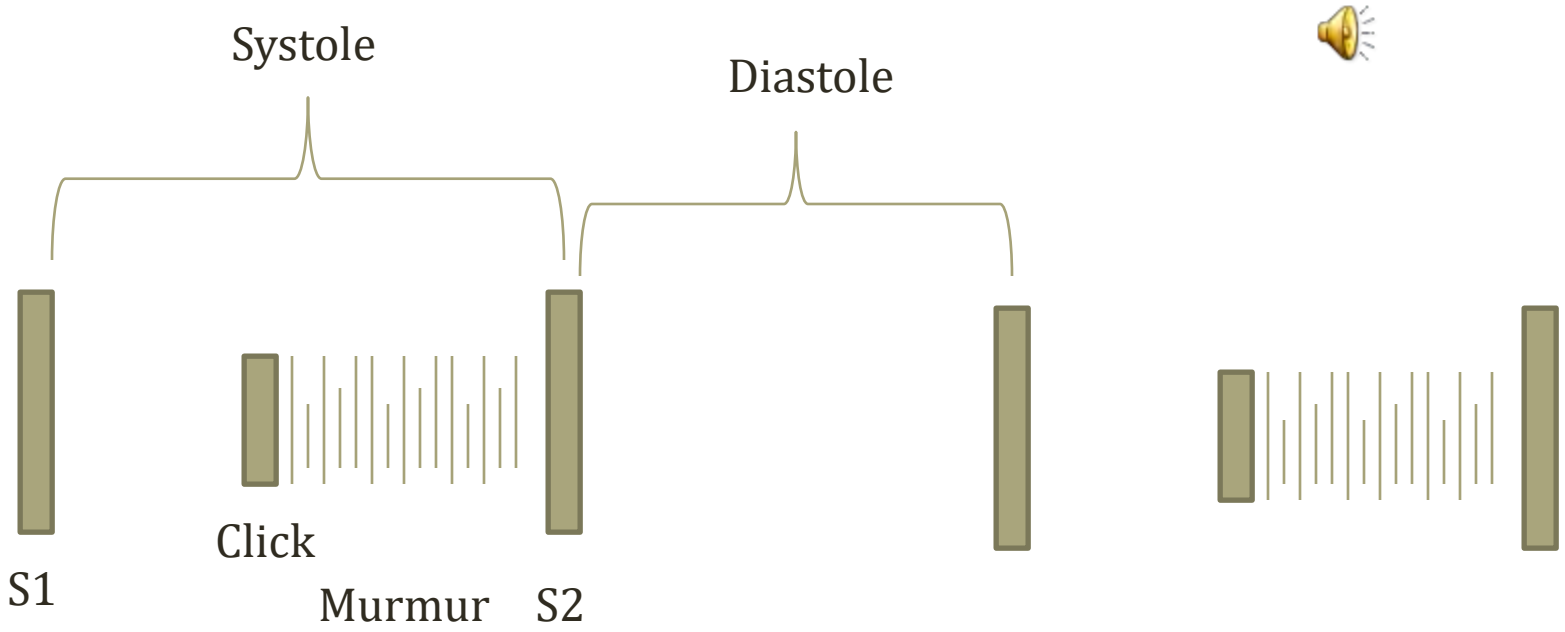
# Mitral Valve Prolapse

- **Billowing** of mitral valve leaflets above annulus
- Common cause of **mitral regurgitation**
- Causes a **systolic click**
  - Don't confuse with opening snap of mitral stenosis

| Mitral Valve Disorders |
| --- |
| Proclick |
| Stenosnap |



# Mitral Valve Prolapse



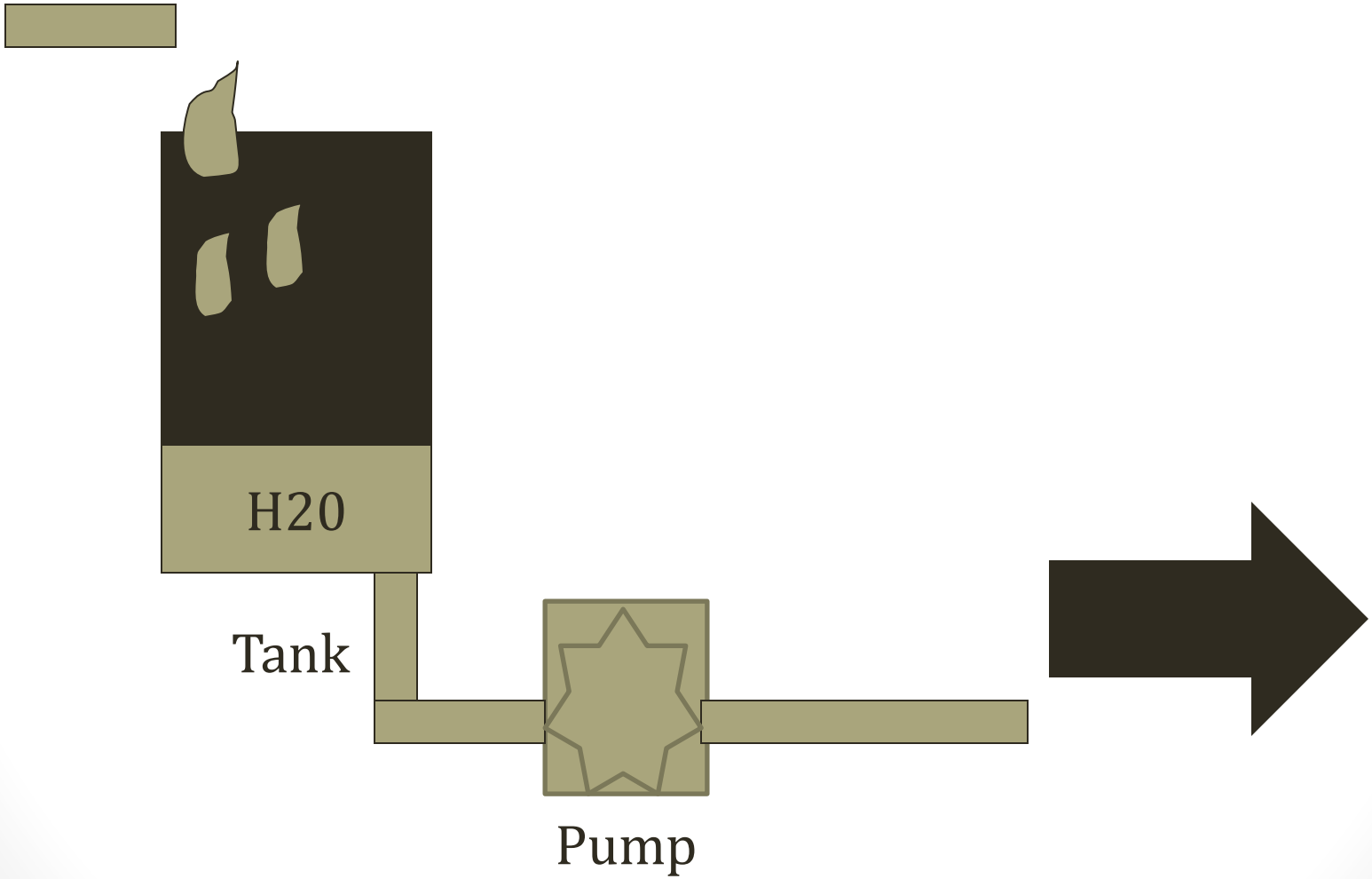
# Heart Failure Basics

Jason Ryan, MD, MPH

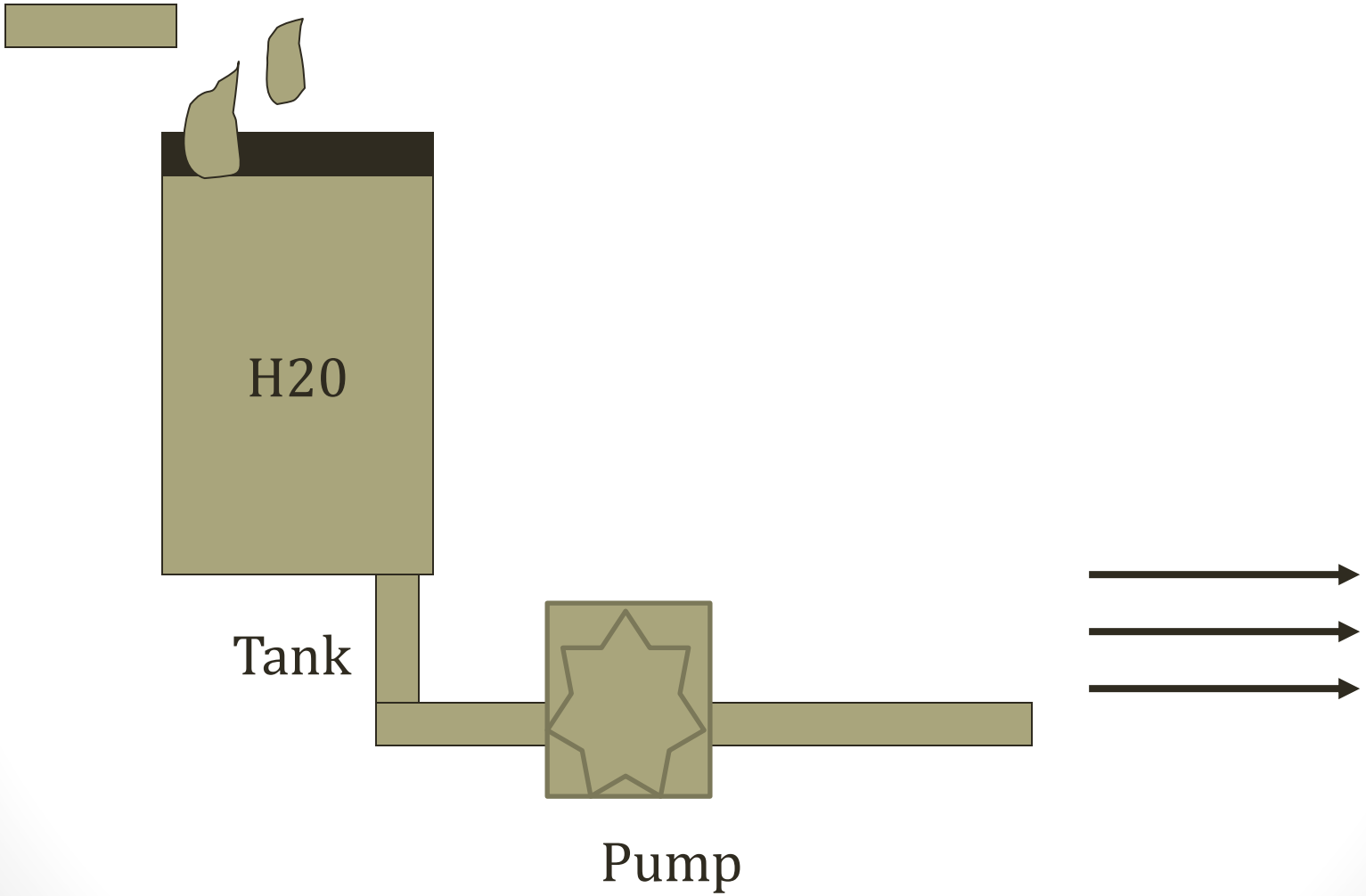
# Heart Failure

- Impaired ability of the heart to pump blood
- Hallmark: **Low cardiac output**

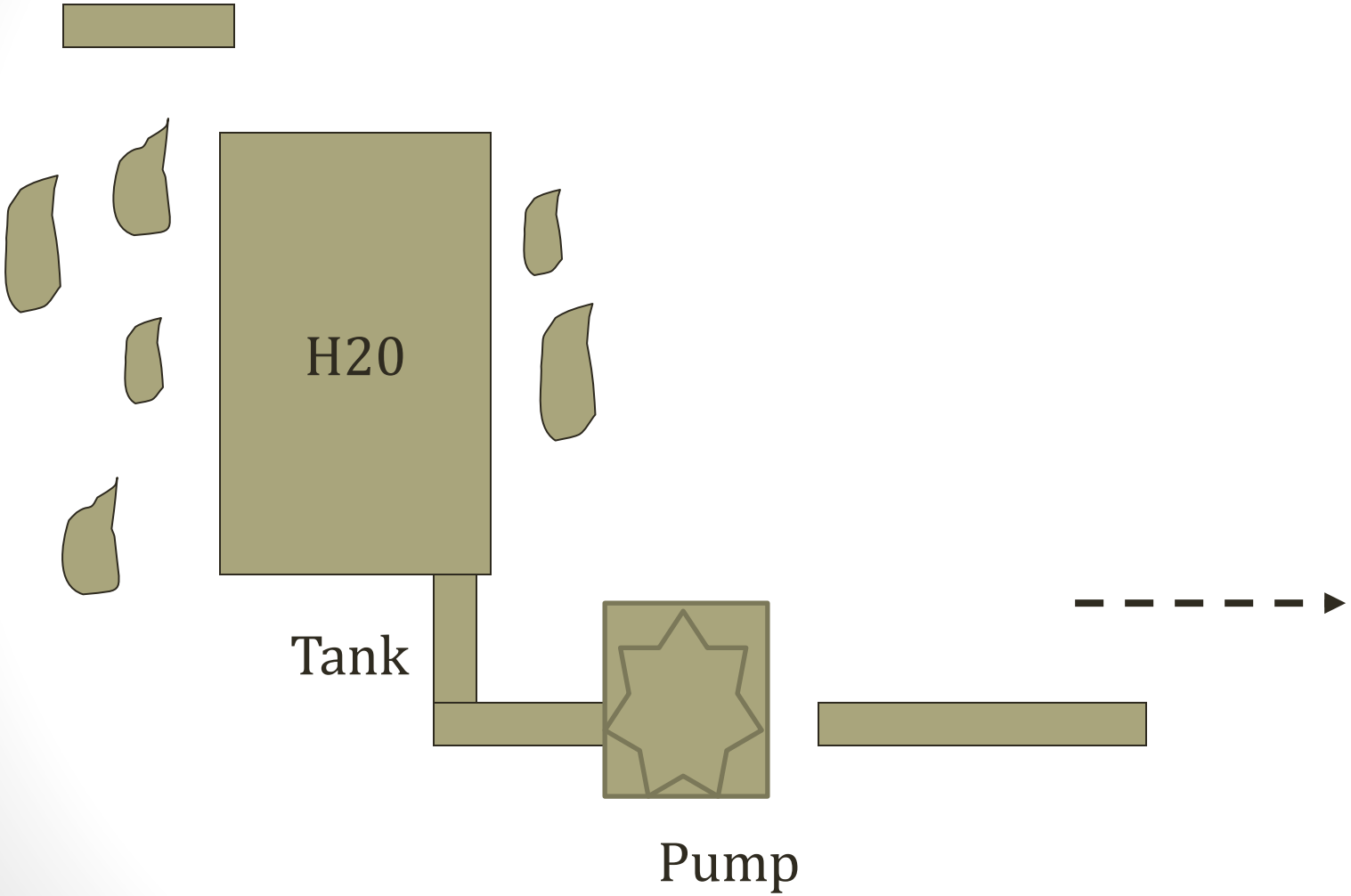
# Heart Failure



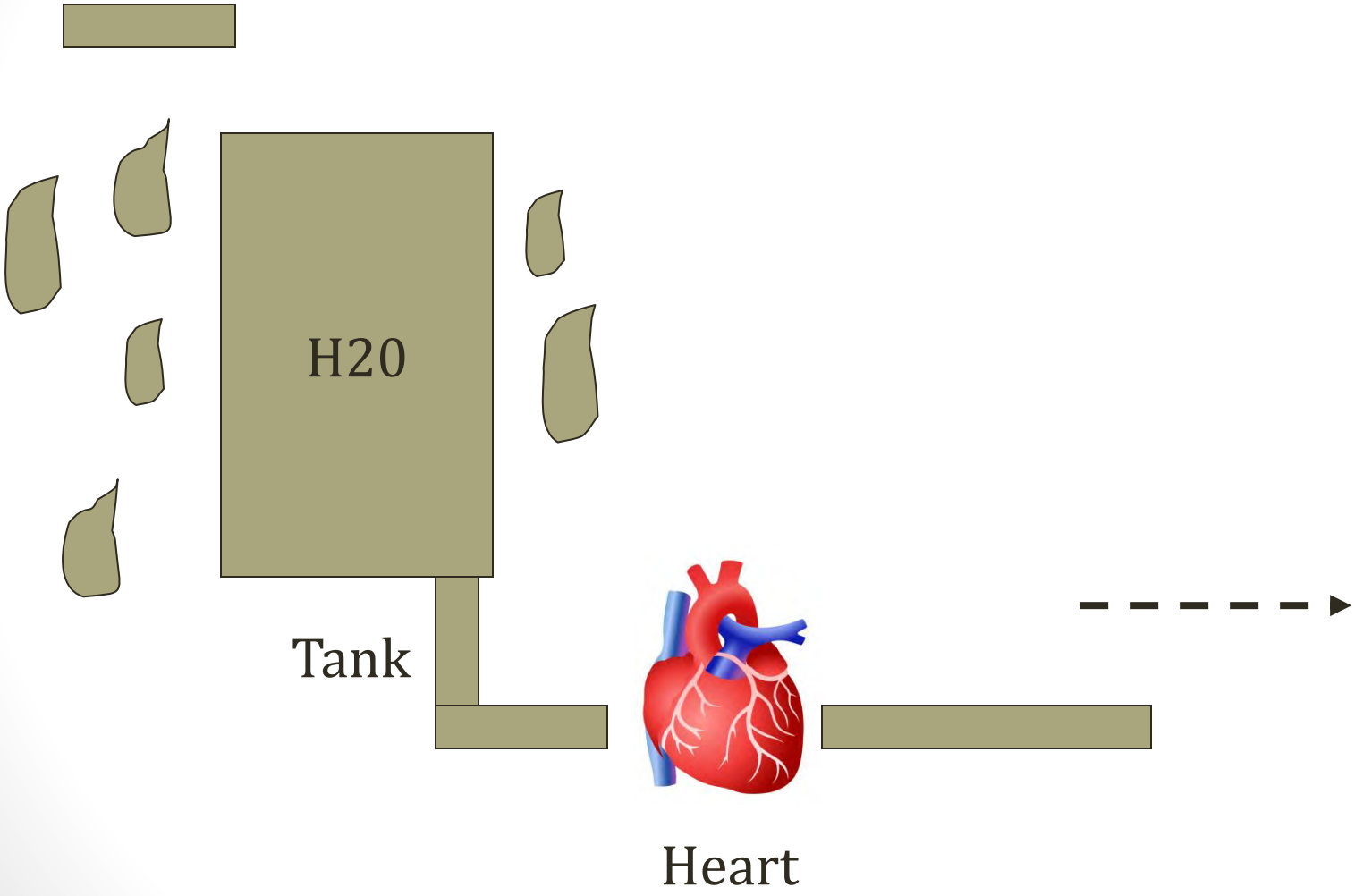
# Heart Failure



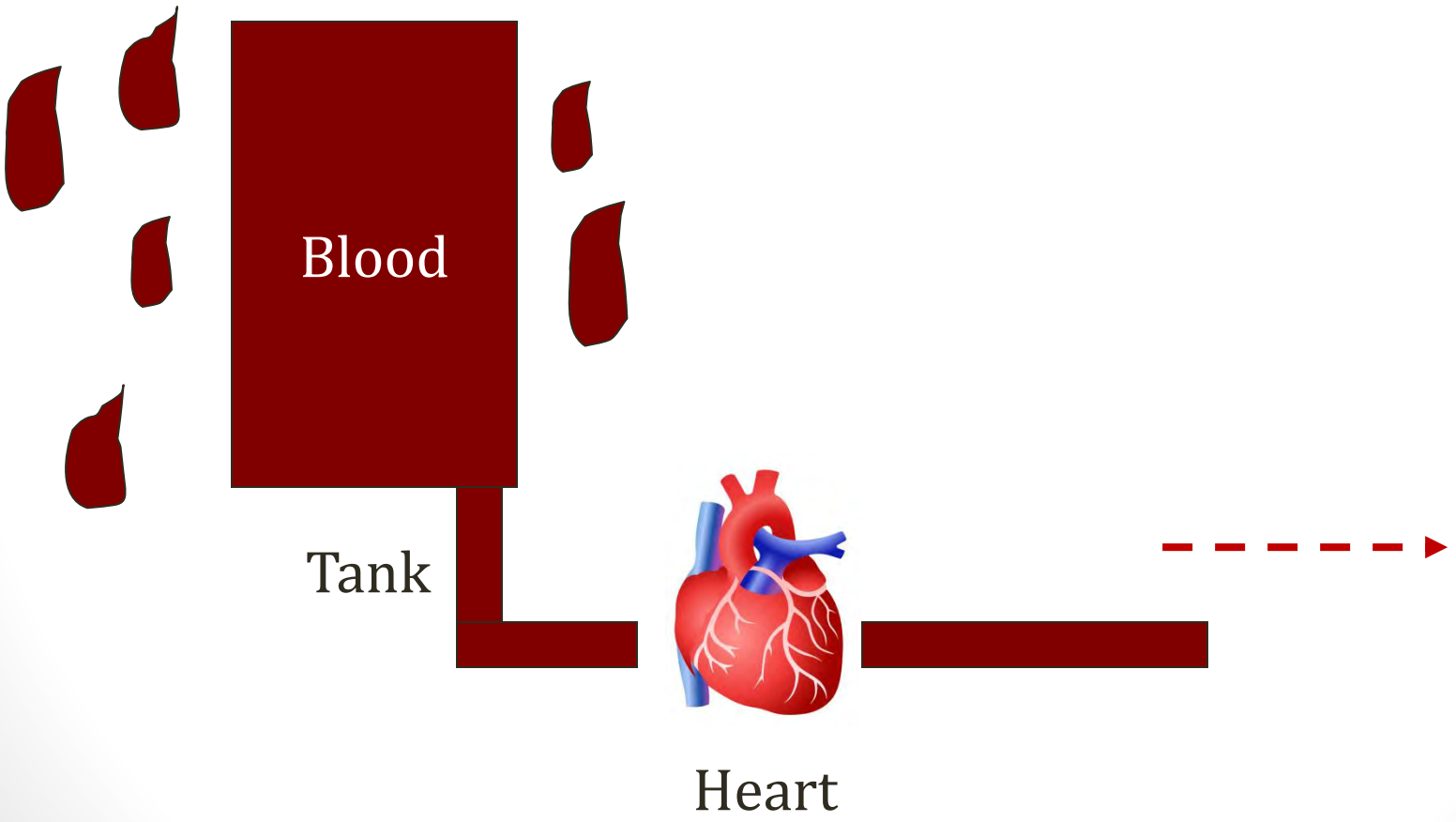
# Heart Failure



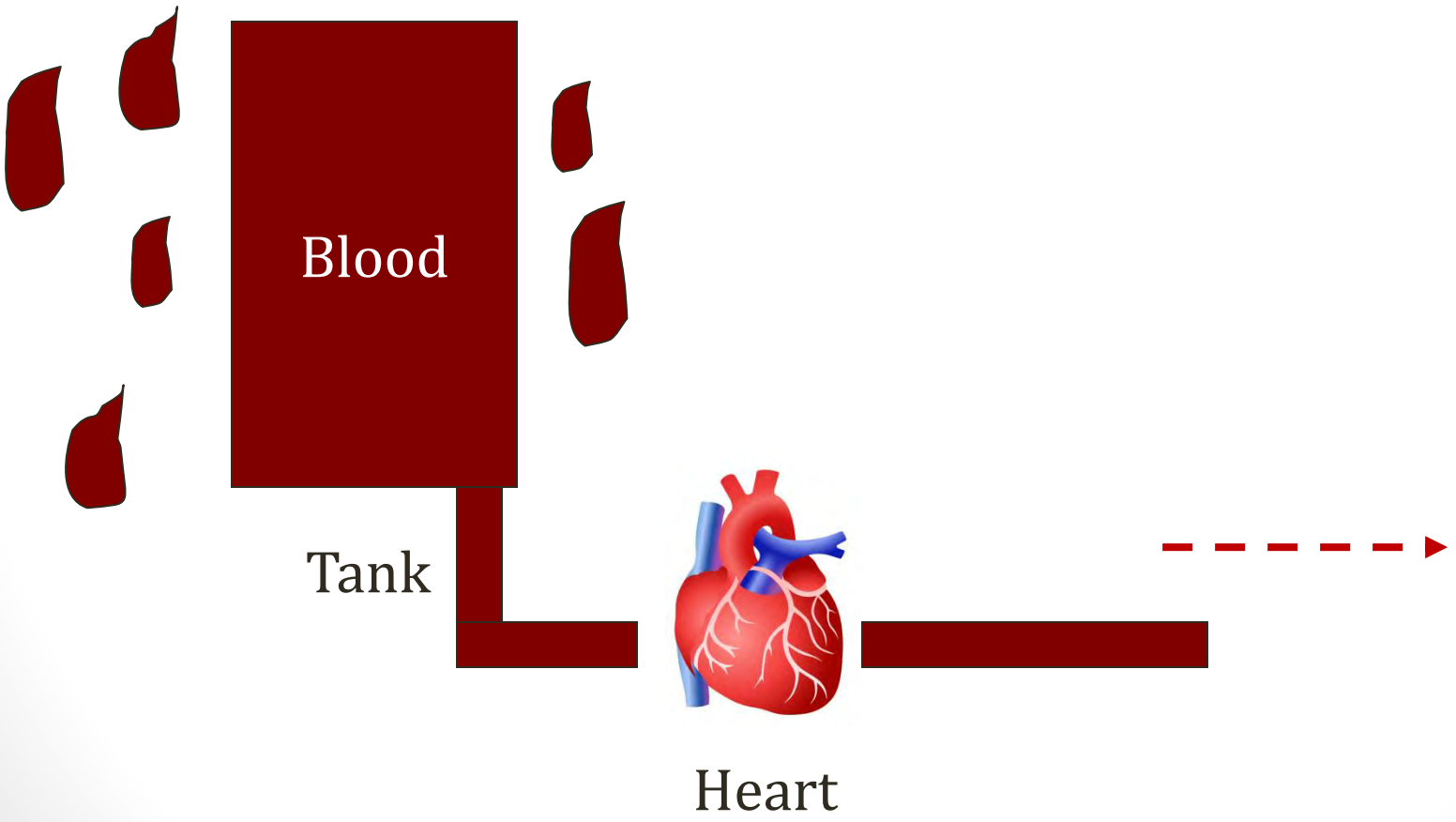
# Heart Failure



# Heart Failure

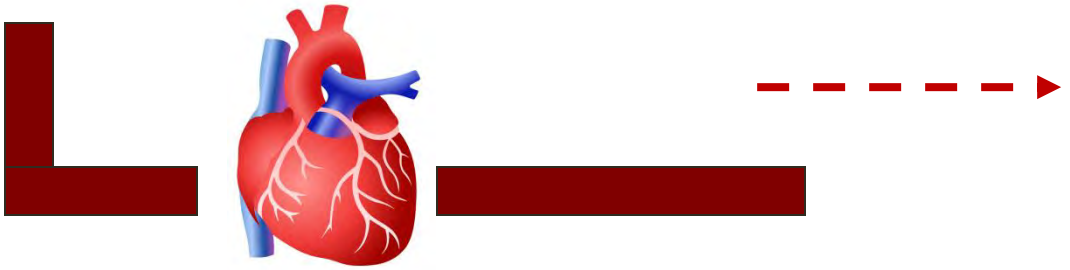


# Heart Failure



# Heart Failure

Lungs
&
Veins



Heart

# Heart Failure

## Pathophysiology

- "Failing" chambers → Increased pressures
- **Pressures** rise in cardiac chambers

# Heart Failure

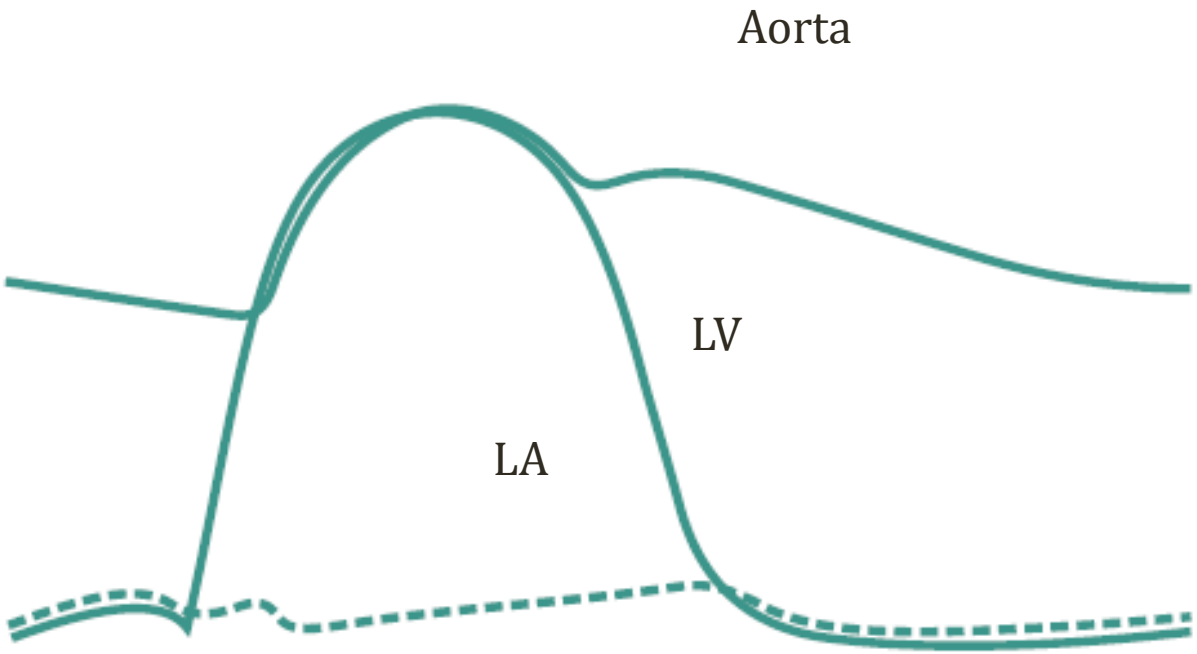
## Pathophysiology

- Left ventricular failure → ↑ LV pressure
  - LV systolic pressure: depends on contractility (can be low)
  - **LVEDP** = always **high** in left heart failure
  - Hallmark of left heart failure
  - Less blood pumped out → more left behind → more pressure
  - Stiff ventricle (diastolic HF) → high pressure

# Heart Failure

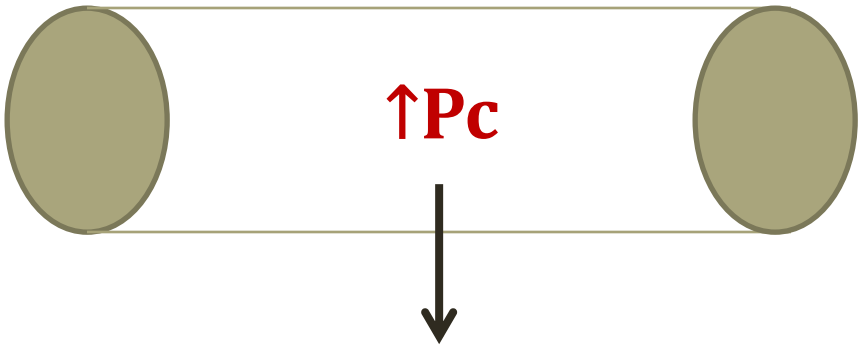
## Pathophysiology

- ↑ LVEDP → ↑ LA pressure
- ↑ pulmonary capillary pressure
  - **Dyspnea**
  - **Pulmonary edema**



# Heart Failure

## Pathophysiology



# Heart Failure

## Pathophysiology

- ↑ pulmonary capillary pressure → ↑ PA pressure
- ↑ PA pressure → ↑ RV pressure
- ↑ RV pressure → ↑ RA pressure
  - Right atrial pressure = central venous pressure
  - **High pressure in venous system**
  - **↑ jugular venous pressure (neck veins)**
  - **Capillary leak → pitting edema**

# Heart Failure

## Signs/Symptoms

- Physiologic effects of lying flat (supine)
  - Increased venous return
  - Redistribution of blood volume
  - From lower extremities and splanchnic beds to lungs
- Little effect in normal individuals
- Impaired ventricle cannot tolerate changes
- Worsens pulmonary congestion and breathing

# Heart Failure

## Signs/Symptoms

- Left heart failure
  - Dyspnea especially on exertion
  - Paroxysmal nocturnal dyspnea (wake up SOB)
  - Orthopnea (can't breathe lying flat)
- Right heart failure
  - Increased jugular venous pressure
  - Lower extremity edema
  - Liver congestion (rarely can cause cirrhosis)
- "Backward failure"

# Heart Failure

## Right Heart Failure

- Most common cause R heart failure: Left heart failure
- Occasionally right heart failure occurs in isolation
  - Normal left atrial pressure
  - High pulmonary artery, right ventricular, right atrial pressure
  - Usually secondary to a lung process
  - Pulmonary hypertension
  - COPD
  - This is often called “cor pulmonale”

# Heart Failure

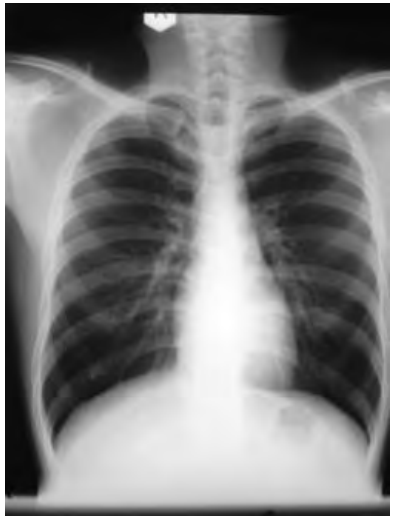
## Signs/Symptoms

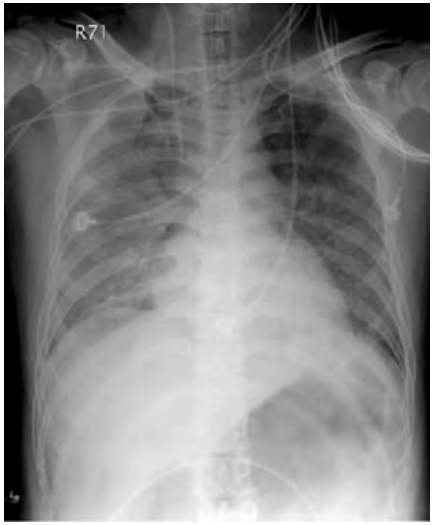
- Low flow signs/symptoms ("forward failure")
  - Loss of appetite
  - Weight loss (cachexia)
  - Confusion
  - Cool extremities
  - "Narrow pulse pressure"
- Seen only with very low cardiac output (systolic HF)
- Not seen in diastolic heart failure

# Heart Failure

## Lung Findings

- Classic finding is **rales**
  - Fluid filled alveoli "pop" open with inspiration
- Chest X-ray shows congestion
- Lungs/CXR can be clear in chronic heart failure
  - ↑lymphatic drainage

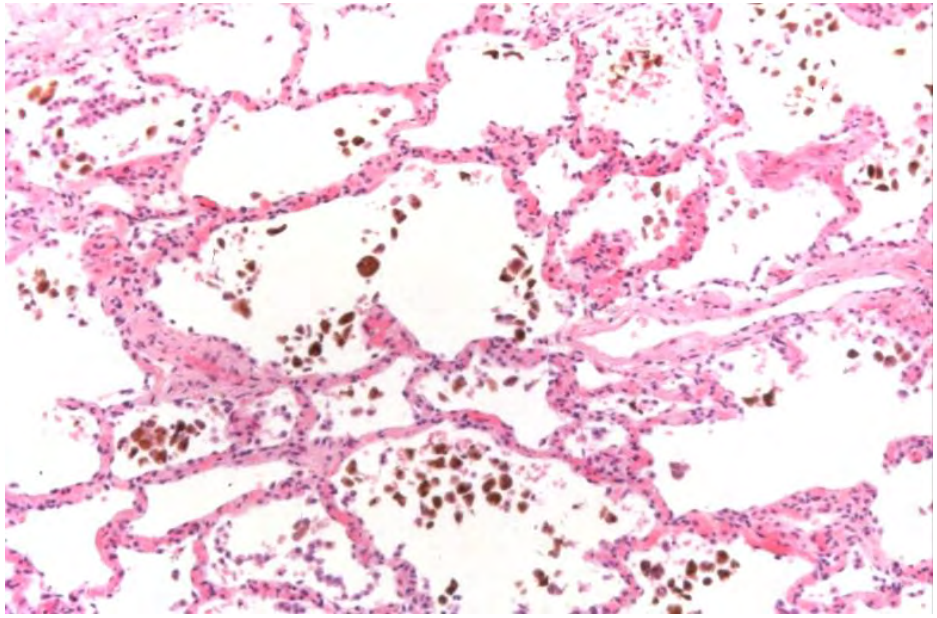




# Heart Failure

## Lung Findings

- Heart failure cells
- Hemosiderin (iron) laden macrophages
- Brown pigment in macrophages

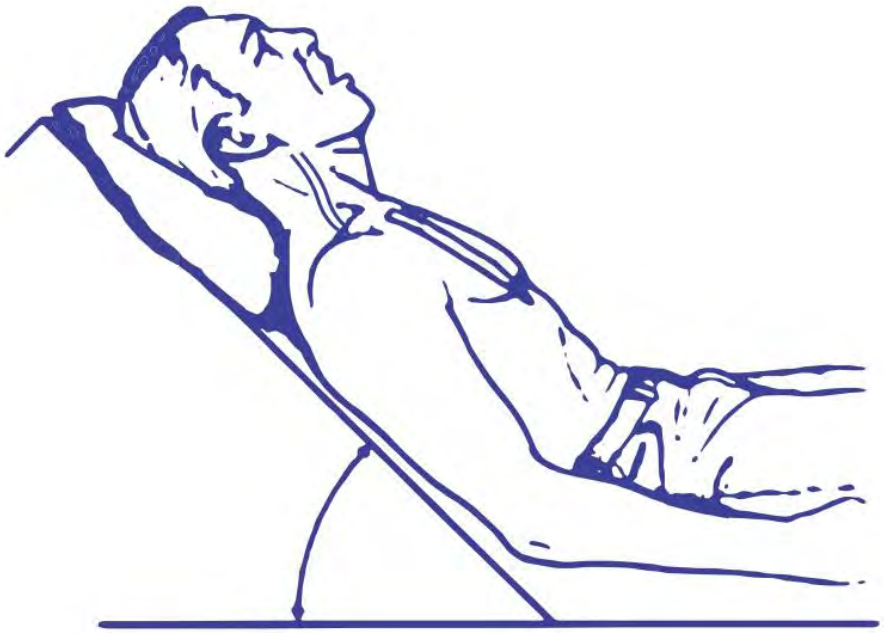


Zorkun/Wikipedia

# Heart Failure

## Signs/Symptoms

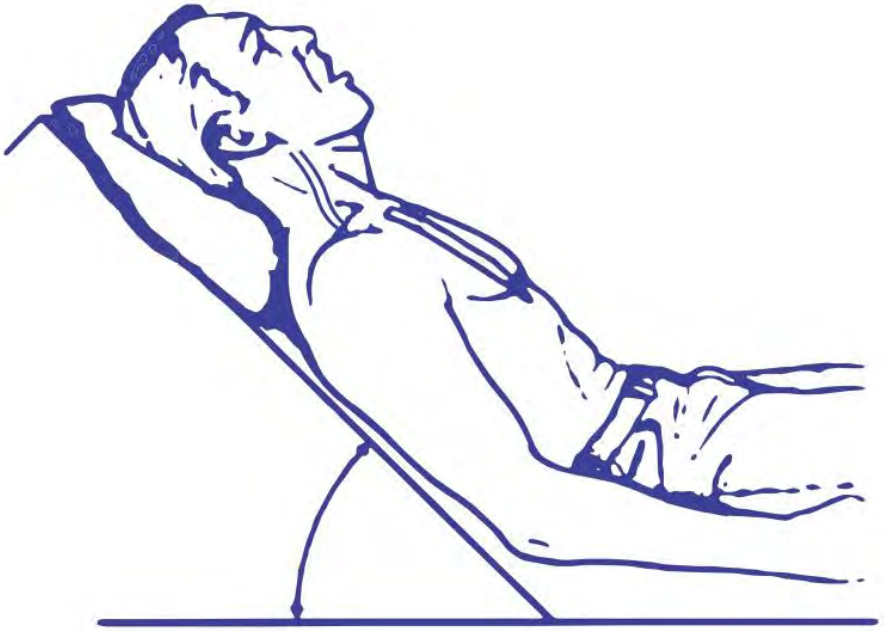
- Elevated **jugular venous pressure** (normal 6-8cmH2O)
- Look for height of double bounce (cause by a and v waves)



# Heart Failure

## Hepatojugular Reflux

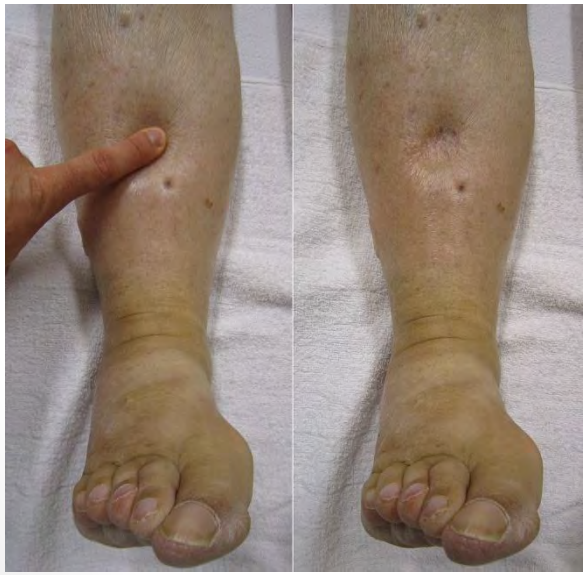
- Pressure on abdomen raises JVP 1-3cm normally
- With failing RV, increase is greater



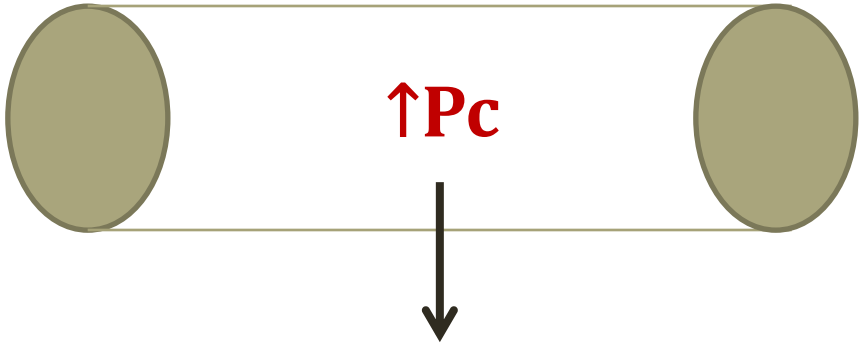
# Heart Failure

## Signs/Symptoms

- **Lower extremity pitting edema**
- Increased capillary hydrostatic pressure
- Fluid leak from capillaries → tissues
- Gravity pulls fluid to lower extremities



James Heilman, MD



# Heart Failure

## Abnormal Heart Sounds

- **S3** (associated with high left atrial pressure)
- S4 (associated with stiff left ventricle)
- Displaced apical impulse – enlarged heart

# Heart Failure

## Pathophysiology

- All forms of heart failure lead to **↓ cardiac output**
- Activates two physiologic systems
  - Activation of **sympathetic nervous system**
  - Activation of **renin-angiotensin-aldosterone system**
  - All RAAS hormone levels will rise
- Both systems lead to two key effects:
  - Increased peripheral vascular resistance (vasoconstriction)
  - Retention of sodium/water (kidneys)

# Heart Failure

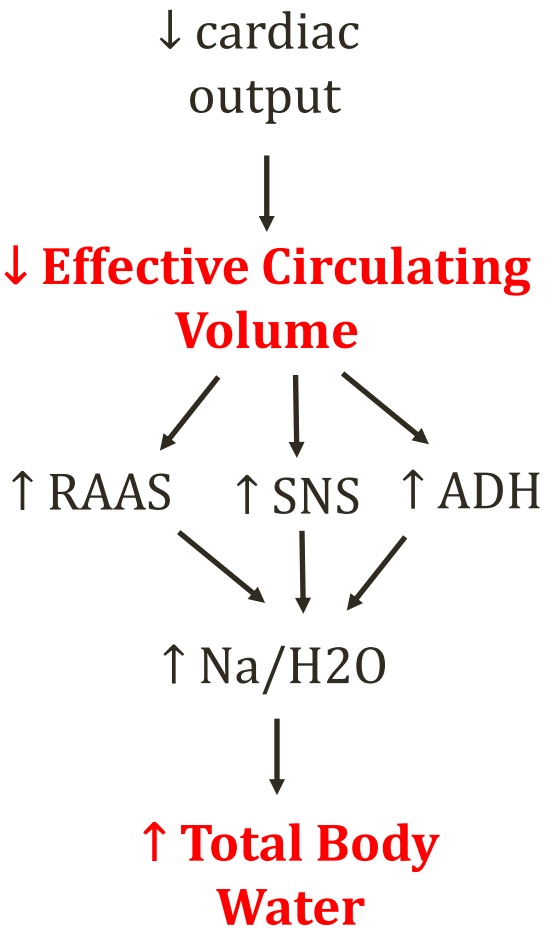
## Total Peripheral Resistance

- Cardiac output falls → vasoconstriction
- Angiotensin II, sympathetic nervous system
- **TPR always high**
- Blood pressure often high but may be low
- Depends on combined changes CO and TPR

**BP = CO X TPR**

# Heart Failure

## Sodium/Water Retention



# Heart Failure

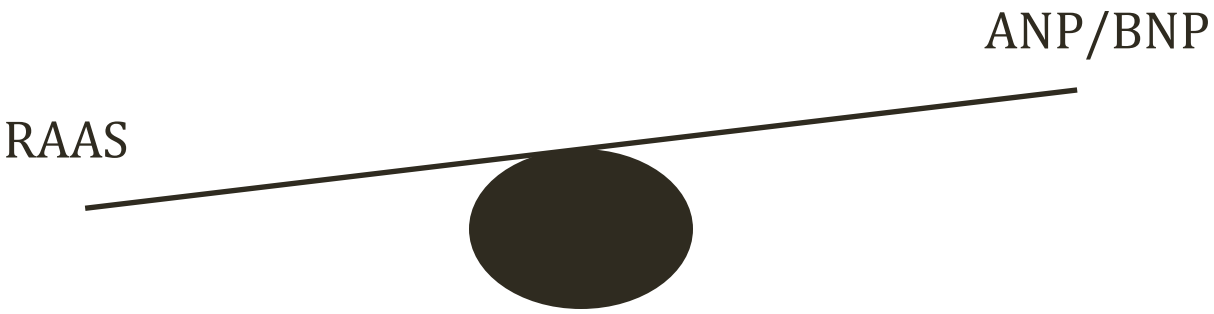
## Other Hormones

- **ANP (Atrial natriuretic peptide)**
- Atrial stretch (pressure/volume) → ANP release
- Vasodilator (↓TPR)
- Constricts renal efferents/dilates afferents
- ↑ diuresis
- Opposite effects of RAAS system

# Heart Failure

## Other Hormones

- ANP released by atrial myocytes
- **BNP (brain natriuretic peptide):** Ventricles
- Both rise with volume/pressure overload
- Both counter effects of RAAS system
- BNP sometimes used for diagnosis in dyspnea
  - High levels suggest heart failure
  - Low levels suggest other causes of dyspnea



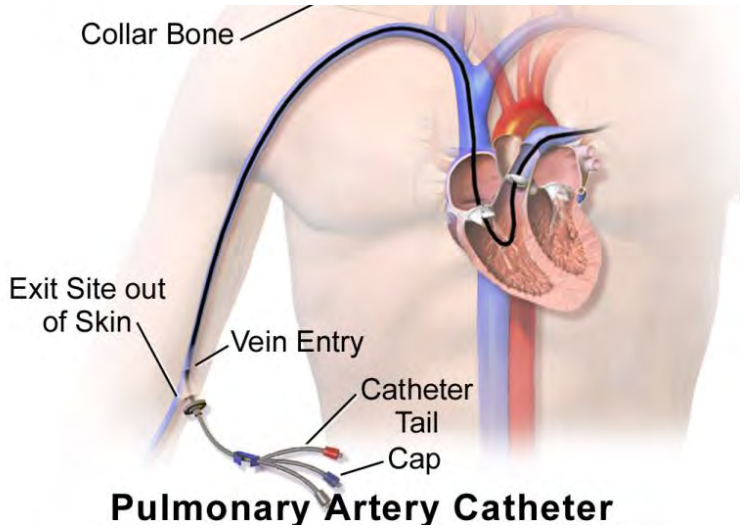
# Nesiritide

- Recombinant **BNP**
- Vasodilation
- ↓ afterload, ↑CO
- Failed to show benefit in clinical trials

# Heart Failure

## Diagnosis

- Most common: typical signs/symptoms
- Elevated BNP level
- **Heart catheterization**
  - Increased LVEDP = left heart congestion/failure
  - Increased RA, RVEDP = right heart congestion/failure



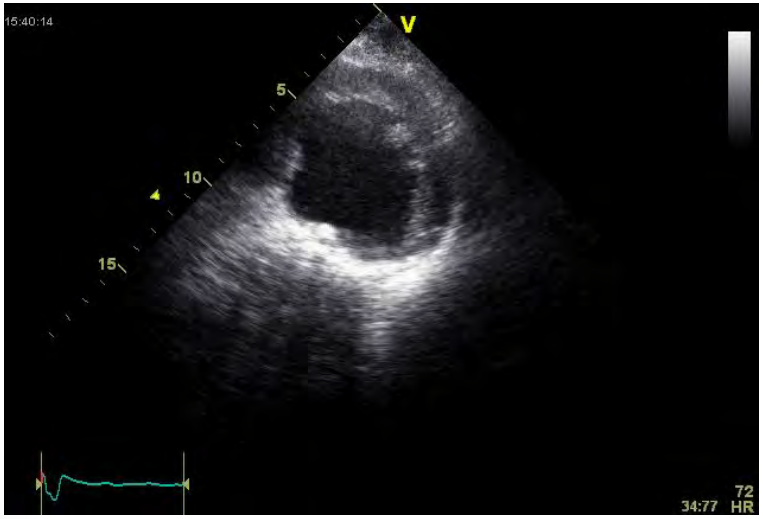
# Systolic and Diastolic Heart Failure

Jason Ryan, MD, MPH

# Heart Failure

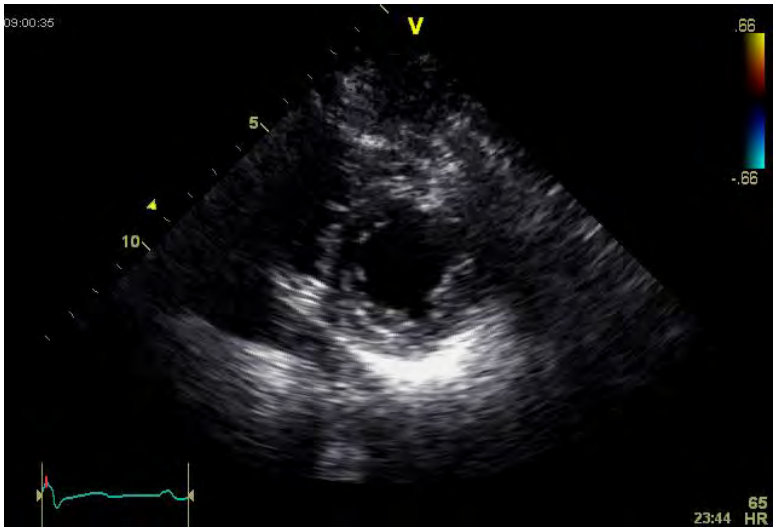
## Systolic and Diastolic

### Systolic Heart Failure




Ejection fraction is <u>reduced</u>

### Diastolic Heart Failure




EF is <u>normal</u> (55-65%)

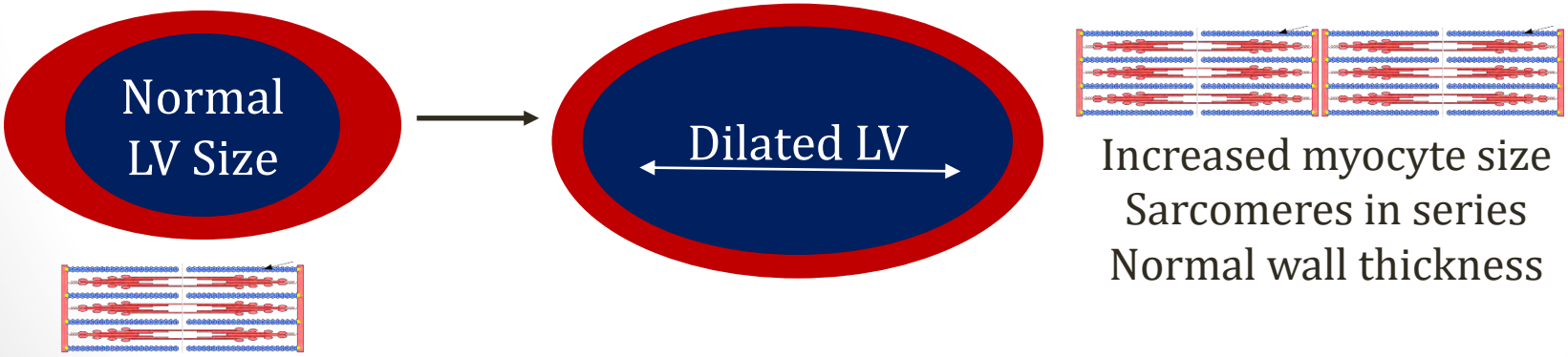
# Heart Failure

## Systolic and Diastolic

- Same congestive signs/symptoms
  - Dyspnea, orthopnea, paroxysmal nocturnal dyspnea
  - Rales, ↑ JVP, pitting edema
- Exception: **Low flow symptoms** in systolic only
  - Cool extremities
  - Cachexia
  - Confusion

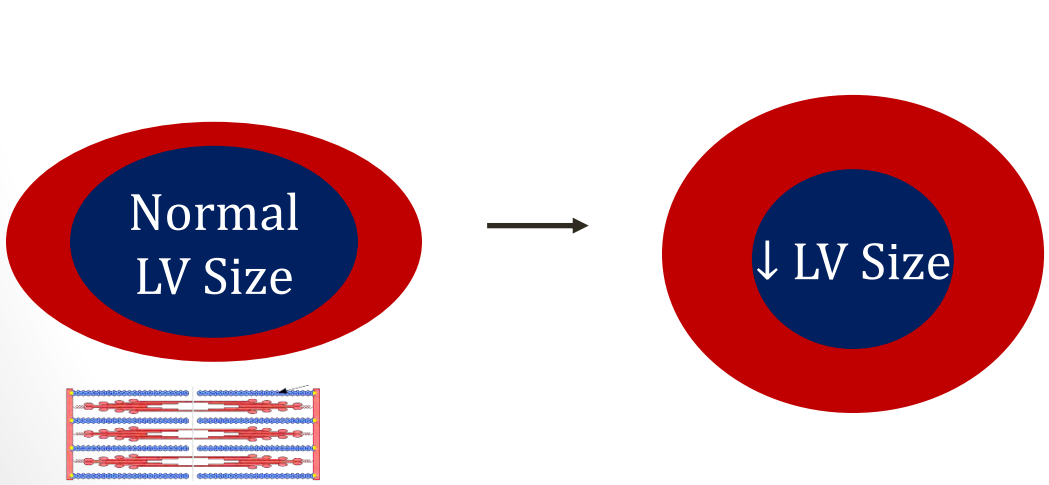
# Dilated Cardiomyopathy

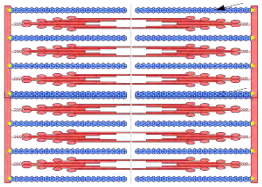
- Systolic heart failure with LV cavity dilation
- **"Eccentric" hypertrophy**
  - Volume overload (chronic retention of fluid in cavity)
  - Longer myocytes
  - Sarcomeres added in series



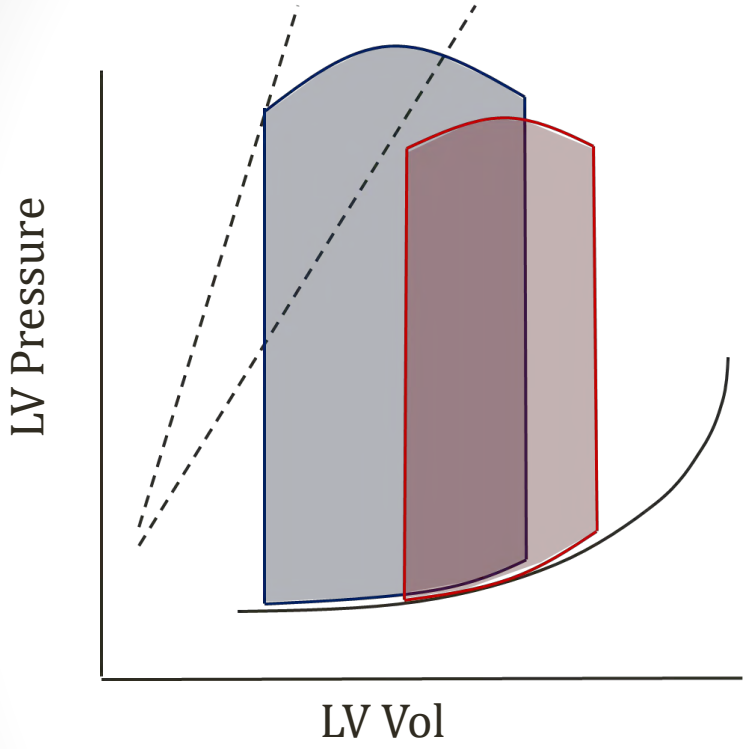
# Concentric Hypertrophy

- Pressure overload
- Chronic ↑↑ pressure in ventricle: HTN, Aortic stenosis
- Decreased compliance (stiff ventricle)
- Often seen in diastolic heart failure



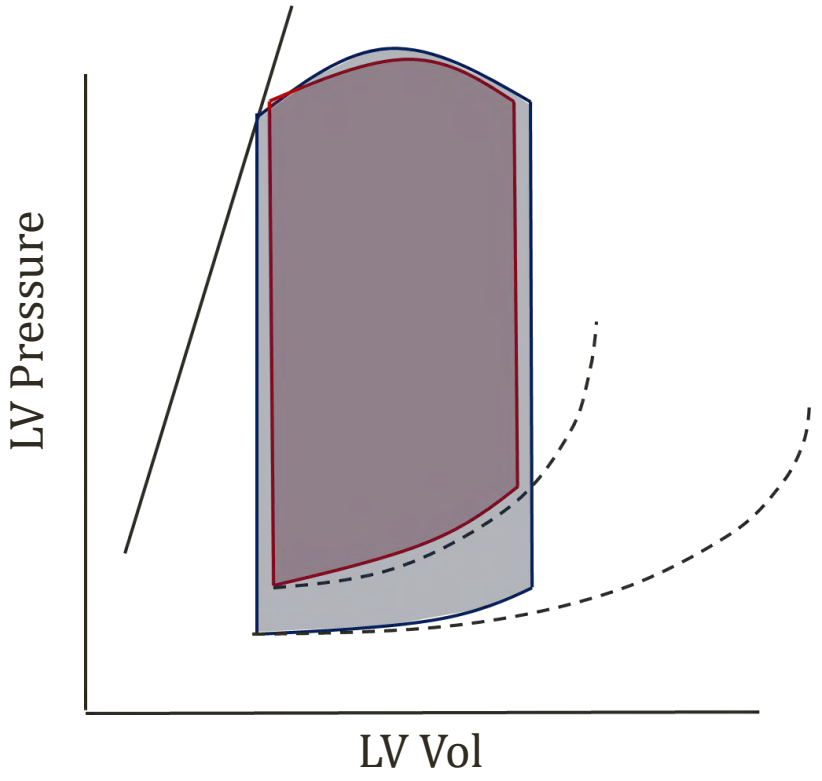



Increased myocyte size
Sarcomeres in parallel
Increased wall thickness




Systolic Heart Failure

**↓ Contractility**



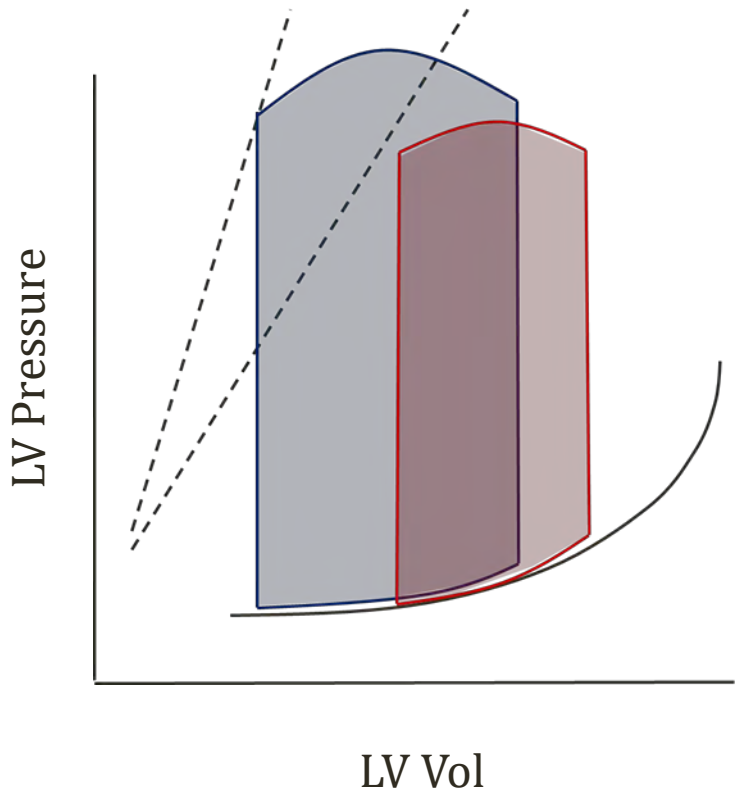

Diastolic Heart Failure

**↓ LV Compliance**

**↓ Lusitropy**

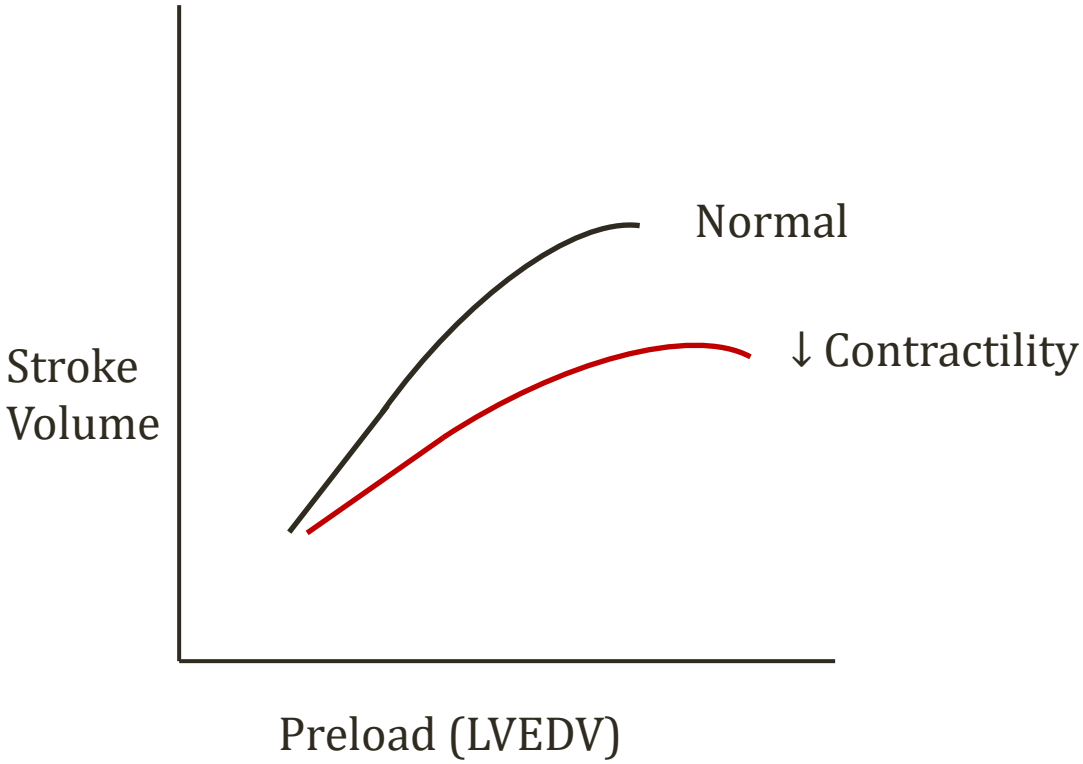
# Systolic Heart Failure

- ↓ Cardiac output
- Problem in SYSTOLE
- Can't get blood out
- ↓ Stroke volume
  - SV = EDV – ESV
  - ↑ ↑ ESV (↓ contractility)
  - ↑ EDV (↑ESV + VR)
  - ↑ LVEDP



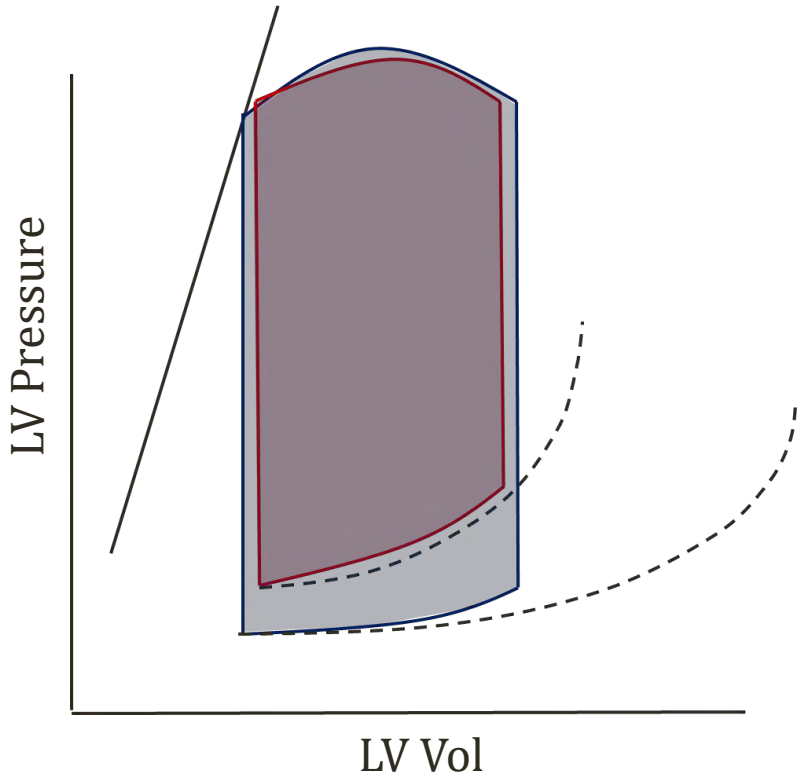

Systolic Heart Failure
**↓ Contractility**

# Frank-Starling Curve



# Diastolic Heart Failure

- ↓ Cardiac output
- Problem in DIASTOLE
- Can't get blood in
- Small ↓ stroke volume
  - ↓ EDV (↓ filling)
- ↑↑ **LVEDP** (stiff ventricle)




Diastolic Heart Failure
**↓ LV Compliance**
**↓ Lusitropy**

# Systolic vs. Diastolic

| | Normal | Systolic/Dilated | Diastolic |
|---|---|---|---|
| EDV | 100 | 200 | 90 |
| ESV | 40 | 160 | 40 |
| SV/CO | 60 | 40 | 50 |
| EF % | 60 | 20 | 56 |

# Systolic Heart Failure

- Most common cause: **Myocardial infarction**
  - Myocytes replaced by scar tissue
  - "Ischemic" cardiomyopathy
- Many causes of "non-ischemic" cardiomyopathy
  - About 50% idiopathic
  - Many other causes: viral, familial, peri-partum, chemotherapy toxicity, HIV, alcoholic, sarcoidosis, tachycardia-mediated

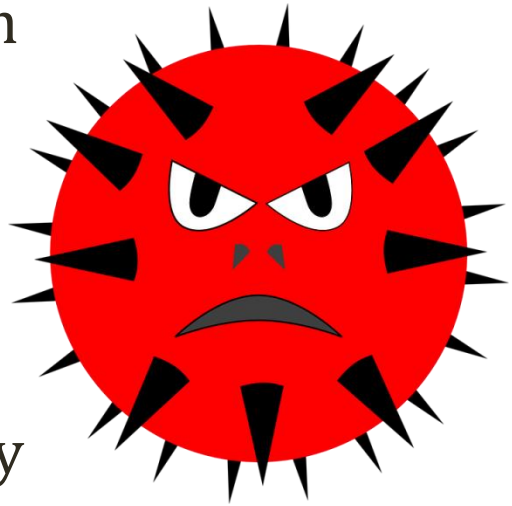
# Diastolic Heart Failure

- Exact cause unknown
- Many cases have **concentric hypertrophy**
- Many associated conditions
  - Age, diabetes, hypertension
- Terms:
  - Heart failure preserved EF
  - HFpEF
  - Diastolic dysfunction

# Nonischemic Cardiomyopathy

## Viral

- May follow upper respiratory infection
- Many associated viruses
  - **Coxsackie**
  - Influenza, adenovirus, others
- Virus enters myocytes
- Causes myocarditis → cardiomyopathy
- Myocarditis phase may go undiagnosed
- No specific therapy for virus



Pixabay/Public Domain

# Nonischemic Cardiomyopathy

## Peri-partum

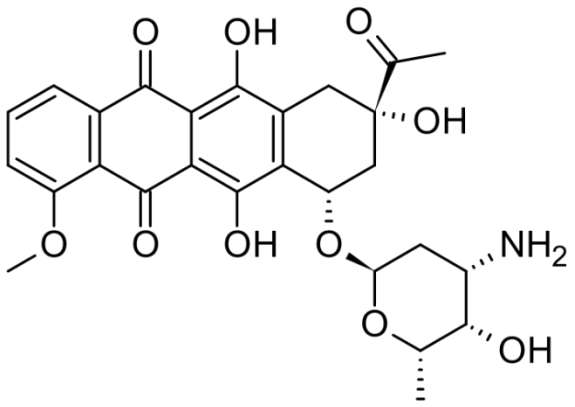
- Late in pregnancy or early post-pregnancy
- Exact cause unknown (likely multifactorial)
- Women often advised to avoid future pregnancy

Øyvind Holmstad/Wikipedia

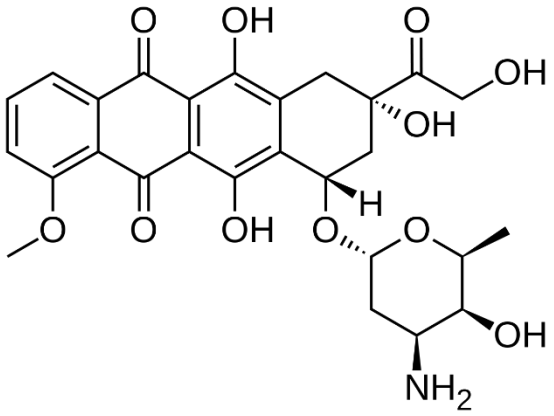
# Nonischemic Cardiomyopathy

## Chemotherapy

- Usually after treatment with anthracyclines
  - Antitumor antibiotics
  - Doxorubicin and daunorubicin




Daunorubicin

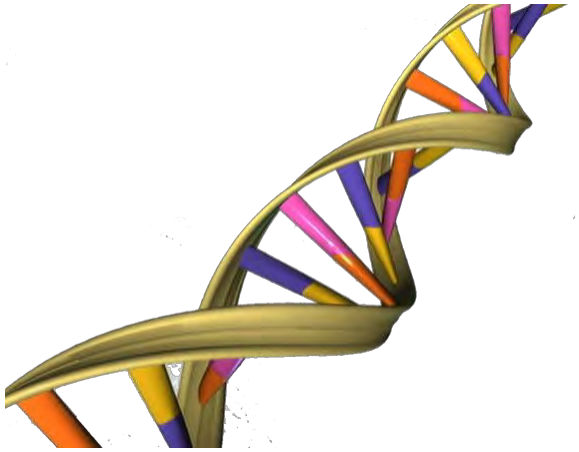



Doxorubicin
(Adriamycin)

# Nonischemic Cardiomyopathy

## Familial

- Mutations
  - Often sarcomere proteins
  - Beta myosin heavy chain
  - Alpha myosin heavy chain
  - Troponin
- Many autosomal dominant
- X-linked, autosomal recessive also described

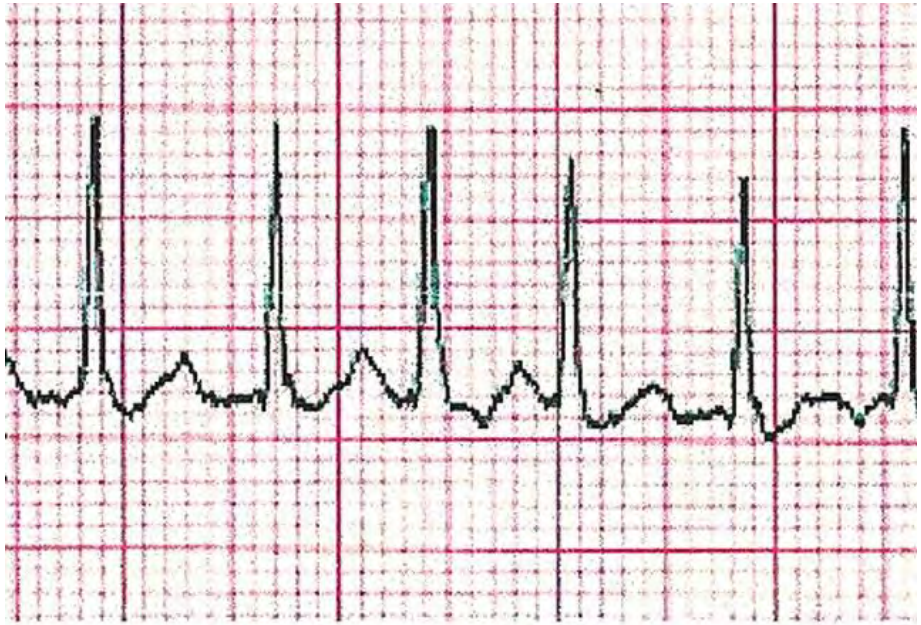


Wikipedia/Public Domain

# Nonischemic Cardiomyopathy

## Tachycardia-mediated

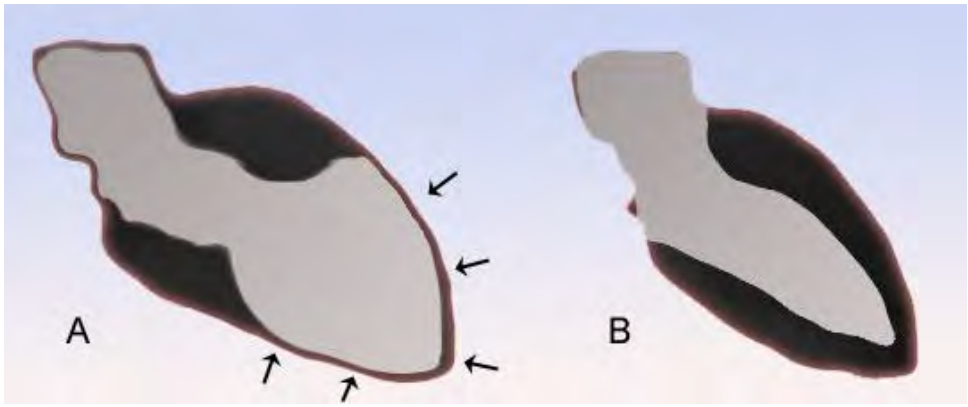
- Constant, rapid heart rate for weeks/months
- Leads to depression of LV systolic function
- **Reversible** with slower heart rate



# Nonischemic Cardiomyopathy

## Takotsubo/Apical ballooning

- **Stress-induced** cardiomyopathy
- Occurs after severe emotional distress
- Markedly reduced LVEF
- Increase CK, MB, Troponin; EKG changes
- Looks like anterior MI (but no coronary disease)
- Usually recovers 4-6 weeks




Jheuser/Wikipedia

# Alcohol

- Chronic consumption can cause cardiomyopathy
- Believed to be due to toxic metabolites
- Can recover with cessation of alcohol

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# High Output Heart Failure

John Liu/Flikr

- Heart in overdrive
  - Severe anemia
  - Thyroid disease
  - Thiamine (B1) vitamin deficiency (beriberi)
  - A-V fistulas (post-surgical)
- Exact mechanism unclear
  - Decreased LV filling time
- Defining characteristic: **HIGH cardiac output**
  - Heart failure symptoms in absence of low output
  - ↑JVP, pulmonary edema

# Restrictive Cardiomyopathy

Jason Ryan, MD, MPH

# Restrictive Heart Disease

- Something "infiltrates" the myocardium
  - Granulomas (Sarcoid)
  - Amyloid protein (Amyloidosis)
- Heart cannot relax and fill
- SEVERE diastolic dysfunction


MarkBuckawicki/Wikipedia

# Restrictive Heart Disease

- **LVEF = normal**
- Left ventricular volume = normal (not dilated)
- Restricted filling = ↑ atrial pressure
- Dilated left and right atria
- Classic imaging findings:
  - Normal left ventricular function/size
  - Bi-atrial enlargement

# Restrictive Heart Disease

## Clinical Features

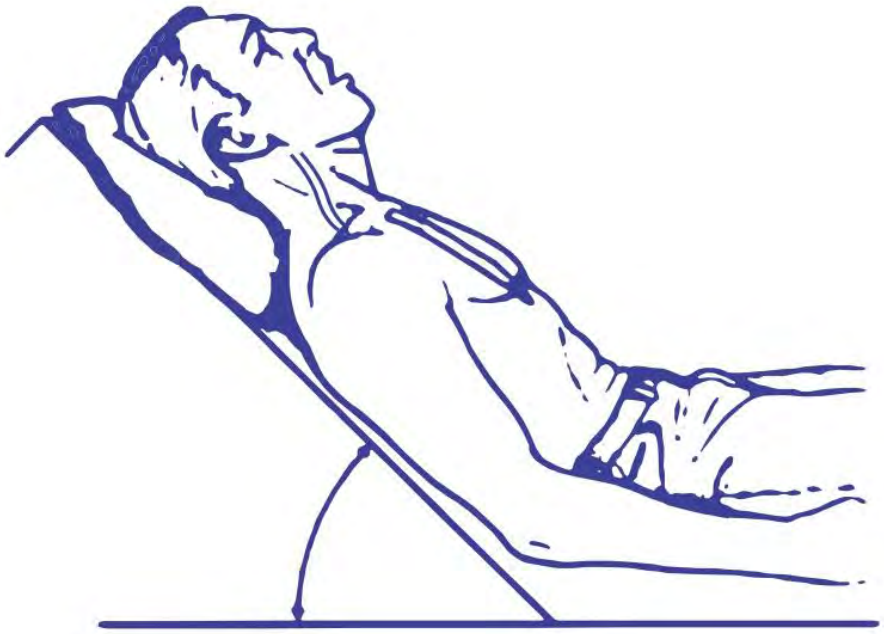
- Dyspnea
- Prominent **right heart failure**
  - Markedly elevated jugular venous pressure
  - Lower extremity edema
  - Liver congestion
  - May lead to cirrhosis ("nutmeg liver")

David Monniaux/Wikipedia

# Restrictive Heart Disease

## Classic signs

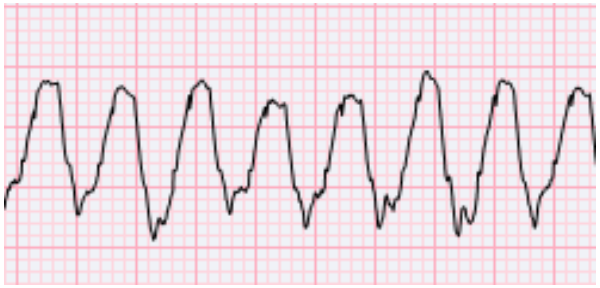
- Kussmaul's sign
  - Inspiration causes rise in JVP



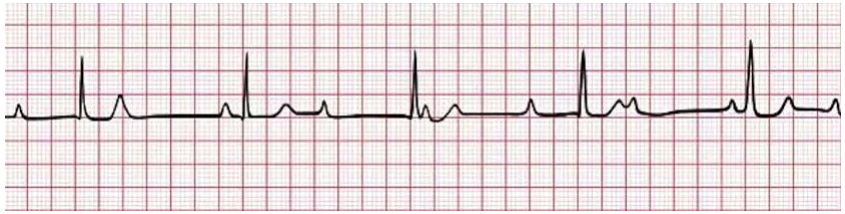
# Restrictive Heart Disease

## Rhythm Disturbances

- Myocardial infiltration may disrupt electrical activity
- Arrhythmias (sudden death)
- AV block



Ventricular Tachycardia

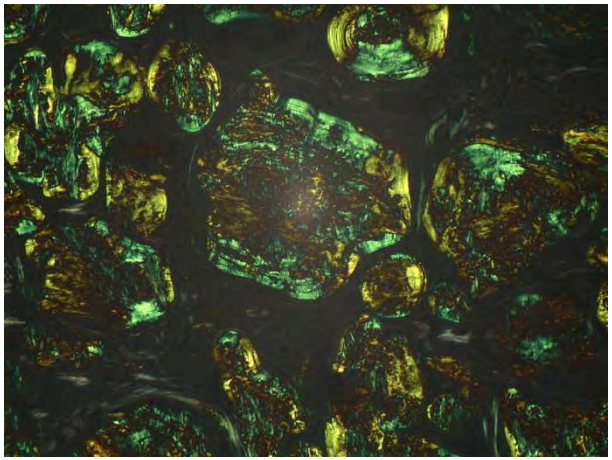


3rd Degree Heart Block

# Restrictive Heart Disease

## Major Causes

- Amyloidosis
  - Amyloid protein deposits in heart
  - Various forms (primary, secondary, etc.)

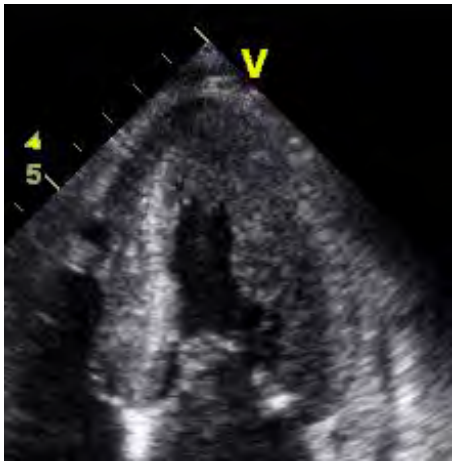


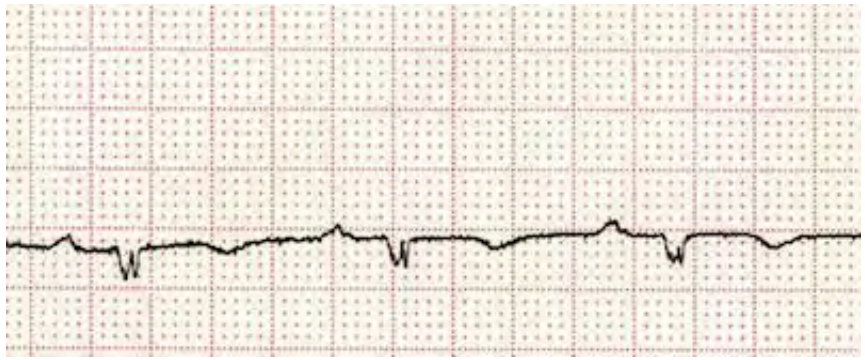
Ed Uthman, MD

# Restrictive Heart Disease

## Classic signs

- Can see thickened myocardium
- **Low** voltage on EKG
- Classic finding in amyloidosis and Fabry's disease

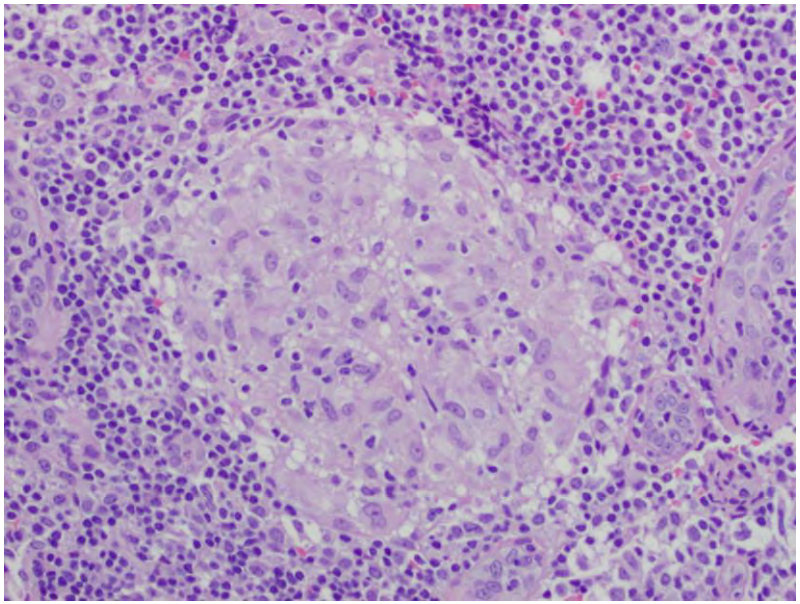


# Restrictive Heart Disease

## Major Causes

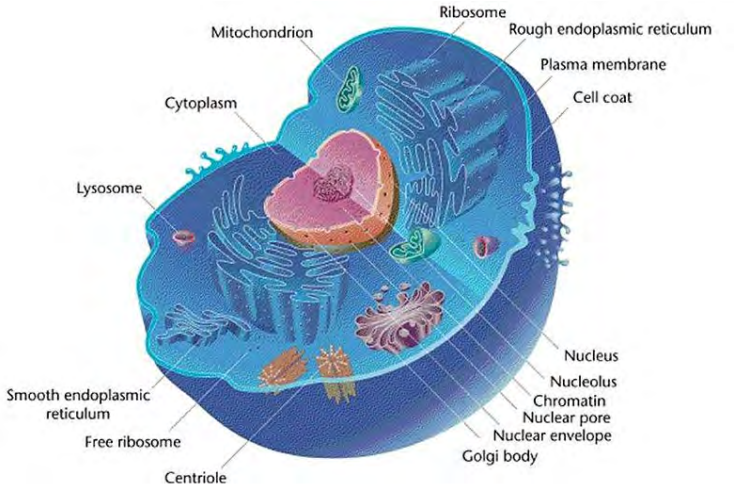
- Sarcoidosis
  - Granuloma formation
  - Usually involves lungs
  - Extra-pulmonary organs include heart



# Restrictive Heart Disease

## Major Causes

- **Fabry disease**
  - Lysosomal storage disease
  - Deficiency of α-galactosidase A
  - Accumulation of ceramide trihexoside




Mediran/Wikipedia

# Restrictive Heart Disease

## Major Causes

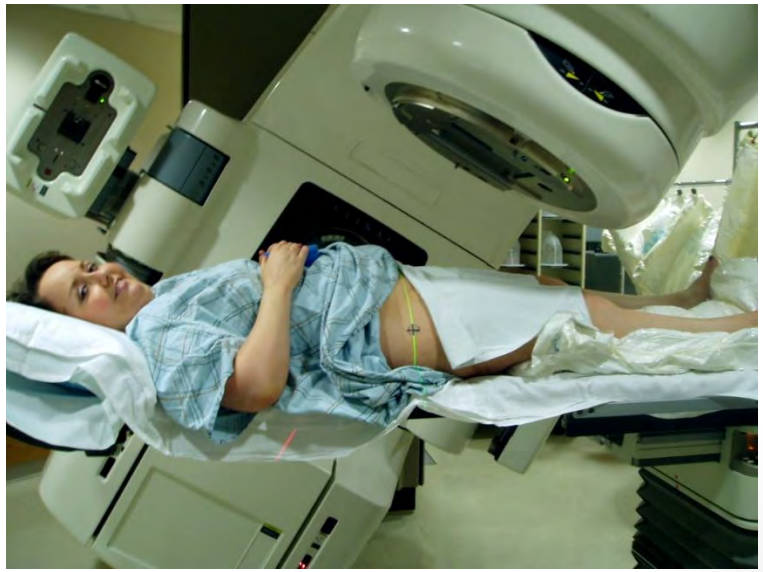
- **Hemochromatosis**
  - **Iron** excess
  - Commonly causes dilated cardiomyopathy
  - Rarely may cause restrictive

Tomihahndorf

# Restrictive Heart Disease

## Major Causes

- **Post-radiation**
- Acutely: May cause inflammation
- Fibroblast recruitment
- **Extra-cellar matrix deposition**
- Collagens and fibronectin



Dina Wakulchik/Wikipedia

# Restrictive Heart Disease

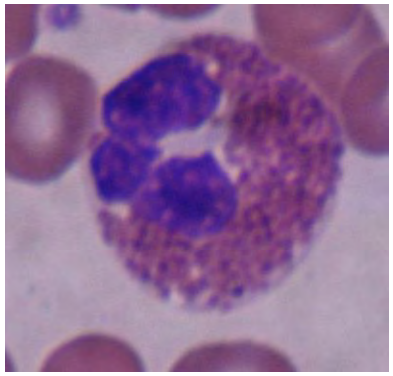
## Major Causes

- Pericarditis may occur acutely after therapy
- Long term effects
  - Pericardial disease
  - Coronary artery disease
  - Valvular disease
  - Conduction abnormalities
- Restrictive cardiomyopathy
  - **Fibrous tissue** accumulation
  - Diastolic dysfunction

# Restrictive Heart Disease

## Major Causes

- Loeffler's syndrome
  - **Hypereosinophilic syndrome**
  - High eosinophil count
  - Eosinophilic infiltration of organs
- Skin (eczema)
- Lungs (fibrosis)



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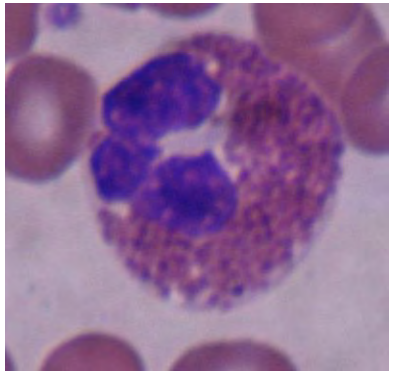
# Restrictive Heart Disease

## Major Causes

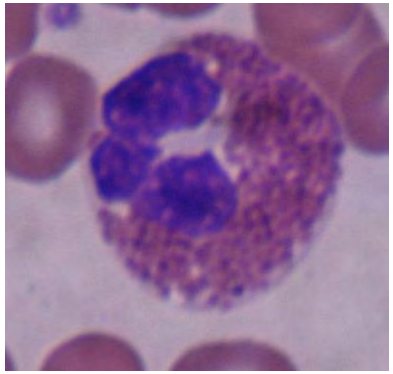


Bobjgalindo/Wikipedia

- Primary HES
  - Neoplastic disorder
  - Stem cell, myeloid, or eosinophilic neoplasm
- Secondary HES
  - Reactive process
  - Eosinophilic overproduction due to cytokines
  - Occurs in parasitic infections (ascaris lumbricoides)
  - Some tumors/lymphomas
- Idiopathic HES

# Restrictive Heart Disease

## Major Causes



Bobjgalindo/Wikipedia

- Eosinophilic infiltration of myocardium
  - Common mode of death
- Acute phase
  - Myocarditis (often asymptomatic)
- Chronic phase
  - Endomyocardial fibrosis and myocyte death
  - Can see restrictive heart disease
  - **Thrombus** formation common (embolic stroke)

# Restrictive Heart Disease

## Major Causes

- Endocardial fibroelastosis
  - **Endocardial** thickening (innermost myocardium)
  - Infants in first year of life
  - Thick myocardium
  - Proliferation of **fibrous (collagen) and elastic fibers**
- Restrictive cardiomyopathy

Avsar Aras

# Acute Heart Failure

Jason Ryan, MD, MPH

# Heart Failure

## Acute vs. Chronic

**Acute**

- Congested/Swollen
- Pulmonary Edema
- Pitting Edema
- ↑JVP

**Chronic**

- Euvolemic
- Clear lungs
- No pitting edema
- JVP flat

# Acute Exacerbations

## Causes

- #1: Dietary indiscretion
  - High salt intake
- #2: Poor medication compliance

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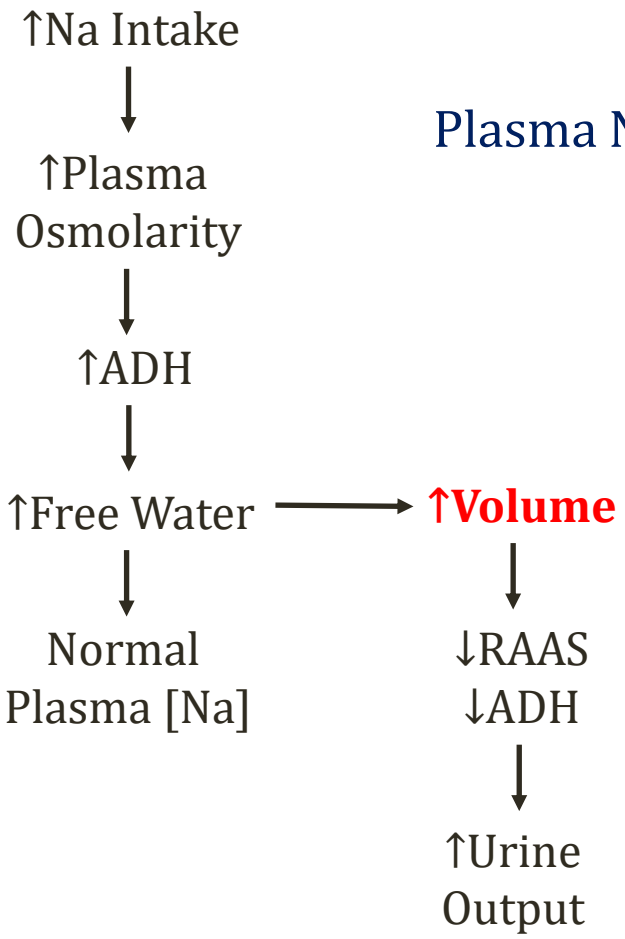
# Dietary Indiscretion




Plasma Na = 140meq/L

# Acute Exacerbations

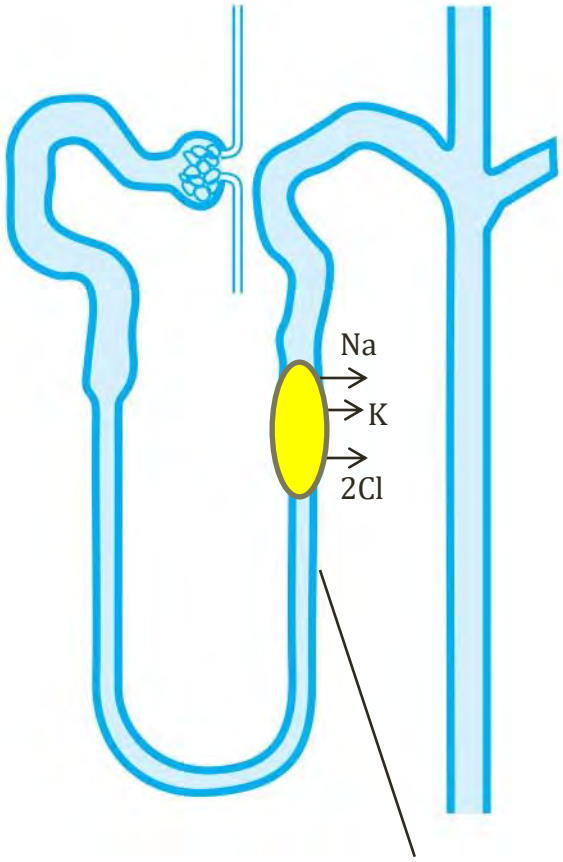
## Causes

- Infection/trauma/surgery
  - Activation of sympathetic nervous system
- Ischemia (rare)
  - Decreased cardiac output
- **NSAIDs**
  - Inhibit cyclooxygenase (COX) → ↓ prostaglandins
  - Prostaglandins maintain renal perfusion
  - Result: Less renal perfusion → salt/water retention

# Acute Heart Failure Therapy

- Often treated in the hospital
- Goal: Symptom relief
  - Contrast with chronic HF: reduce mortality/hospitalizations
- Often same therapies for diastolic versus systolic

# Loop Diuretics




Ascending Limb
Loop Diuretics

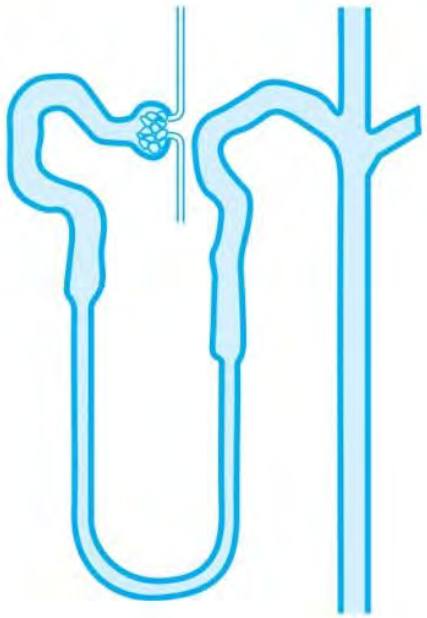
# Loop Diuretics

## Furosemide, Bumetanide, Torsemide, Ethacrynic Acid

- Inhibit Na-K-Cl pump in ascending loop of Henle
- Result in salt-water excretion
- Relieve congestion
- IV better than PO (gut is swollen)
- Key side effects
  - Hypokalemia
  - Volume depletion (Renal failure; hypotension)
- Sulfonamide drugs: allergy (except ethacrynic acid)

# Metolazone

- Thiazide-like diuretic
- Inhibits Na-Cl reabsorption distal tubule
- Gives loop diuretics a “kick”
- Vigorous diuresis
- Side effects: additional fluid, K+ loss

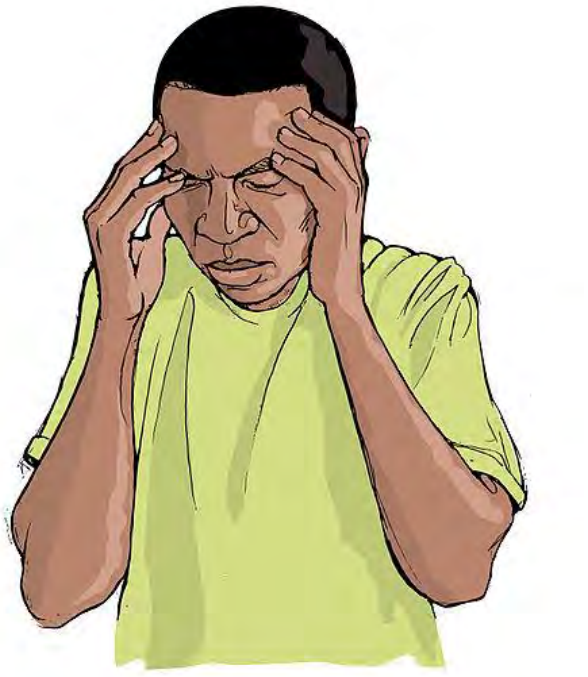


# Nitrates

- Predominant mechanism is **venous dilation**
  - Bigger veins hold more blood
  - Takes blood away from left ventricle
  - Lowers LVEDV (preload), LA pressure
  - Less pulmonary edema → improved dyspnea

# Nitrates

- Side effects
  - Headache (meningeal vasodilation)
  - Flushing
  - Hypotension



Wikipedia/Public Domain

# Vasodilators

## "Afterload reduction"

- ACE inhibitors
- Hydralazine
- Cause peripheral vasodilation
- Reduced afterload → increased cardiac output

# Nitrates plus Hydralazine

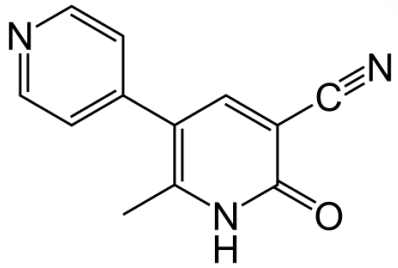
- Combination therapy for **acute and chronic** HF
  - Studied in systolic heart failure
  - Reduction in preload (nitrates) and afterload (hydralazine)
  - Acute therapy: Improves symptoms
  - Chronic therapy: Lowers mortality in some studies
- Largely replaced by ACE inhibitors

# Inotropes

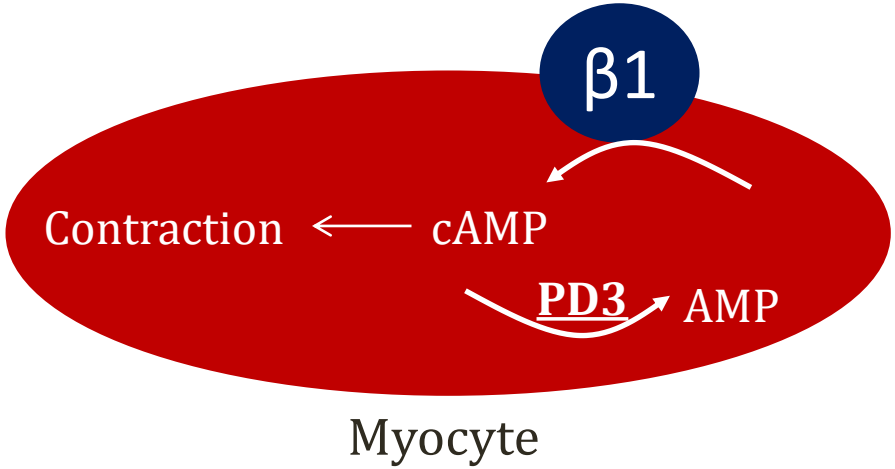
- Increase contractility
- Only for **systolic heart failure**
  - No role in diastolic heart failure (normal contractility)
- All activate **β1 pathways in myocytes**
  - Increased HR and contractility
- Can also active **β2 pathways in smooth muscle**
  - Vasodilation → hypotension

# Inotropes

## Milrinone

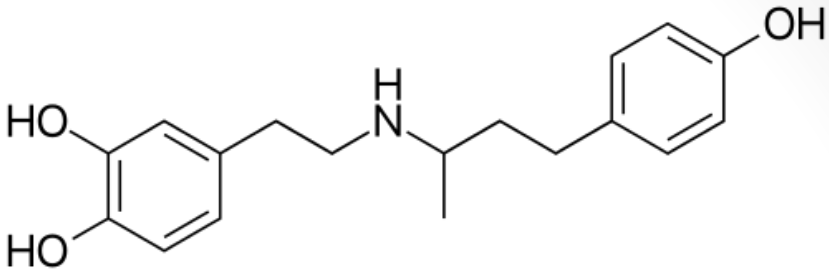



- **Phosphodiesterase 3 inhibitor**
  - PD3 breaks down cAMP in myocyctes
  - Inhibition → ↑cAMP → contraction
  - Vascular smooth muscle ↑cAMP (β2) → dilation
- ↑Inotropy
- ↑Vasodilation
- Hypotension

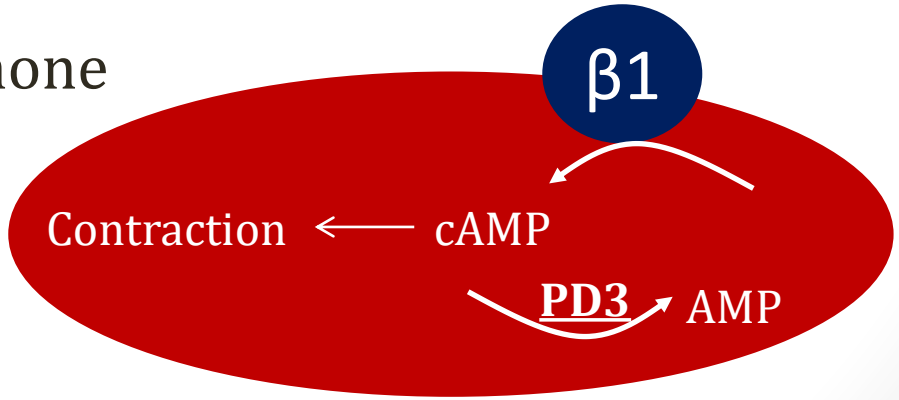


# Inotropes

## Dobutamine



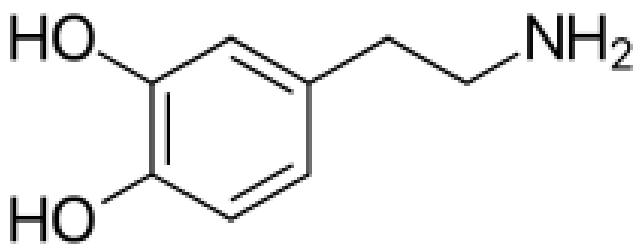

- **Mostly beta-1 agonist**
  - Increases heart rate and contractility
- Weak beta-2 agonist
  - Vasodilation
- ↑Inotropy
- ↑Vasodilation
- Hypotension
- Similar effects to milrinone



# Inotropes

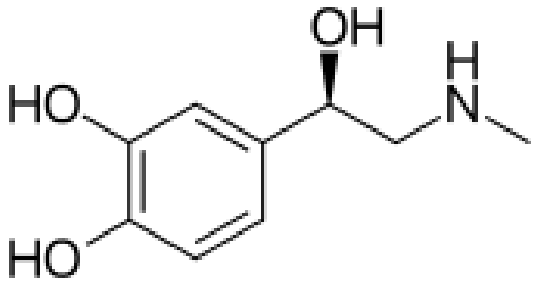
## Dopamine

- Does not cross blood brain barrier (no CNS effects)
- Peripheral effects highly dependent on dose
- Low dose: dopamine agonist
  - Vasodilation in kidneys
- Medium dose: beta-1 agonist
  - Increased heart rate and contractility
- High dose: alpha agonist
  - Vasoconstriction



# Inotropes

## Epinephrine




- Also dose dependent effects
- Low dose: beta-1 and beta-2 agonist
  - Increased heart rate & contractility, vasodilation
- High dose: alpha agonist
  - Vasoconstriction

# Inotrope Risks

- Numerous registries and clinical trials demonstrate increased mortality with routine use of inotropes
- **Dangerous drugs** used in very sick patients under monitored conditions

# A Typical Acute Heart Failure Course

- ER presentation:
  - Dyspnea, edema, sleeping in chair
- Admitted to hospital
  - Nitro drip to relieve dyspnea
  - IV Furosemide to remove fluid
- Hospital Day 2
  - Weight down 4kg, feels better
  - Nitro drip stopped
  - Changed to oral furosemide
- Hospital Day 3: Discharge

# A More Complex Heart Failure Course

- ER presentation:
  - Dyspnea, edema, sleeping in chair
  - Known LVEF 10%
- Admitted to hospital
  - Nitro drip to relieve dyspnea
  - IV Furosemide to remove fluid
- Hospital Day 2
  - Poor urine output, Cool extremities, Cr rises 1.1→1.4
  - Dobutamine drip started

# A More Complex Heart Failure Course

- Hospital Day 3-5
  - Good urine output
  - Weight loss 4kg
  - Breathing improves
- Hospital Day 6
  - Dobutamine stopped
  - Furosemide drip stopped
- Hospital Day 7
  - Oral furosemide given
- Hospital Day 8: Discharge

# Heart Failure Readmission

- Recurrence of HF after discharge common
  - Post-discharge follow-up VERY important
  - "Readmissions" a focus of public health policy
  - **High risk of readmission within 30 days**
  - Highest risk category among Medicare population

# Acute Heart Failure

- Most patients require chronic, daily diuretic
  - Helps to maintain euvolemic status
  - Often oral furosemide or other loop diuretic
- Some patients require daily long acting nitrate
  - Often oral isosorbide mononitrate

# Acute Heart Failure

- Rare patients: continued treatment for **low output**
  - Systolic heart failure only
  - Chronic, IV infusion inotrope (i.e. “home dobutamine”)
  - Left ventricular assist device (LVAD)
  - Heart transplant

# Digoxin

- Only available ***oral*** inotrope
- "Dig and diuretic" once the mainstay of HF treatment
- What changed?
  - Digoxin shown to have no mortality benefit
  - Digoxin not effective for diastolic heart failure
    - About 50% of all cases
  - Digoxin carries significant risk of side effects

# Digoxin Mechanism

## Two important cardiac effects

- #1: Inhibits Na-K-ATPase pump
  - More Na in cell → more Ca++ in cell
  - More Ca++ → more contractility
- #2 Suppresses AV node conduction (parasympathetic)
  - Can be used to slow heart rate in rapid atrial fibrillation

# Digoxin

## Benefits in Heart Failure

- Useful for **systolic HF** patients
  - Symptoms despite maximal therapy on other drugs
  - i.e. persistent dyspnea despite good volume status
- Can be administered for acute heart failure
- Can be administered long term to maintain CO

# Digoxin

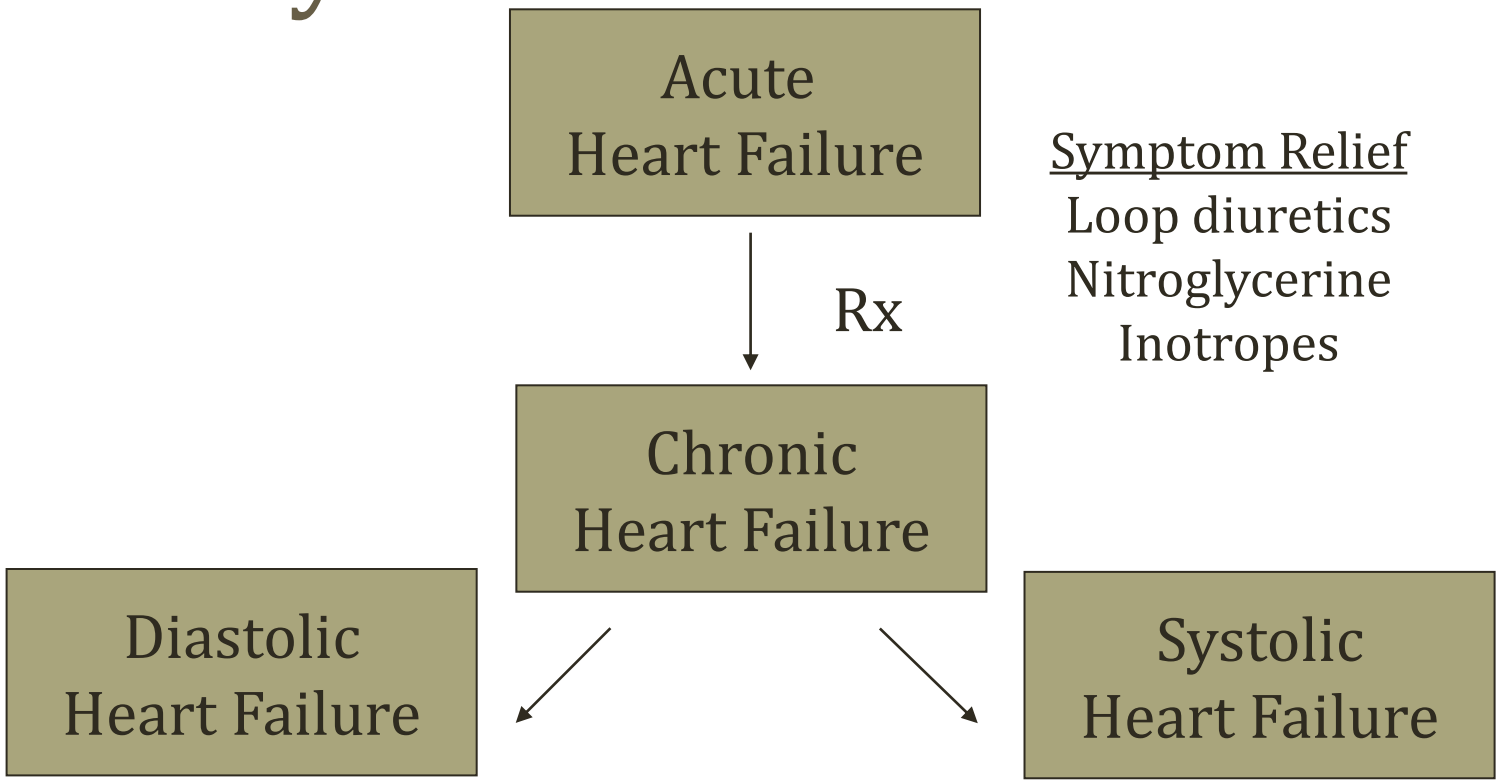
## Benefits in Heart Failure

- Increased cardiac output
- Improved symptoms and quality of life
- No established mortality benefit

# Chronic Heart Failure

Jason Ryan, MD, MPH

# Heart Failure Treatment Pathway



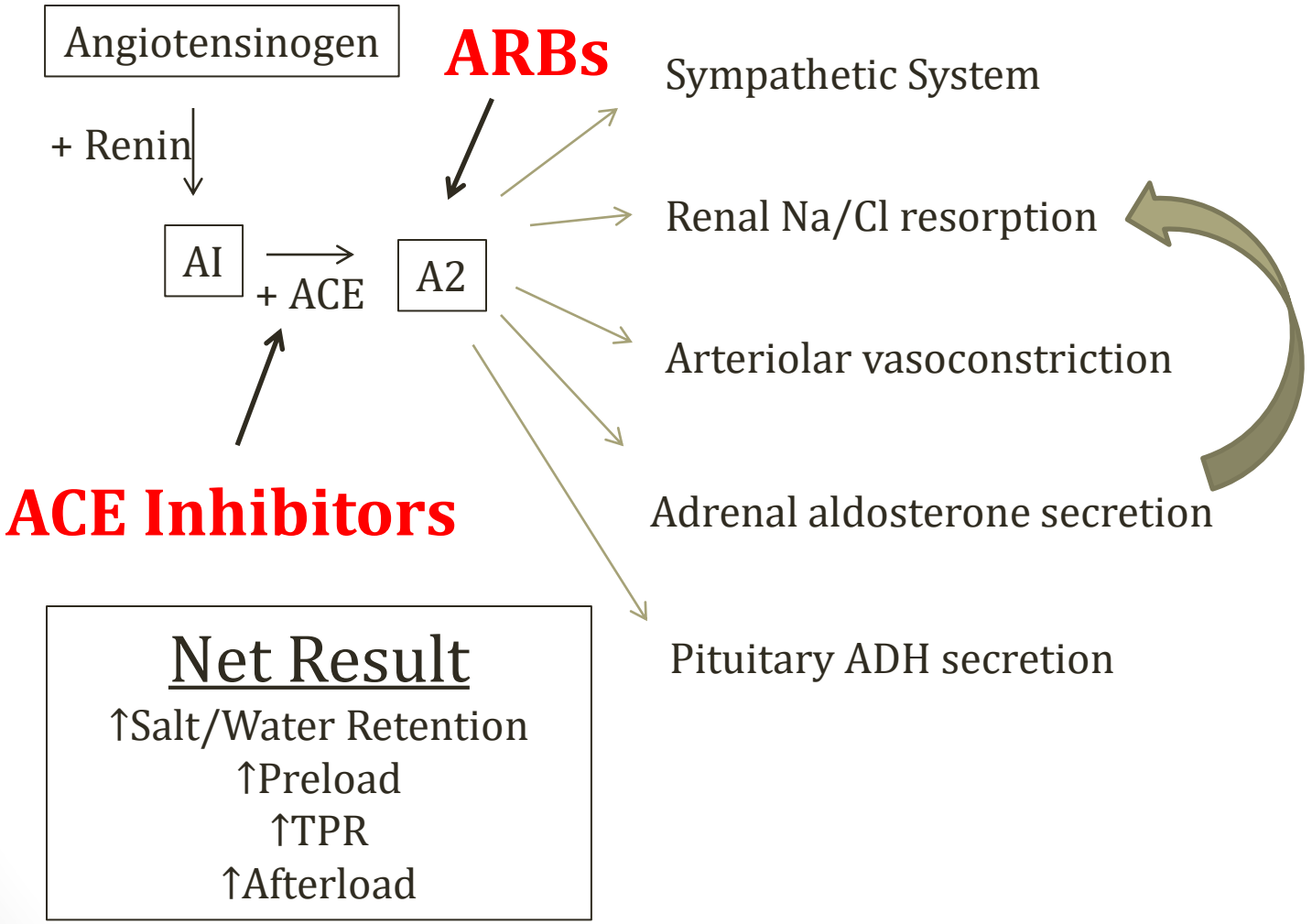
# Chronic Heart Failure

- **LOTS** of therapies for systolic heart failure
  - Drugs: ACE-inhibitors, beta blockers, aldosterone antagonists
  - Defibrillators
  - Bi-ventricular pacemakers
- NO direct therapies for diastolic heart failure
  - Guidelines recommendations: treat HTN, diabetes, A. fib
  - Mainstay of therapy: monitor for symptoms, diuretics

# Systolic Heart Failure

- Chronic over-activation of two physiologic systems
- **Renin-angiotensin-aldosterone system**
- **Sympathetic nervous system (β1 stimulation)**
- Blockade → ↓ mortality and disease progression

# Renin-Angiotensin System




**Net Result**

↑Salt/Water Retention
↑Preload
↑TPR
↑Afterload

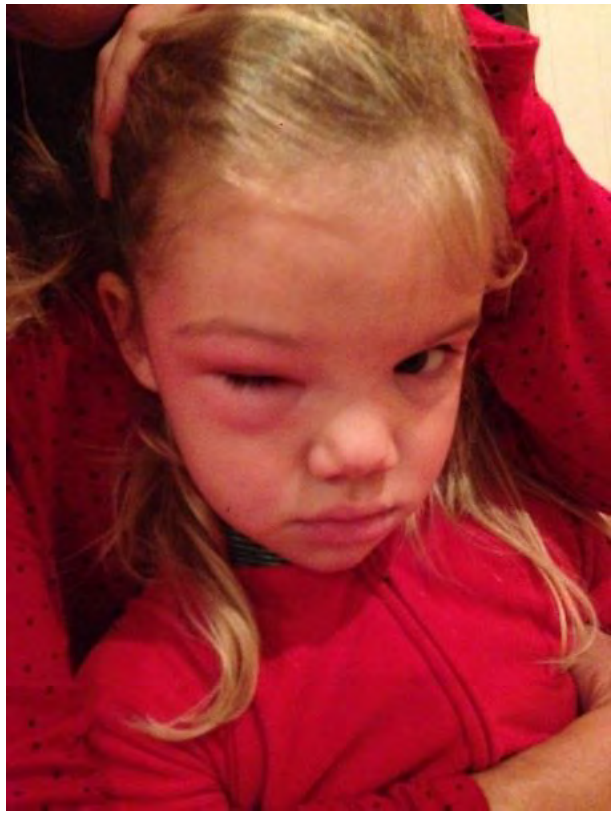
# RAAS Drugs

- **ACE Inhibitors**
  - Captopril, Enalapril, Lisinopril, Ramipril
  - Block conversion AI → AII
- **Angiotensin Receptor Blockers (ARBs)**
  - Candesartan, Irbesartan, Valsartan
  - Directly block AII receptor
- Both classes: **↓ mortality**, **↓ hospitalizations**
- Side effects
  - Hyperkalemia (↓aldosterone)
  - Renal failure (↓GFR)

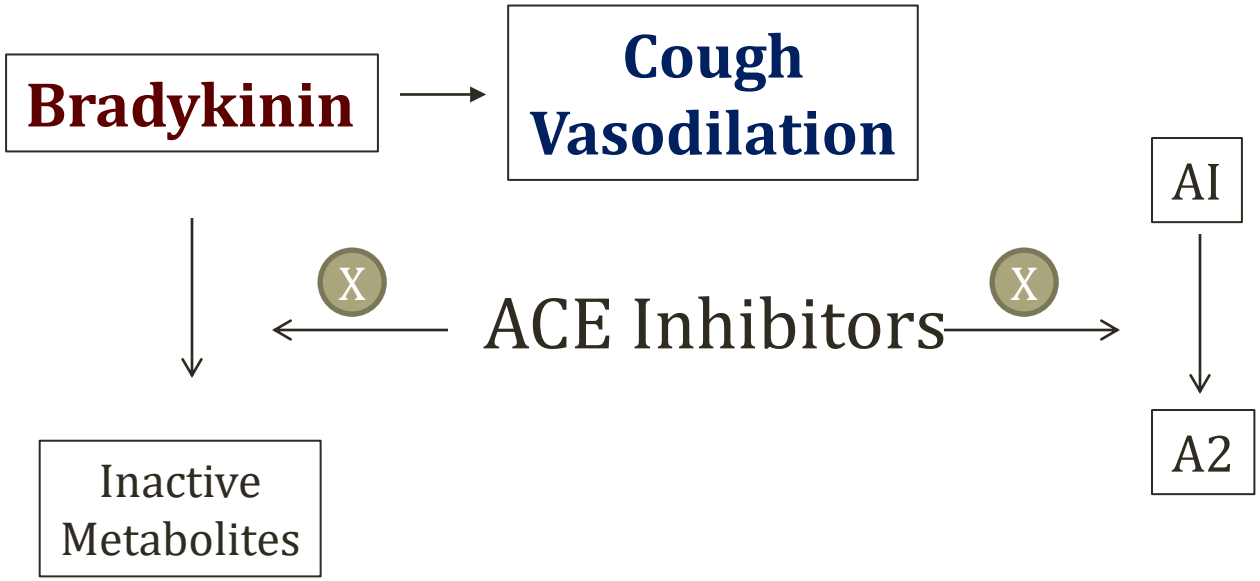
# ACE Inhibitors

## Unique Side Effects

- Due to increased **bradykinin**
- Dry Cough
  - Occurs in ~10% of patients
- Angioedema
  - Swelling of face, tongue
  - Can be life-threatening



# Bradykinin



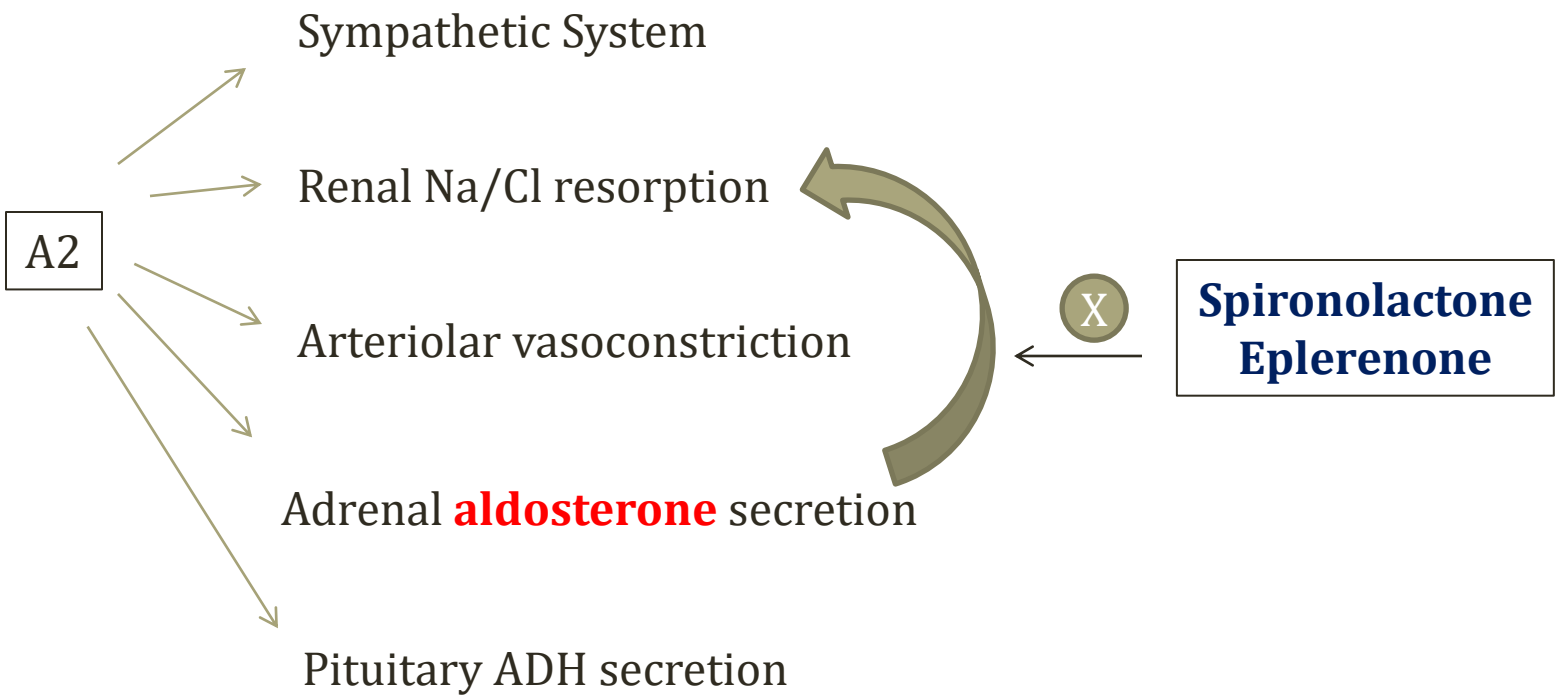
# Beta Blockers

- Once contraindicated in systolic heart failure
  - Negative inotropes
- Not used in acute heart failure
  - May worsen cardiac output and symptoms

# Beta Blockers

- Three agents beneficial in chronic systolic HF
  - Metoprolol (β1)
  - Carvedilol (β1β2α1)
  - Bisoproplol (β1)
- **↓ mortality, ↓ hospitalizations**

# Aldosterone Antagonists



# Spironolactone, Eplerenone

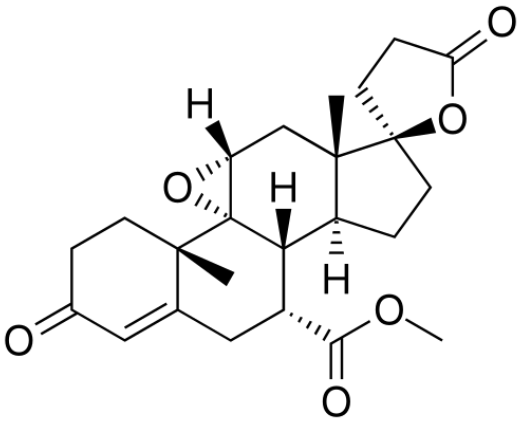
## Potassium-sparing diuretics

- ↑$Na/H_2O$ excretion (diuretics)
- "Spare" potassium
  - Unlike other diuretics, do not increase $K^+$ excretion
- HYPERkalemia is side effect
- Reduced mortality
- Reduced hospitalization rate

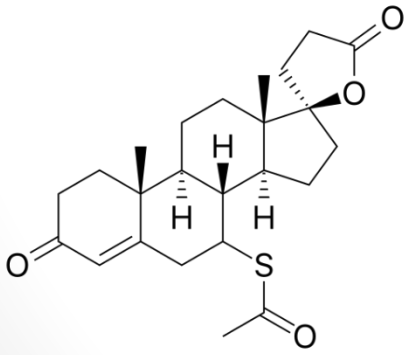
# Spironolactone, Eplerenone

## Potassium-sparing diuretics

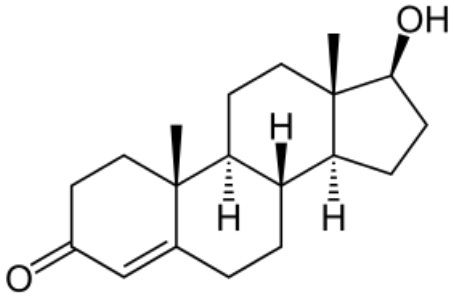
- Similar structure to testosterone
  - Blocks testosterone effects
  - **Gynecomastia** in men
  - Eplerenone: No gynecomastia
- Derivative of progesterone
  - Activates progesterone receptors
  - **Amenorrhea** in women



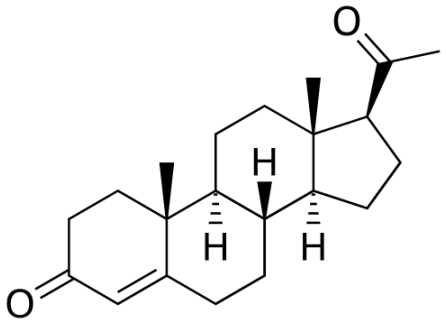

Eplerenone




Spironolactone




Testosterone

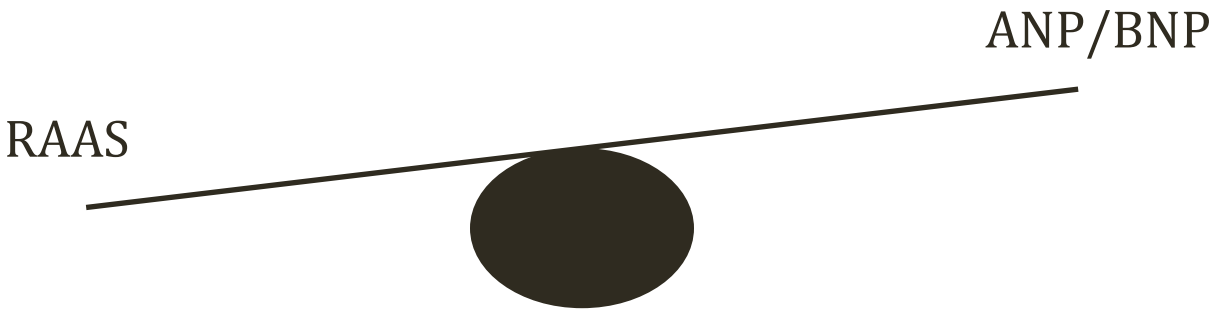



Progesterone

# Neprilysin Inhibitors

## Sacubitril

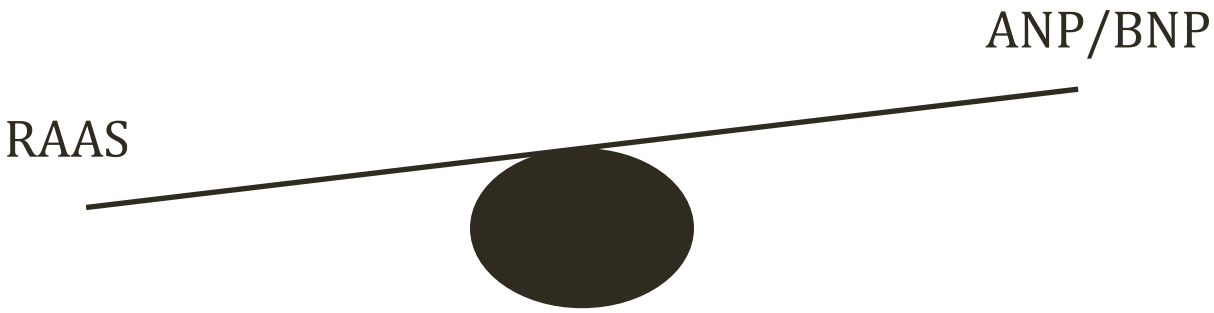
- Neprilysin: Degrades atrial/brain natriuretic peptide
- Inhibition → **↑ANP/BNP**
  - Antagonists to RAAS system
  - Vasodilatation
  - Natriuresis (sodium excretion)
  - Diuresis (water excretion)
  - Reduced sympathetic tone



# Neprilysin Inhibitors

## Sacubitril

- Entresto: oral combination sacubitril/valsartan
  - Valsartan: angiotensin receptor blocker (ARB)
- **↓ mortality**
- **↓ hospitalizations**



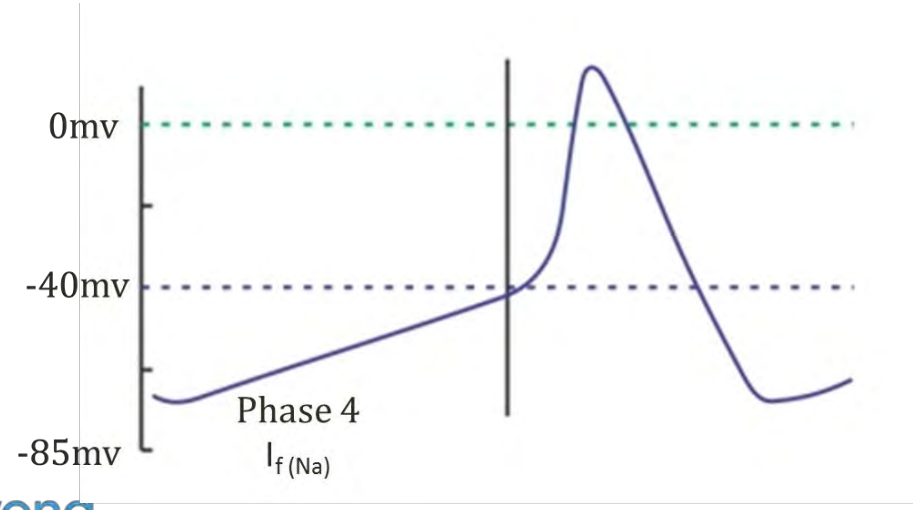
# Neprilysin Inhibitors

## Side Effects

- Studied in combination with valsartan
- Many side effects similar to ARBs
- Hypotension
- Hyperkalemia
- Angioedema
  - Rare, feared adverse effect
  - Neprilysin also degrades bradykinin (like ACE)
  - Angioedema may occur
  - Cannot be given together with ACE inhibitors

# Ivabradine

- Selective sinus node inhibitor
- Elevated HR → worse prognosis
- Slows heart rate without ↓ contractility
- Inhibits SA pacemaker **"funny current" ($I_f$)**
- Used in patients on max-dose beta blocker with ↑HR
- Limited evidence of ↓ mortality and ↓hospitalizations



# Chronic Systolic Heart Failure

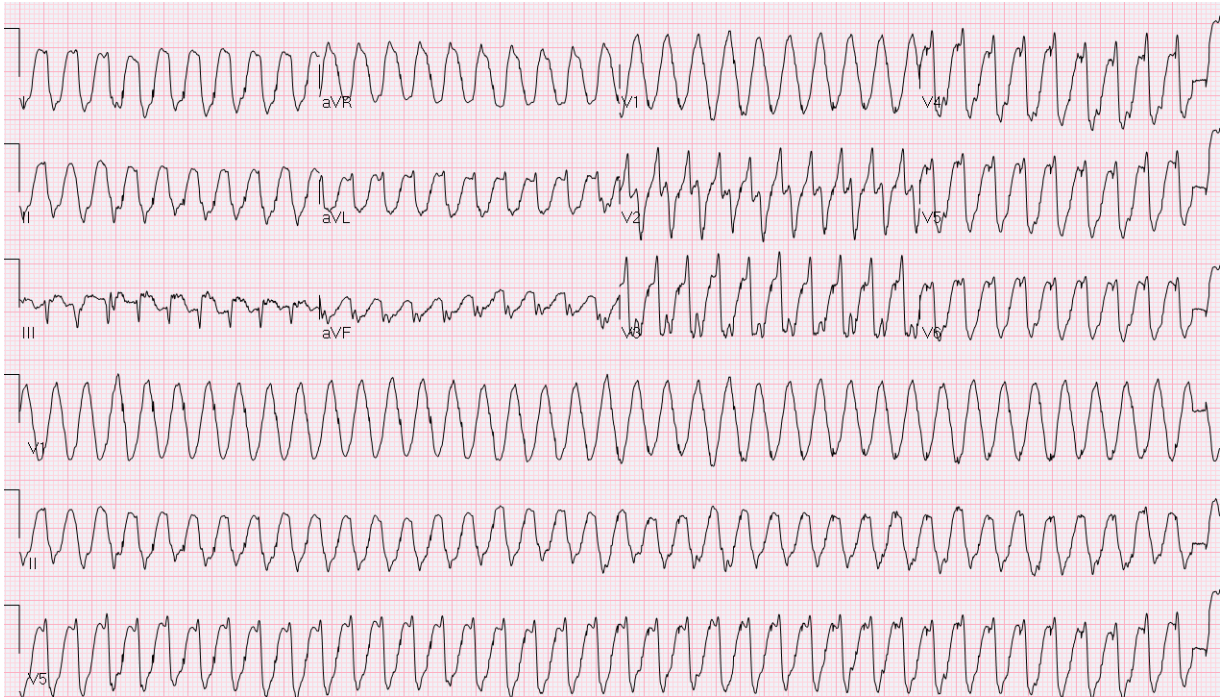
## Drug Therapy

- ACE inhibitors/ARB
- Beta Blockers
- Aldosterone antagonists
- Neprilysin inhibitors
- Ivabradine

# ICD

## Implantable Cardiac Defibrillator

- Annual risk SCD >20% some studies
- Most due to ventricular tachycardia



# ICD

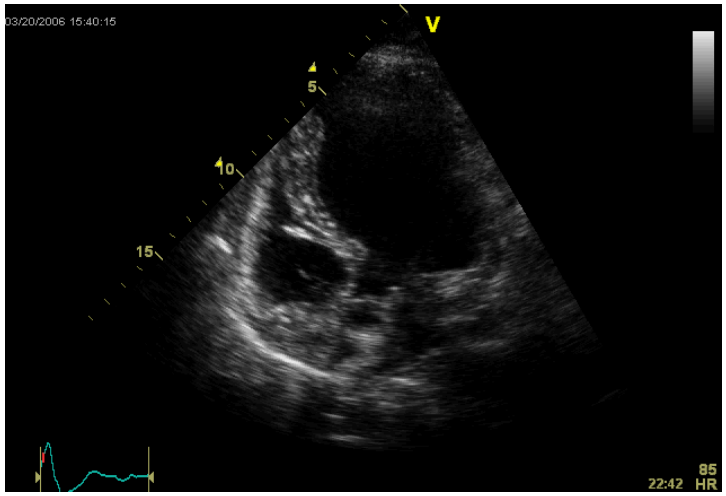
## Implantable Cardiac Defibrillator

- Improve mortality in appropriate patients
- Implantation carries some risk:
  - Bleeding, infection
  - Inappropriate shocks

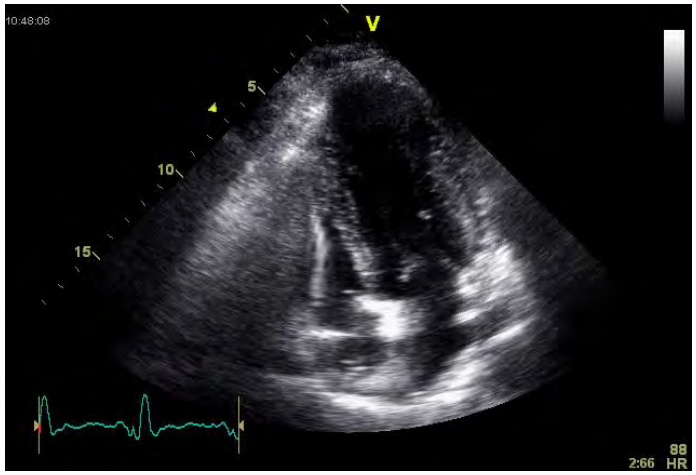
# Biventricular Pacemakers

## Cardiac Resynchronization Therapy (CRT), BiV pacer

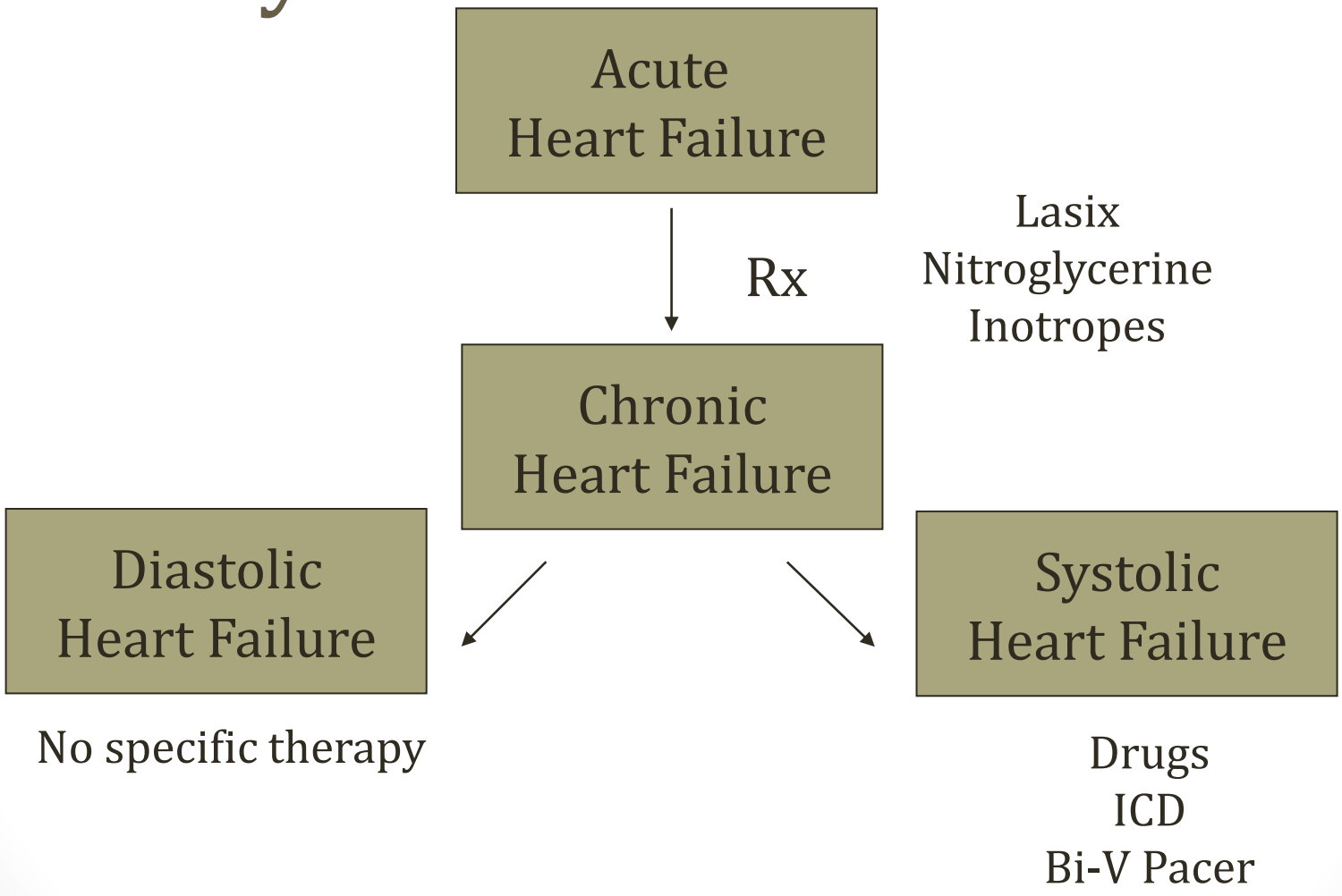
**Out of Synch**




**After Pacemaker**



# Heart Failure Treatment Pathway

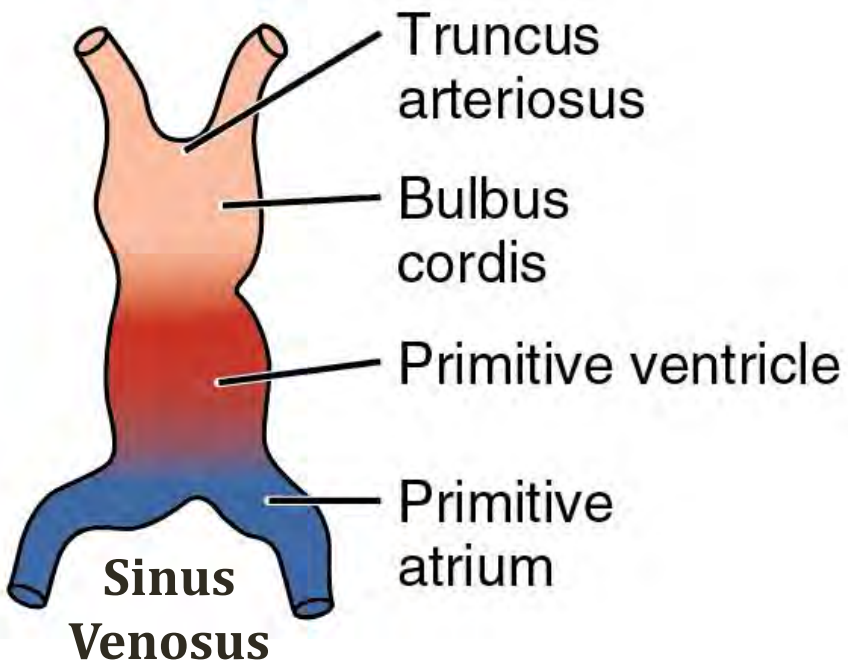


# Cardiac Embryology

Jason Ryan, MD, MPH

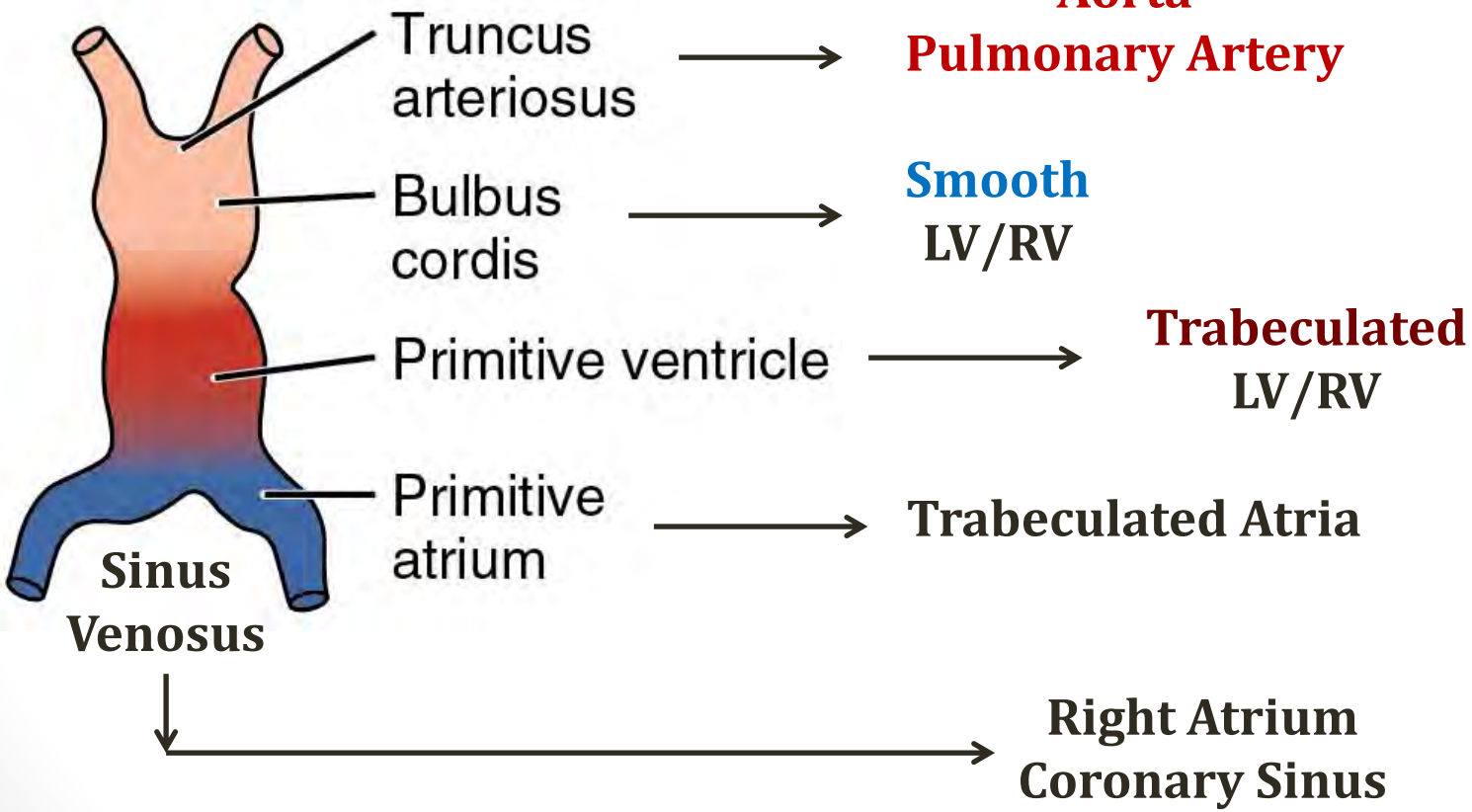
# Primitive Heart

22 days



# Primitive Heart

22 days




OpenStax Colleg/Wikipedia

# Sinus Venosus

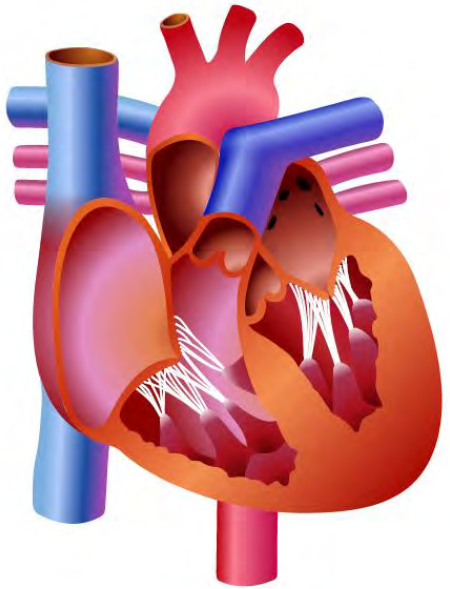

**Smooth Right Atrium (sinus venarum)**

**Coronary Sinus**

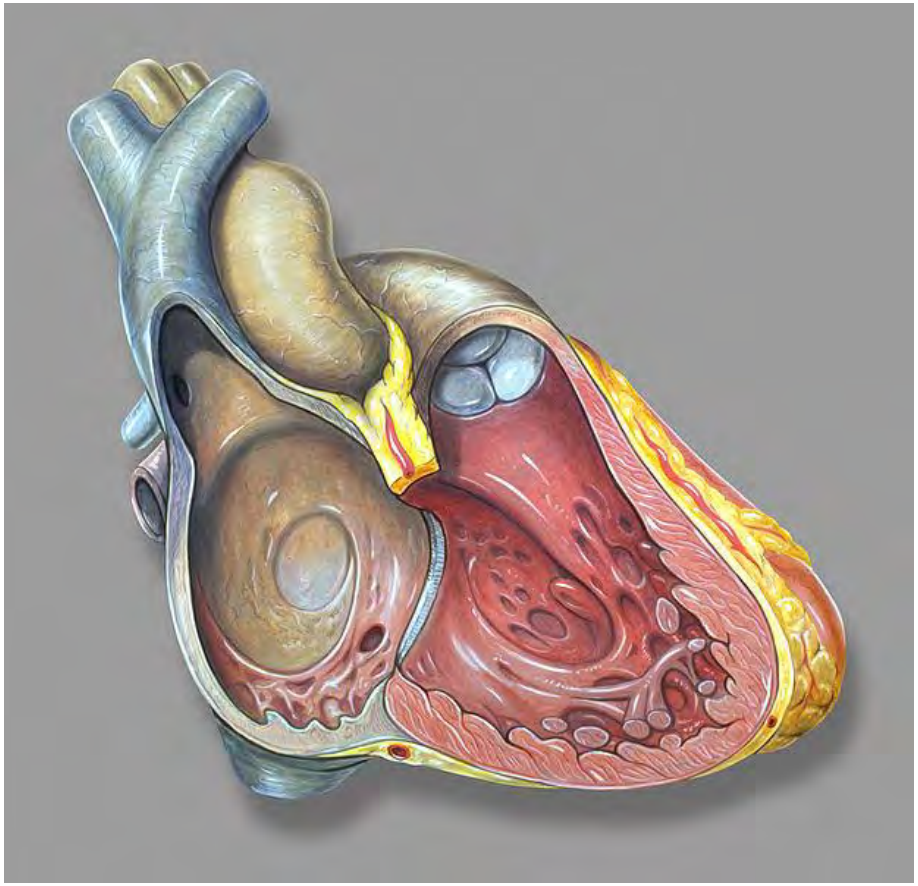
OpenStax Colleg/Wikipedia

# Cardinal Veins

- Form SVC/IVC (not from heart tube)
- Connect to right atrium
- Superior vena cava
  - R common cardinal vein and R anterior cardinal vein
- Inferior vena cava
  - Posterior veins

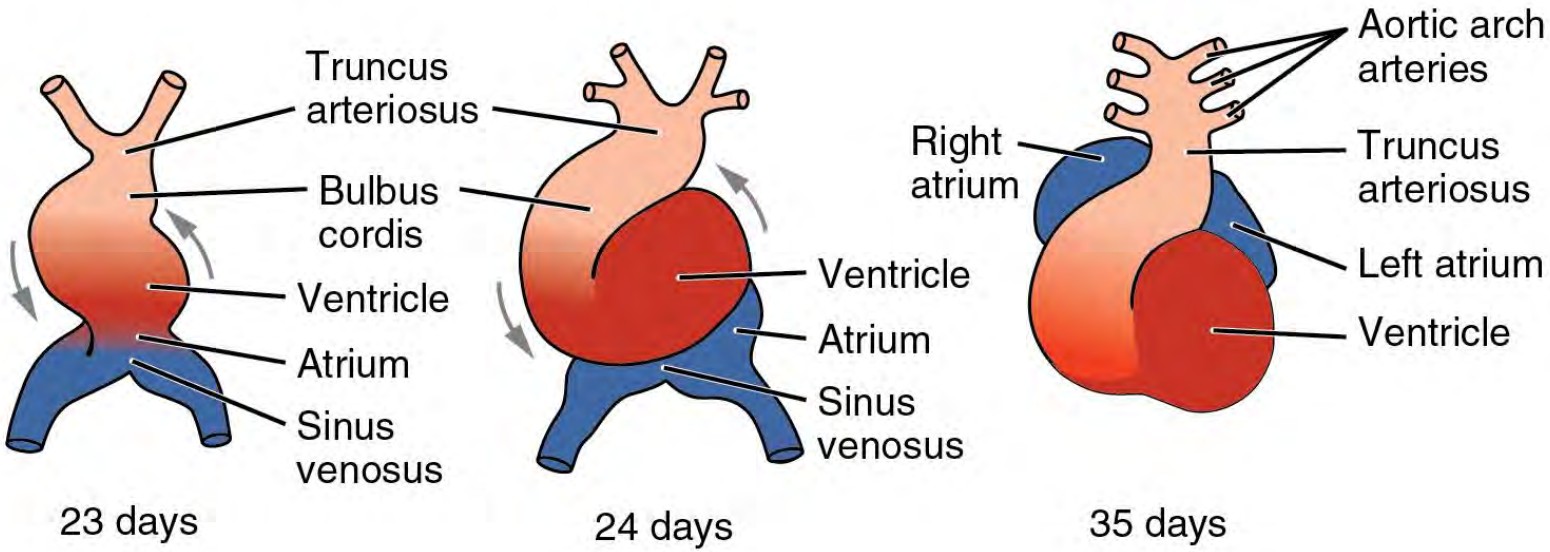


# Adult Heart



Patrick J. Lynch, medical illustrator/Wikipedia

# Primitive Heart

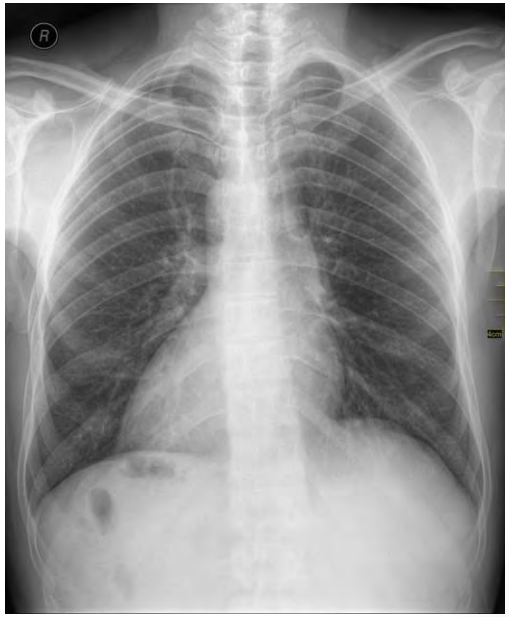





OpenStax Colleg/Wikipedia

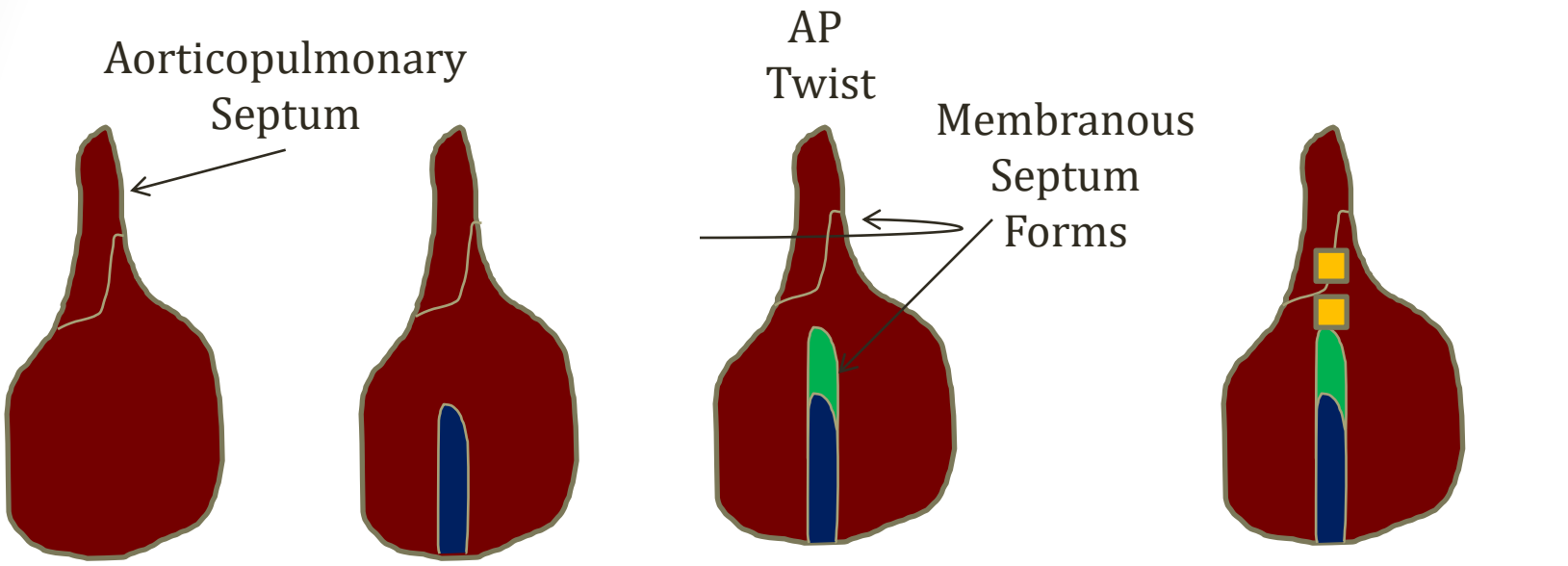
# Cardiac Looping

- Heart tube "loops" at about 4 weeks gestation
- Establishes left-right orientation in chest
- Requires **cilia** and **dynein**
- Dextrocardia (heart on the right side of body)
  - Seen in in Kartagener syndrome
  - Part of primary ciliary dyskinesia



Nevit/Wikipedia

# Ventricular Septum Formation



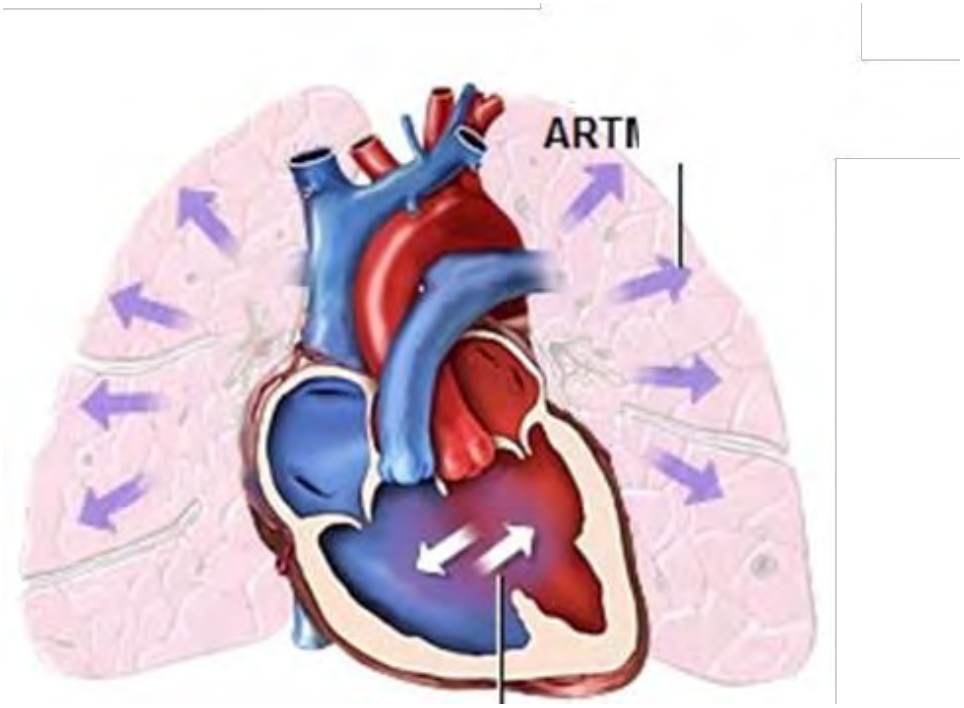

Muscular Ventricular Septum

AP Fuses Muscular Septum

Endocardial Cushions Separate R/L atria R/L ventricle

# Ventricular Septum Pathology

- Membranous VSD (most common type)
- Muscular VSD

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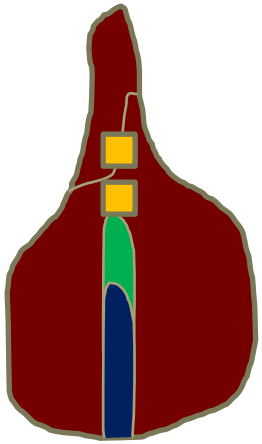
# Endocardial Cushions

- Contribute to several cardiac structures
  - Atrial septum
  - Ventricular septum
  - AV valves (mitral/tricuspid)
  - Semilunar valves (aortic/pulmonic)
- **Endocardial cushion defects**
  - Atrioventricular canal defects
  - Atrioventricular septal defects
  - ASD, VSD, Valvular malformations
  - Common in **Down syndrome**

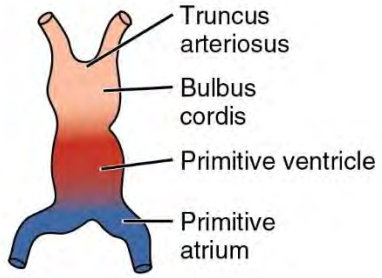


Endocardial Cushions
Separate R/L atria
R/L ventricle

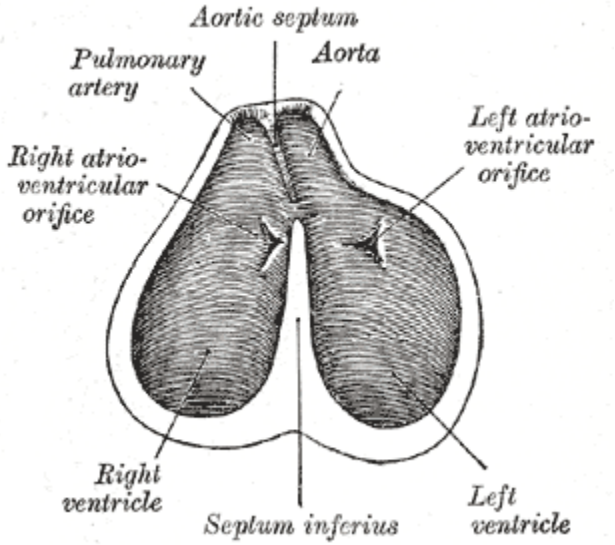
# Aorticopulmonary septum

## Spiral Septum

- Formed from **neural crest cells**
- Migrate to truncal and bulbar ridges
- Separates aorta and pulmonary arteries
- Fuses with  interventricular septum




OpenStax Colleg/Wikipedia

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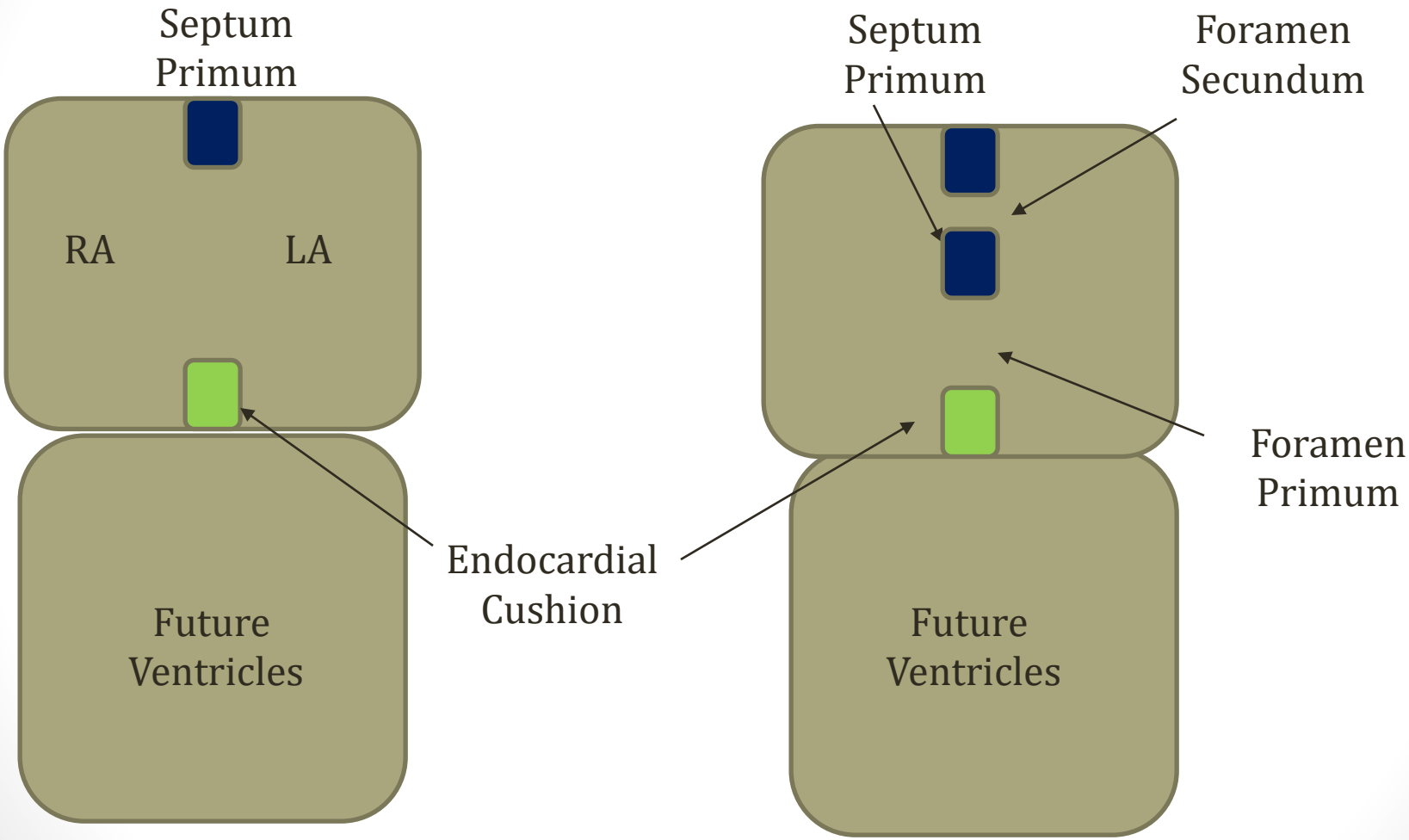
# Aorticopulmonary septum

## Spiral Septum

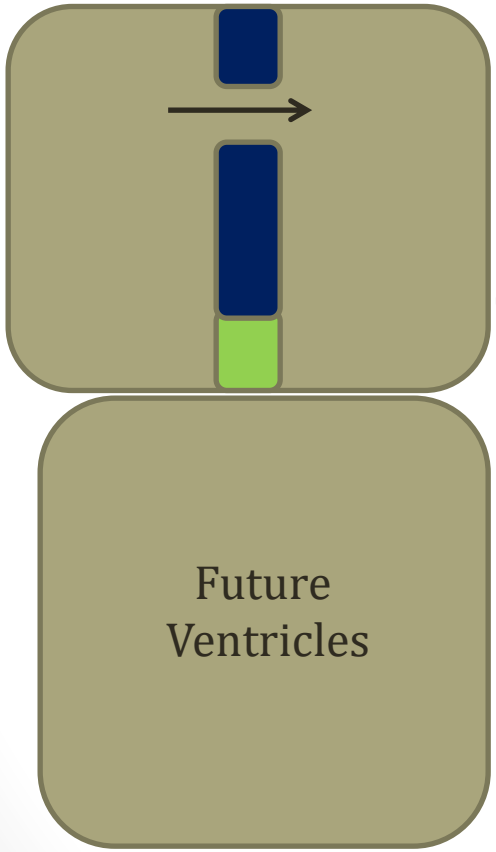
- Abnormal formation → congenital pathology
- Transposition of great vessels
  - Failure to spiral
- Tetralogy of Fallot
  - Skewed septum development
- Persistent truncus arteriosus
  - Partial/incomplete septum development

# Atrial Septum



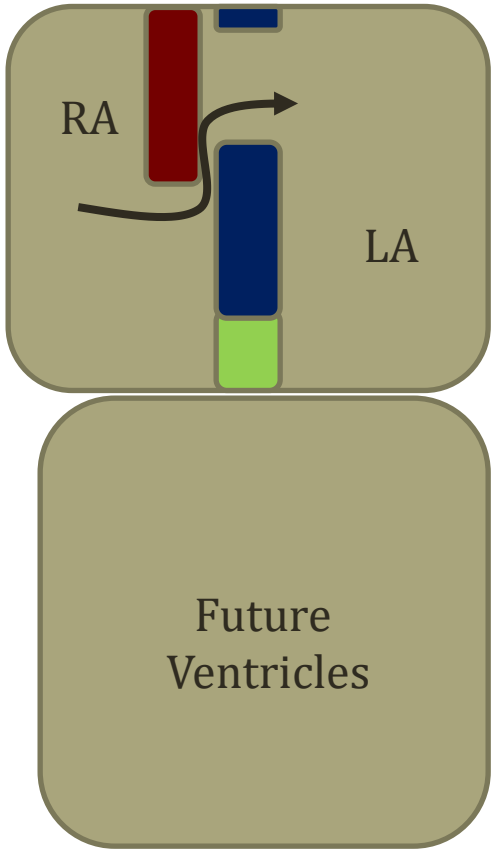
# Atrial Septum

Septum primum fuses
Endocardial cushion




Foramen
Secundum

Septum secundum grows

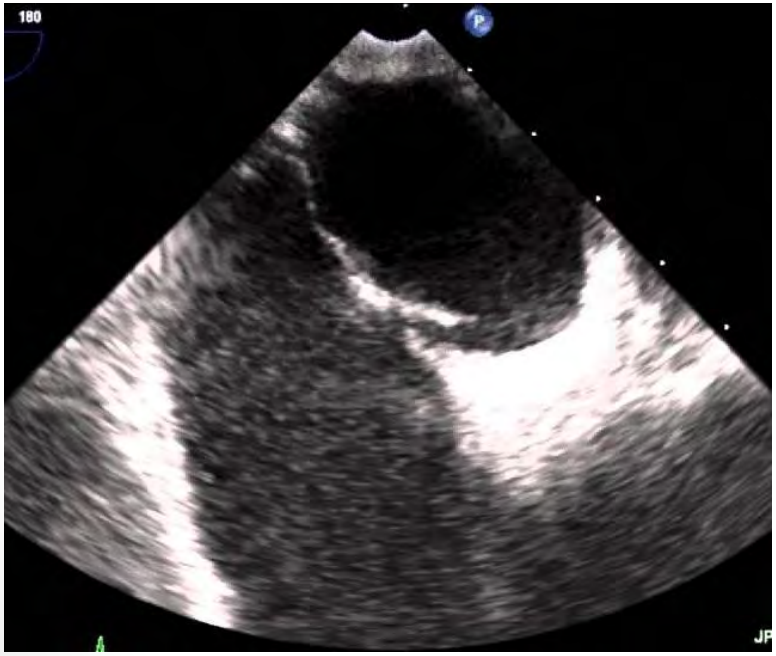


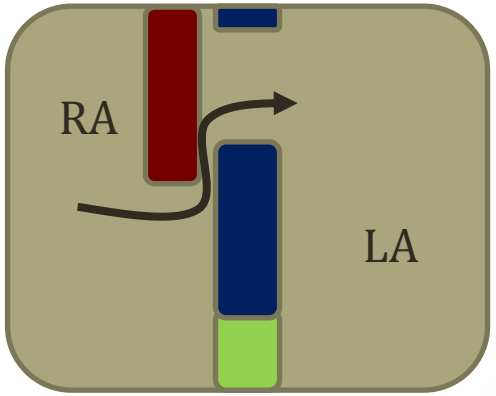

Remaining
Opening
Foramen
Ovale

# PFO

## Patent Foramen Ovale

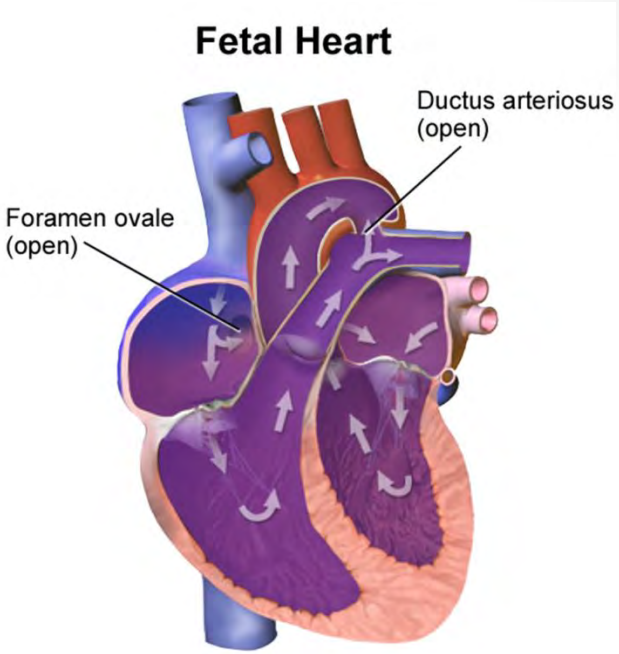
- Found in ~25% adults
- Failure of foramen ovale to close after birth
- Septum primum/secundum fail to fuse



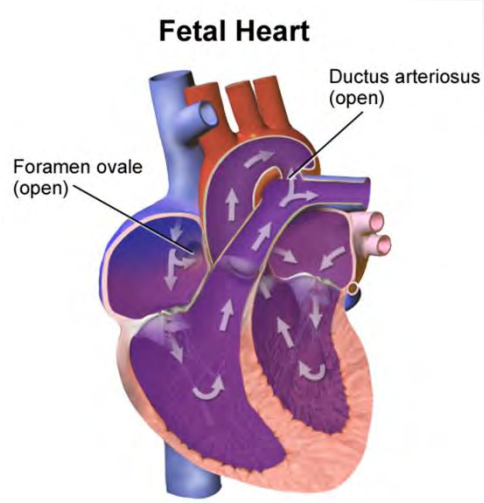
# Fetal Circulation

- **High resistance to flow** in lungs
- Oxygenated blood umbilical veins
  - About 80% saturated (30mmHg O2)
- Travels directly to right atrium
  - Bypasses liver via ductus venosus
- Bypasses lungs via foramen ovale
- Some blood gets to RV (SVC)
  - Bypasses lungs via **ductus arteriosus**
  - Left pulmonary artery to aorta




BruceBlaus/Wikipedia

# Changes at Birth



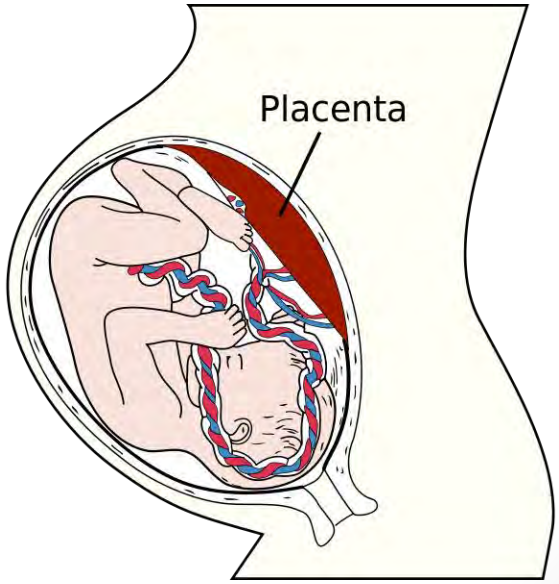
BruceBlaus/Wikipedia

- **Pulmonary resistance falls**
- More blood to left atrium
- LA pressure > RA pressure
- Foramen ovale closes (fossa ovalis)
- Ductus arteriosus closes
  - In utero: ↓ O2, ↑ prostaglandins maintain patency
  - Birth: ↑ O2, ↓ prostaglandins (loss of placenta)

| | PVR | RA | LA |
|---|---|---|---|
| In Utero | ↑ | ↑ | ↓ |
| Birth | ↓ | ↓ | ↑ |

# Changes at Birth

- Placenta has **low resistance to flow**
- In utero: helps keep LA pressure low
- At birth: **increase in peripheral resistance**
- Rise in systemic blood pressure
- Rise in left ventricular pressure
- Contributes to rise in LA pressure

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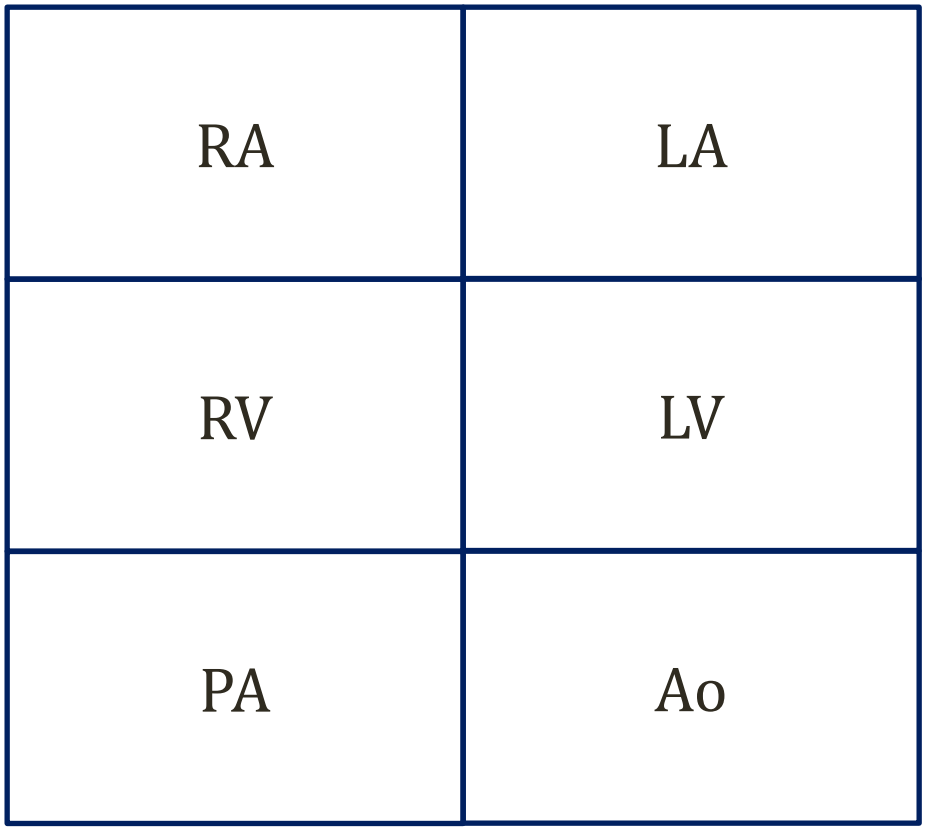
# Shunts

Jason Ryan, MD, MPH

# Shunts



# Shunts

- Left side pressures >> Right side pressures
  - LA ~10mmHg >> RA ~6mmHg
  - LV ~120/10 >> RV ~24/6
  - Ao ~ 120/80 >> PA ~24/12
- Left to right connection → Left to right flow
  - VSD (LV→RV)
  - ASD (LA→RA)
  - PDA (Aorta → Left pulm artery)

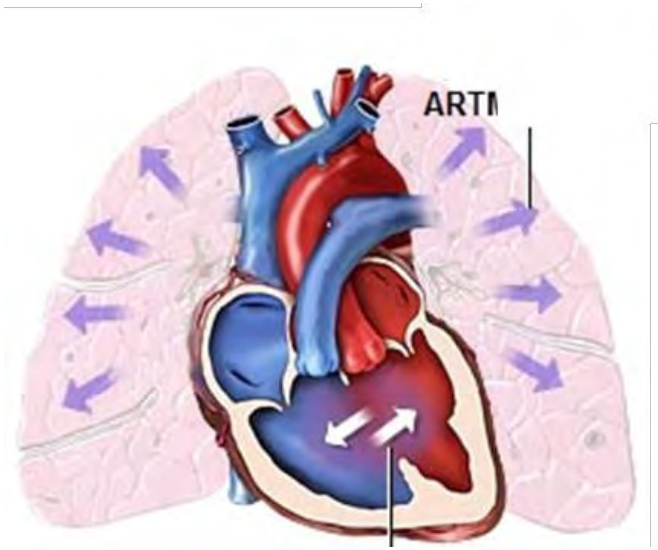
# Shunts

- At birth:
  - Left to right flow → volume overload of right heart
  - Blood flow to lungs unimpaired → no cyanosis
- YEARS later (untreated)
  - Pulmonary vessels become stiff/thick
  - Right ventricle hypertrophies
  - **Right sided pressures rise**
  - Shunt reverses (now R → L)
  - Cyanosis occurs (Eisenmenger syndrome)
- "Blue kids" not "blue babies"

# VSD

## Ventricular Septal Defect

- Most common congenital anomaly
- Communication LV/RV
- **Harsh, holosystolic murmur**
  - Tricuspid area (LLSB)

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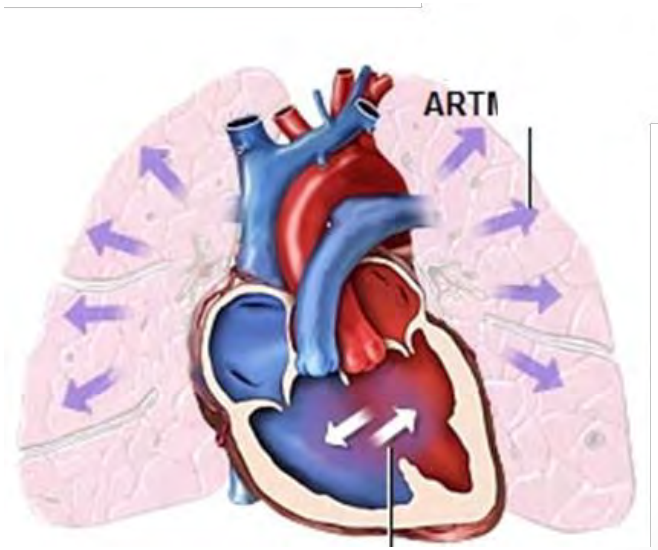
# VSD

## Ventricular Septal Defect

- Characterized in many ways
  - Size
  - Location
  - Associated defects

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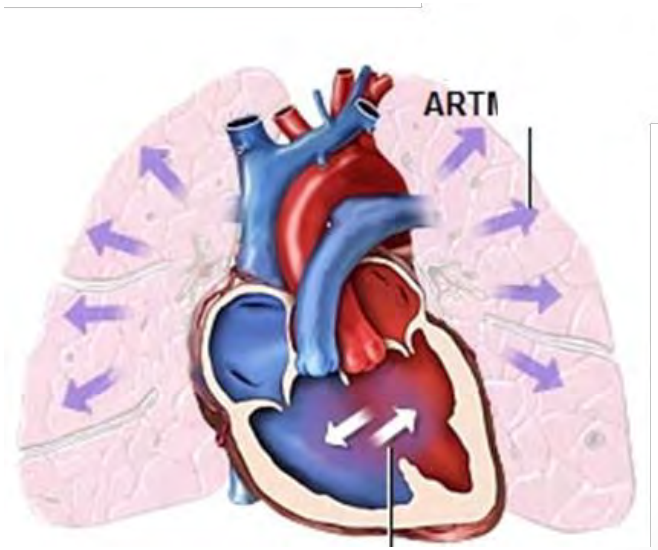
# VSD

## Ventricular Septal Defect

- Small VSD
  - Tiny hole → resists flow across defect ("restrictive")
  - Lots of turbulence → loud murmur
  - Small shunt (small volume of flow across defect)
- Large VSD
  - Large hole ("non-restrictive")
  - Significant shunting
  - Often closed surgically

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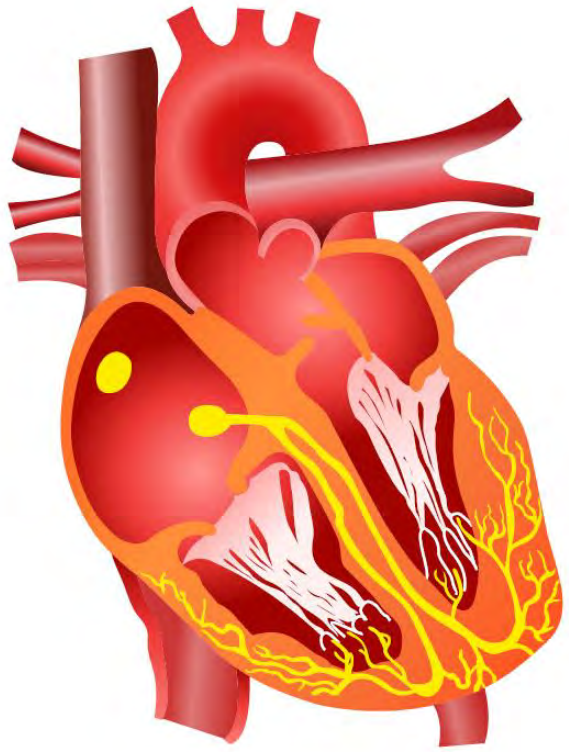
# ASD

## Atrial Septal Defect

- Communication between left/right atrium
- Adds volume to RA/RV
- Delays closure of pulmonic valve
- **Wide, fixed splitting of S2**
- Increased flow across PV/TV
- **Systolic ejection murmur**
- Rarely a mid-diastolic murmur

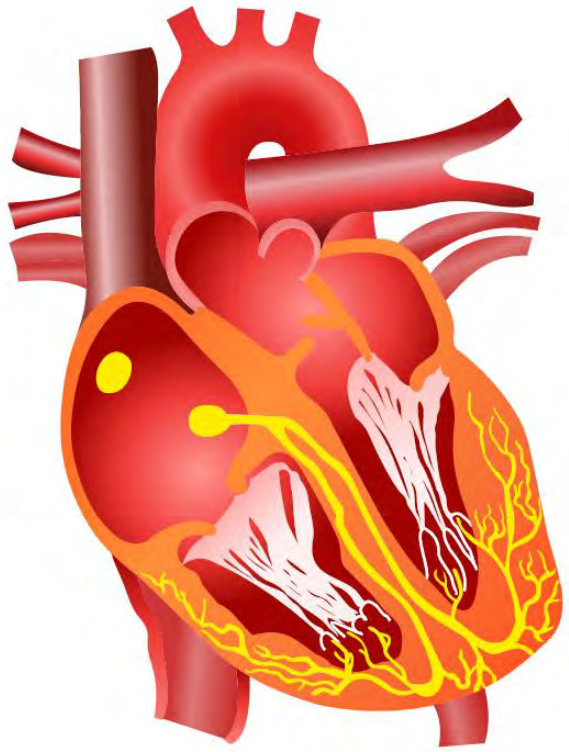


# ASD

## Atrial Septal Defect

- Oxygenated blood LA → RA
- ↑ O2 saturation in RA, RV, PA
- "Shunt run"
  - Series of blood samples
  - SVC = 65%
  - IVC = 65%
  - RA = 75%
  - RV = 75%
  - PA = 75%

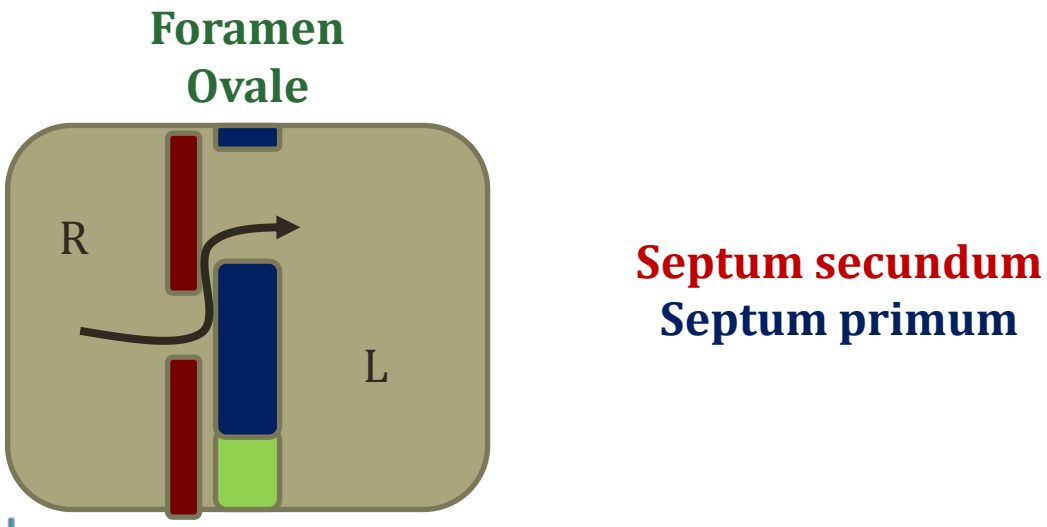
**"Step up"**



# ASD

## Atrial Septal Defect

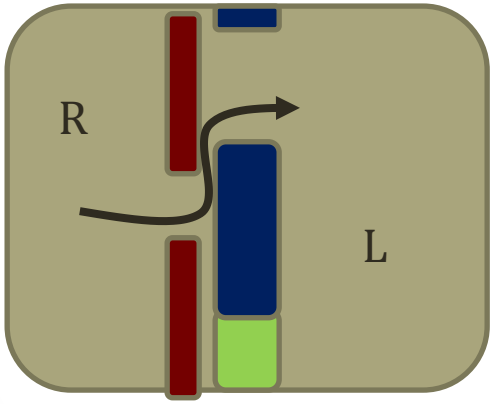
- **Secundum type** is most common
  - Defects at site of foramen ovale/ostium secundum
  - Poor growth of secundum septum
  - Or excessive absorption of primum septum
  - Located mid-septum
  - Often isolated defect



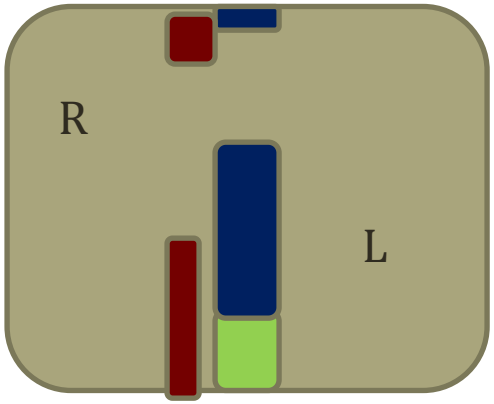
# ASD

## Atrial Septal Defect

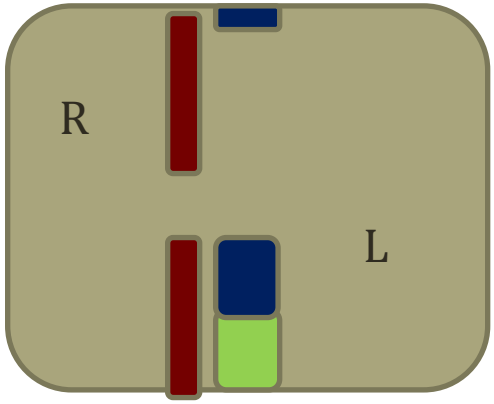
**Foramen Ovale**




**Septum Secundum Too Short**



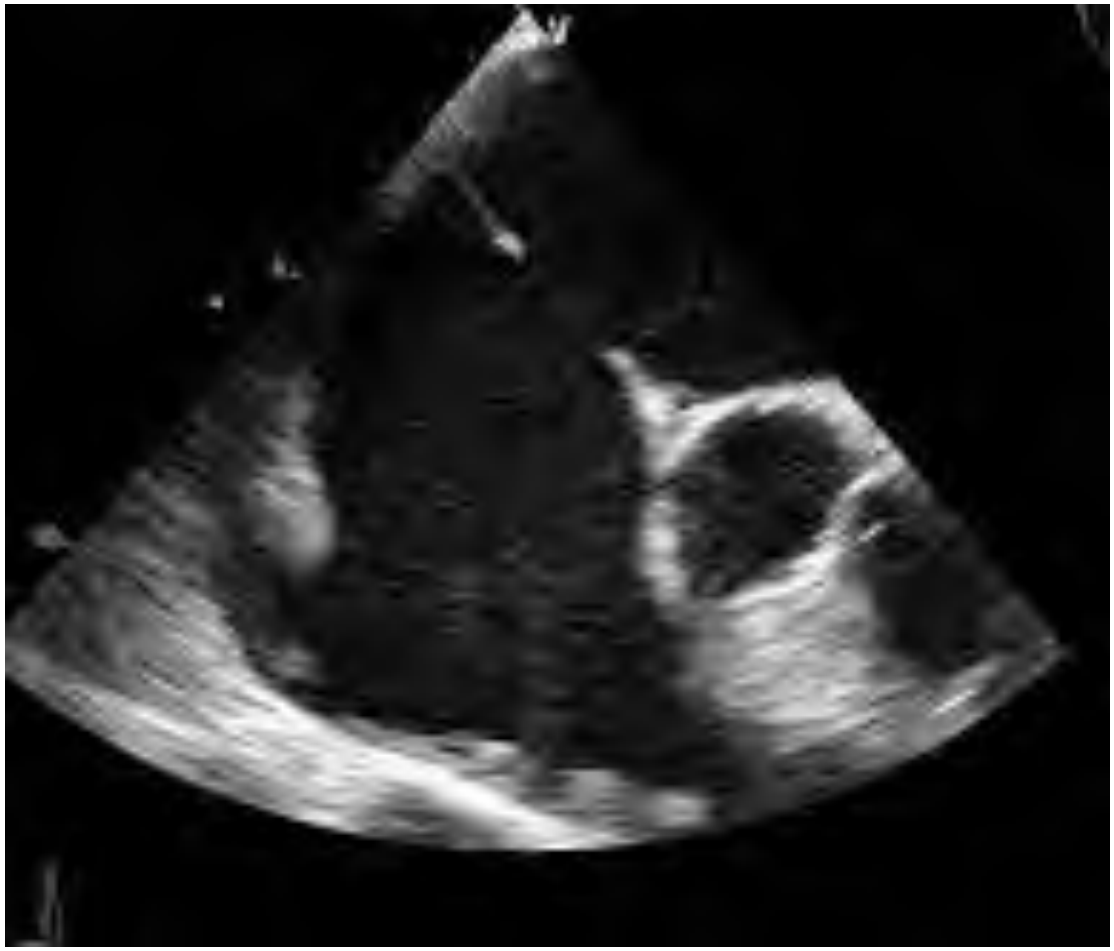

**Septum Primum Excessive Reabsorption**




**Septum secundum**
**Septum primum**

# ASD

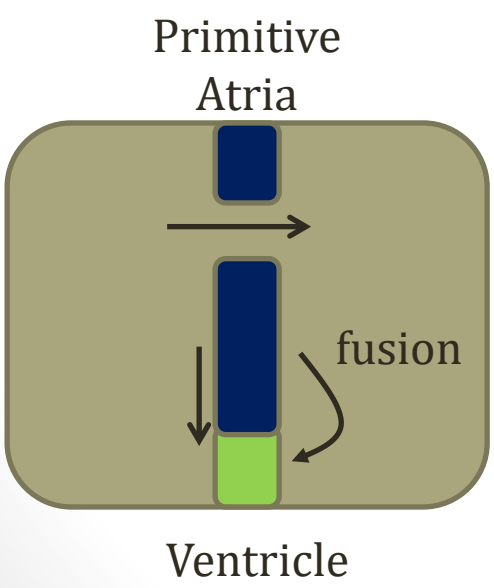
## Atrial Septal Defect

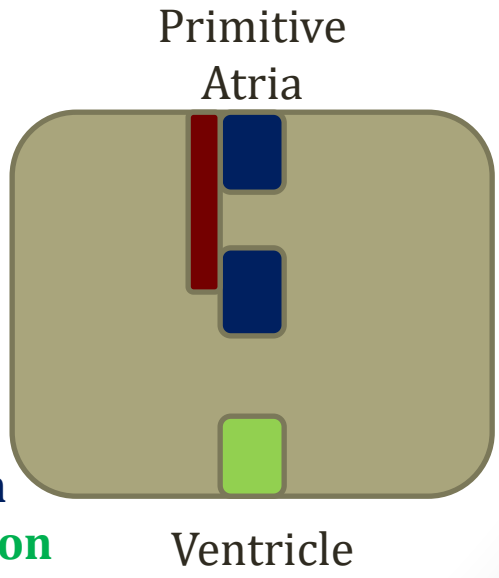


# ASD

## Atrial Septal Defect

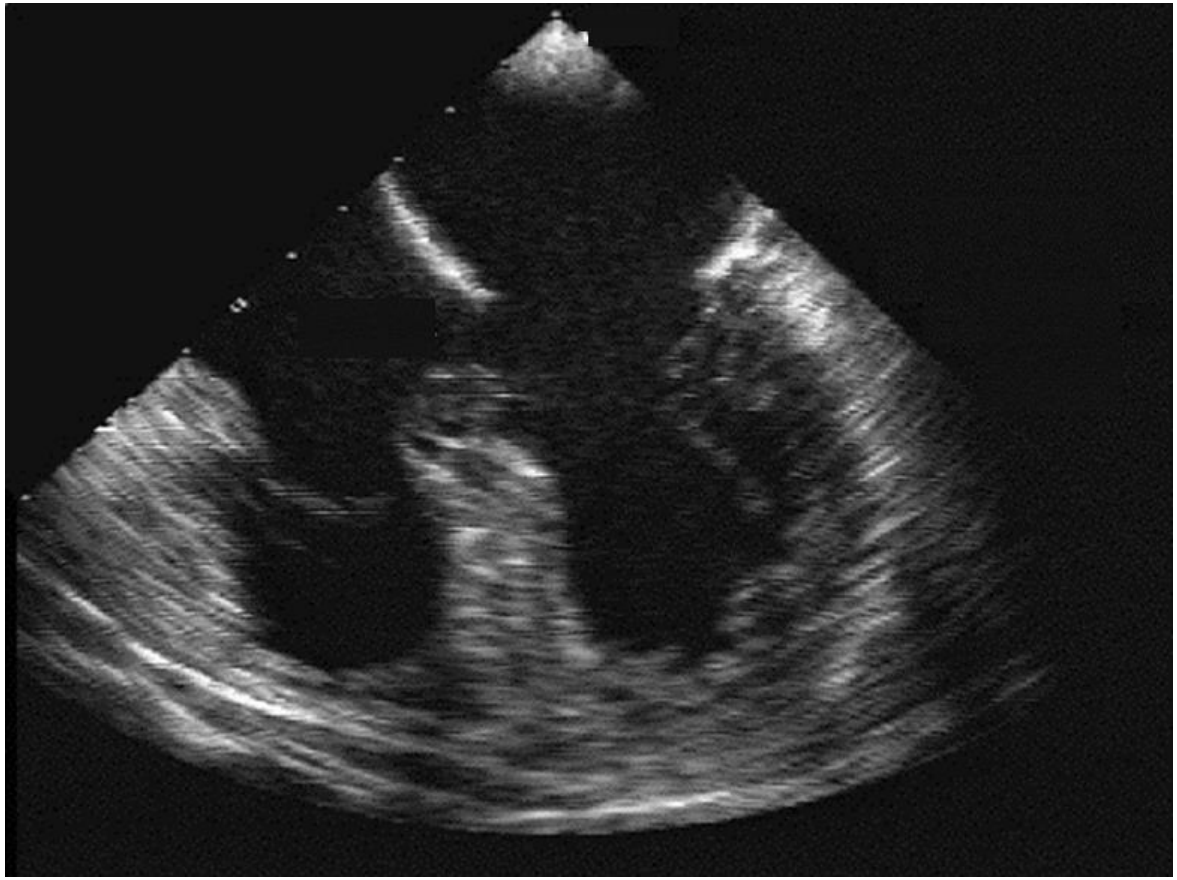
- **Primum type**
  - Defect at site of ostium primum
  - Failure of primum septum to fuse with endocardial cushions
  - Located near AV valves; often occurs with other defects
  - Seen in endocardial cushion defects (Down syndrome)



# ASD

## Atrial Septal Defect



# PDA

## Patent Ductus Arteriosus

- Ductus arteriosus shunts blood in utero
  - Left pulmonary artery → aorta
- Closes close after birth
  - "Functional" closure 18 to 24 hours (smooth muscle)
  - "Anatomic" occlusion over next few days/weeks
  - Becomes **ligamentum arteriosum**
- Patency maintained by prostaglandin E2
  - Major source in utero is placenta

# PDA

## Patent Ductus Arteriosus

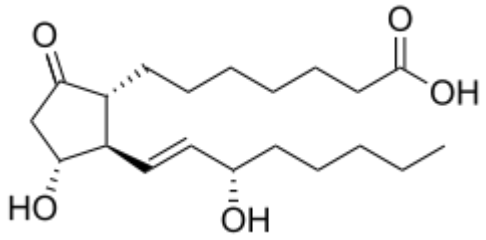
- Rarely remains patent (3 to 8 per 10,000 births)
- Associated with **congenital rubella syndrome**
  - ToRCHeS infection
  - Mother: Rash, fever, lymphadenopathy
  - Baby: Deafness, cataracts, cardiac disease
  - PDA common
  - Rare in developed countries (vaccination)
  - Consider in infants whose mothers are immigrants

# PDA

## Patent Ductus Arteriosus

- **Continuous**, machine-like murmur
- **Widened pulse pressure**
  - Loss of volume in arterial tree through PDA
  - Low diastolic pressure → Increased pulse pressure
- **Differential cyanosis**
  - Occurs when shunt reverses R → L
  - Blue toes, normal fingers

# Alprostadil




- **Prostaglandin E1**
- Maintains patency of ductus arteriosus
- Key effect: delivers blood to lungs
- Useful when poor RV → PA blood flow
  - Tetralogy of Fallot
  - Pulmonary atresia

# Indomethacin

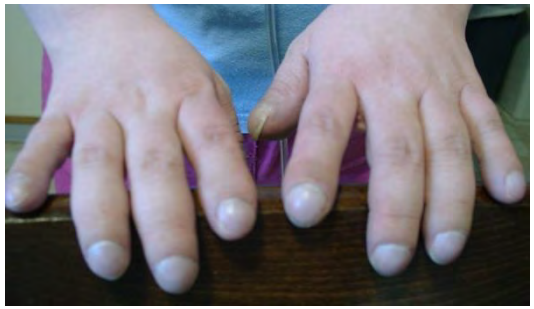
- **NSAID**
- Inhibits cyclooxygenase
- Decreases prostaglandin formation
- Can be used to close PDA

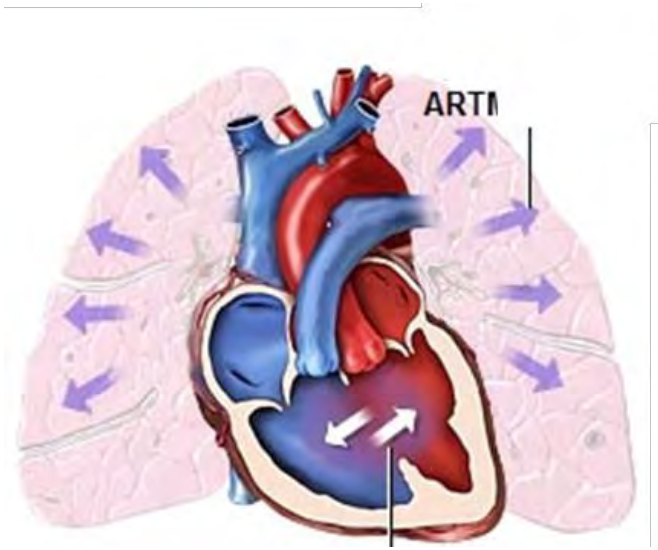
# Qp:Qs

- Qp = Pulmonary blood flow
- Qs = Systemic blood flow
- Qp:Qs should be 1:1
- In shunts, Qp:Qs may be > 1:1
  - 1.5:1, 2:1, 3:1, etc.

# Eisenmenger's Syndrome

- Uncorrected ASD/VSD/PDA
- Right heart chronically overloaded
  - RV Hypertrophy
  - Pulmonary hypertension
- Shunt reverses right → left
  - Cyanosis
  - Clubbing
  - Polycythemia (very high Hct)



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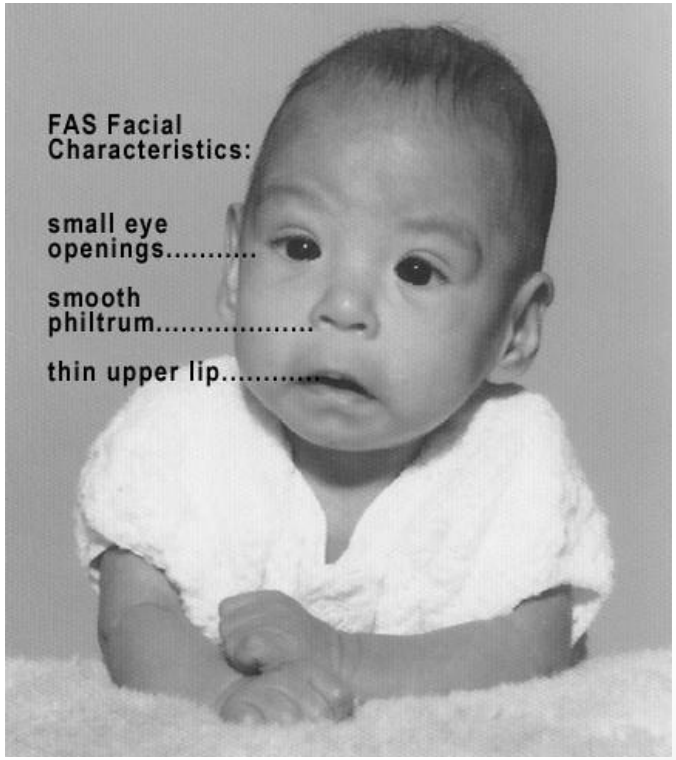
# Fetal Alcohol Syndrome

- Caused by prenatal exposure to alcohol (teratogen)
- Characteristic facial features
- Impaired neurologic function
- **Congenital heart defects**
  - Atrial septal defect
  - Ventricular septal defect
  - Tetralogy of Fallot

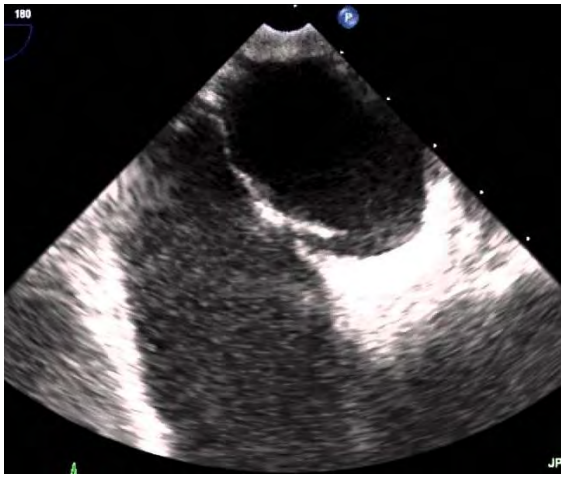



Teresa Kellerman/Wikipedia

# PFO

## Patent Foramen Ovale

- Found in ~25% adults
- Failure of foramen ovale to close after birth
- Can lead to **stroke** in patients with DVT/PE

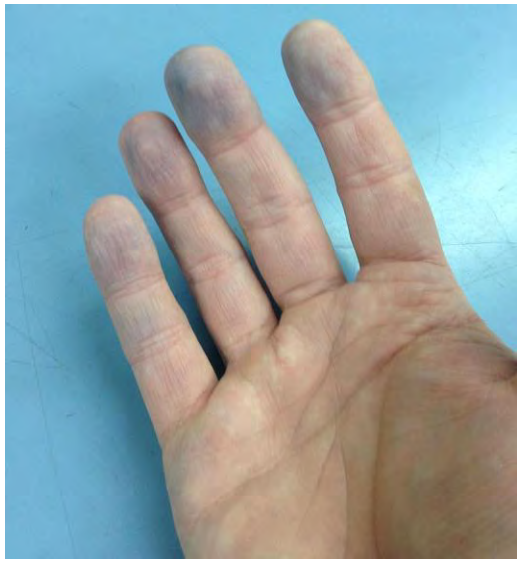


# Cyanotic Congenital Heart Disease

Jason Ryan, MD, MPH

# Cyanosis

- **Central** cyanosis
  - Cardiac output normal
  - Blood is flowing
  - Not enough O2
  - Lips
  - Nail beds
  - Conjunctivae
  - Warm extremities
- Peripheral cyanosis
  - Low blood flow
  - Severe heart failure
  - Cold extremities



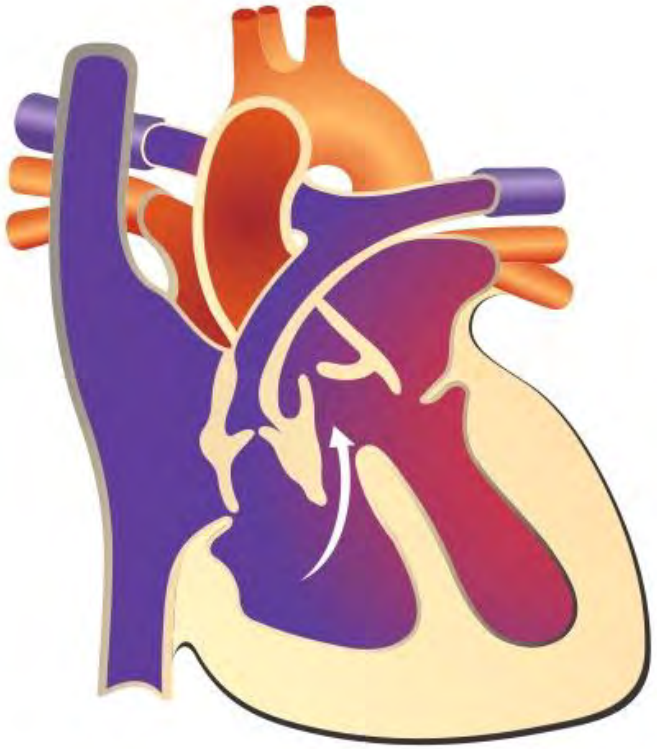
WaltFletcher/Wikipedia

# Blue Babies

- **Central cyanosis** early in life
- Blood not going through lungs after birth
  - Tetralogy of Fallot
  - Transposition of great vessels
  - Truncus arteriosus
  - Tricuspid atresia
  - Total anomalous pulmonary venous return

# Tetralogy of Fallot

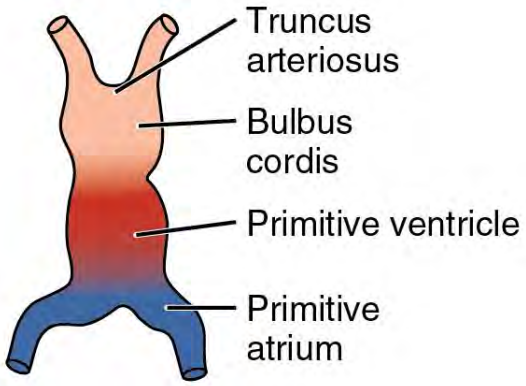
- Constellation of four abnormalities
  - Ventricular septal defect (VSD)
  - Rightward deviation of aortic valve ("overriding aorta")
  - Subpulmonary stenosis
  - Right ventricular hypertrophy



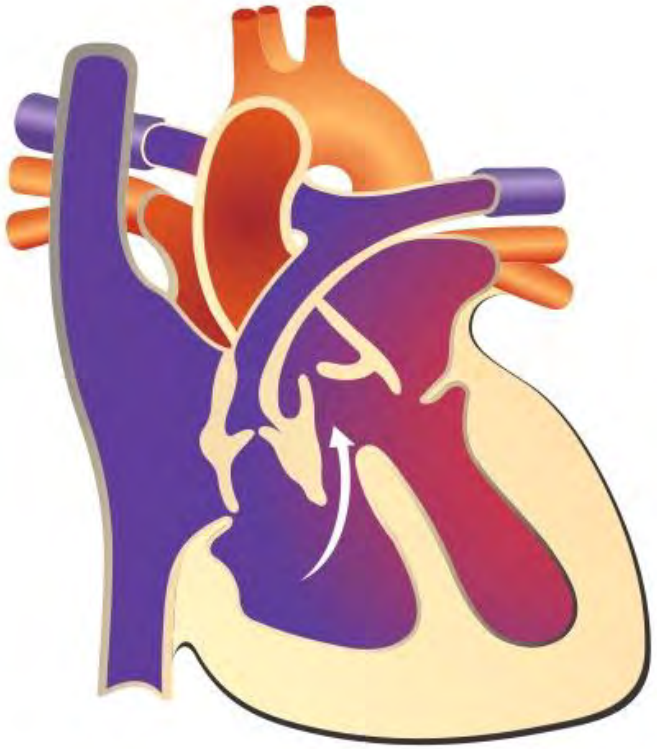
# Infundibulum

## Conus Arteriosus

- "Funnel" leading to pulmonic valve
- Develops from **bulbus cordis**
- Smooth, muscular structure at RV outflow to PA



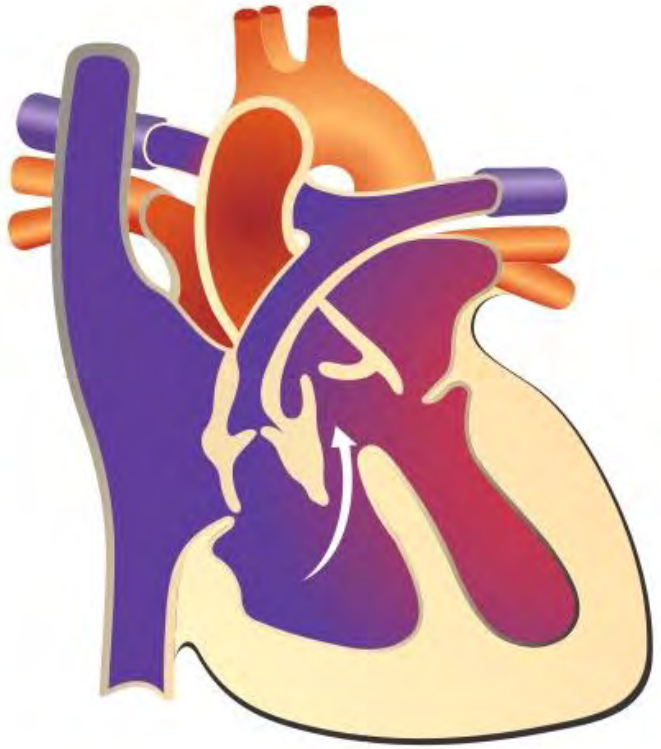

OpenStax Colleg/Wikipedia



# Infundibulum

## Conus Arteriosus

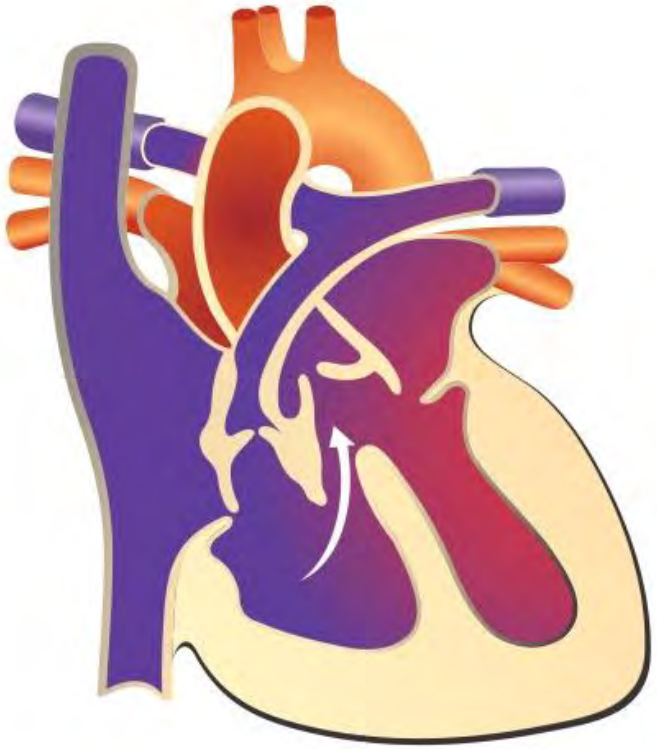
- **Septum displaced (moves toward RV) in TOF**
- Causes "overriding aorta"
  - 5-95% of aorta may lie over RV
- Causes VSD
  - Usually large ("non-restrictive")



# Infundibulum

## Conus Arteriosus

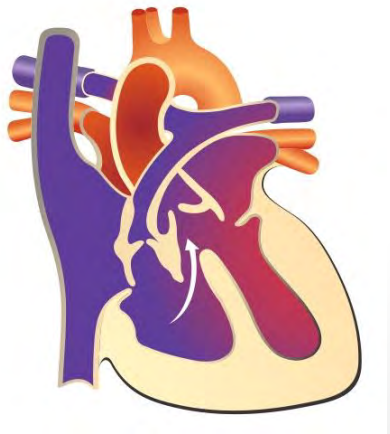
- **"Infundibular stenosis"**
  - Subpulmonary stenosis
  - RV outflow tract obstruction
- Abnormal pulmonary valve
  - Rarely main cause of obstruction
- Flow obstruction → RVH



# Tetralogy of Fallot

## Physiology

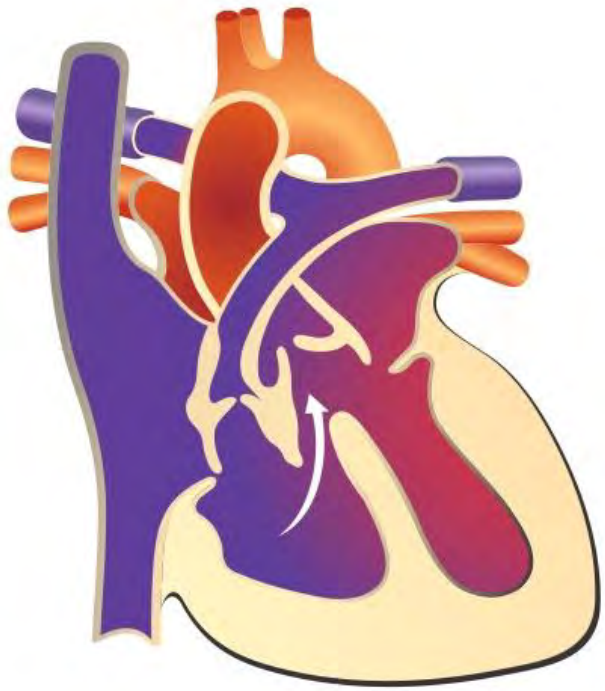
- High **resistance to flow** RV → pulmonary artery
  - RV outflow pulmonic stenosis
- Diverts blood across VSD to left ventricle
- **Severity of flow obstruction determines symptoms**
- Severe obstruction: severe cyanosis
- Mild obstruction: less shunting ("pink" tets)



# Tetralogy of Fallot

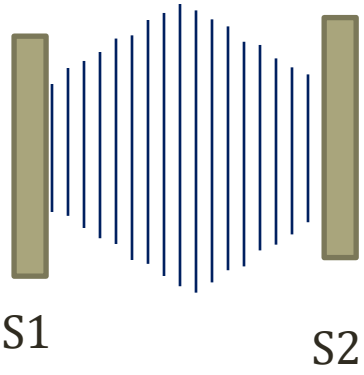
## Physiology

- Poor blood flow RV → lungs
- Left to right shunts beneficial
  - Bring back to pulmonary artery
  - Diverts blood to lungs
  - Improves oxygenation
  - **Patent ductus arteriosus**
  - Aortopulmonary collateral arteries
  - Surgical shunt



# Tetralogy of Fallot

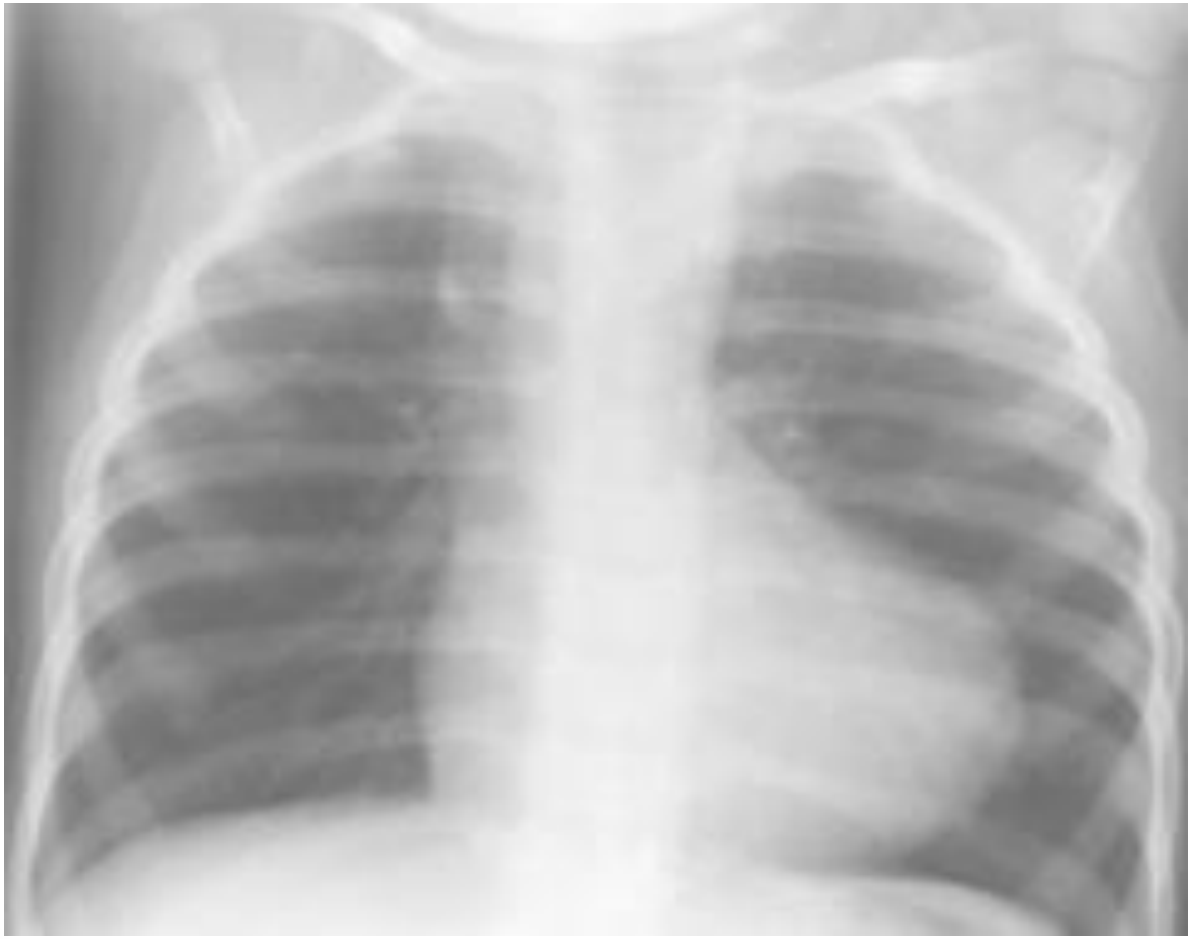
## Murmur




- Systolic ejection murmur
  - Crescendo-decrescendo
  - RV outflow and pulmonic stenosis
  - Heard best at left sternal border
- Single S2
  - S2 = closure of aortic and pulmonic valves
  - TOF: Diseased pulmonic valve → no sound
- VSD murmur (holosystolic) not typically heard
  - Large VSD → no murmur

# Tetralogy of Fallot

X-ray



# Tetralogy of Fallot

## Other Features

- **Squatting** improves symptoms
  - Increased **afterload/TPR** (resists flow out of LV)
  - Pressure rises in the aorta/left ventricle
  - Less blood shunted RV → LV via VSD
  - More blood to lungs

Sherif Salama/Flikr

# Tetralogy of Fallot

## Other Features

- **"Tet spells"**
  - Sudden cyanosis often when agitated
  - **Severe/complete RVOT obstruction**
  - O2, knees to chest, beta blockers (propranolol)

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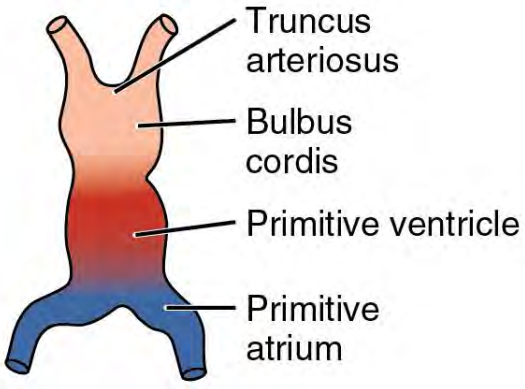
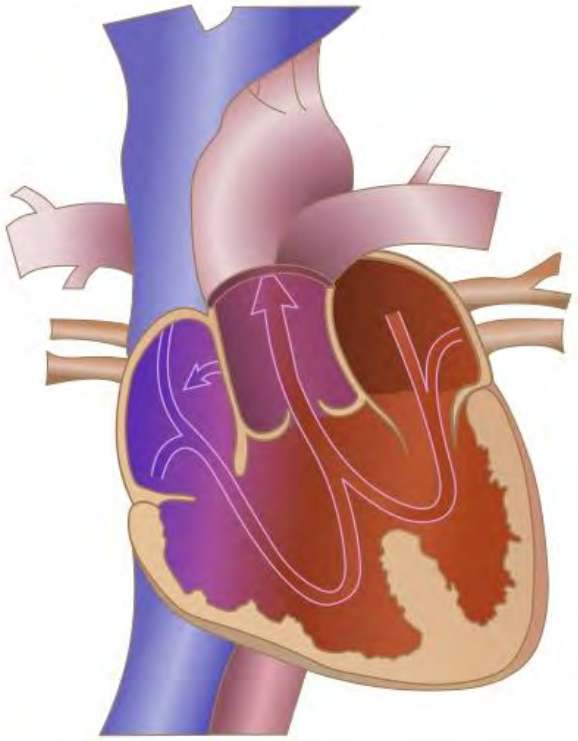
# Truncus Arteriosus

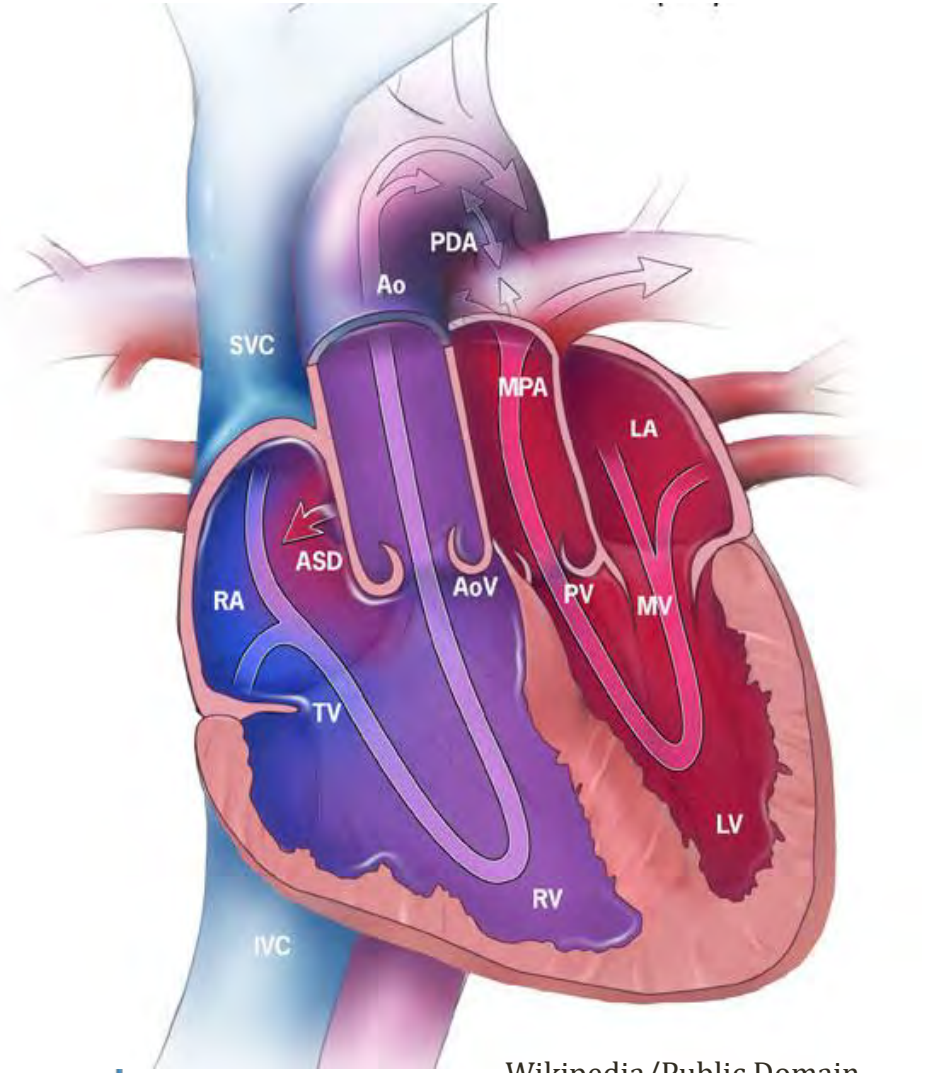
- Common arterial trunk → Mixing of blood
- Failure of **neural crest cells** to drive formation of **aorticopulmonary septum**
- **Almost always has VSD**




OpenStax Colleg/Wikipedia



# Transposition of Great Vessels

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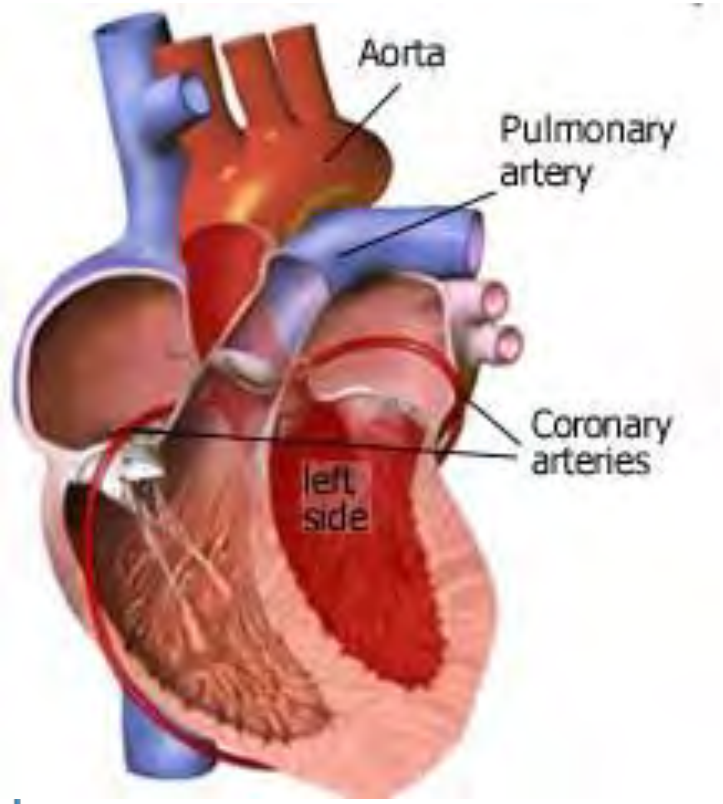
# Transposition of Great Vessels

- Normal heart:
  - **Aorta is posterior** and to right of pulmonary artery

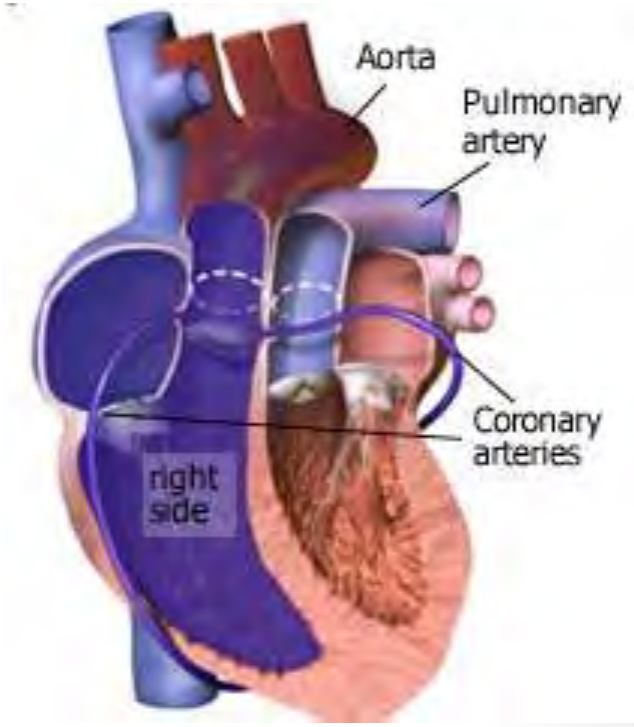





Kshafer/WikiDoc

# Transposition of Great Vessels

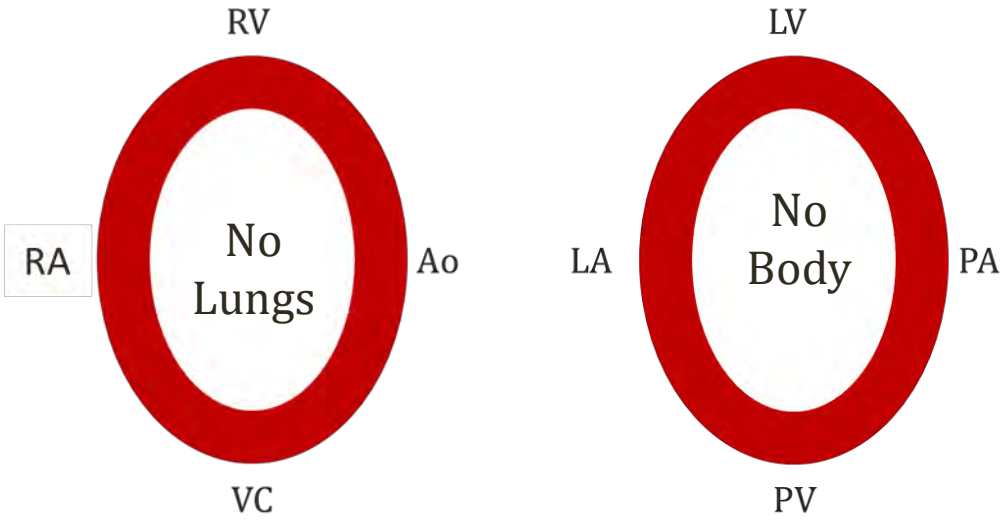
- D-transposition (most common type):
  - **Aorta forms anterior** and rightward of pulmonary artery
  - Aorta arises from right ventricle
  - Pulmonary artery from left ventricle




Kshafer/WikiDoc

# Transposition of Great Vessels

- RV → Aorta → body → RA → RV
- LV → Pulmonary artery → LA → LV
- Two completely separate circuits
- NOT compatible with life unless shunt present
  - Usually PDA or VSD



# L-TGA

## L-Transposition of the Great Arteries

- "Double switch": Aorta/PA and LV/RV
- "Congenitally corrected TGA"
- Venous blood → RA → LV → PA → Lungs
- Lungs → PV → LA → RV → Aorta
- Two circuits *not* separated
- Wrong connections (RV-Aorta, LV-PA)
- **Eventually right ventricle fails**

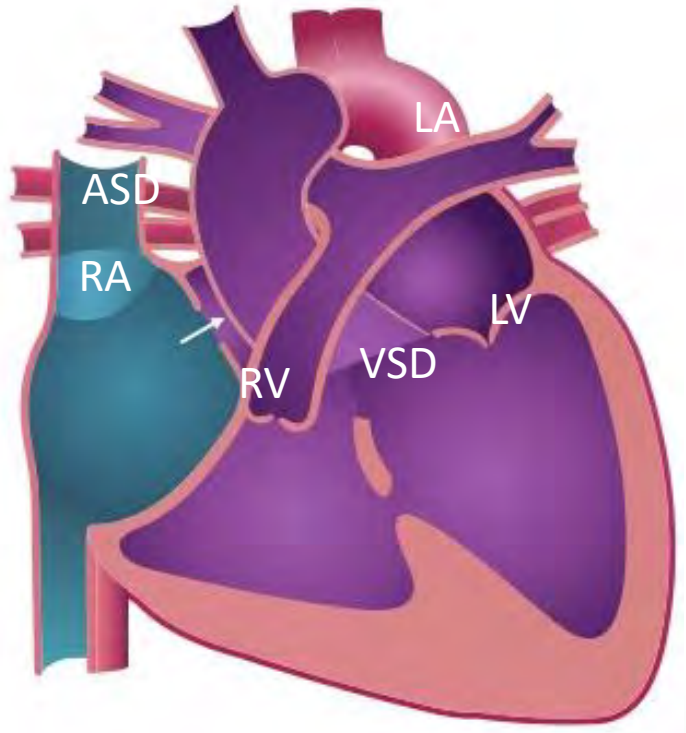
# Maternal Diabetes

- Infants at increased risk congenital anomalies
- Common congenital heart defects
  - **Transposition of great vessels**
  - Truncus arteriosus
  - Tricuspid atresia
  - VSD
  - PDA

Øyvind Holmstad/Wikipedia

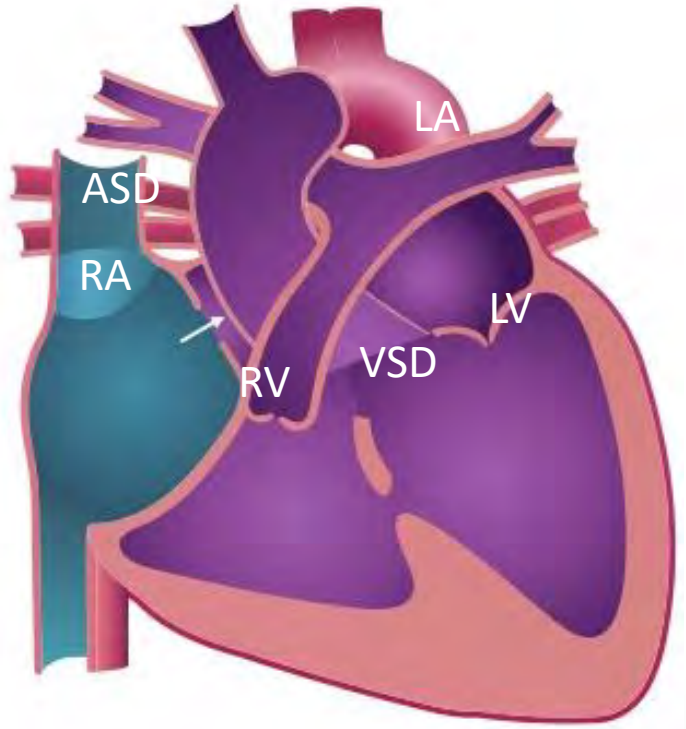
# Tricuspid Atresia

- Abnormal AV valves from endocardial cushions
- **No tricuspid valve**
- No blood RA → RV



# Tricuspid Atresia

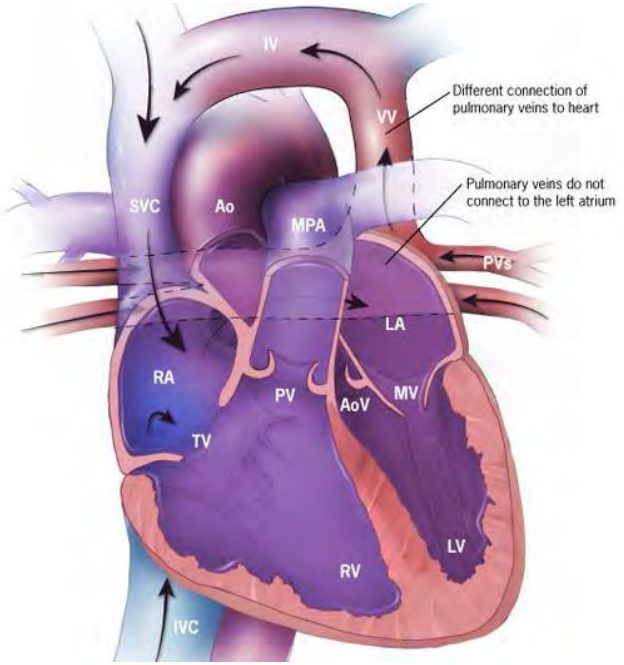
- All cases have R→L shunt
  - Always seen with ASD
  - Allows blood flow to LA
- All cases have L→R shunt
  - Allows blood flow to lungs
  - LV→ RV via VSD
  - Ao → PA via PDA



# TAPVR

## Total Anomalous Pulmonary Venous Return

- Normal: pulmonary veins drain to left atrium
- TAPVR: pulmonary veins drain to venous system
  - Innominate (brachiocephalic) veins → SVC
  - Coronary sinus
  - Portal vein

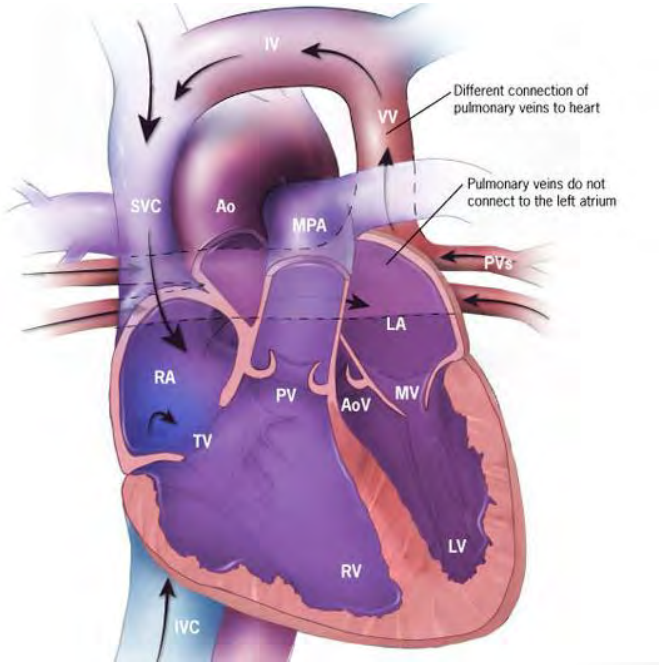



Wikipedia/Public Domain

# TAPVR

## Total Anomalous Pulmonary Venous Return

- RV → Lungs → Pulm Veins → RA → RV
- RA and RV dilate
- Must have a right to left shunt
  - **ASD** (most common)
  - **PDA**
- Mixed (low O2) blood to body

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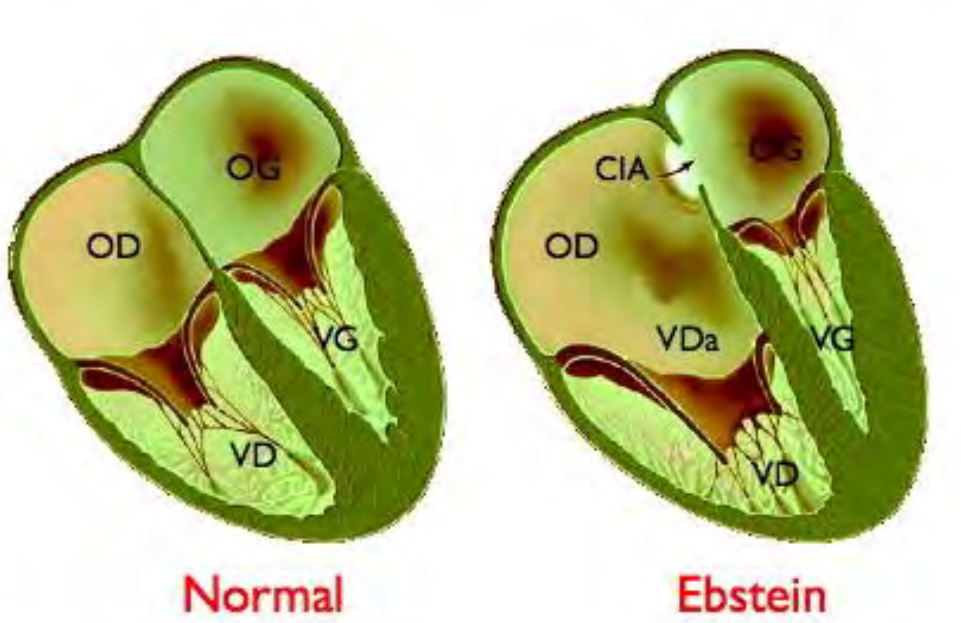
# Ebstein's Anomaly

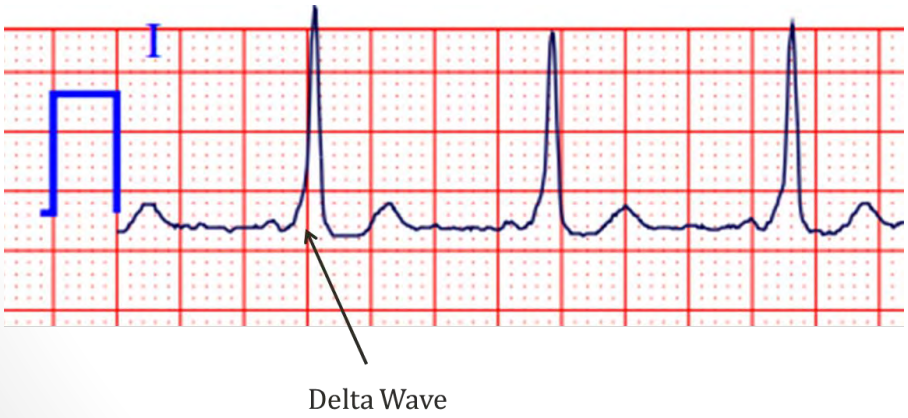
- Apical displacement of TV → small RV
- "Atrialization" of RV tissue
- Severe tricuspid regurgitation
- Can lead to right heart failure

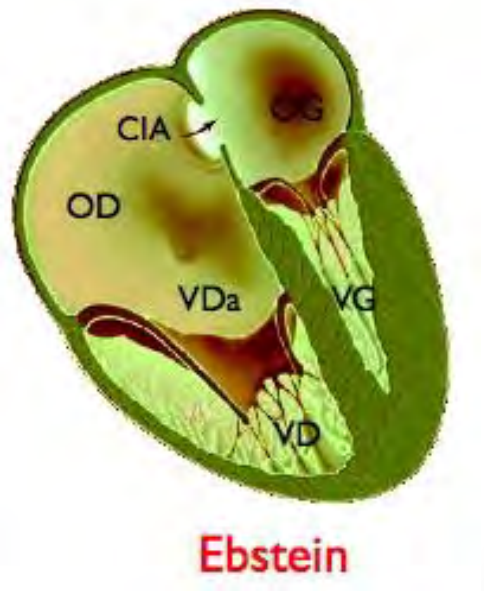



Wikipedia Commons

# Ebstein's Anomaly

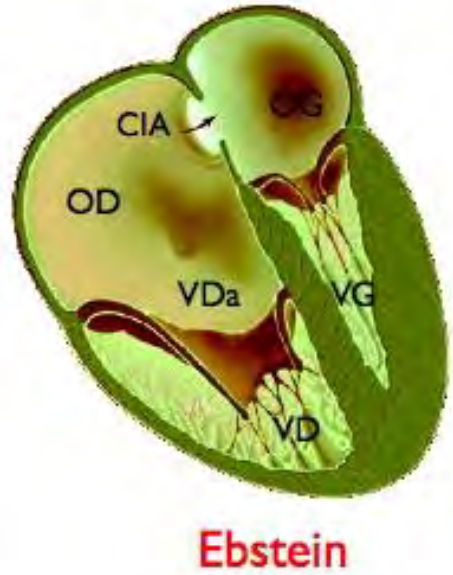
- Right to left shunting and cyanosis if ASD
  - High RA pressure
- Associated with **WPW**
  - Electrical bypass tract often present
  - Delta wave on EKG



# Maternal Lithium

- Teratogen
- Completely equilibrates across the placenta
- Teratogenic effects primarily involve heart
- **Ebstein's anomaly** most common



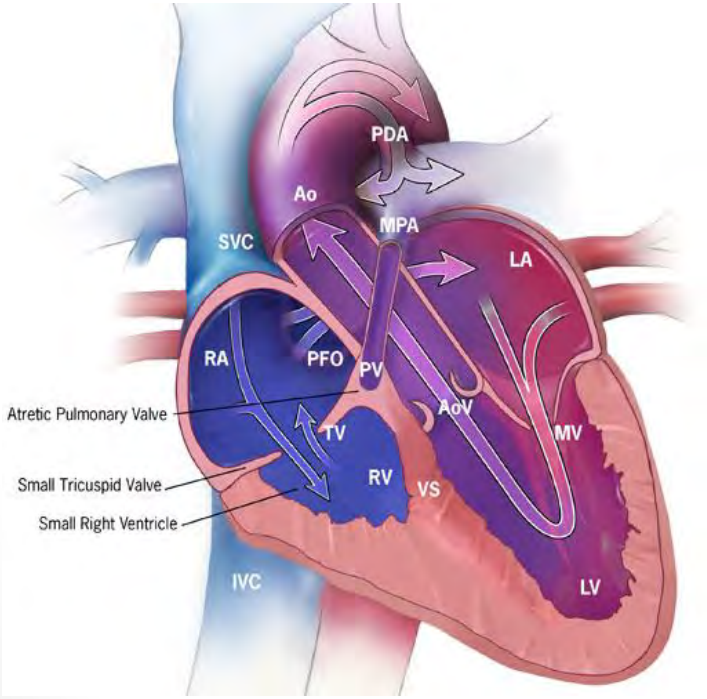

Øyvind Holmstad/Wikipedia

# Pulmonary Atresia

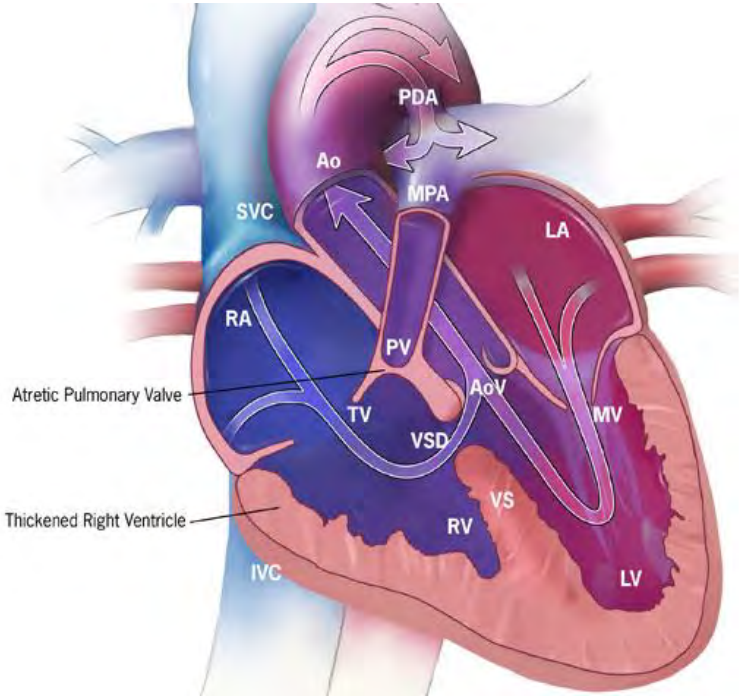
- Failure of pulmonic valve orifice to develop
- No flow from RV to lungs
- In utero blood bypasses lungs (normal development)
- At birth: No blood flow to lungs through PV
  - PVR should fall but does not
- Often co-exists with VSD for outflow of RV
  - Similar to a severe form of Tetralogy of Fallot
- Survival depends on ductus arteriosus
- **Alprostadil** given to keep DA open

# Pulmonary Atresia

**No VSD**

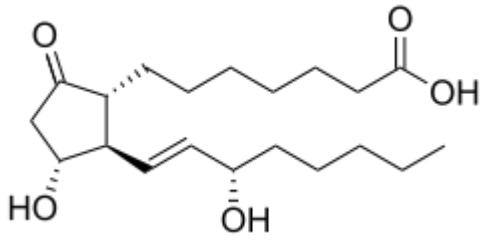



**VSD**




CDC/Public Domain

# Alprostadil




- Prostaglandin E1
- Maintains patency of ductus arteriosus
- Key effect: **delivers blood to lungs**
- Useful when poor RV → PA blood flow
  - Tetralogy of Fallot
  - Pulmonary atresia

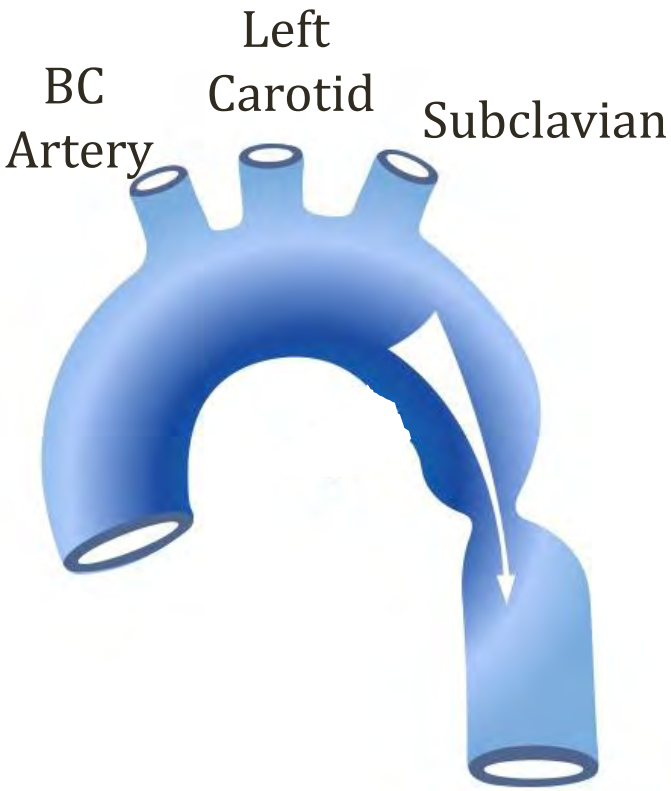
# Conotruncal Heart Defects

- Outflow tract anomalies
  - Trunk = Truncus arteriosus
  - Conus = Conus arteriosus
- Tetralogy of Fallot
- Truncus arteriosus
- Transposition of the great arteries
- **22q deletion syndromes**
  - DiGeorge syndrome (Thymic Aplasia)
  - Immunodeficiency, hypocalcemia
  - **Conotruncal anomalies**

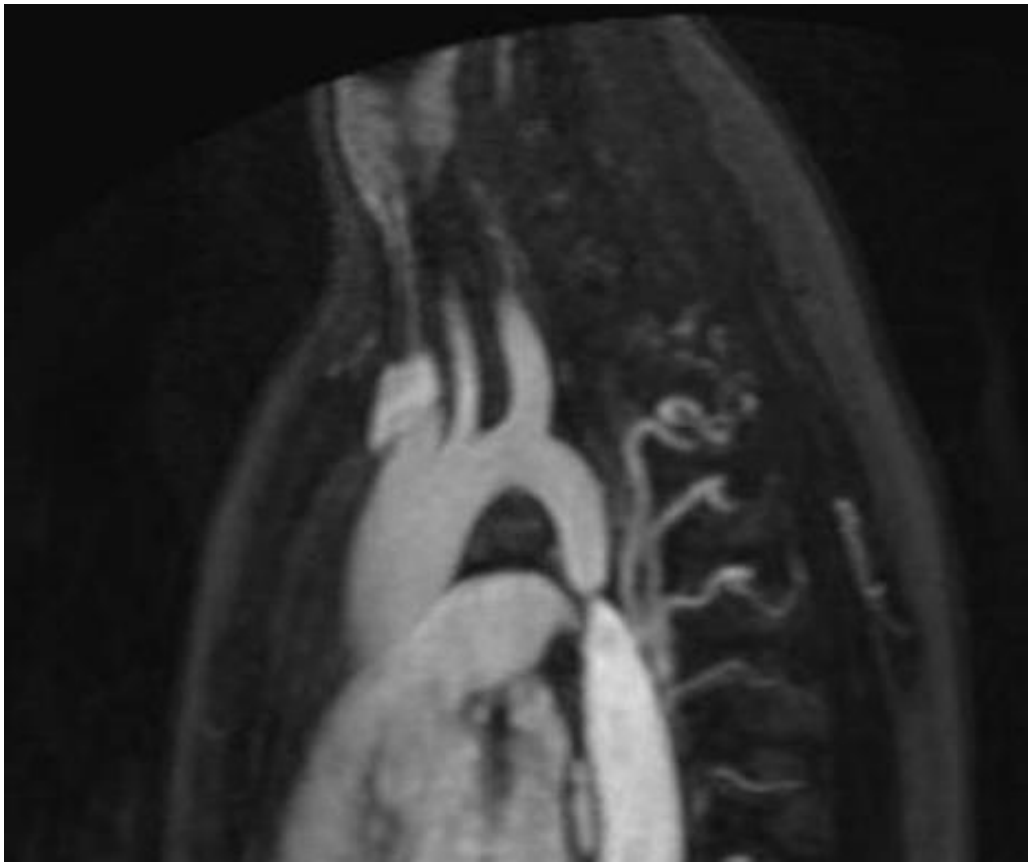
# Coarctation of the Aorta

Jason Ryan, MD, MPH

# Coarctation of the Aorta

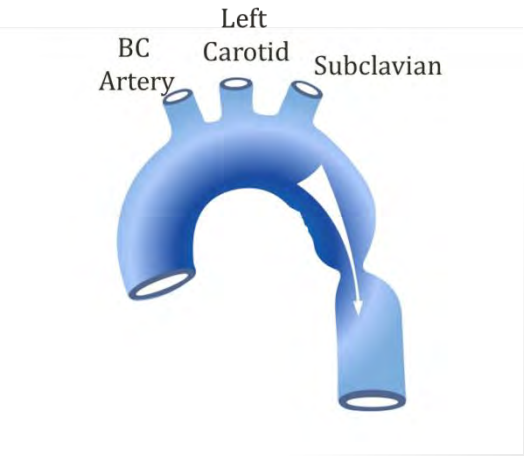


# Coarctation of the Aorta

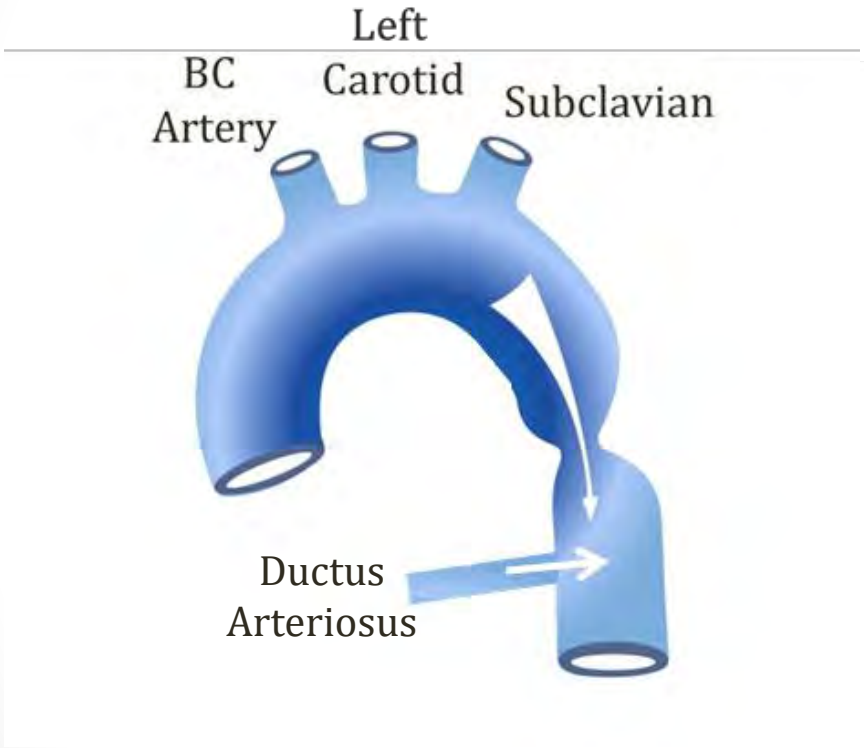


# Coarctation of the Aorta

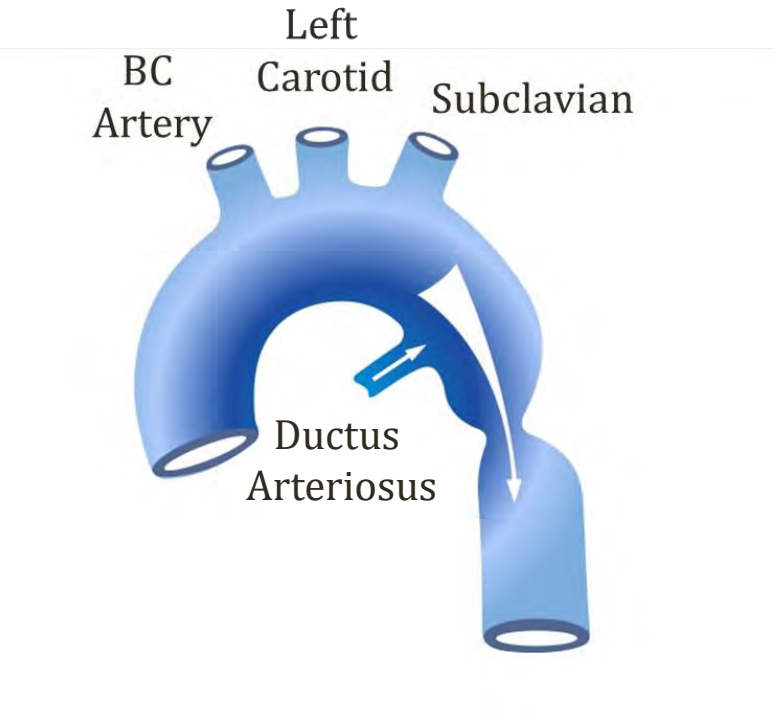
- Congenital disorder
- Usually involves thoracic aorta distal to subclavian
- Near insertion of ductus arteriosus
- “Juxtaductal” aorta
- Subtypes based on location of ductus arteriosus
- High **resistance to flow** in aorta



# Coarctation of the Aorta




**Pre-ductal Coarctation**




**Post-ductal Coarctation**

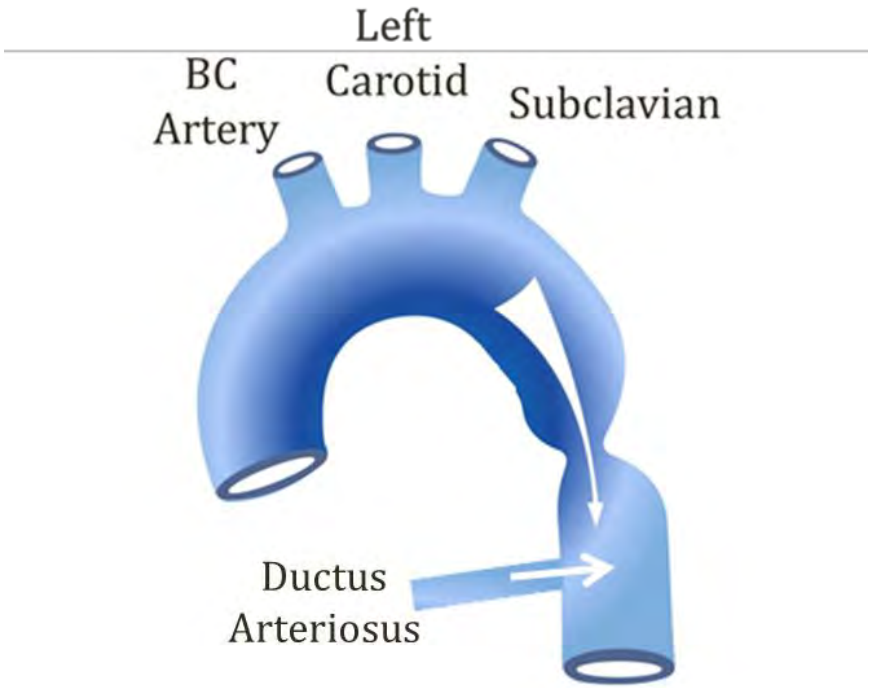
# Ductus Arteriosus

- Shunts blood in utero
- Left pulmonary artery → aorta
- Patency maintained by ↓O2 and ↑ prostaglandins
- At birth: ↑O2 and ↓ prostaglandins
- "Functional" closure 18 to 24 hours after birth
  - Smooth muscle constriction
- "Anatomic" occlusion over next few days/weeks
- Becomes **ligamentum arteriosum**

# Coarctation of the Aorta

## Preductal or Infantile

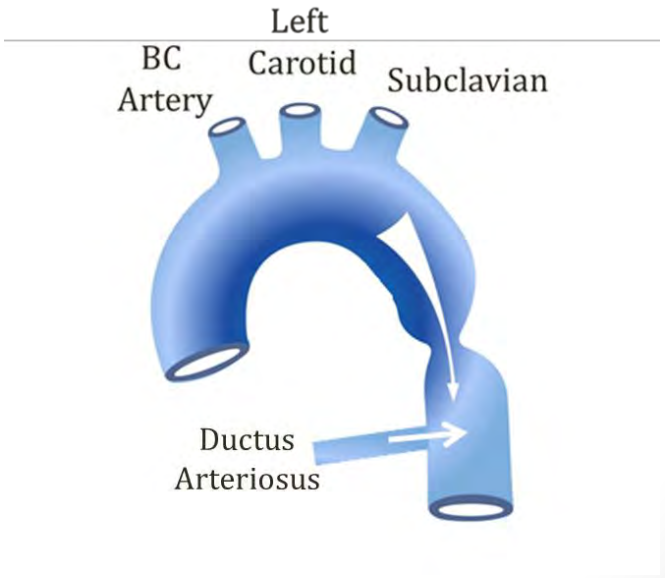
- Ductus arteriosus supplies lower extremities
- Poor development of **collateral vessels**



# Coarctation of the Aorta

## Preductal or Infantile

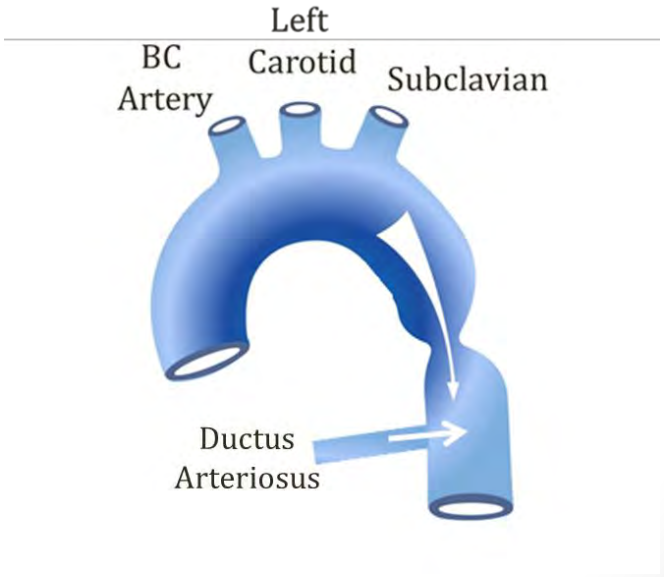
- At birth ductus arteriosus open (not closed yet)
- Deoxygenated blood to lower extremity
- **Lower extremity cyanosis** may occur



# Coarctation of the Aorta

## Preductal or Infantile

- Ductus closure → symptoms may develop
- All flow through aorta with severe narrowing
- **Abrupt increase afterload**
- Rise in LVEDP
- Acute heart failure
- LV can dilate → fail → shock
- All caused by **closure of DA**



# Coarctation of the Aorta

## Preductal or Infantile

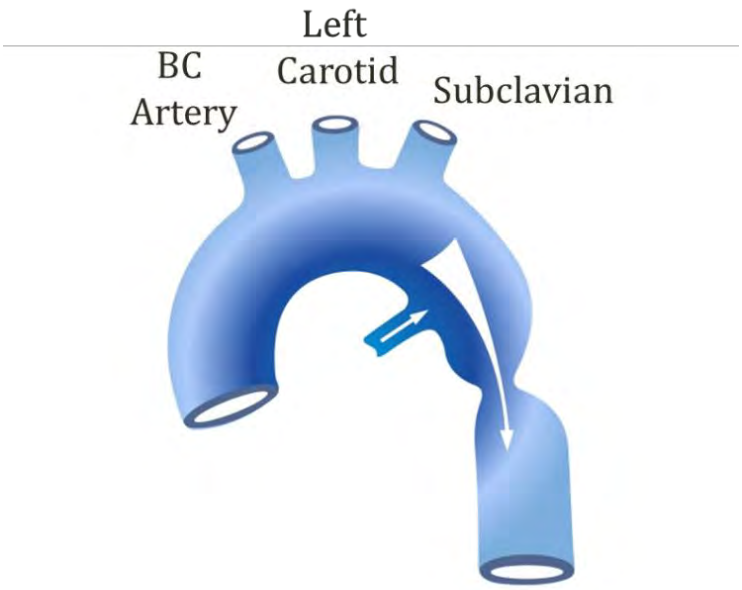
- Key associations: Turner syndrome (45, XO)
- Short stature, webbed neck
- 5-10% have coarctation of the aorta

Johannes Nielsen/Wikipedia

# Coarctation of the Aorta

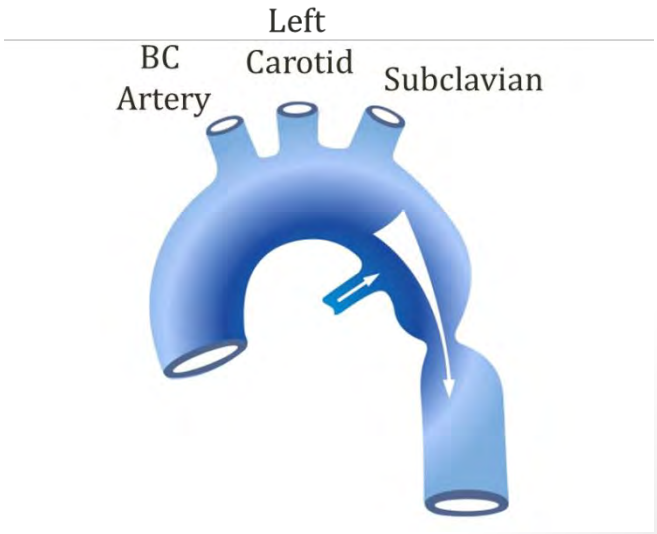
## Postductal or Adult type

- Ductus arteriosus does not supply lower extremities
- Collaterals develop
- May go undetected until adulthood



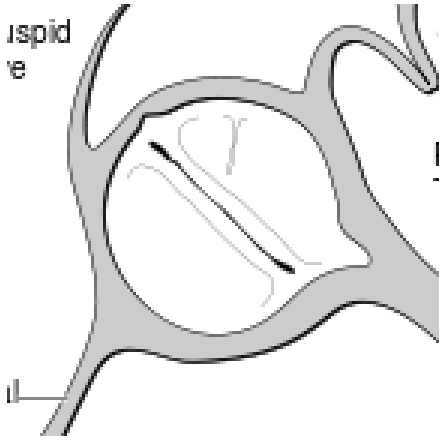
# Coarctation of the Aorta

- Lower extremities → low blood pressure
  - ↑ Renin release
  - Salt/water retention
  - Vasoconstriction (AII)
  - Weak pulses ("brachio-femoral delay")
- Upper extremities and head → **high blood pressure**
- **Secondary hypertension**



# Coarctation of the Aorta

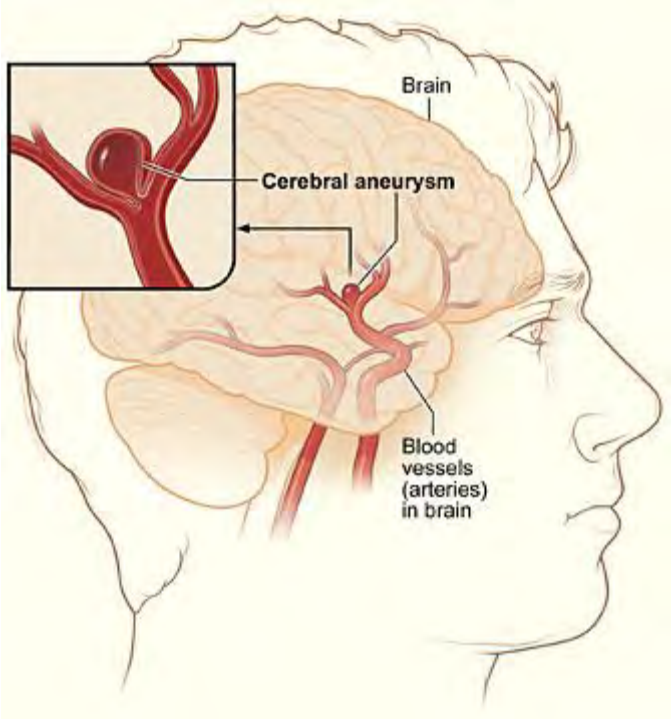
- Key association: **bicuspid aortic valve**
- Found in up to 60% of coarctation cases



Patrick J. Lynch, medical illustrator

# Coarctation of the Aorta

- Key association: **intracranial aneurysms**
- Occur in about 10% of patients with coarctation




Wikipedia/Public Domain

# Coarctation of the Aorta

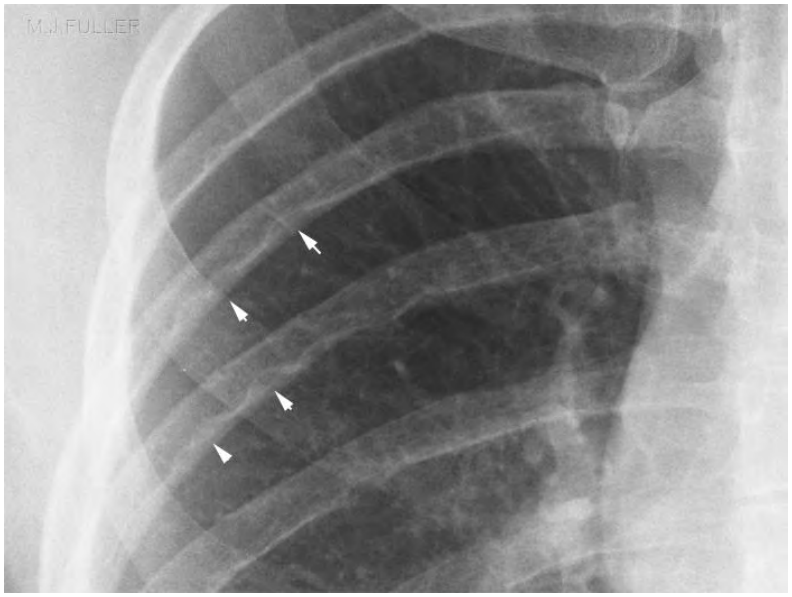
## Signs/Symptoms

- Only sign may be **hypertension** in arms
- Murmur over back between **scapula**
- Weak femoral pulses
- Pain with walking (claudication)

# Coarctation of the Aorta

## Signs/Symptoms

- **Rib notching**
  - High pressure above coarctation
  - Intercostals enlarge to carry blood around obstruction
  - Bulge into ribs
  - “Rib notching” seen on chest x-ray

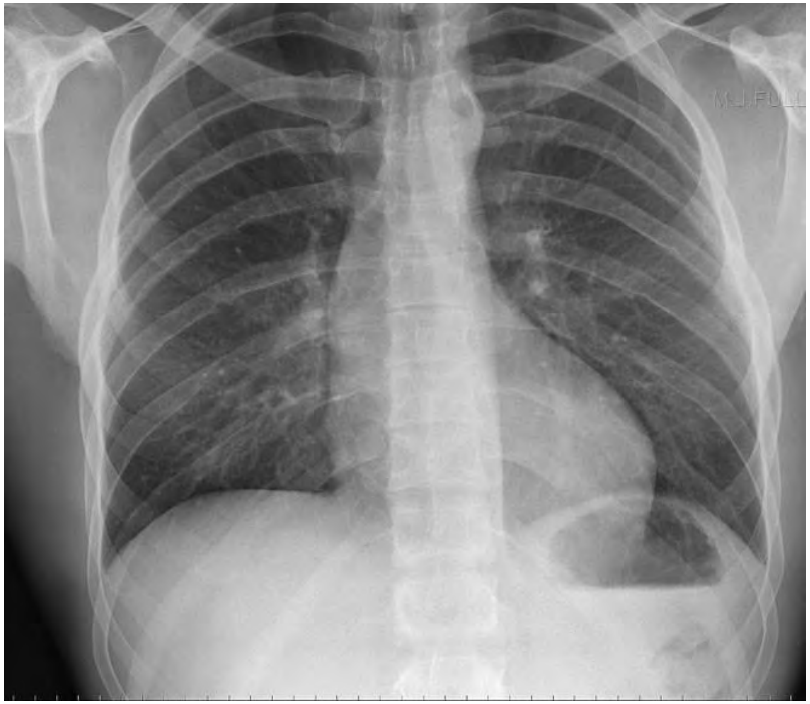



WikiRadiography

# Coarctation of the Aorta

## Signs/Symptoms

- **3-sign**
  - Bulge before and after coarctation
  - "3 sign" on chest x-ray



WikiRadiography

# Coarctation of the Aorta

## Physiology

- **Autoregulation** maintains regional blood flow
  - Normal upper/lower perfusion despite high/low pressures
- Upper extremities
  - High blood pressure → high flow
  - Arterioles constrict to limit flow to normal level
  - Local effect – not mediated by sympathetic/parasympathetic
  - Resistance to flow is high ($Q = \Delta P / R$)
- Lower extremities
  - Low blood pressure
  - Arterioles dilate to increase flow to normal level ($Q = \Delta P / R$)
- Result is normal ("compensated") flow

# Coarctation of the Aorta

## Complications

- Heart failure
  - Pressure overload of left ventricle
- Aortic rupture/dissection
- **Endocarditis/endarteritis**
  - High-low pressure across narrowing
  - Endothelial injury
  - Low pressure distal to narrowing
  - Bacteria may attach more easily

# Hypertension

Jason Ryan, MD, MPH

# Hypertension

- Normal blood pressure: 120/80
- Stage 1 hypertension:
  - Systolic 130-139
  - Diastolic 80-89
- Need more than one measurement

# Etiology

- Most (90%) is primary ("essential") HTN
  - Cause not clear
- Remainder (10%) secondary

# Hypertension

## Risk Factors

- Family history
- African-American race
- High salt intake
- Alcohol
- Obesity
- Physical inactivity

# Sodium Intake

Wikipedia/Public Domain

↑ Na

↓

↑ Posm

↓

↑ ADH

↓

↑ H2O → ↑ ECV → **↑ BP**

↓

**[Na] = 140meq/L**

# Hypertension

## Associations

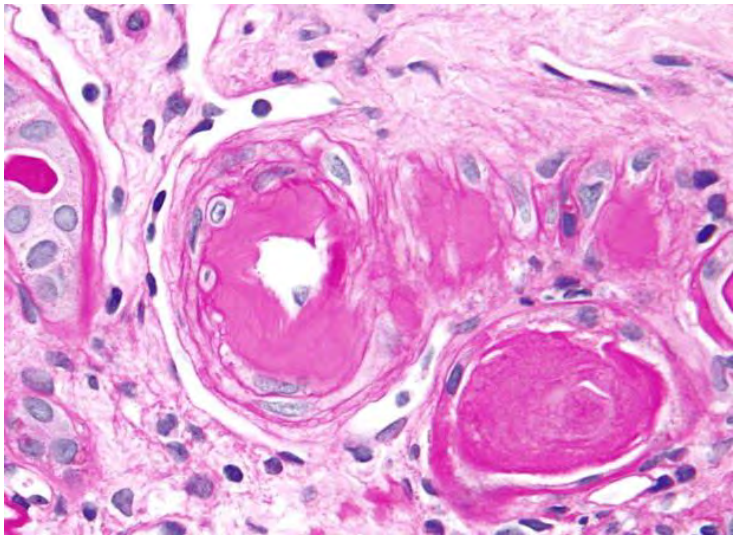
- Stroke
- Heart disease
  - MI
  - Heart failure
- Renal failure
- Aortic aneurysm
- Aortic dissection

# Hypertension Effects

- Atherosclerosis – lipid/fibrous plaques in vessels
- Arteriosclerosis – thickening of artery wall
  - Response to chronic hypertension

# Hypertension Effects

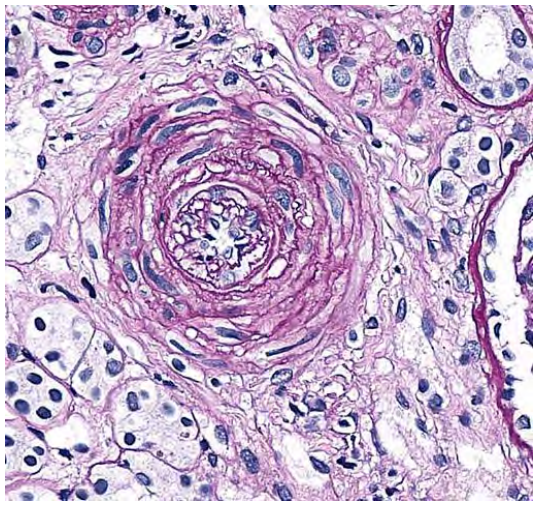
- **Hyaline** arteriosclerosis
  - Thickening of small arteries
  - Seen with aging
  - Also common with diabetes



Nephron/Wikipedia

# Hypertension Effects

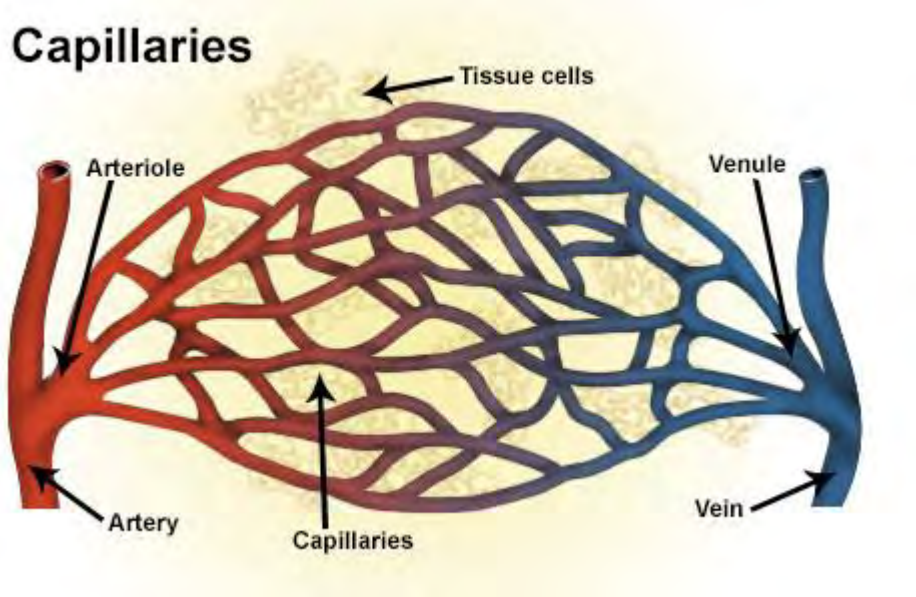
- **Hyperplastic** arteriosclerosis
  - Arteries look like "onion skin"
  - Occurs when hypertension is severe (usually DBP>120)
  - "Malignant" hypertension
  - Retinal hemorrhages, exudates, or papilledema



Pacolarosa/Wikipedia

# Arteriolar Rarefaction

- Loss of arterioles
- Arterioles close off and get resorbed




Wikipedia/Public Domain

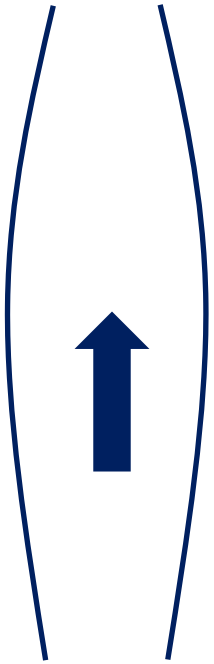
# Hypertension Effects

$$C = \Delta V / \Delta P$$

$$\downarrow$$

$$\Delta P = \Delta V / C$$

- Pulse pressure may increase
  - Example: Normal 120/80; HTN 170/100
  - Stiff arteries → ↓compliance

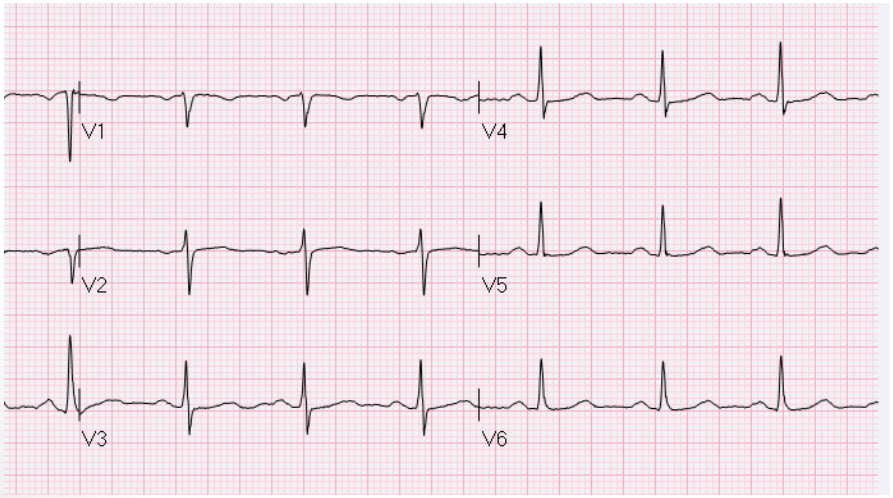


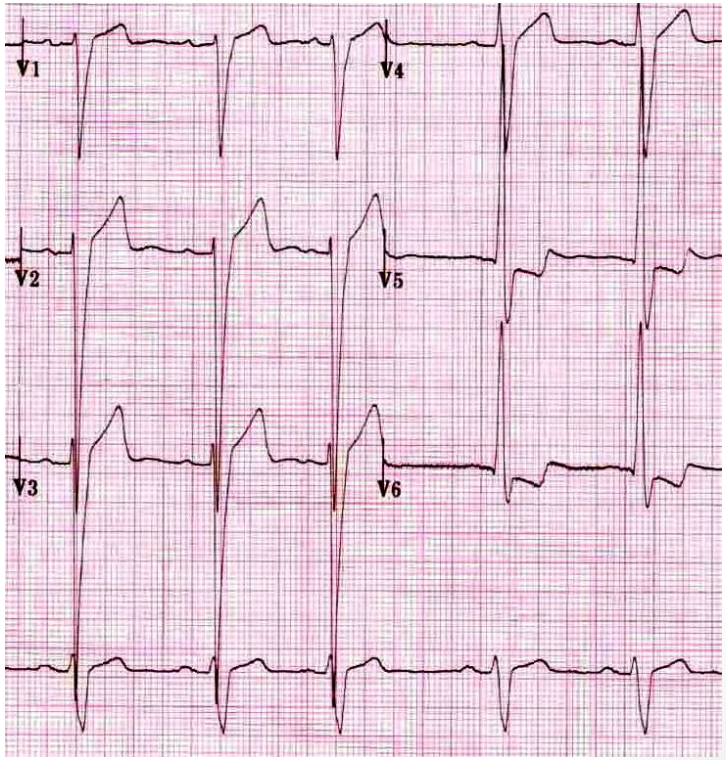
Distensible Vessel 120/80

Stiff Vessel 170/100

# Hypertension Effects

- Afterload on heart is increased
- Left ventricle: concentric hypertrophy
  - Large voltage on EKG
  - Displaced apical impulse
  - S4



# Hypertensive Urgency

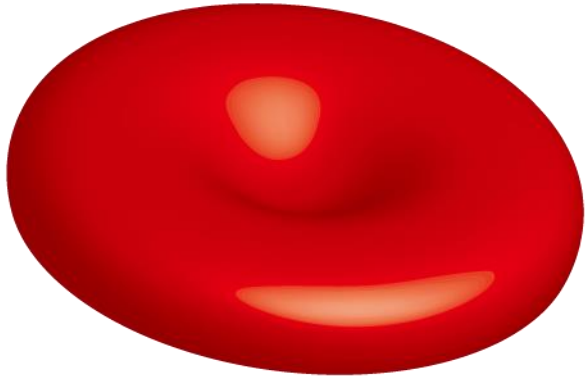
- Severe hypertension without end-organ damage
- No agreed upon BP value
- Usually >180/120

# Hypertensive Emergency

- Also no definite value
- BP usually >180/120
- Patient longstanding HTN, stops meds
- Neurologic impairment
  - Retinal hemorrhages, encephalopathy
- Renal impairment
  - Acute renal failure
  - Hematuria, proteinuria
- Cardiac ischemia

# Hypertensive Emergency

- Associated with MAHA
- Endothelial injury → thrombus formation
- Improved with BP control



Databese Center for Life Science (DBCLS)

# Malignant Hypertension

- Historical term
- Most cases hypertension: “benign”
  - Modestly elevated blood pressure
  - Stable over years
- “Malignant hypertension”
  - Rare form, often fatal
  - Severe elevation of blood pressure (diastolic >120mmHg)
  - Rapidly progressive over 1 to 2 years
  - Renal failure, retinal hemorrhages, ischemia

# Secondary Hypertension

Jason Ryan, MD, MPH

# Etiology

- Most (90%) is primary ("essential") HTN
  - Cause not clear
- Remainder (10%) secondary

# Blood Pressure

## Determinants

- Cardiac output
  - Increased with renal salt/water retention
- Total peripheral resistance
  - Key vessels: arterioles
  - Increased by vasoconstrictors (i.e. catecholamines)
  - Increased by sympathetic nervous system

**BP = CO X TPR**

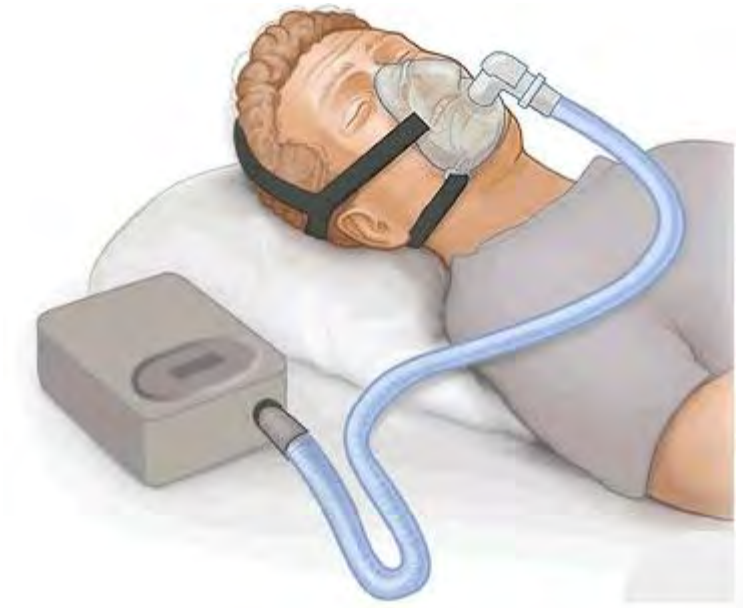
# Chronic Kidney Disease

- Over 80% of patients have hypertension
- Multiple causes:
  - Sodium retention
  - Increased renin-angiotensin-aldosterone activity
  - Increased sympathetic nervous system activity


Anna Frodesiak/Wikipedia

# Obstructive Sleep Apnea

- Sleep-related breathing disorder
- Apnea during sleep
- Often associated with hypertension
- Treatment may reduce BP

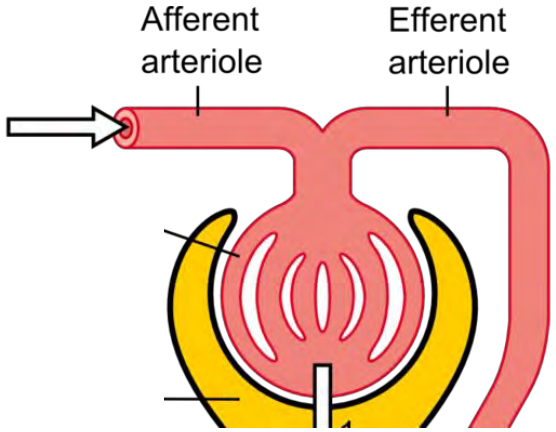


PruebasBMA /Wikipedia

# NSAIDs

## Ibuprofen, naproxen, indomethacin, ketorolac, diclofenac

- Nonsteroidal anti-inflammatory drugs
- Inhibit cyclooxygenase in kidneys
- Decrease synthesis of prostaglandins
- PGE-2: Renal vasodilator




Madhero88 /Wikipedia

# NSAIDs

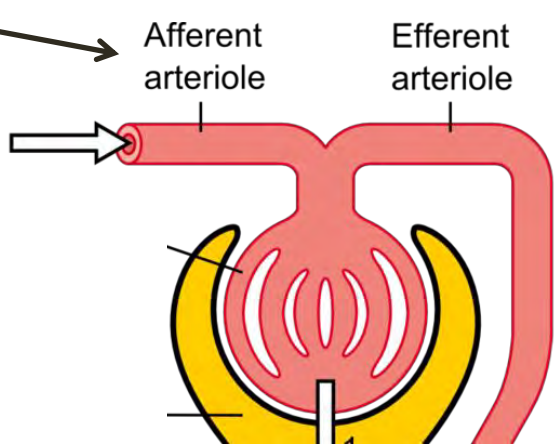
## Ibuprofen, naproxen, indomethacin, ketorolac, diclofenac

- ↓ Na/Water excretion
- May cause **hypertension**
- May exacerbate **heart failure**

**Vasoconstriction**

**↓RBF**

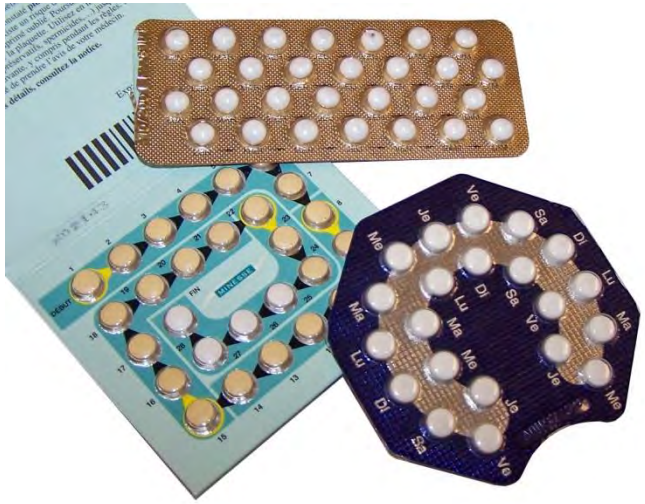
**↓GFR**



# Oral Contraceptive Pills

## OCPs

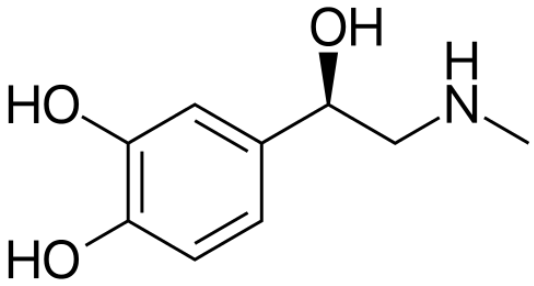
- Estrogen and progesterone analogs
- Cause mild increase in blood pressure



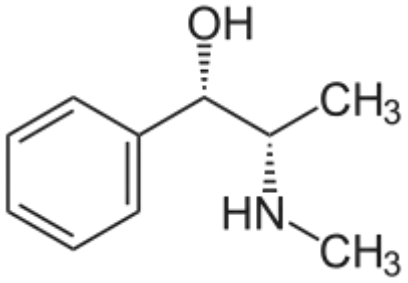
Ceridwen/Wikipedia

# Pseudoephedrine

- Nasal decongestant
- Alpha-1 agonist
- Vasoconstriction → ↓ nasal blood flow




Epinephrine



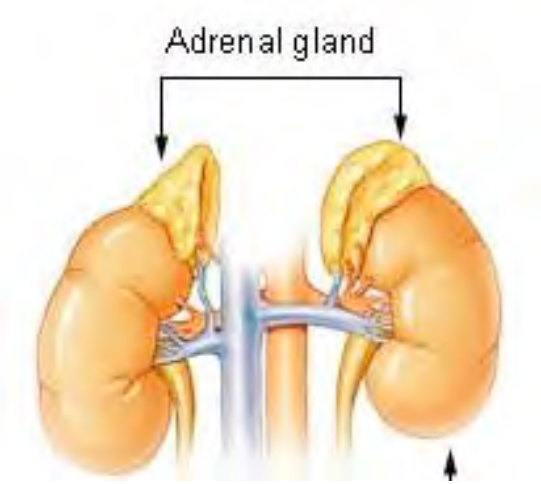

Pseudoephedrine

# Cyclosporine & Tacrolimus

- Immunosuppressants
- Calcineurin inhibitors
- **Renal vasoconstriction** → salt/water retention
- **Diltiazem**: drug of choice
  - Impairs metabolism (↑ drug levels)
  - Treats HTN and allows lower dose cyclosporine to be used

# Primary Aldosteronism

- Excessive levels of aldosterone secretion
- Not due to increased activity of RAAS system
- Adrenal adenoma (Conn's syndrome)
- Bilateral idiopathic adrenal hyperplasia




Wikipedia /Public Domain

# Primary Aldosteronism

- ↑Na reabsorption distal nephron
- ↑ECV → ↑CO → Hypertension
- ↑K excretion → hypokalemia

# Aldosterone Escape

- Excess aldosterone does not lead to volume overload
- Usually no pitting edema, rales, increased JVP
- Na/Fluid retention → hypertension
- Compensatory mechanisms activated
  - Increased ANP
- Increased sodium and free water excretion
- Result: diuresis → **normal volume status**

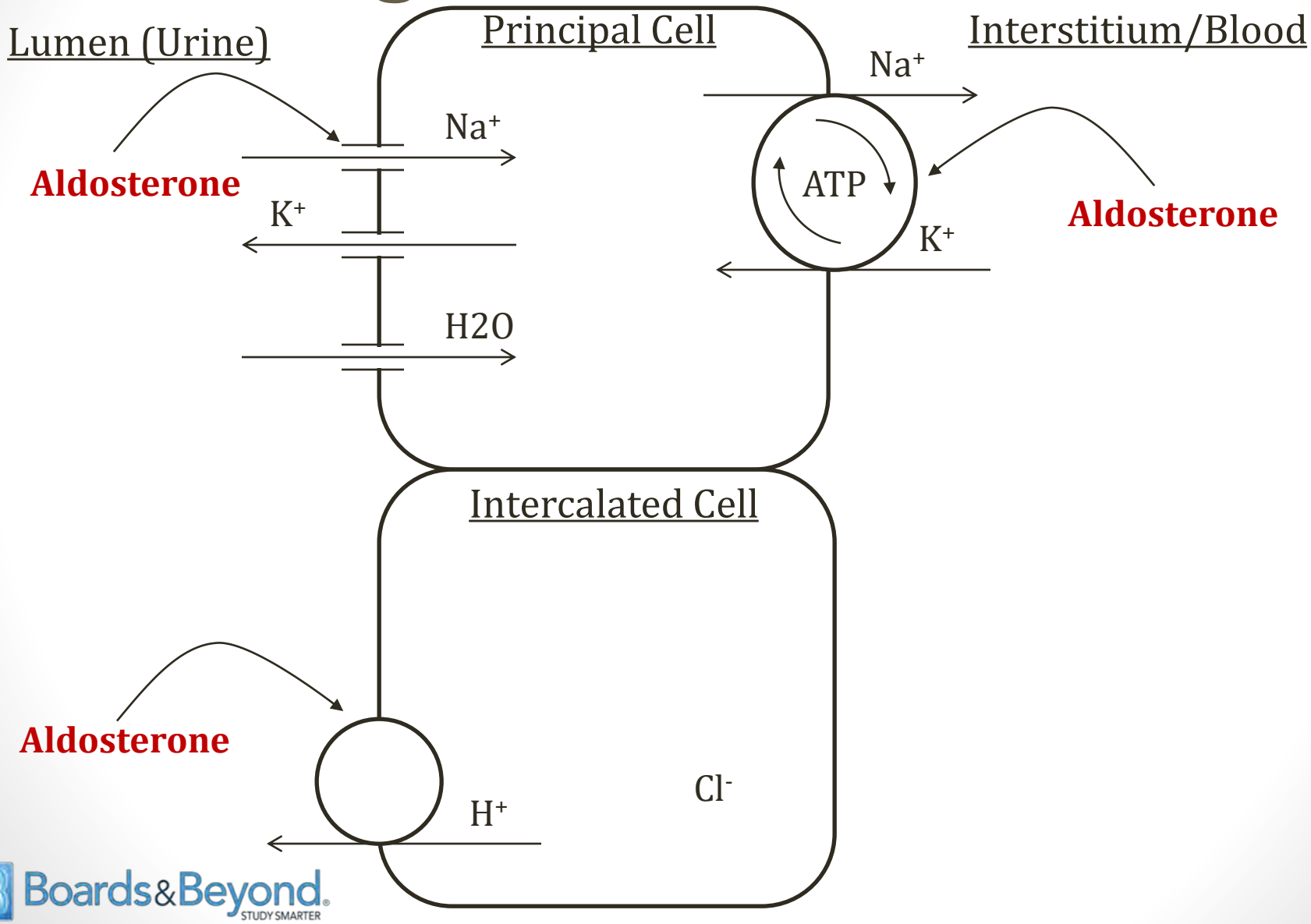
# Primary Aldosteronism

- Clinical features
  - Resistant hypertension
  - Hypokalemia
  - Normal volume status on physical exam
- Diagnosis
  - **Renin-independent** aldosterone section
  - Low plasma renin activity
  - High aldosterone levels
- Drugs of choice: **Spironolactone/Eplerenone**
  - Aldosterone antagonists

# Liddle Syndrome

- Genetic disorder
- **Increased activity of ENaC**
- Similar clinical syndrome to hyperaldosteronism
  - Hypertension
  - Hypokalemia
- **Aldosterone levels low**

# Collecting Duct



# Pheochromocytoma

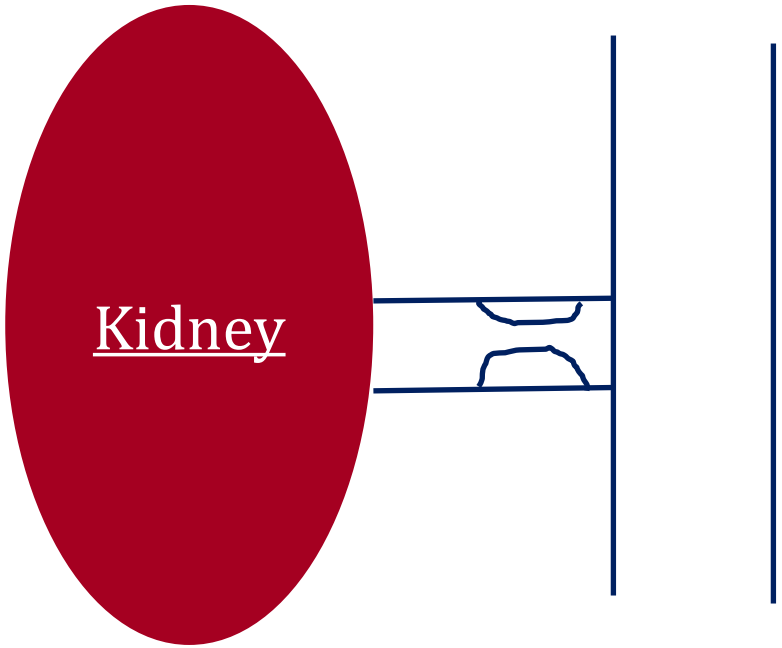
- **Catecholamine-secreting tumor**
  - Epinephrine, norepinephrine, dopamine
- Usually arises from adrenal gland
- Triad: Palpitations, headache, episodic sweating
  - PHEochromocytoma
- Most patient have hypertension
- Diagnosis: Catecholamines breakdown products
  - Metanephrines
  - Vanillylmandelic acid (VMA)

# Cushing's Syndrome

- Excess **cortisol**
- Often from steroid administration
- Other causes
  - Cushing's Disease (pituitary oversecretes ACTH)
  - Tumors (i.e. small cell lung cancer secretes ACTH)
  - Adrenal tumor secretes cortisol
- Cortisol → hypertension
  - Increased vascular sensitivity to adrenergic agonists

# Renal Artery Stenosis

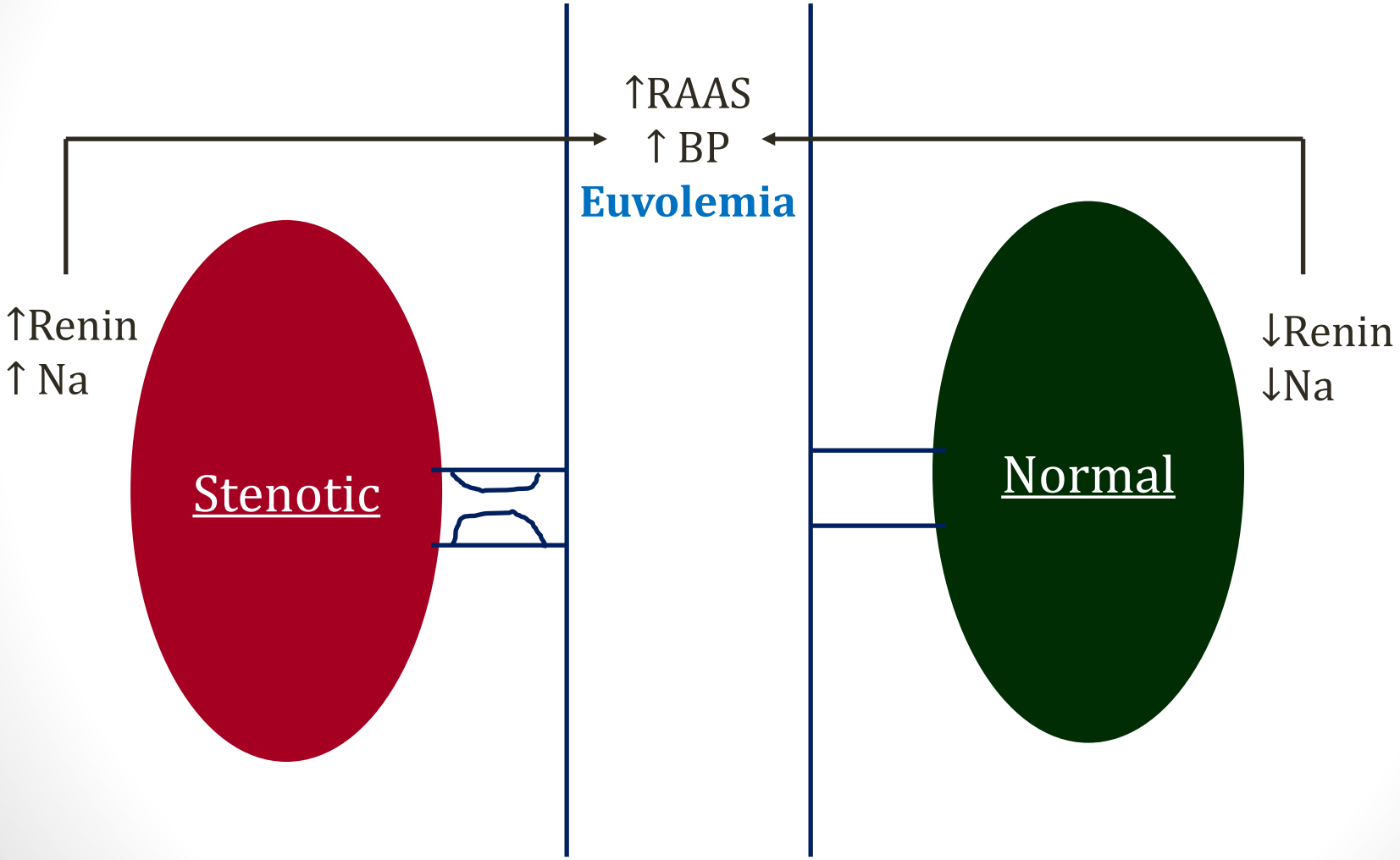
- Vascular disease of renal arteries
- Decreased blood flow to kidneys
- Key exam finding: **renal bruit**



# Renal Artery Stenosis

- Increased renin, salt-water retention → HTN
- Often unilateral stenosis
- Normal kidney compensates
- Results: **No signs of volume overload**

# Renal Artery Stenosis



# Renal Artery Stenosis

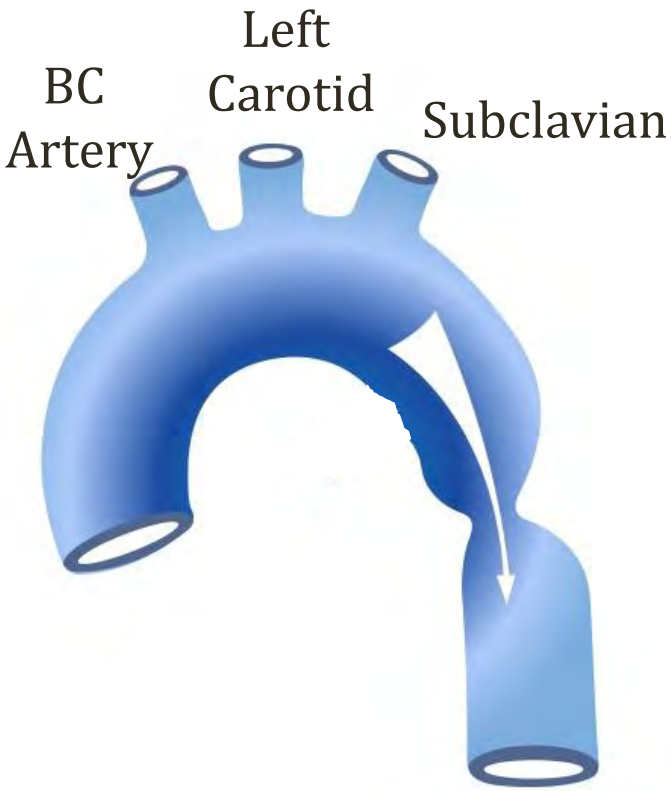
## Angiotensin II

- Normal GFR depends on **angiotensin II**
  - AII → efferent arteriole vasoconstriction
  - Maintains GFR
- ACE inhibitors can precipitate renal failure

# Fibromuscular Dysplasia

- Vascular disease → obstruction to flow
- Common among **women**
- Often occurs in 40s-50s
- Non-atherosclerotic, non-inflammatory
- Often involves **medial layer** fibroplasia
- Stenosis and aneurysms of vessels ("string of beads")
- Most common in renal and carotid arteries
- Can lead to renal artery stenosis

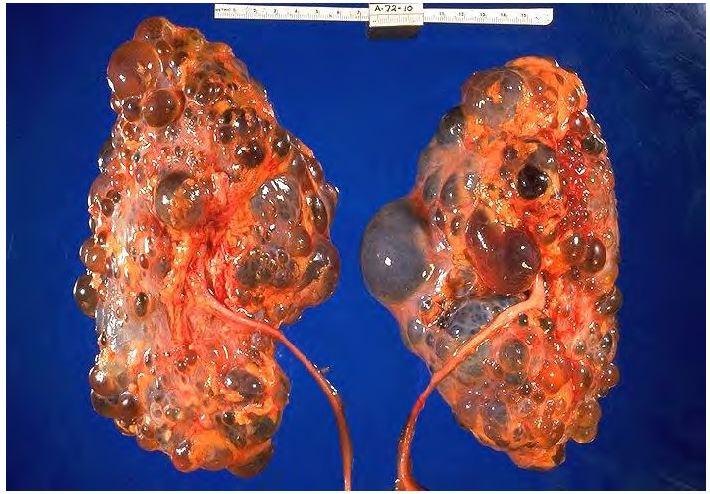
# Coarctation of the Aorta



# ADPKD

## Autosomal dominant polycystic kidney disease

- Genetic disorder
- Mutations of PKD1 or PKD2
- Presents in adulthood with HTN and renal cysts
- Increased RAAS activity

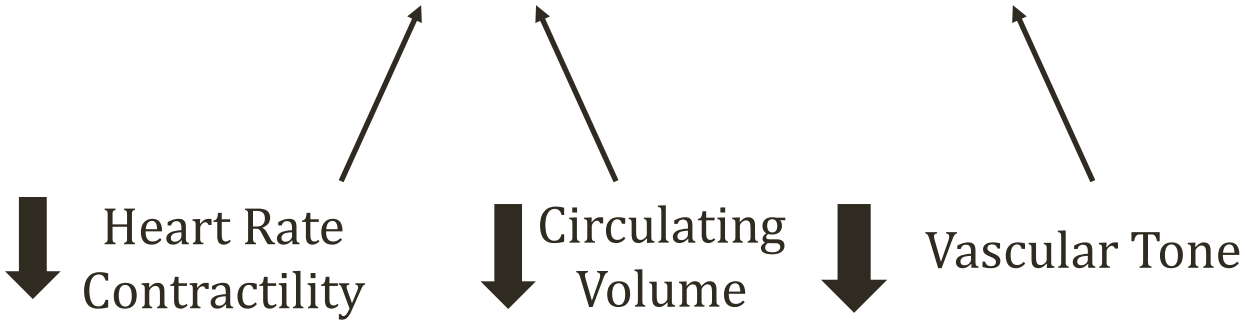


Wikipedia/Public Domain

# Antihypertensives

Jason Ryan, MD, MPH

# BP = CO X TPR



# Beta Receptors

- β1 receptors in heart, kidneys
  - Increase heart rate and contractility
  - Stimulate renin release
  - Blockade → ↓ CO, ↓ ECV → ↓ BP
- β2 receptors
  - Dilate blood vessels (muscle, liver)
  - Bronchodilate
  - Blockade does not lead to lower blood pressure

# Beta Blockers

## β1-selective antagonists

- Atenolol, Metoprolol, Esmolol
- Used for hypertension
  - Blockade → ↓ CO, ↓ ECV → ↓ BP
- Metoprolol: Systolic heart failure
  - Blocks sympathetic stimulation of heart
  - Reduces mortality

# Beta Blockers

## β1β2 (nonselective) antagonists

- Propranolol, Timolol, Nadolol
- Can be used for hypertension
- Nadolol, Propranolol: Used in **portal hypertension**
  - Beta 1 blockade: ↓ CO, ↓ ECV → ↓ BP
  - Beta 2 blockade: ↓ portal blood flow
- Timolol: Used in **glaucoma**
  - Beta 1 and Beta 2 → aqueous humor production

# Beta Blockers

## β1β2α1

- Carvedilol, Labetalol
- Labetalol: Hypertensive Emergency
  - Rapid reduction in blood pressure
- Carvedilol: Systolic heart failure
  - Blocks sympathetic stimulation of heart
  - Reduces mortality

# Beta Blockers

## Partial Agonists

- Pindolol: β1β2 (nonselective)
- Acebutolol: β1-selective
- "Intrinsic sympathomimetic activity"
  - Beta agonist when sympathetic activity is low
  - Beta blocker when sympathetic activity is high
- Can cause **angina** through beta 1 activation
- Special pharmacologic properties

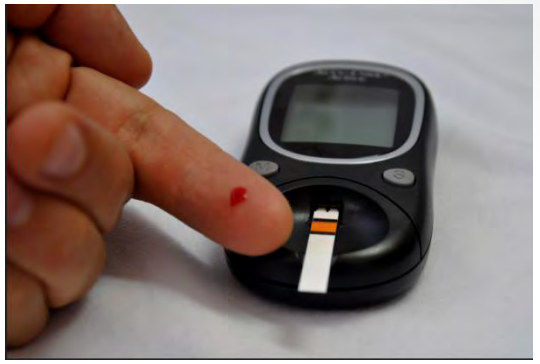
# Beta Blockers

## Side effects

- Fatigue, erectile dysfunction, depression
  - More common with older beta blockers (propranolol)
- Hyperlipidemia
  - Mild increase in triglycerides
  - Mild decrease in HDL
  - Effect varies with different beta blockers

# Beta Blockers

## Side effects



Victor/Flikr

- Caution in **diabetes**
- Blockade of epinephrine effects
  - Epinephrine raises glucose levels
  - Blockade → hypoglycemia
- Blockade of hypoglycemia symptoms
  - ↓ glucose → sweating/tachycardia
  - Symptoms "masked" by beta blockers

# Beta Blockers

## Side effects

- Caution in **asthma/COPD**
  - β2 receptors: bronchodilators
  - β2 blockade may cause a flare
  - β1 blockers ("cardioselective") often used
- Decompensated **heart failure**
  - β1 blockers lower cardiac output → worsening of symptoms
  - Commonly used in compensated heart failure
  - Mortality benefit

# Beta Blockers

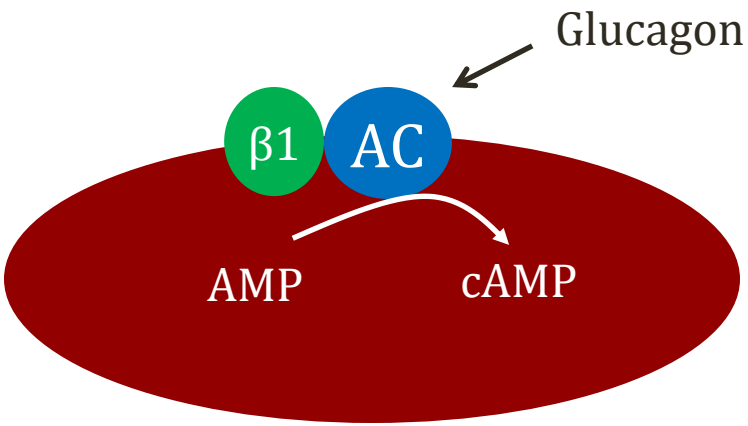
## Overdose

- Depression of myocardial contractility → shock
- Bradycardia/AV block

# Beta Blockers

## Overdose

- Treatment: **Glucagon**
  - Activates adenyl cyclase at different site from beta receptors
  - ↑ cAMP → ↑ intracellular Ca
  - Increased contraction and heart rate



# α1 Blockers

## Tamsulosin, Alfuzosin, Doxazosin, Terazosin

- α1 receptors in periphery: vasoconstrict
- Blockade → vasodilation → ↓ TPR → ↓ BP
- Used in **benign prostatic hypertrophy**
  - Relax smooth muscle of bladder/prostate
  - Increase urine flow
- Common side effect: **Postural hypotension**
- Tamsulosin: "Uroselective"
  - Less hypotension effect

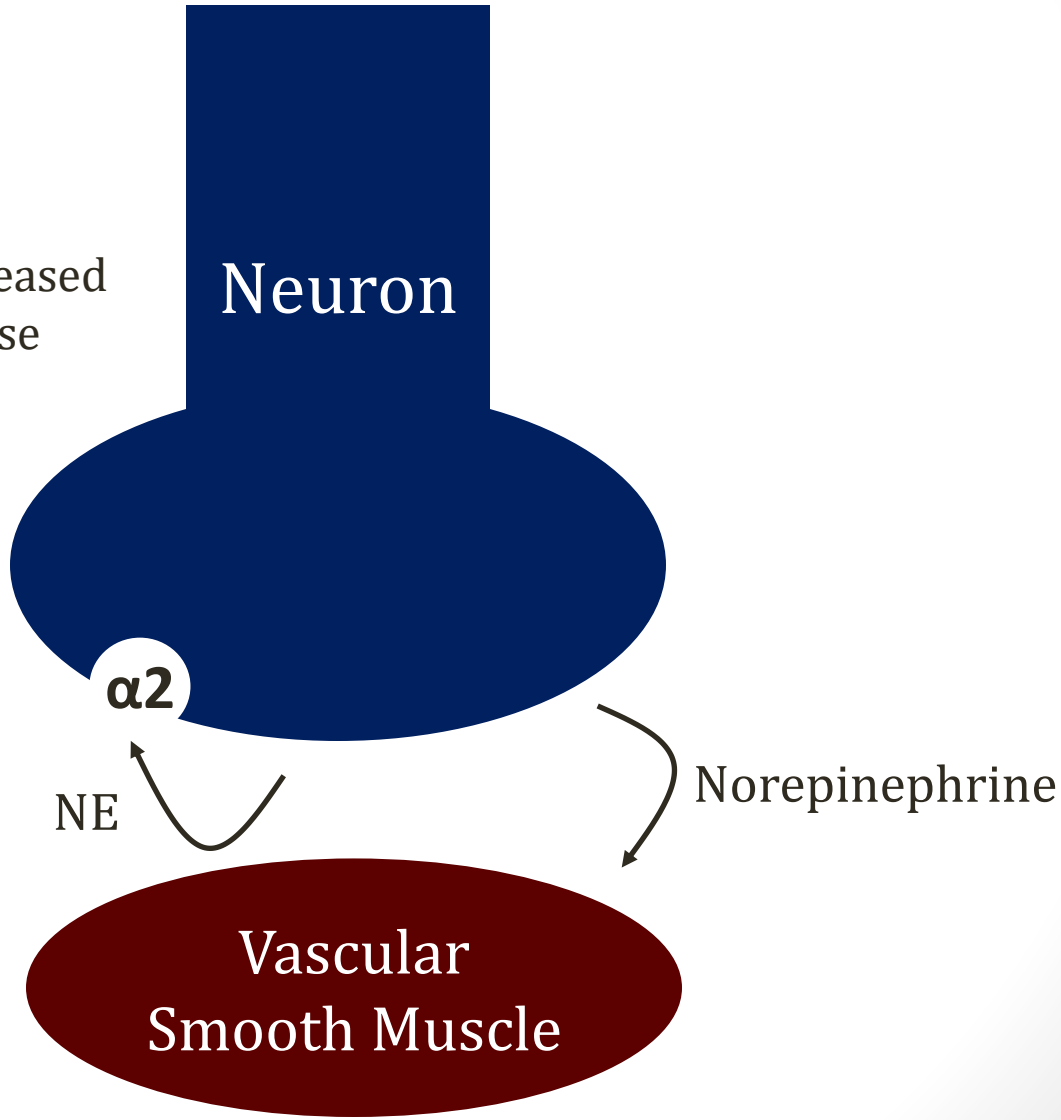
# Alpha 2 Receptors

α2 receptors in CNS

Presynaptic receptor

Feedback to nerve when NE released

Activation leads to ↓NE release



# Clonidine

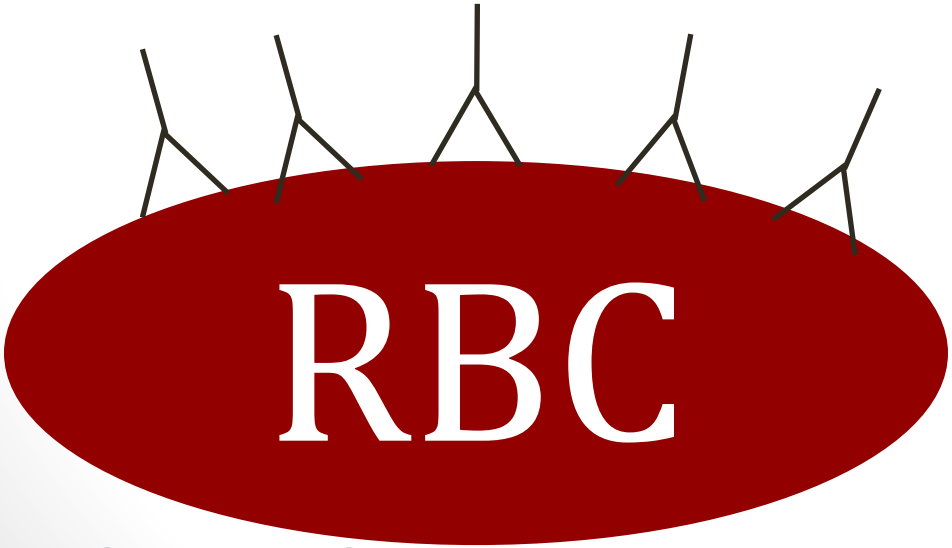
## α2 agonist

- Old, rarely used hypertension drug
- Key side effect: **Rebound hypertension**
  - Abrupt cessation of drug (usually at high dose)
  - Severe hypertension (SBP>200; DBP>120)
  - Symptoms of high BP and sympathetic over-activity
  - Nervousness, sweating, headache, chest pain
- Also causes **sedation**

# Methyldopa

## α2 agonist

- Drug of choice in **pregnancy**
- Also causes sedation
- Key side effect (rare): **Hemolytic anemia**




Øyvind Holmstad/Wikipedia

# Calcium Channel Blockers

- Three major classes of calcium antagonists
  - dihydropyridines (nifedipine)
  - phenylalkylamines (verapamil)
  - benzothiazepines (diltiazem)
- **Vasodilators** and **negative chronotropes/inotropes**

# Calcium Channel Blockers

- Vascular smooth muscle effects
  - Nifedipine>Diltiazem>Verapamil
- Heart rate/contractility effects
  - Verapamil>Diltiazem>Nifedipine

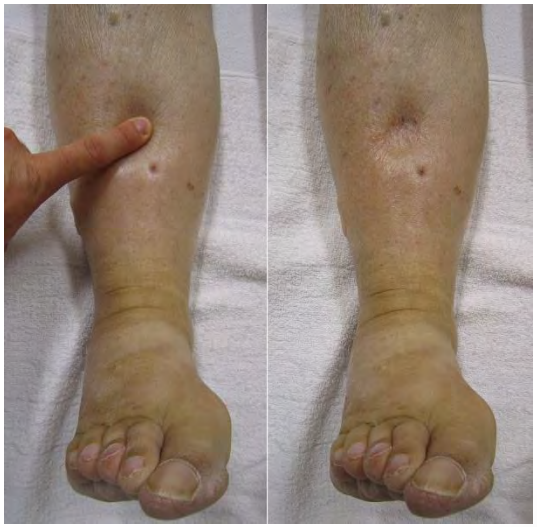
# Calcium Channel Blockers

- Dihydropyridines (nifedipine) → vasodilators
  - Main effect: ↓TPR
- Non-dihydropyridines (Verapamil, diltiazem)
  - Similar to β1 blockers
  - Main effects: ↓HR; ↓ contractility

# Calcium Channel Blockers

## Dihydropyridines (nifedipine)

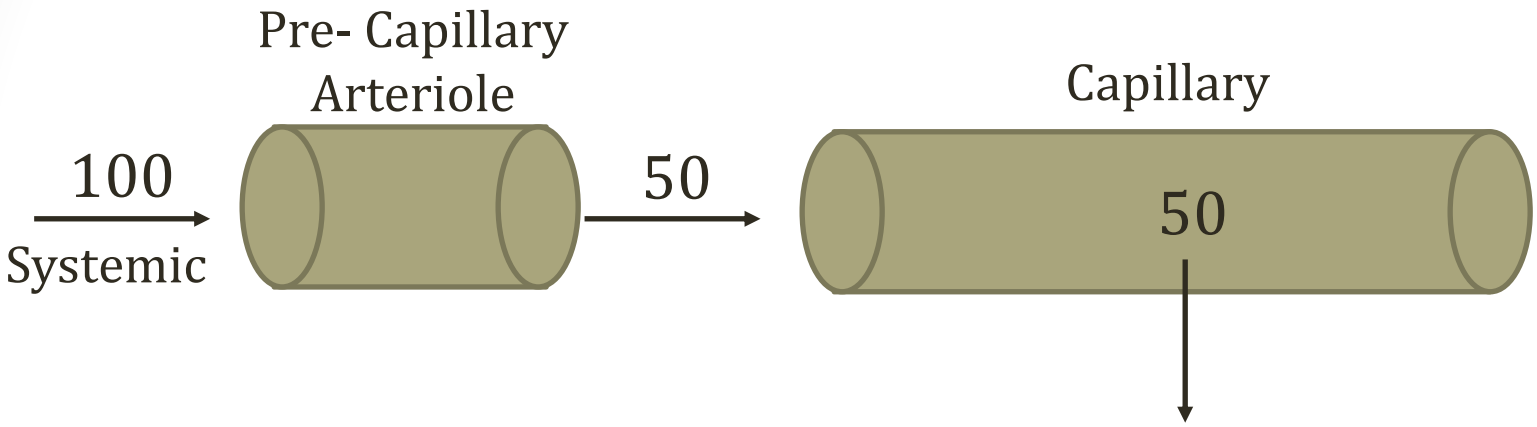
- Used for hypertension
- Flushing, headache, hypotension
  - Peripheral vasodilation
- Key side effect: edema
  - Increased ***capillary*** hydrostatic pressure
  - **Pre-capillary arteriolar vasodilation**

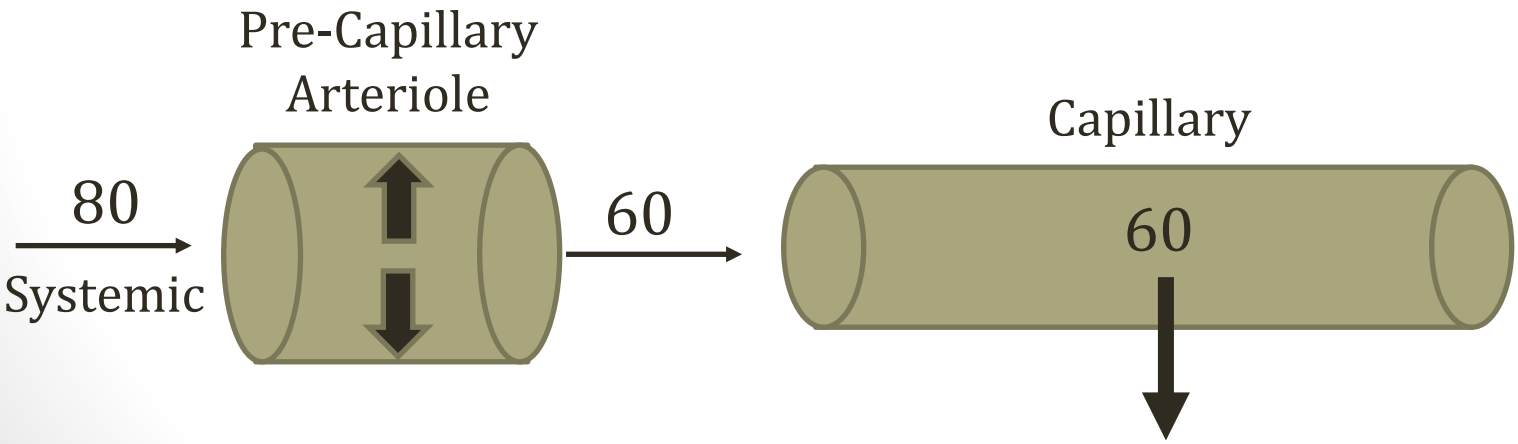


James Heilman, MD/Wikipedia

# Calcium Channel Blockers

## Dihydropyridines (nifedipine)



# Calcium Channel Blockers

## Verapamil, diltiazem

- Used for hypertension
- Also used in heart disease
  - Arrhythmias (atrial fibrillation)
  - Stable angina (lower oxygen demand)
- Potential side effect: Negative inotropes
  - Can precipitate heart failure

# Calcium Channel Blockers

## Other Side Effects

- Constipation
  - Most commonly with **verapamil**

Elya/Wikipedia

# Calcium Channel Blockers

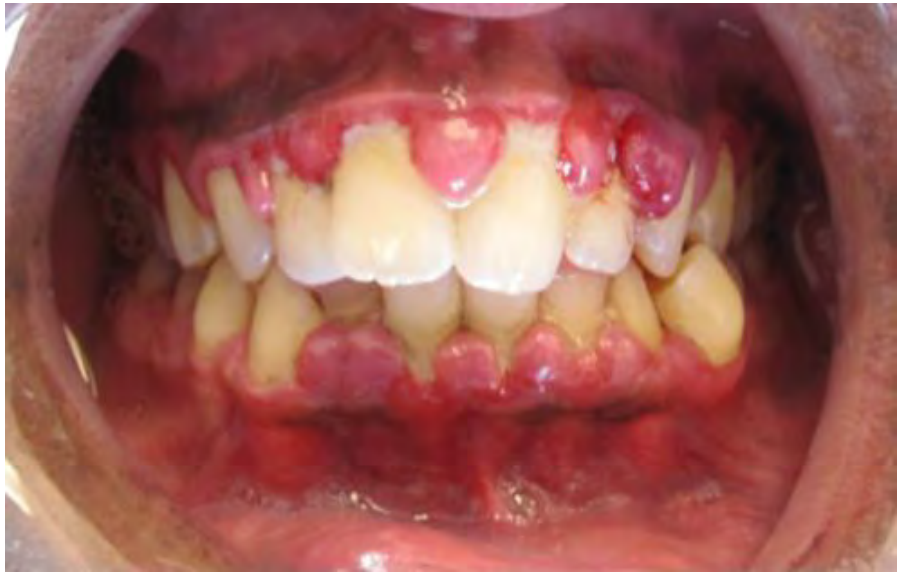
## Other Side Effects

- Hyperprolactinemia
  - Seen with **verapamil**
  - Blocks calcium channels CNS → ↓ dopamine release
  - Causes hypogonadism
  - Men: ↓ libido, impotence
  - Pre-menopausal women: irregular menses, galactorrhea

# Calcium Channel Blockers

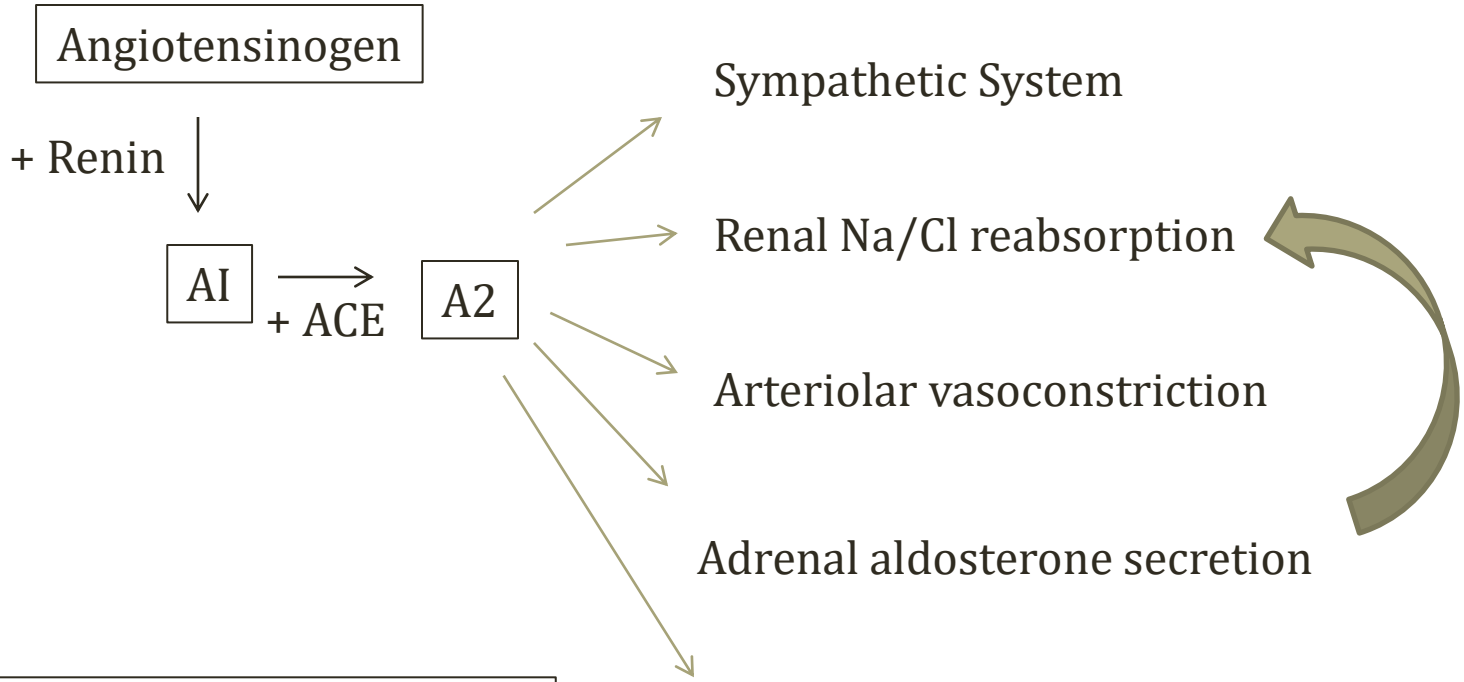
## Other Side Effects

- Gingival hyperplasia
  - Seen in all types CCB
  - Also with phenytoin, cyclosporine



Lesion/Wikipedia

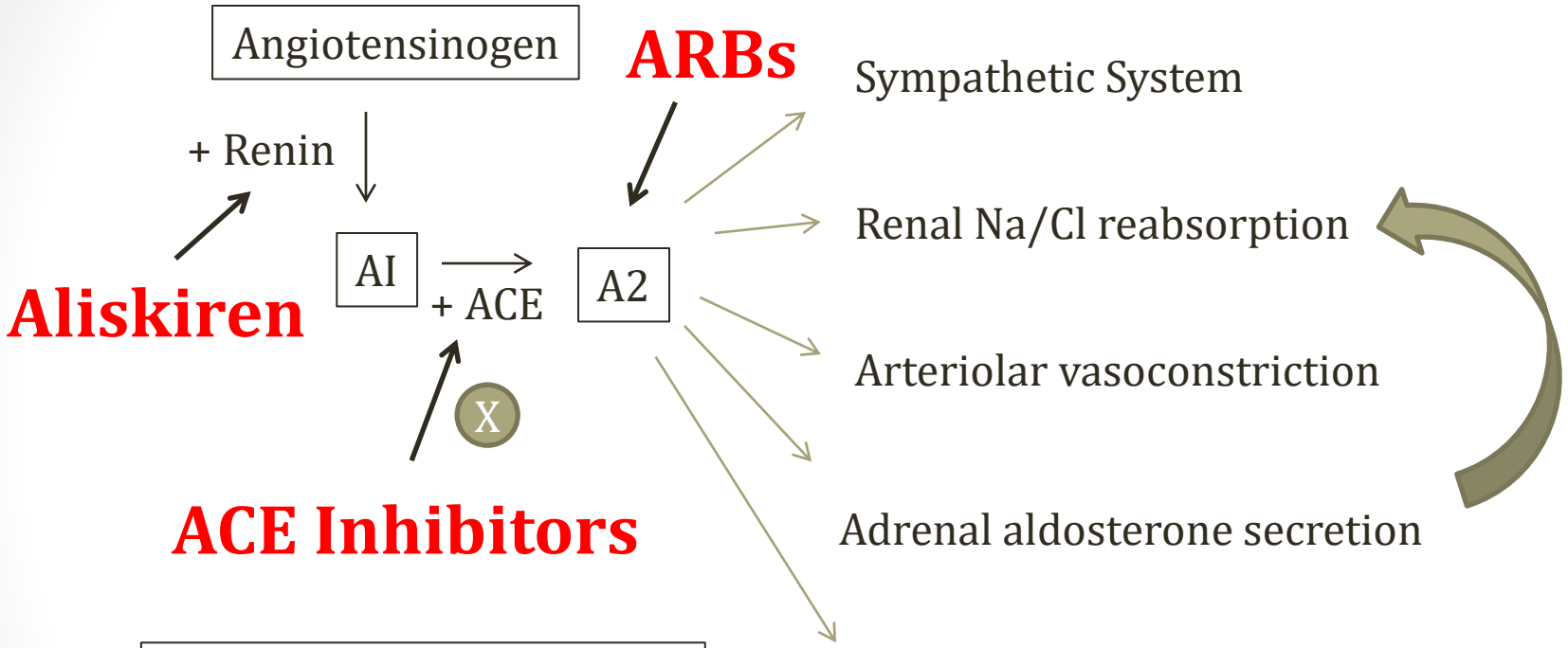
# Angiotensin II




## Net Result

↑Salt/Water Retention
↑Preload
↑Afterload
**↑BP**

# Angiotensin II Inhibition



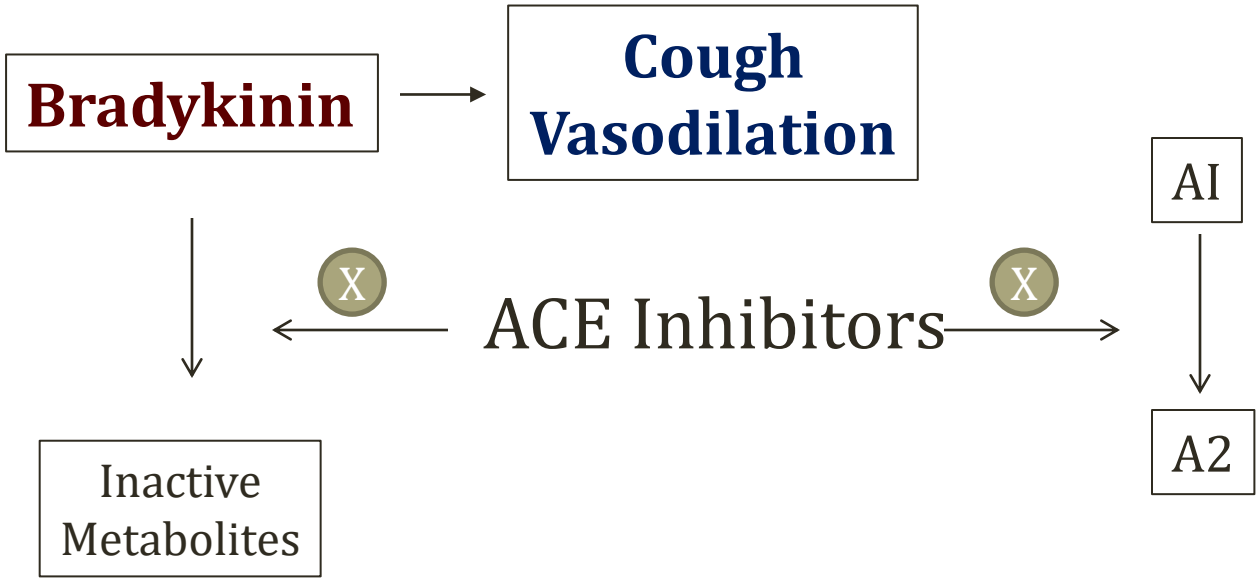

## Net Result

↑Salt/Water Retention
↑Preload
↑Afterload
**↑BP**

# AII Drugs

- ACE Inhibitors
  - Captopril, Enalapril, Lisinopril, Ramipril
- Angiotensin Receptor Blockers (ARBs)
  - Candesartan, Irbesartan, Valsartan
- Side effects
  - Hyperkalemia (↓aldosterone)
  - Renal failure (↓GFR)

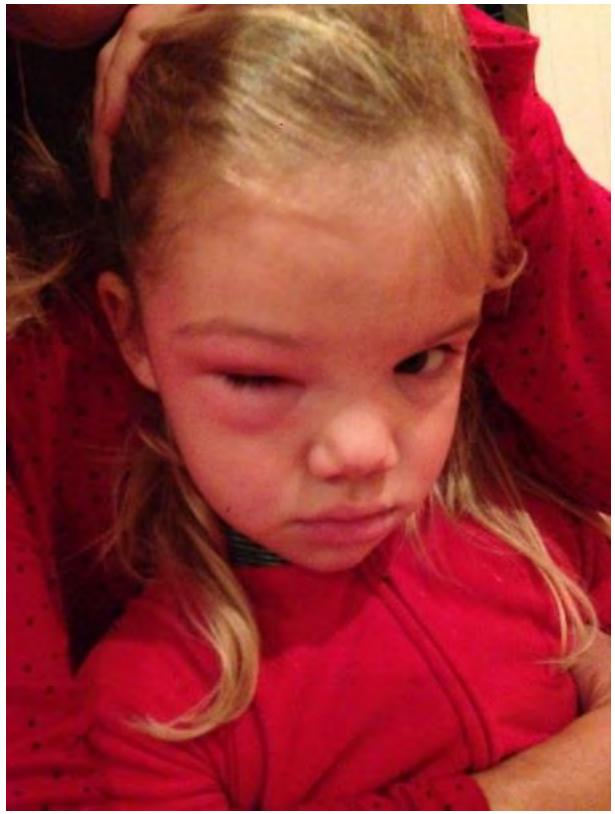
# Bradykinin



# ACE Inhibitors

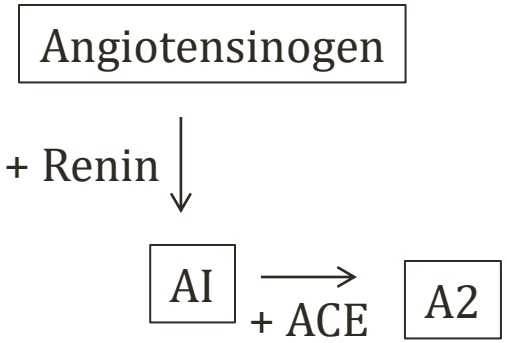
## Unique Side Effects

- Due to increased **bradykinin**
- Dry Cough
  - Occurs in ~10% of patients
- Angioedema
  - Swelling of face, tongue
  - Can be life-threatening



# Aliskiren

- Direct renin inhibitor
- Reduces angiotensin I levels (unique effect)



# Diuretics

- Loop diuretics
  - Furosemide, bumetanide, torsemide, ethacrynic acid
- Thiazide diuretics
  - **Hydrochlorothiazide**; chlorthalidone; metolazone
- Potassium sparing diuretics
  - Spironolactone, Eplerenone, Triamterene, Amiloride

# Hydralazine

- Direct arteriolar vasodilator
- Rarely used for hypertension
- Combined with nitrates for heart failure
- Safe in pregnancy
- Causes drug-induced lupus

# Drug-induced Lupus

- Syndrome similar to lupus
  - Often rash, arthritis, low blood cell counts
  - Milder than SLE
  - Usually no associated renal failure/CNS disease
- Key finding: **anti-histone antibodies**
- Three drugs
  - Hydralazine
  - Procainamide
  - Isoniazid

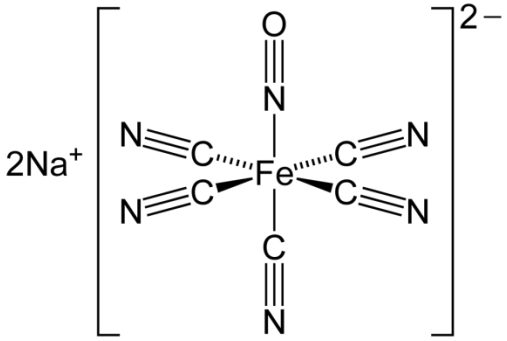
# Hypertensive Emergency

- Unique drugs used for therapy
  - Intravenous, rapid acting
- Lowering BP too fast can cause ischemia
  - Autoregulation of vascular beds → vasoconstriction


KOMUNews/Flikr

# Hypertensive Emergency

- **Nitroprusside**
  - Short acting drug
  - ↑ intracellular cGMP
  - ↑ nitric oxide release
  - Venous and arteriolar vasodilation
  - ↓ preload (VR); ↓ afterload
- **Cyanide toxicity** with prolonged use
  - Multiple cyanide groups per molecule
  - Inhibits electron transport
  - Toxic levels with prolonged infusions



Sodium Nitroprusside

# Hypertensive Emergency

- **Fenoldopam**
  - D1 agonist
  - Arteriolar vasodilation
  - Increased urinary sodium/water excretion
  - Maintains renal perfusion while vasodilating

# Hypertensive Emergency

- Labetalol
  - β1 and α1 Blocker
- Esmolol
  - Rapid acting intravenous β1 blocker
- Nicardipine, Clevidipine
  - Intravenous dihydropyridine calcium channel blocker

# Orthostatic Hypotension

## Postural Hypotension; Orthostasis

- ↓blood pressure due to gravity with standing
- Compensation from **sympathetic nervous system**
  - Increased VR, CO, HR, TPR
  - Impaired with **low volume, low TPR, blunted ANS**
- Severe ↓BP (>20mmHg) = orthostatic hypotension
  - Dizziness, syncope
- Common etiologies:
  - Hypovolemia
  - Hypertensive medications

# Orthostatic Hypotension

## Postural Hypotension; Orthostasis

- Alpha-1 blockers
- ACE-inhibitors
  - Especially in patients on diuretics
  - Volume depletion → ↑RAAS
  - "First dose hypotension"

# Reflex Tachycardia

- Vasodilation → ↓BP → ↑SNS
- Reflex response: ↑ HR
- Can be caused by vasodilators
  - Hydralazine
  - Alpha-1 blockers
  - Dihydropyridine calcium channel blockers
  - Nitroglycerine
- May exacerbate chronic stable angina
- Drugs may be co-administered with β blocker

# Choosing Drugs

- Diabetes
  - ACE inhibitors: Protective of kidneys
  - Beta blockers can lower glucose and mask hypoglycemia
  - HCTZ can increase glucose
- Systolic Heart Failure
  - ACEi, beta blockers, aldosterone blockers: mortality benefit
  - Calcium channel blockers → ↓ contractility

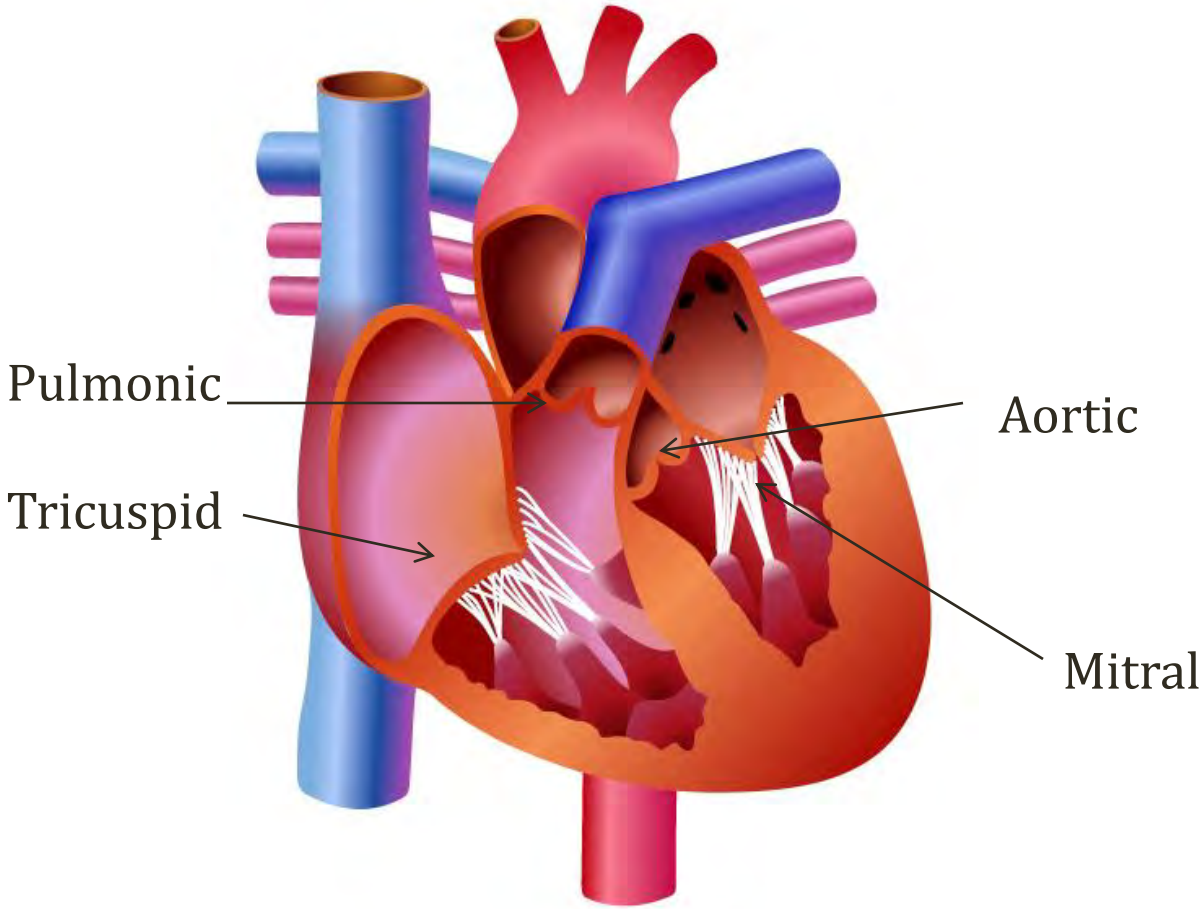
# Choosing Drugs

- Hypertension in Pregnancy
  - Methyldopa
  - Beta blockers, nifedipine, hydralazine
  - Avoid: **ACE inhibitors, ARBs, direct renin inhibitors**
  - Associated with congenital malformations
- Significant renal failure or ↑K
  - Avoid: ACE-inhibitors, ARBs (↓AII, ↓aldsoterone)
  - Avoid: Potassium sparing diuretics (↑ K)
  - Avoid: Other diuretics (↓ECV → ↓GFR)
  - Calcium blockers, beta blockers usually ok

# Valve Disease

Jason Ryan, MD, MPH

# Heart Valves



# Valve Disease

- **Stenosis**
  - Stiffening/thickening of valve leaflets
  - Obstruction to forward blood flow
- **Regurgitation**
  - Malcoaptation of valve leaflets
  - Leakage of blood flow backwards across valve

# Valve Lesions - Systole

- Occur when heart contracts/squeezes
- Aortic stenosis
- Mitral regurgitation
- Pulmonic stenosis
- Tricuspid regurgitation

# Valve Lesions - Diastole

- Occur when heart relaxes/fills
- Aortic regurgitation
- Mitral stenosis
- Pulmonic regurgitation
- Tricuspid stenosis

# Valve Disorders

## Treatments

- Only **severe** valvular lesions treated
- Mostly **surgical diseases**
- Surgical repair
  - Often done for mitral valve prolapse → mitral regurgitation
- Valve replacement
  - Bioprosthetic (pig or cow)
  - Mechanical (requires life-long anticoagulation)
- Valvuloplasty (stenotic lesions)

# Stenotic Valve Disorders

- Stiff valve
- “Gradient” across valve
- High pressure upstream
- Lower pressure downstream

# Rheumatic Fever

- Occurs weeks after **streptococcal pharyngitis**
- Common in **children**
- Autoimmune: type II hypersensitivity reaction
- Antibodies to bacterial **M proteins** cross-react

# Rheumatic Fever

- **Jones** criteria
  - **J**oints: Polyarthritis (>5 joints)
  - ❤: Carditis (valvulitis, myocarditis, pericarditis)
  - **N**odules (subcutaneous)
  - **E**rythema marginatum (rash on trunk)
  - **S**ydenham chorea  (jerking movement disorder)

# Rheumatic Heart Disease

- Damage to heart valves by rheumatic fever
- **Mitral valve** most commonly involved
- Often presents years after acute rheumatic fever
- Many patients do not recall acute symptoms
- Common in **developing countries**
  - Limited access to medical care for pharyngitis
  - Often seen in **immigrants** to US

# Carcinoid Heart Disease

- Caused by carcinoid tumors of intestines
- Secrete **serotonin**
- Fibrous deposits **tricuspid/pulmonic valves**
- Leads to stenosis and regurgitation
- Serotonin inactivated by lungs
- Left sided lesions rare

# Aortic Stenosis

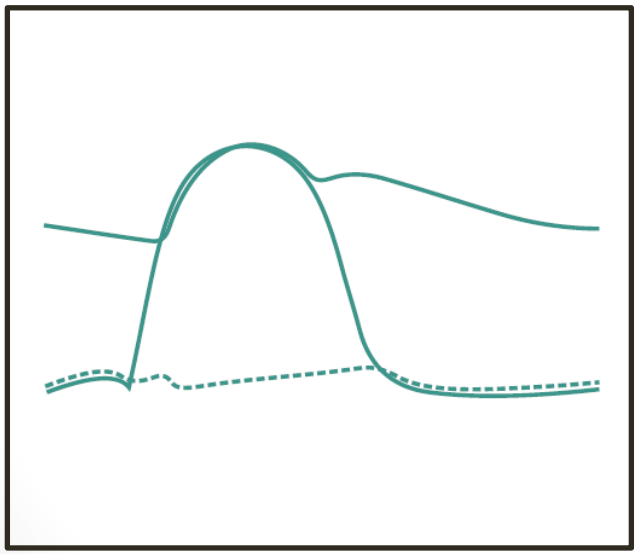
## Pathophysiology

- Stiff aortic valve
- Systolic problem
- **Increased afterload**

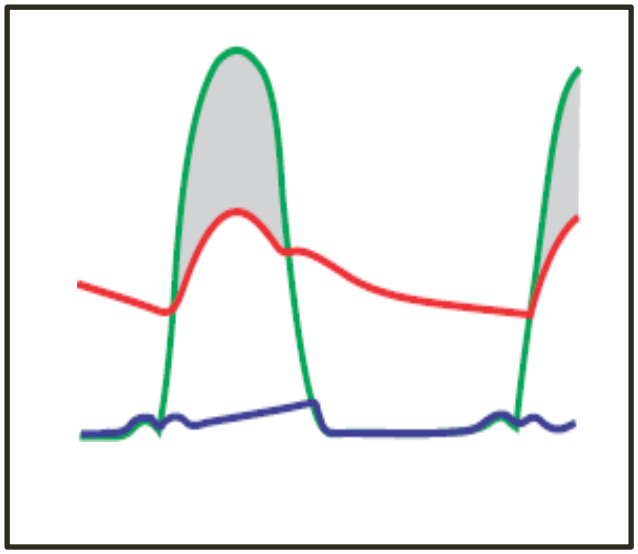
# Aortic Stenosis

## Hemodynamics

- **LV pressure systolic >> aortic pressure**
  - LVSP = 160mmHg (normal = 120)
  - SBP = 120mmHg (normal = 120)
  - Gradient = 40mmHg
- ↑ **LVEDP** due to ↑ afterload



Normal



Aortic Stenosis

# Aortic Stenosis

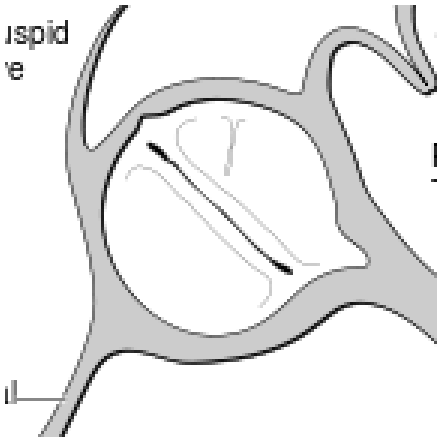
## Clinical features

- Systolic crescendo-decrescendo murmur
- **Syncope:** failure to ↑CO due to ↑ afterload
- **Angina**: ↑ LVEDP → ↓ coronary blood flow
- **Left heart failure**: ↑ LVEDP

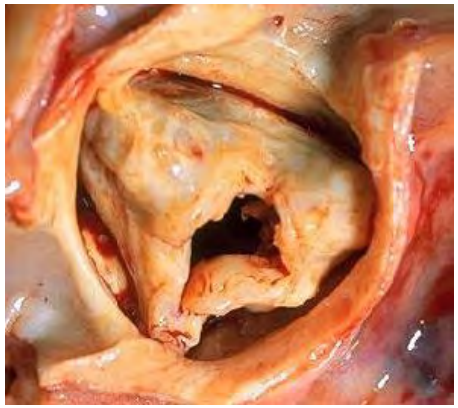
# Aortic Stenosis

## Causes

- **Senile aortic stenosis**
  - "Wear and tear"
  - Collagen breakdown
  - Calcium deposition
- **Bicuspid aortic valve**
- Rarely rheumatic heart disease



Patrick J. Lynch, medical illustrator



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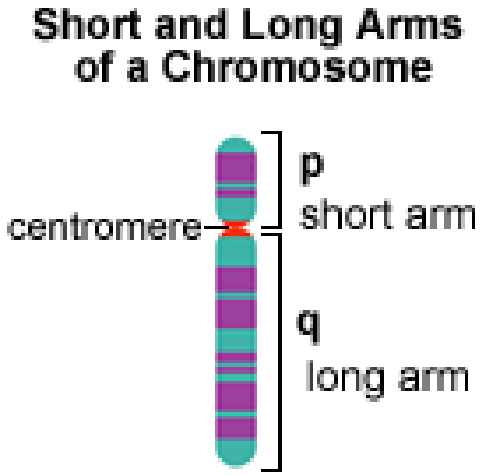
# Supravalvular Aortic Stenosis

- Narrowing of ascending aorta above aortic valve
- Seen in **Williams syndrome**
- Genetic deletion syndrome

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# Mitral Stenosis

## Pathophysiology

- Stiff mitral valve
- Diastolic problem
- **LA pressure >> LV diastolic pressure**
  - Left atrial pressure 20mmHg (normal = 10)
  - LVEDP 5mmHg (normal = 10)
  - Gradient = 15mmHg
- **Decreased preload**

# Mitral Stenosis

## Clinical features

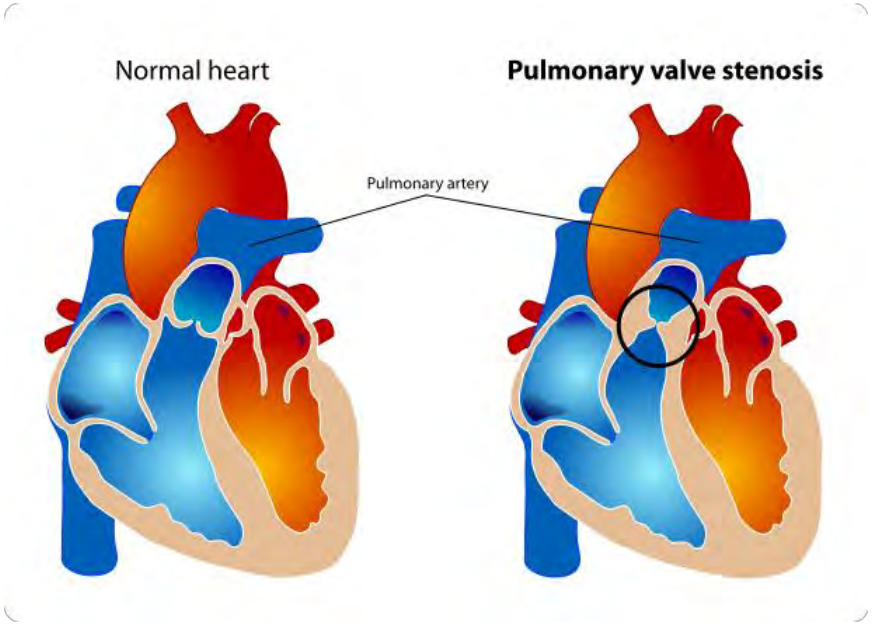
- Caused by **rheumatic fever**
- Most common symptom: dyspnea
  - ↑ LA pressure → pulmonary congestion
- Murmur: diastolic rumble with opening snap

# Tricuspid Stenosis

- Very rare valve disorder
- **Diastolic murmur at left lower sternal border**
- Caused by rheumatic fever (with mitral disease)
  - Tricuspid regurgitation more common
- Carcinoid heart disease

# Pulmonic Stenosis

- **Congenital defect** in children
  - Fused commissures with thickened leaflets
- Carcinoid heart disease

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# Regurgitant Lesions

- Acute and chronic forms
- Acute regurgitation (often from endocarditis)
  - May cause shock
  - Activation of sympathetic nervous system
  - Increased contractility
  - Increased afterload
- Chronic regurgitation
  - No shock
  - Leads to chronic heart failure
  - Sympathetic activation only if severe heart failure

# Aortic Regurgitation

## Pathophysiology

- Blood leaks across aortic valve
- Diastolic problem
- **Increased preload, stroke volume**
- Increased afterload
  - More stroke volume → aorta → ↓ compliance (stiffening)
- Blowing diastolic murmur

# Aortic Regurgitation

## Causes

- **Dilated aortic root** → leaflets pull apart
  - Often from HTN or other aortic aneurysm
  - Rarely from tertiary syphilis (aortitis)
- **Bicuspid aortic valve**
  - Turner syndrome
  - Coarctation of the aorta
- Endocarditis
- Rheumatic heart disease
  - Almost always with mitral disease

# Aortic Regurgitation

## Clinical features

- Leaking blood back into LV causes **low diastolic BP**
  - 120/80 (normal) → 120/40
  - Low diastolic pressure
- **Wide pulse pressure**
  - High cardiac output with low diastolic pressure
- Wide pulse pressure symptoms
  - "Water hammer" pulses
  - Head bobbing
  - Many, many others (mostly historical)

# Mitral Regurgitation

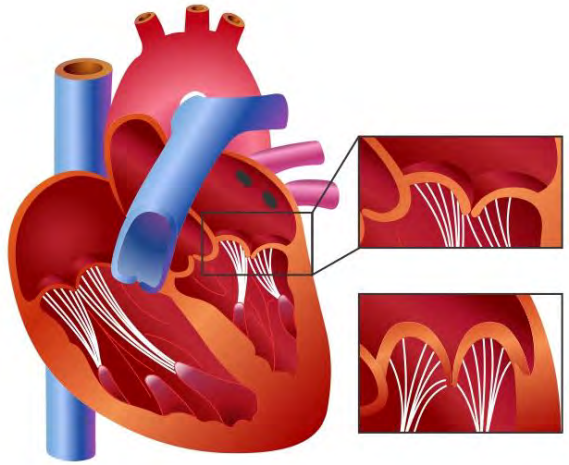
## Pathophysiology

- Blood leaks across mitral valve
- Increased LA volume → Starling mechanism
- Increased left ventricular filling from LA
- **Increased preload, stroke volume**
- Reduced afterload

# Mitral Regurgitation

## Causes

- Primary MR caused by **mitral valve prolapse**
  - Also called degenerative or myxomatous
- Billowing of mitral valve leaflets above annulus
- Common cause of **mitral regurgitation**
- Causes a **systolic click**
  - Don't confuse with opening snap of mitral stenosis



# Mitral Regurgitation

## Secondary causes

- Ischemia → damage to papillary muscle
- Left ventricular dilation
  - Dilated cardiomyopathy
  - Leaflets pulled apart
  - **"Functional" MR**
- Hypertrophic cardiomyopathy

# Mitral Regurgitation

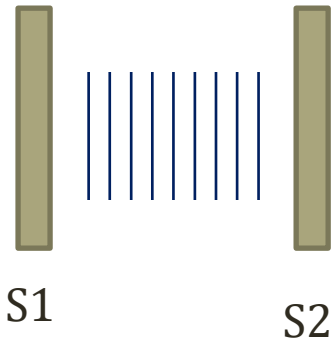
## Causes

- Endocarditis
- Rheumatic heart disease
- Congenital
  - Cleft mitral valve
  - Endocardial cushion defect
  - Down syndrome

# Mitral Regurgitation

## Clinical Features

- Holosystolic murmur at apex



# Afterload Reduction

## Aortic and Mitral Regurgitation

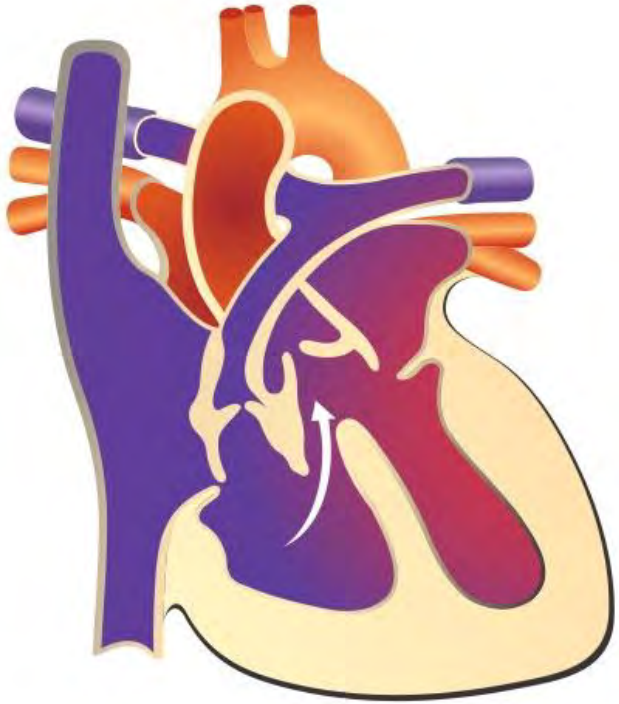
- In theory, ↓ afterload can improve forward flow
- For severe, acute regurgitation this helps
- For chronic disease, clinical trials with mixed results
- In general, these are surgical diseases
- Common test scenario “Best medical option?”

# Tricuspid Regurgitation

- Small amount of TR normal ("physiologic TR")
- Holosystolic murmur at left sternal border
- Pathologic causes
  - Functional TR from **RV enlargement**
  - **Endocarditis - classically IV drug users**
  - Carcinoid
  - Ebstein's anomaly

# Pulmonic Regurgitation

- Most common cause: repaired **Tetralogy of Fallot**
  - Repair of RVOT obstruction damages valve
- Endocarditis (rare)
- Rheumatic heart disease (rare)



Tetralogy of Fallot

# Shock

Jason Ryan, MD, MPH

# Shock

- Life-threatening fall in blood pressure
- Poor tissue perfusion
- **Low cardiac output**
  - Loss of contractility
  - Low intravascular volume
- **Peripheral vasodilation**

**BP = CO X TPR**

# Types of Shock

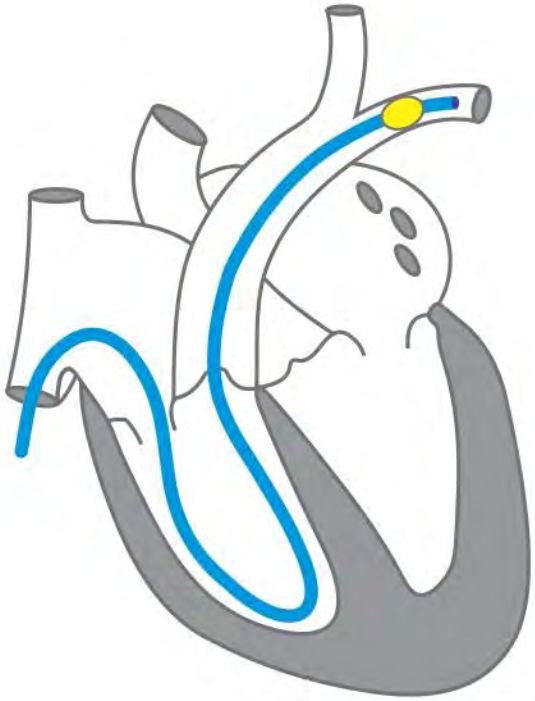
- Cardiogenic
  - Cardiac disorder → fall in cardiac output
- Hypovolemic
  - Fall in intravascular volume → fall in cardiac output
  - Hemorrhage
- Distributive
  - Peripheral vasodilation
  - Septic, anaphylactic
- Obstructive

# Types of Shock

- **Different treatments** for different types of shock
- Often can determine type from **history**
  - Myocardial infarction → cardiogenic shock
  - Massive bleeding → hypovolemic shock
- Shock of unclear etiology: Swan-Ganz catheter

# Swan-Ganz Catheter

## Pulmonary artery catheter



Pulmonary Capillary Wedge Pressure
PCWP
"Wedge Pressure"
Equal to LA pressure

# Swan-Ganz Data

- RA Pressure (Normal ~ 5mmHg)
- RV Pressure (20/5)
- PA Pressure  (20/10)
- PCWP Pressure (10)
- Mixed venous O2 sat
  - Oxygen concentration after all veins mix

# Fick Equation

Oxygen Consumed = O2 Out Lungs – O2 In Lungs

= CO (Art O2 – Ven O2)

**Cardiac Output** = $\frac{\text{O2 Consumption}}{\text{(Art O2 – Ven O2)}}$

O2 Consumption α body size

Arterial O2 Content = O2 sat on finger probe

Venous O2 Content = O2 from Swan-Ganz

**Swan-Ganz catheter gives cardiac output**

# Flow Equation

- Used to determine **systemic vascular resistance**

$$\Delta P = CO * SVR$$

$$MAP - RAP = CO * SVR$$

$$SVR = \frac{MAP - RAP}{CO}$$

**Swan-Ganz Catheter gives SVR**

# Swan-Ganz Data

- Direct
  - RA Pressure (Normal ~ 5mmHg)
  - RV Pressure (20/5)
  - PA Pressure  (20/10)
  - PCWP Pressure (10)
  - Mixed venous O2 sat
- Calculated
  - Cardiac output
  - Systemic Vascular Resistance

# Hemodynamic of Shock

- Four major classes of shock
- All have different hemodynamics from Swan
- Swan can be used to determine etiology of shock
  - Cardiogenic
  - Hypovolemic
  - Distributive
  - Obstructive

# Cardiogenic Shock

- Hallmark is **low cardiac output**
- **High cardiac pressures**
- High SVR (sympathetic response)
- Classic cause: large myocardial infarction
- Also seen in advanced heart failure (depressed LVEF)

# Hypovolemic Shock

- Poor fluid intake
- High fever, insensible losses
- Hemorrhage
- **Low cardiac output**
- **Low cardiac pressures**
- High SVR (sympathetic response)

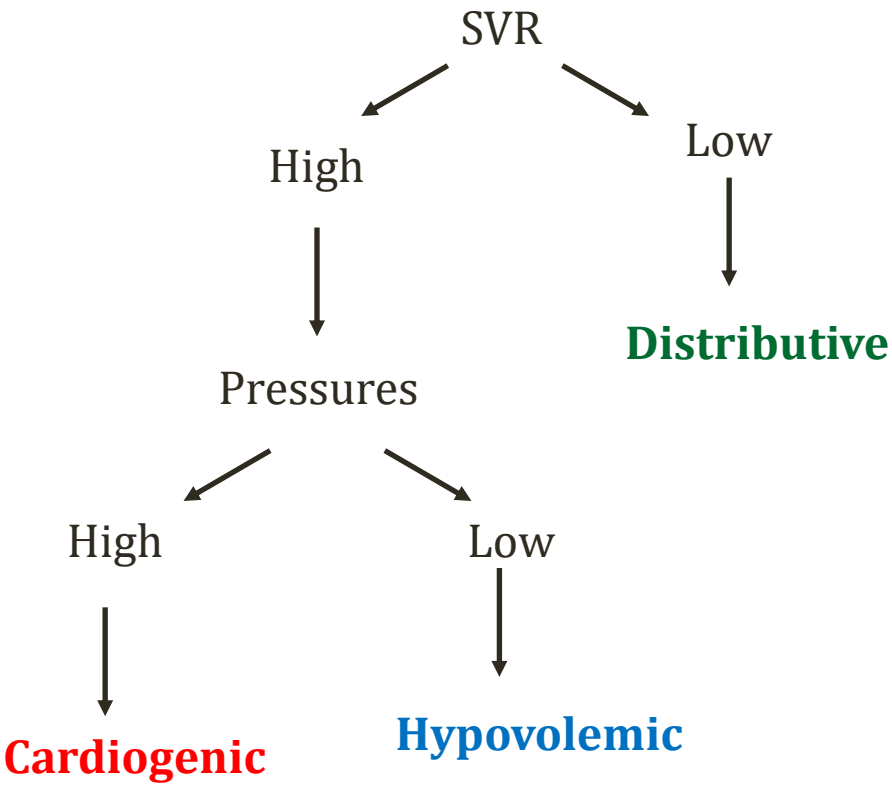
# Distributive Shock

- **Hallmark is low SVR**
- Diffuse vasodilation and/or endothelial dysfunction
- **Sepsis (most common)**
- Anaphylaxis
- Neurogenic
- Cardiac output classically high (variable)
- Cardiac pressures variable

# Type of Shock

| | Cardiogenic | Hypovolemic | Distributive |
|---|---|---|---|
| Blood Pressure | ↓ | ↓ | ↓ |
| HR | ↑ | ↑ | ↑ |
| RA Pressure | ↑ | ↓ | ↓/- |
| RV Pressure | ↑ | ↓ | ↓/- |
| PCWP | ↑ | ↓ | ↓/- |
| Cardiac Output | ↓ | ↓ | ↑ |
| SVR | ↑ | ↑ | ↓ |

# Major Shock Types



# Physical Exam

- Cold skin → high SVR and low CO
  - Cardiogenic
  - Hypovolemic
- Warm skin → low SVR and high CO
  - Distributive
- Jugular venous pressure → high RA pressure
- Pulmonary rales → high LA pressure

# Obstructive Shock

- Obstruction to blood flow from heart
- Low cardiac output despite normal contractility
- Tamponade
- Tension pneumothorax
- Massive pulmonary embolism
- Low cardiac output
- High SVR

# Treatment of Shock

- Cardiogenic: inotropes
  - Milrinone, Dobutamine
- Hypovolemic: volume
  - Blood transfusions, IV fluids
- Distributive: vasopressors
  - Phenylephrine, epinephrine, norepinephrine
- Obstructive: resolve obstruction
  - Treat tamponade, embolism, tension pneumothorax

# Swan in Valve Disease

| | |
|---|---|
| RA (5) | 15 |
| RV (20/5) | 45/15 |
| PA (20/10) | 45/30 |
| PCWP (10) | 30 |
| LV (120/10) | 120/5 |
| Ao (120/80) | 120/80 |

**Mitral Stenosis**

# Swan in Valve Disease

| | |
|---|---|
| RA (5) | 5 |
| RV (20/5) | 20/5 |
| PA (20/10) | 20/10 |
| PCWP (10) | 10 |
| LV (120/10) | 150/10 |
| Ao (120/80) | 120/80 |

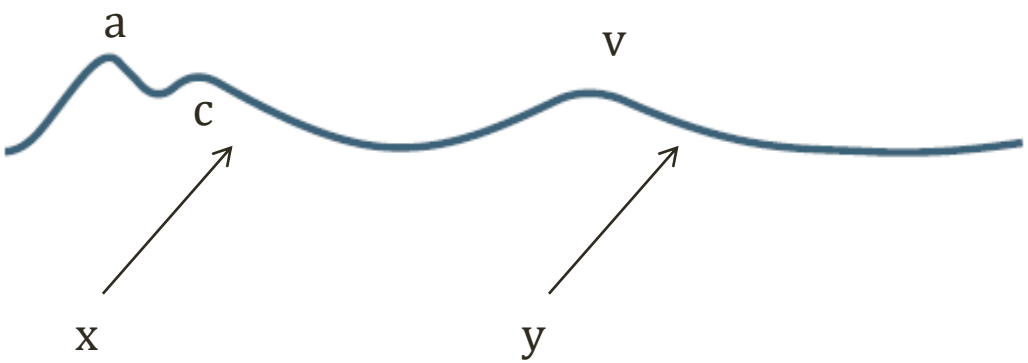
**Aortic Stenosis**

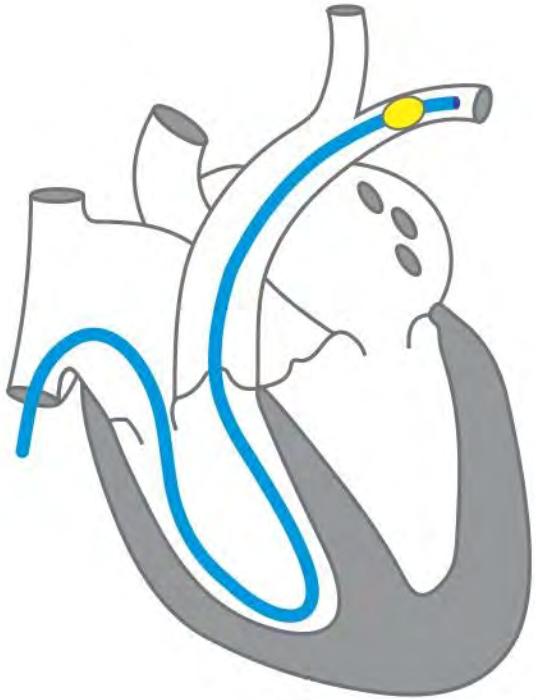
# Swan in Valve Disease

| | |
|---|---|
| RA (5) | 15 |
| RV (20/5) | 45/15 |
| PA (20/10) | 45/30 |
| PCWP (10) | 30 |
| LV (120/10) | 120/30 |
| Ao (120/80) | 120/40 |

**Aortic Regurgitation**

# Left Atrial Pressure



# Giant V waves

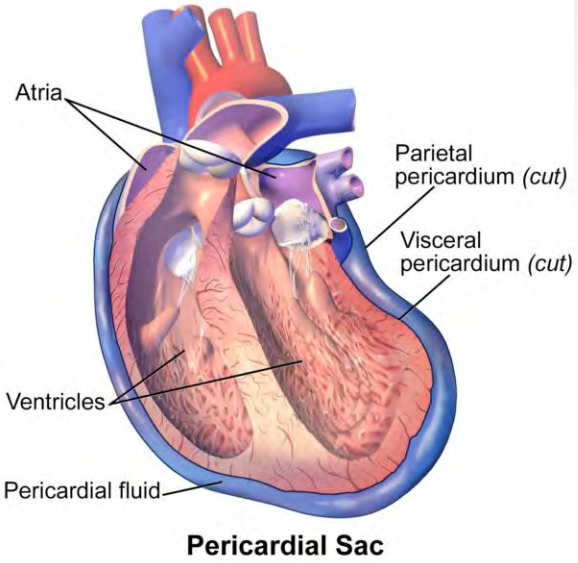
- Seen in **mitral regurgitation** in **PCPW tracing**
- Similar to giant V waves in tricuspid regurgitation
  - Seen in venous pressure tracing

# Pericardial Disease

Jason Ryan MD, MPH

# Pericardium

- Three layers
- Fibrous pericardium
- Serous pericardium
  - Parietal layer
  - Visceral layer
- Pericardial cavity between serous layers
- Innervated by **phrenic nerve**
- Pericarditis → referred pain to the shoulder

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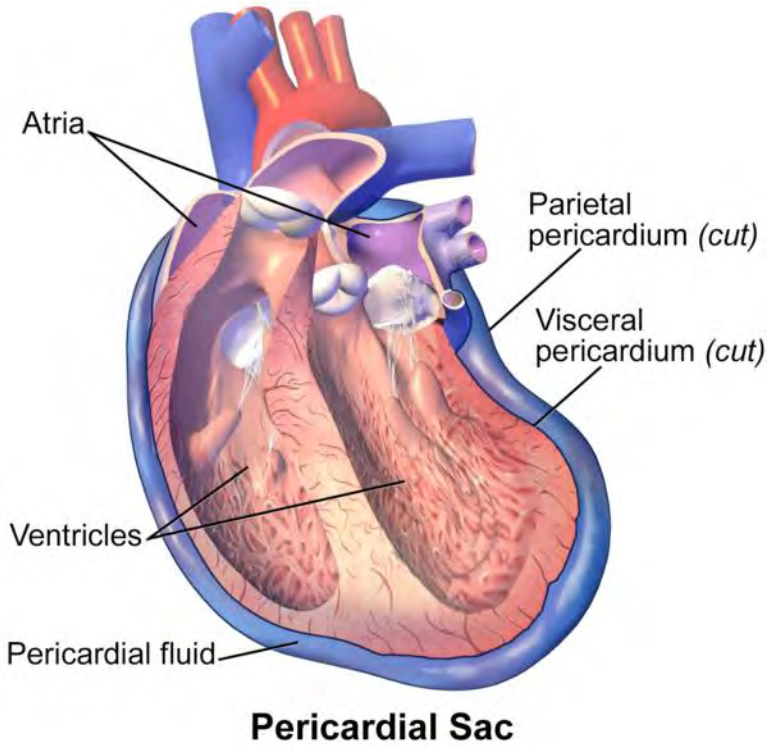
# Pericardial Diseases

- Pericarditis
- Tamponade
- Constrictive pericarditis

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# Pericarditis

- Most common pericardial disorder
- Inflammation of the pericardium
- Immune-mediated (details not known)
- May recur after treatment

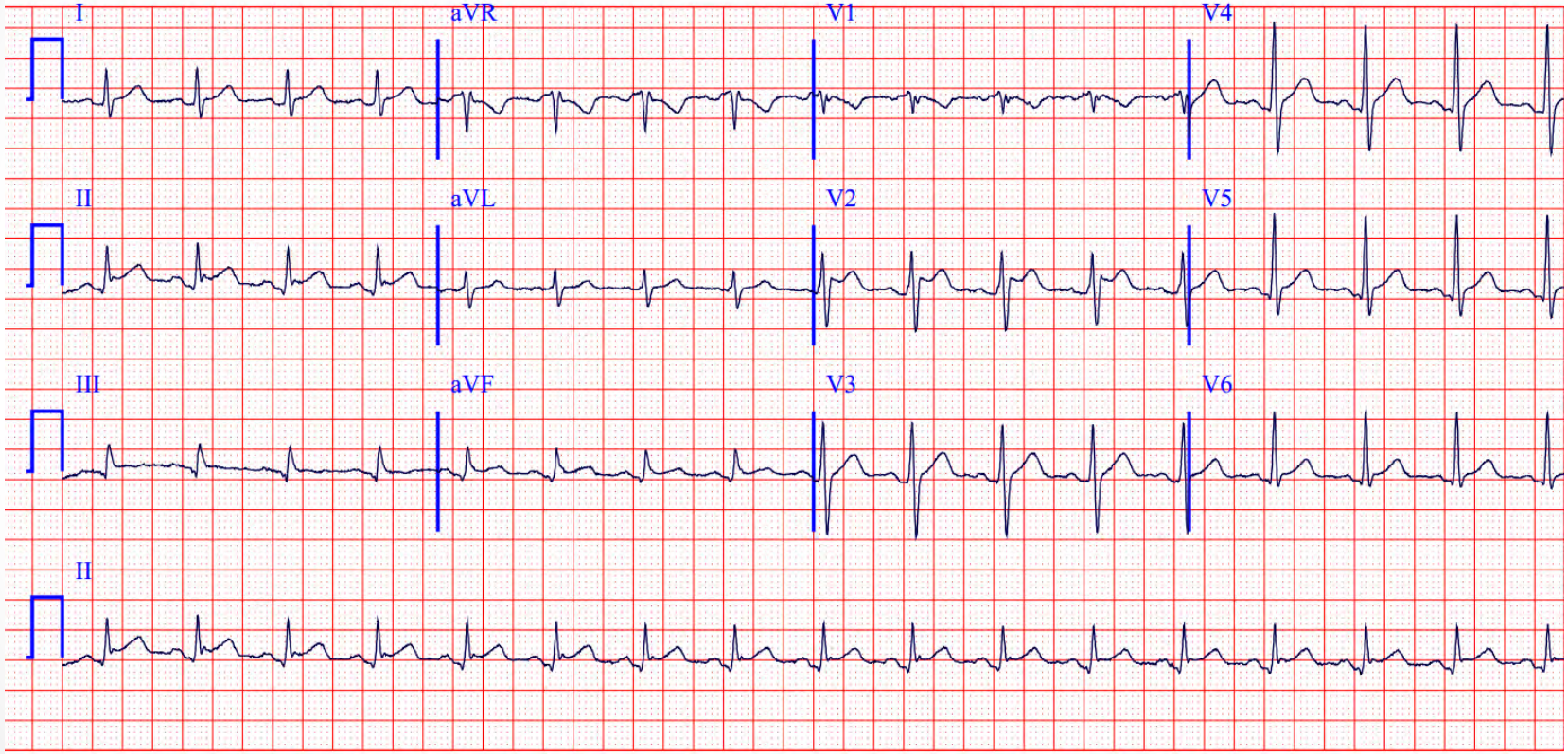
# Pericarditis

## Clinical Features

- Chest pain
  - Sharp
  - Worse with deep breath (pleuritic)
  - Worse lying flat (supine)
  - Better sitting up/leaning forward
- Fever
- Leukocytosis
- Elevated ESR

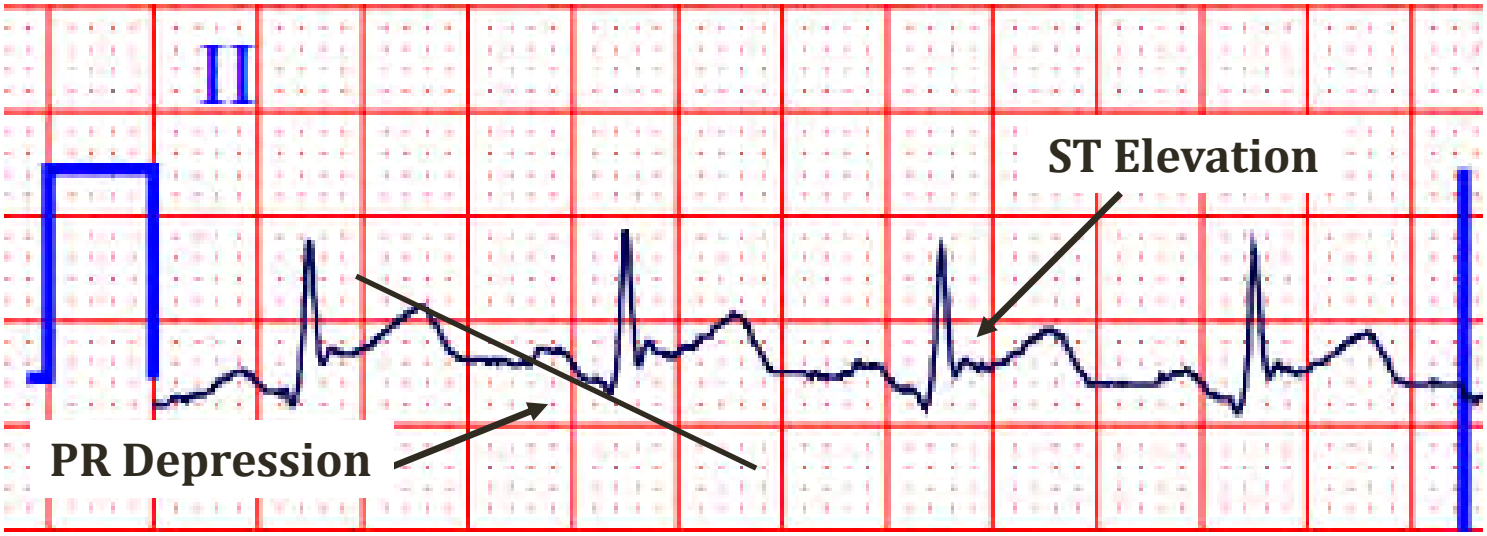
# Pericarditis

## EKG Findings



# Pericarditis

## EKG Findings




<u>Pericarditis</u>
Diffuse ST elevation
PR depression

# Pericarditis

## EKG

- Technically, 4 stages of EKG changes
- Stage 1: diffuse ST elevations, PR depressions
- Stage 2 (~1 week later): Normal
- Stage 3: T wave inversions
- Stage 4: Normal

# Pericarditis

## Physical Exam

- Pericardial friction rub
- **Scratchy** sound
- Systole and diastole

# Pericarditis

## Etiology

- **Usually idiopathic**
- Viral
  - Classic cause is **Coxsackievirus**
  - Often follows viral upper respiratory infection (URI)
- Bacterial
  - Spread of pneumonia
  - Complication of surgery
  - Tuberculosis
- Fungal

# Pericarditis

## Etiology

- Uremic (renal failure)
- Post-myocardial infarction
  - Fibrinous (days after MI)
  - Dressler's syndrome (weeks after MI)
- Autoimmune disease (RA, Lupus)

# Pericarditis

## Treatment

- NSAIDs
- Steroids
- **Colchicine**
  - Inhibits WBCs via complex mechanism
  - Useful in gout and familial Mediterranean fever
  - Added to NSAIDs to lower risk of recurrence

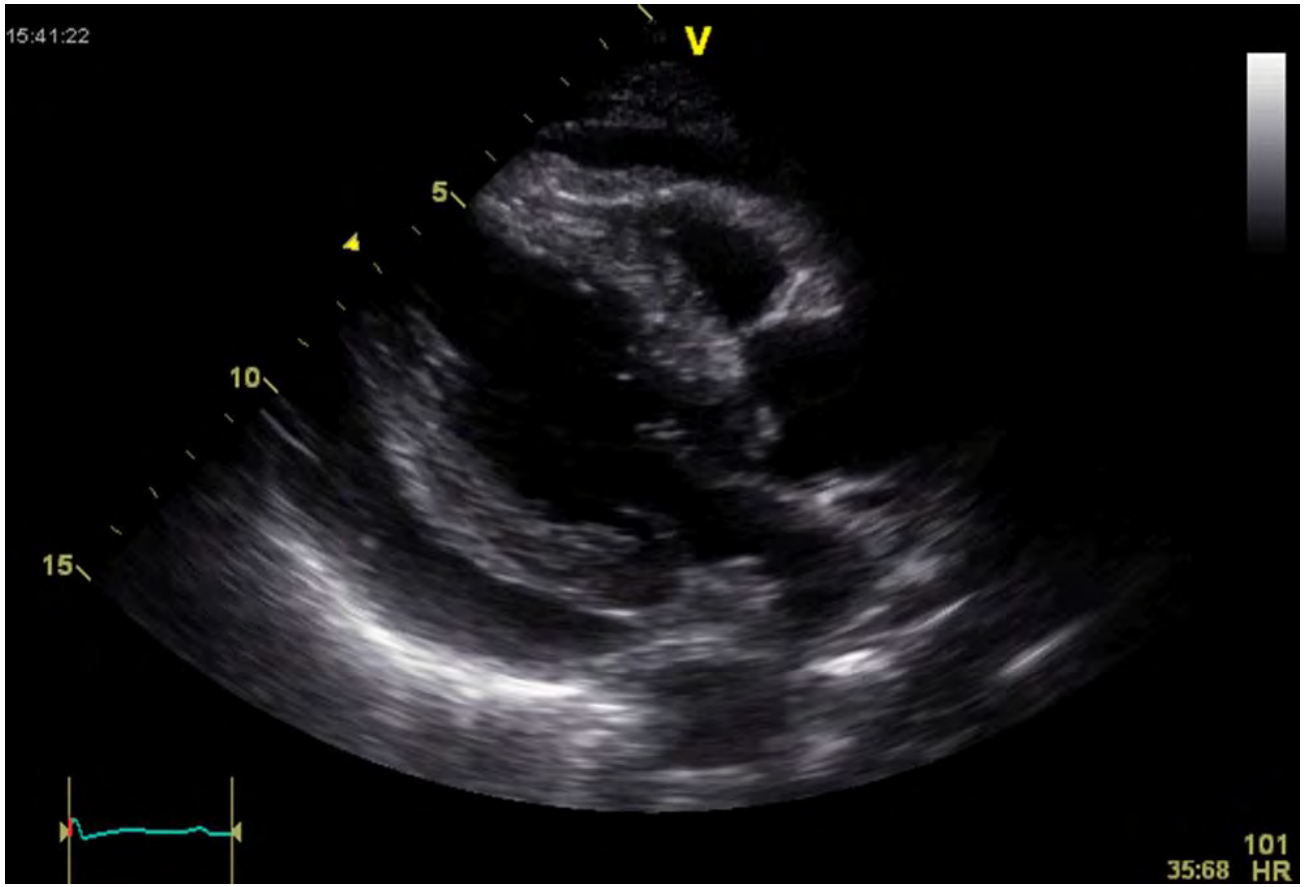
# Myopericarditis

- Myocarditis = inflammation of myocardium
- Similar presentation to ischemia
  - Chest pain
  - EKG changes
  - Increased CK-MB, Troponin

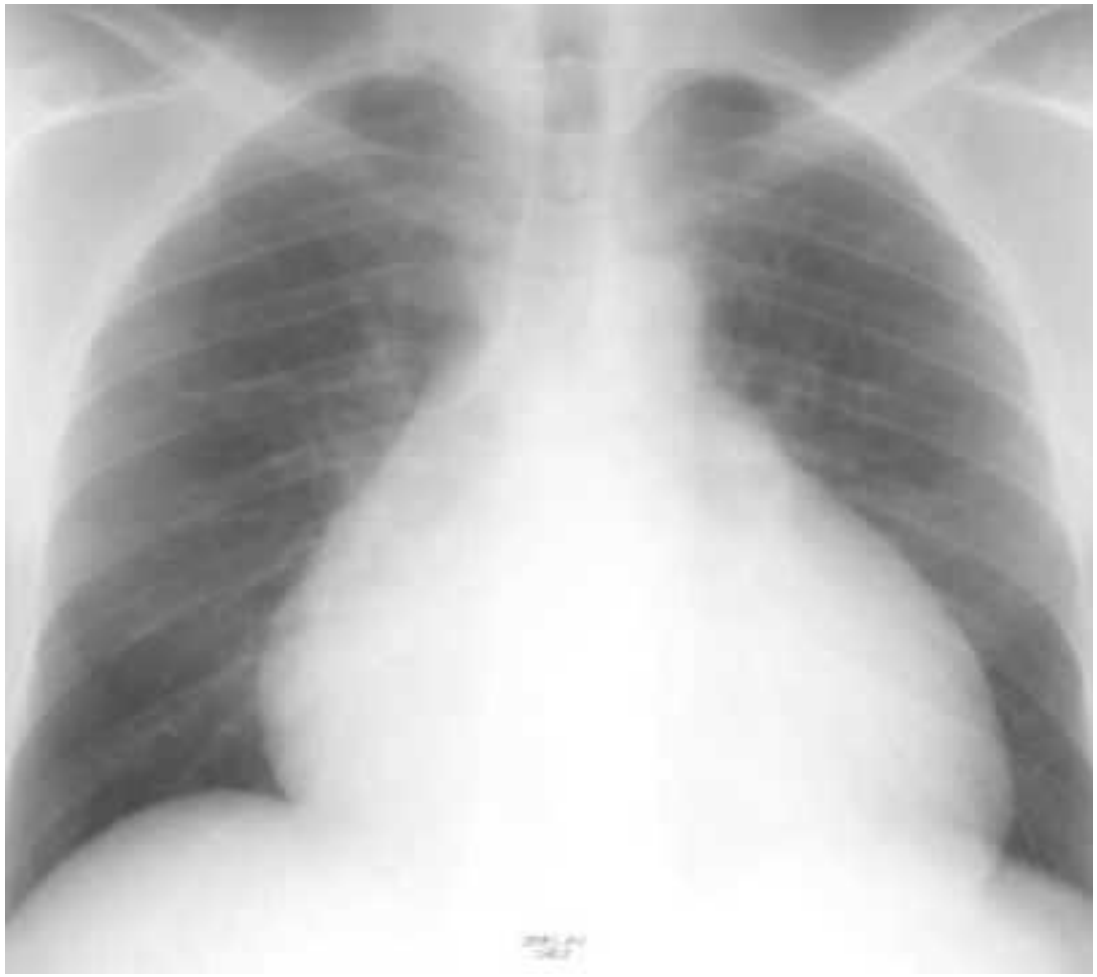
# Tamponade

- Accumulation of pericardial fluid
- **High pericardial pressure**
- Filling restriction of cardiac chambers
- Amount of fluid variable
  - Acute accumulation (bleeding): small amount of fluid
  - Chronic accumulation (cancer): large amount of fluid

# Tamponade



# Water Bottle Sign



# Tamponade

## Causes

- **Cancer metastases** to pericardium
- Uremia
- Pericarditis
- Trauma
- Treatment: Drainage of effusion

# Tamponade

## Clinical features

- Distant heart sounds
- Dyspnea
- Elevated jugular venous pressure

# Tamponade

## Clinical features

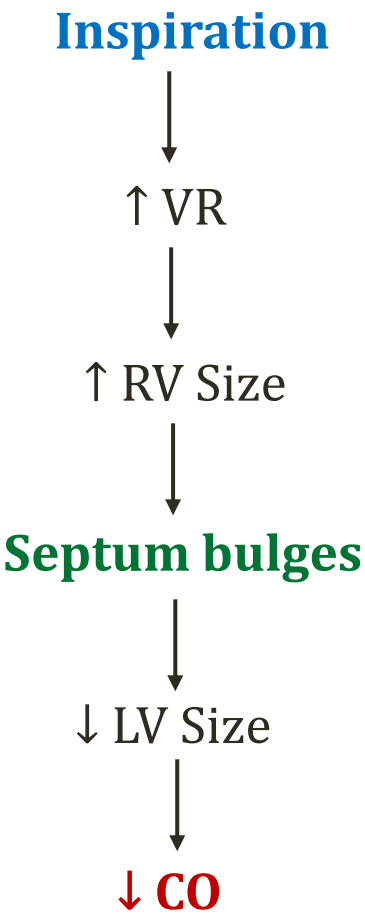
- Beck's Triad
  - Distant heart sounds
  - Elevated JVP
  - Hypotension
- Seen in rapidly-developing traumatic effusions
- Severe impairment LV function → **low cardiac output**
- Slower effusions: Pericardium stretches/dilates

# Pulsus Paradoxus

- Classic finding in tamponade
- Systolic BP always falls slightly on inspiration
- Exaggerated fall (>10mmHg) = pulsus paradoxus
- Severe fall = pulse disappears

Public Domain

# Pulsus Paradoxus



# Pulsus Paradoxus

- Also seen in **asthma and COPD**
- Inspiration: ↓ left sided flow
- Caused by pulmonary pressure fluctuation
- Exaggerated in lung disease
  - Normal lungs: 0 to -5mmHg
  - Lung disease: Change up to 40mmHg
- Large drop in left sided flow → pulsus paradoxus

# Pulsus Paradoxus

## Measurement Technique

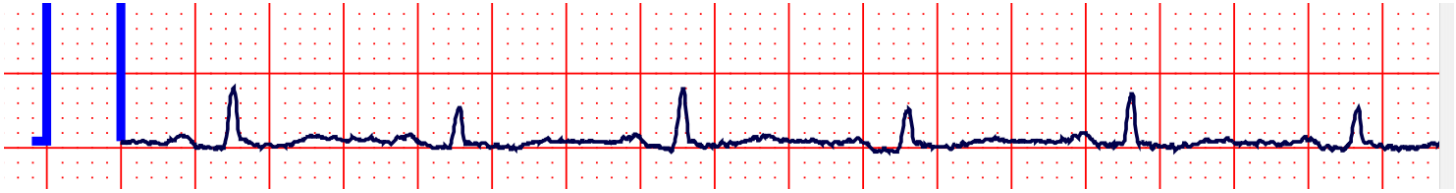
- Raise cuff pressure until no sounds heard
- **NORMAL respirations**
- Slowly lower cuff pressure
- First point (P1): intermittent sounds
- Second point (P2): constant sounds
- Pulsus = P1 – P2

# Tamponade

## EKG

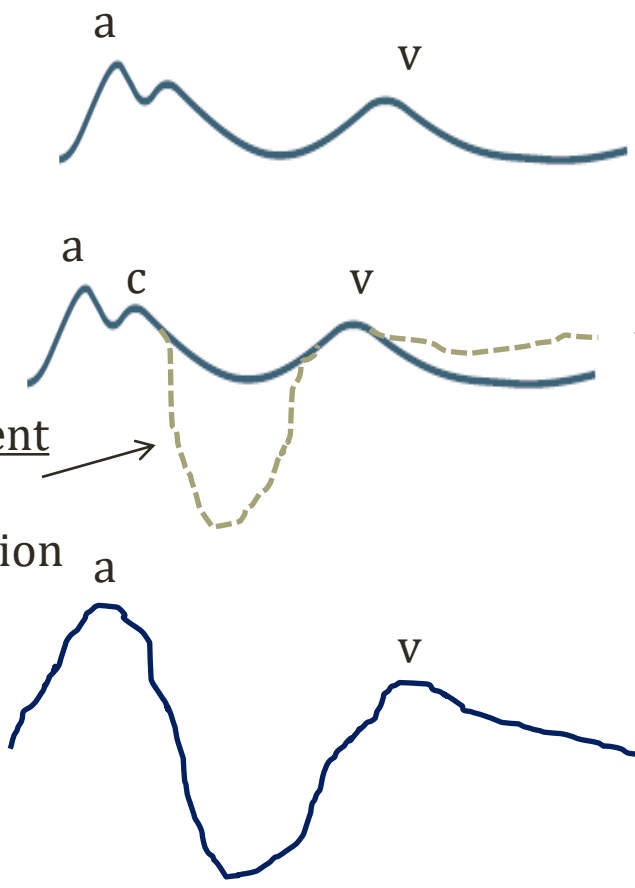
- Sinus tachycardia
- Low voltage – EKG sees less electricity due to effusion

Electrical Alternans



# Tamponade

## Prominent x descent, Blunted y descent




Blunted y descent
Poor RV filling
in diastole

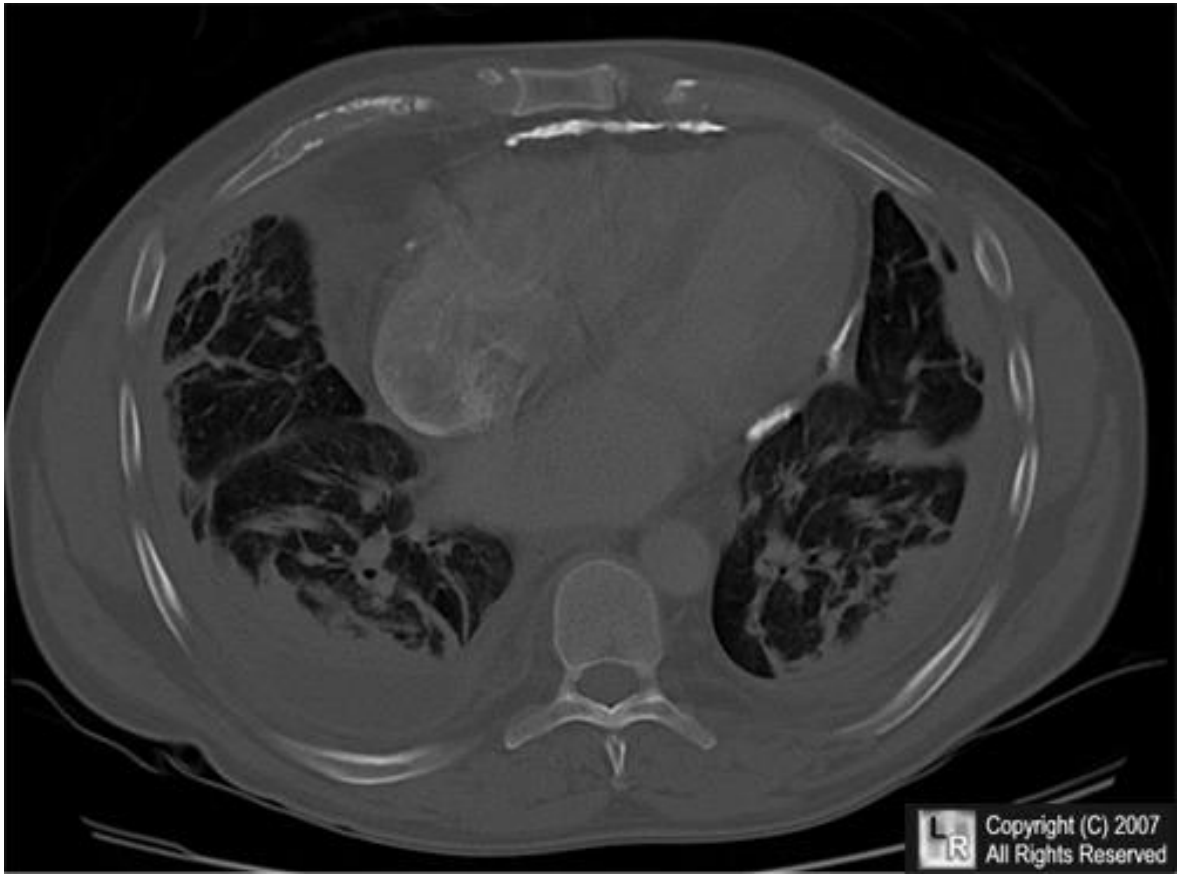
Prominent x descent
↓ RA pressure
during RV contraction
in systole

# Equalization of Pressures

- Occurs when cardiac chambers cannot relax
- Pressure in RA, RV, LA, LV falls but then abruptly stops
- Seen in tamponade and pericardial constriction

| Parameter | Normal | Tamponade |
|---|---|---|
| RA mean | 5 | 20 |
| RV Pressure | 20/5 | 44/20 |
| PCPW Pressure | 10 | 20 |

# Constrictive Pericarditis




www.learningradiology.com, courtesy of Dr. William Herring, MD, FACR. Used with permission.

# Constrictive Pericarditis

- Fibrous, calcified scar in pericardium
- Loss of elasticity: stiff, thickened, sticky
- Can result from many pericardial disease processes
  - Pericarditis
  - Radiation to chest
  - Heart surgery

# Constrictive Pericarditis

## Clinical Features

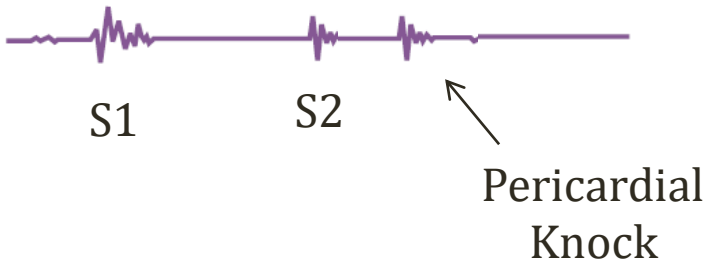
- Dyspnea
- Prominent **right heart failure**
  - Markedly elevated jugular venous pressure
  - Lower extremity edema
  - Liver congestion
  - May lead to cirrhosis ("nutmeg liver")

David Monniaux/Wikipedia

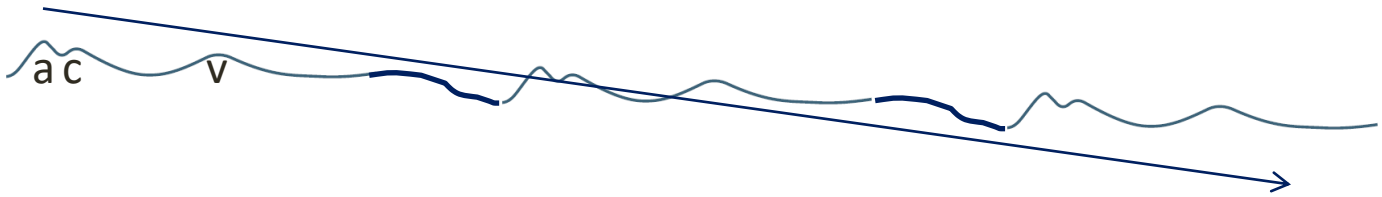
# Constrictive Pericarditis

## Other Features

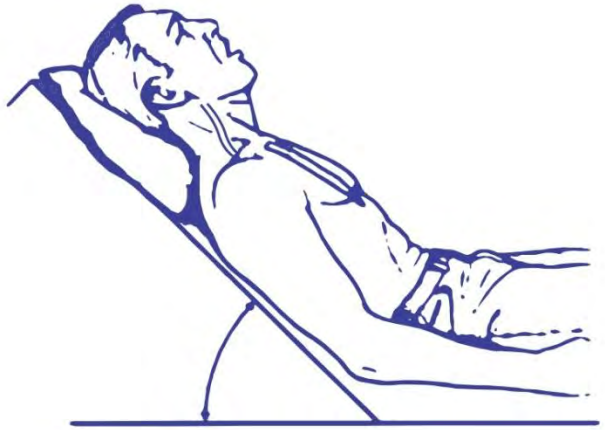
- Pulsus paradoxus uncommon (~20%)
- High RA, RVEDP, PCPW pressures
- Equalization of pressures
- **Pericardial knock**



# Kussmaul's Sign




- Inspiration → ↑ VR → slight fall in mean JVP
- **Kussmaul's sign** = **↑ JVP with inspiration**
  - **Ventricle cannot accept ↑VR**
  - Constrictive pericarditis
  - Restrictive cardiomyopathy
  - RV myocardial infarction
- Not seen in tamponade



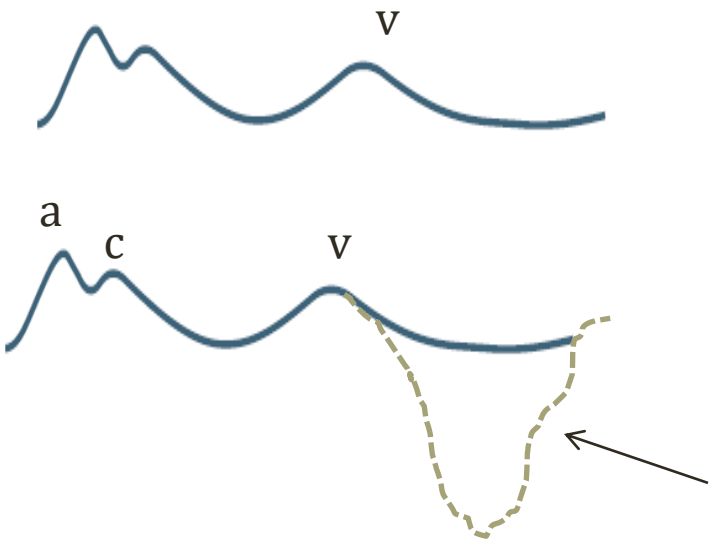
# Pulsus and Kussmaul's

- Pulsus paradoxus: classic sign of tamponade
  - **Pulsus in tamPonade**
- Kussmaul's sign: classic sign of constriction
  - Also seen in restrictive heart disease
  - **Kussmaul's in Konstriction/Restriction**

| | Tamponade | Constriction | Restrictive |
|---|---|---|---|
| Pulsus | Yes | No | No |
| Kussmaul's | No | Yes | Yes |

# Constrictive Pericarditis

## Rapid/prominent y descent




<u>Rapid y descent</u>
Rapid filling of RV
Abrupt stop in filling

Myocardium adherent to pericardium
In diastole: **rapid relaxation** and suction of RA volume

# Venous Pressure Findings

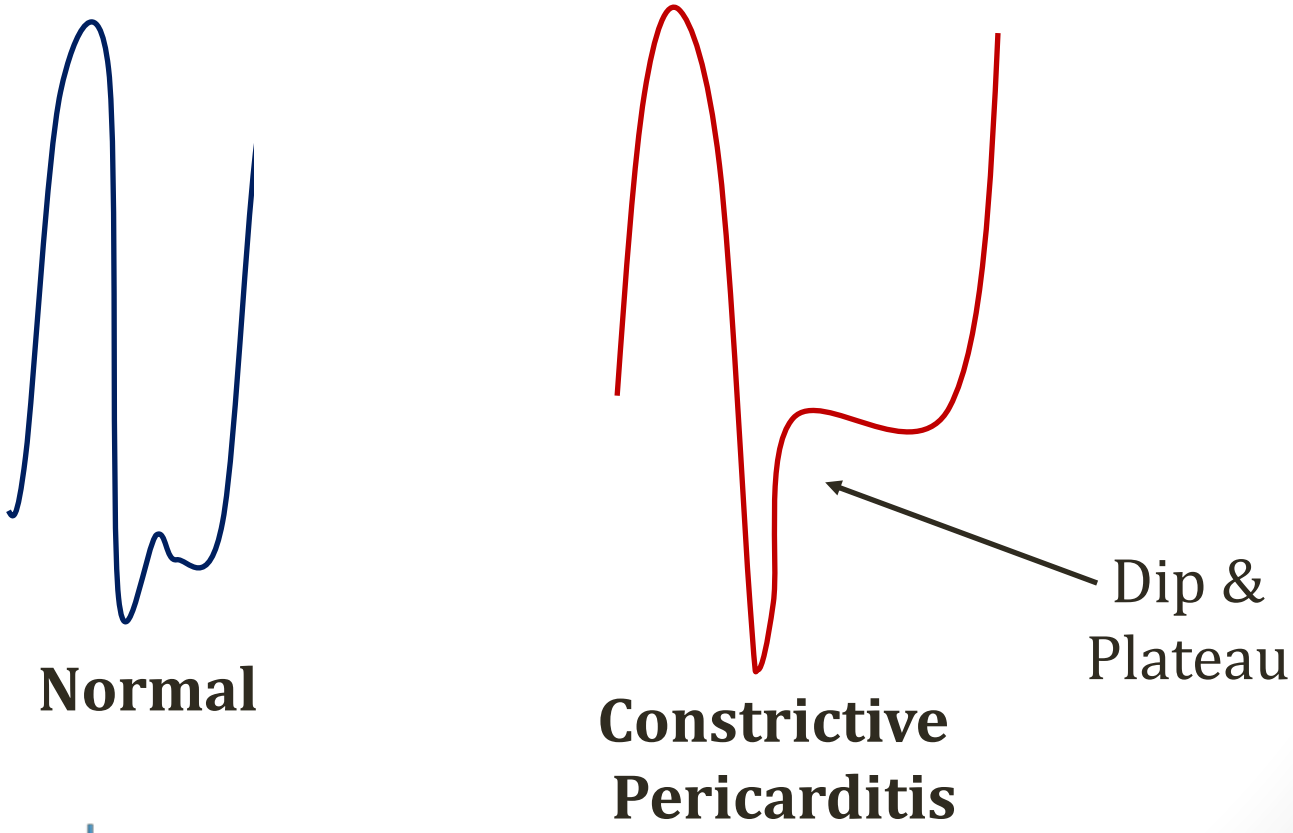
| | Tamponade | Constriction |
|---|---|---|
| x descent | Rapid | -- |
| y descent | Absent | Rapid |

# Dip and Plateau

## Square Root Sign

**Right Ventricular Pressure**

Rapid filling, abrupt stop



# Constriction and Restriction

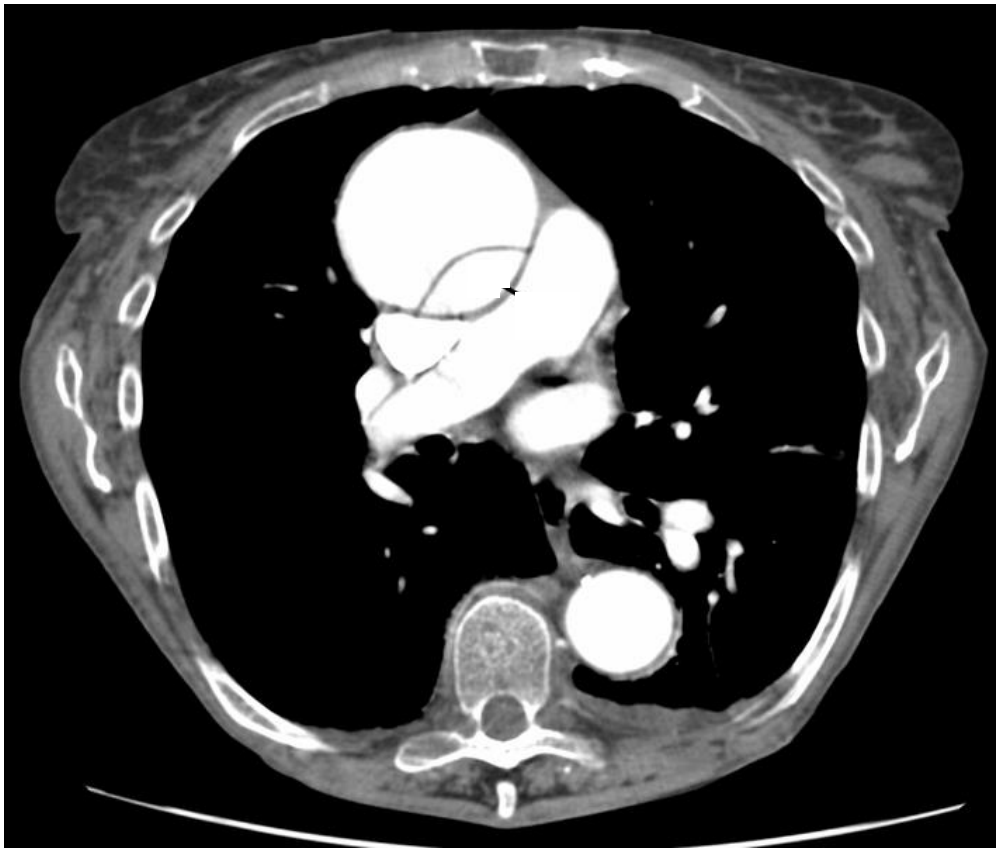
- Constrictive pericarditis/Restrictive heart disease
- **Many common features**
- Prominent right heart failure
- Kussmaul's sign
- Rapid y descent
- Dip and plateau

# Aortic Dissection

Jason Ryan, MD, MPH

# Aortic Dissection

## CT Angiogram

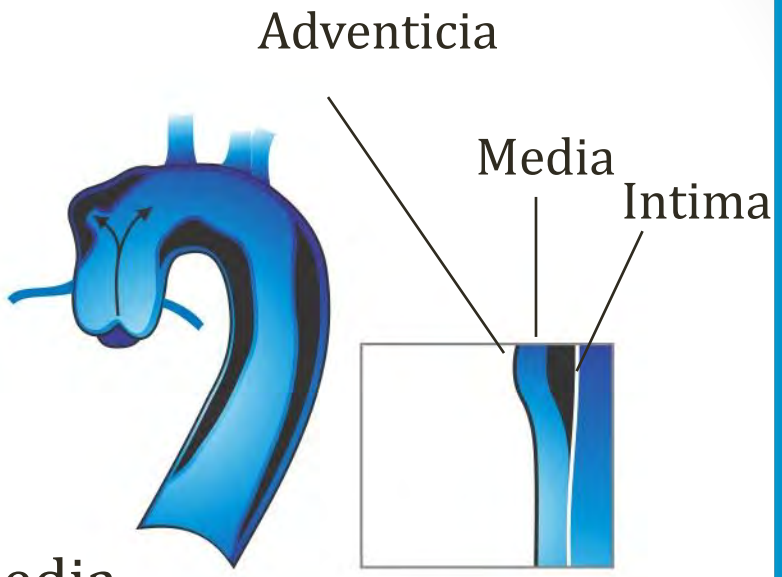




* Images courtesy Dr. James Heilman and Wikipedia; used with permission

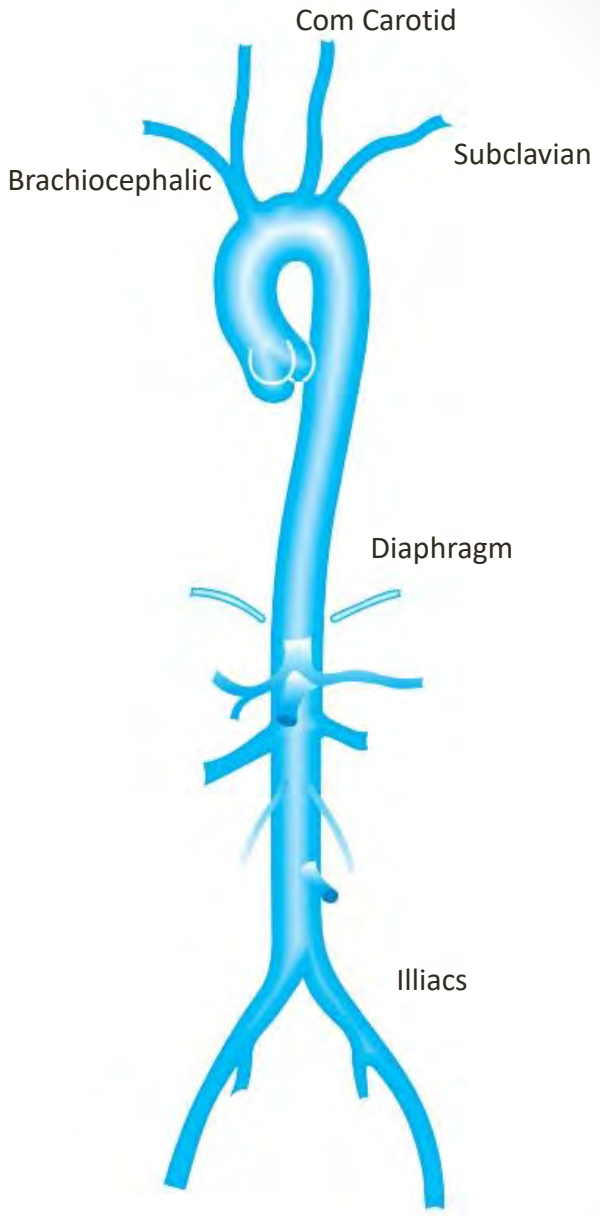
# Aortic Dissection

- Three layers to aorta
  - Intima
  - Media
  - Adventicia
- Dissection → **tear in intima**
- Blood "dissects" intima and media



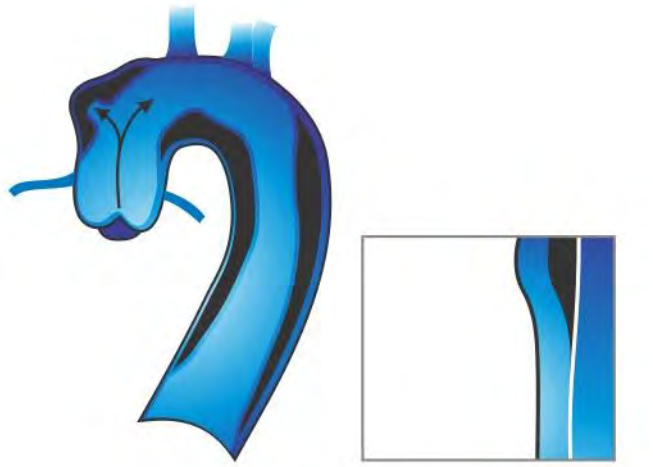
# Propagation

- Blood enters dissection plane
- Spreads proximal, distal
- Can disrupt flow to vessels



# Types

- Type A
  - Involves ascending aorta and/or arch
  - Treated **surgically**
- Type B
  - Descending aorta
  - Can be treated **medically**
  - Control hypertension/symptoms
  - Surgical mortality high

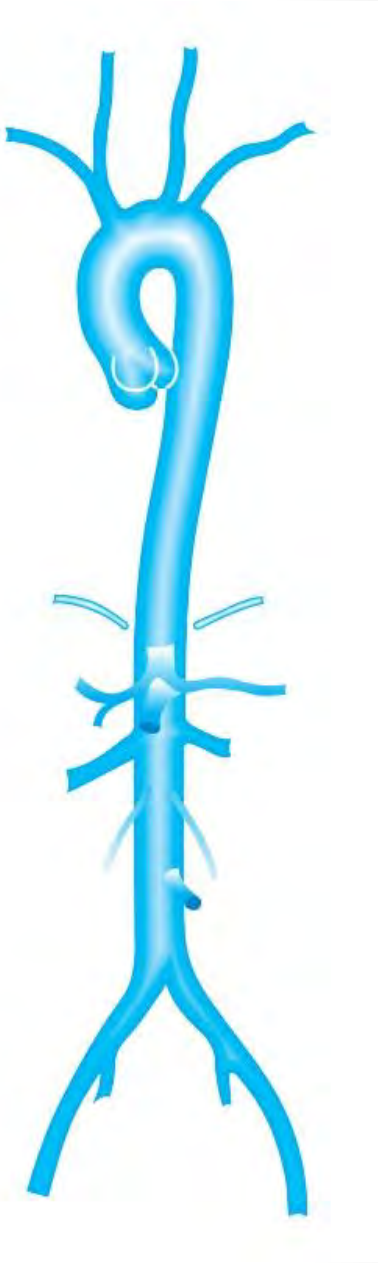


# Symptoms

- “Tearing” chest pain radiating to back

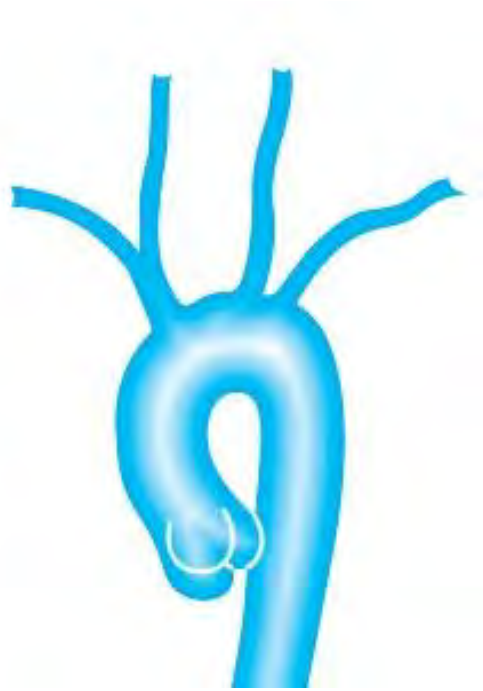
# Other symptoms

- Propagation to aortic root
  - Aortic regurgitation
  - Pericardial effusion/tamponade
  - Myocardial ischemia (obstruction RCA origin)
- Propagation to aortic arch
  - Stroke (carotids)
  - Horner's syndrome
  - Vocal cord paralysis



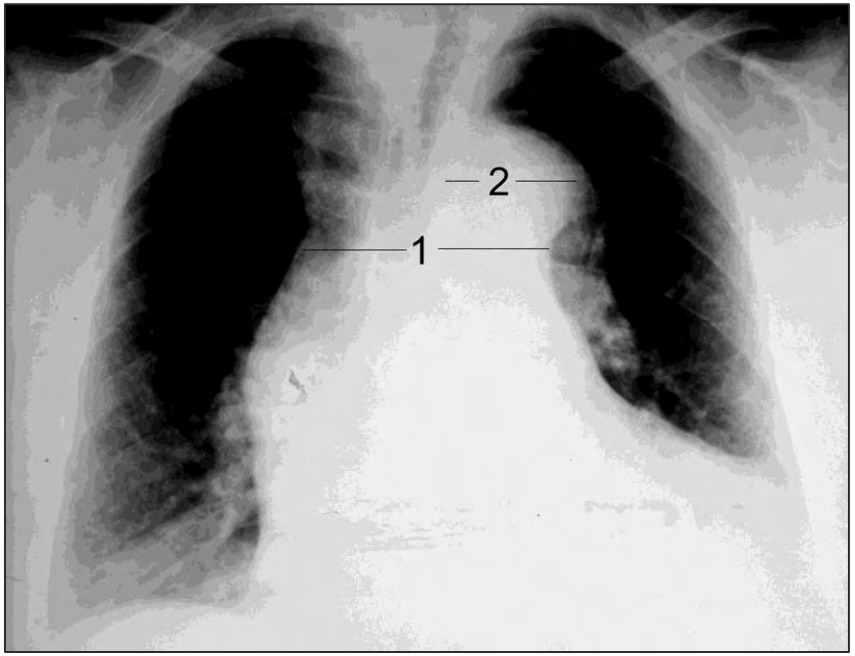
# Recurrent Laryngeal Nerve

- Branch of vagus nerve
- Supplies larynx and voice box
- Compression:
  - Aortic dissection
  - Massive left atrial enlargement



# Other findings

- **Blood pressure differential** between arms
- **Widened mediastinum** on chest x-ray




JHeuser /Wikipedia

# Diagnosis

- Suggested by history, exam, chest x-ray
- Definitive diagnosis
  - **CT scan**
  - MRI
  - Transesophageal echocardiogram (TEE)
- D-dimer
  - Sensitive but not specific
  - Normal value makes aortic dissection unlikely

# Risk Factors

## General Principles

- **Medial layer** of aorta
  - Tensile strength and elasticity
  - Key proteins: **collagen and elastin**
  - Weakness of medial layer → dissection/aneurysms
  - Common aneurysm feature: medial damage/destruction
- **Vasa vasorum**
  - Network of small vessels primarily in adventitial layer
  - Supplies blood to medial layer in thick vessels (i.e. aorta)
  - Thickening (HTN) → weakening of medial layer

# Risk Factors

## General Principles

- Requires **tension** on wall
  - Common in proximal aorta (near aortic valve)
  - High tension from blood moving out of heart
  - Worsened by hypertension
- Requires **weakness of media layer**
  - Also caused by hypertension
  - Seen in collagen disorders (genetic)

# Risk Factors

## General Principles

- **Cystic medial necrosis**
  - Development of cysts and necrosis in medial layer
- Occurs to mild degree with aging
- More rapid with:
  - Bicuspid aortic valve
  - Marfan syndrome
- Common in **ascending thoracic aneurysms**

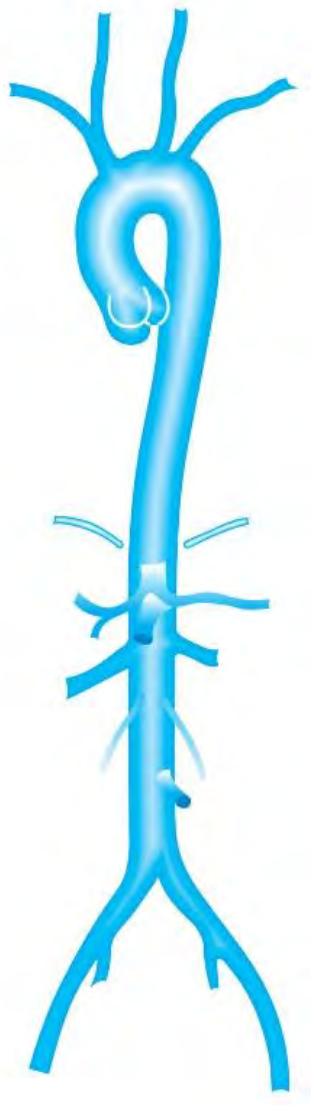
# Risk Factors

## Aortic Dissection

- Aortic damage
  - **HTN - #1 risk factor**
  - Atherosclerosis
  - Thoracic aneurysm
- Abnormal collagen
  - Marfan Syndrome
  - Ehlers-Danlos
- Others
  - Bicuspid aortic valve
  - Turner Syndrome (bicuspid, coarctation)
  - Tertiary syphilis: Aortitis

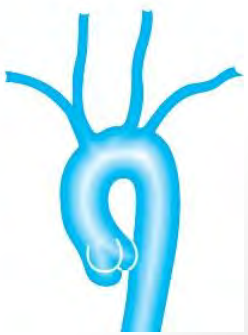
# Aortic Aneurysms

- Dilation/bulge of aorta
- More than 1.5x normal
- Involves all three 3 layers
- Thoracic (TAAs)
- Abdominal (AAAs)



# Thoracic Aortic Aneurysms

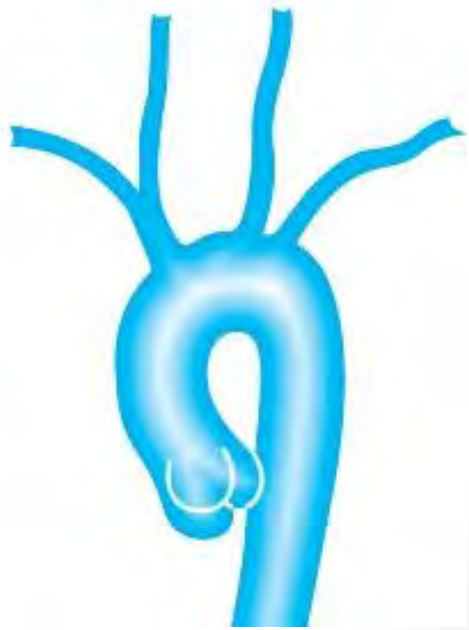
- Important risk factor for dissection
- Usually occur in proximal/ascending aorta
- Usually seen in **association with another disorder**
  - Marfan, Turner, Bicuspid aortic valve, **Syphilis**
- Family history of aneurysm important
- May be associated with **atherosclerosis**
  - More common in descending aorta
  - Occur in association with atherosclerosis risk factors
  - HTN, smoking, high cholesterol



# Thoracic Aortic Aneurysms

## Symptoms

- Most are asymptomatic
- Can cause **aortic regurgitation**
- Surgery if size >5.0cm



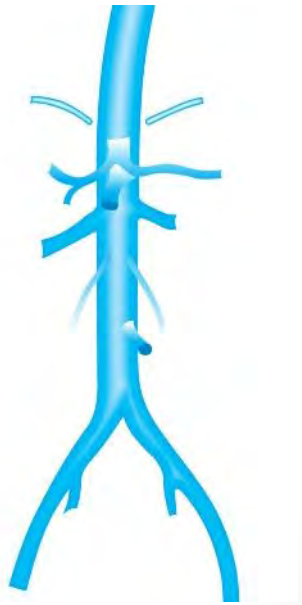
# Abdominal Aortic Aneurysms

- More common than thoracic aneurysms
- Classically taught as a disease of **atherosclerosis**
- **Infrarenal aorta** most affected by atherosclerosis
- Also most common site of AAA
- Current research suggests many factors
  - Genetic, environmental, hemodynamic, immunologic

# Abdominal Aortic Aneurysms

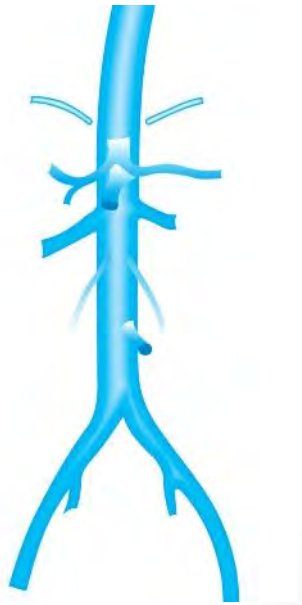
## Risk Factors

- **Smoking:** strongest association with AAA
- Males: 10x more common men vs. women
- Age
  - Rare before 55
  - As high as 5% in men >65
- HTN, hyperlipidemia



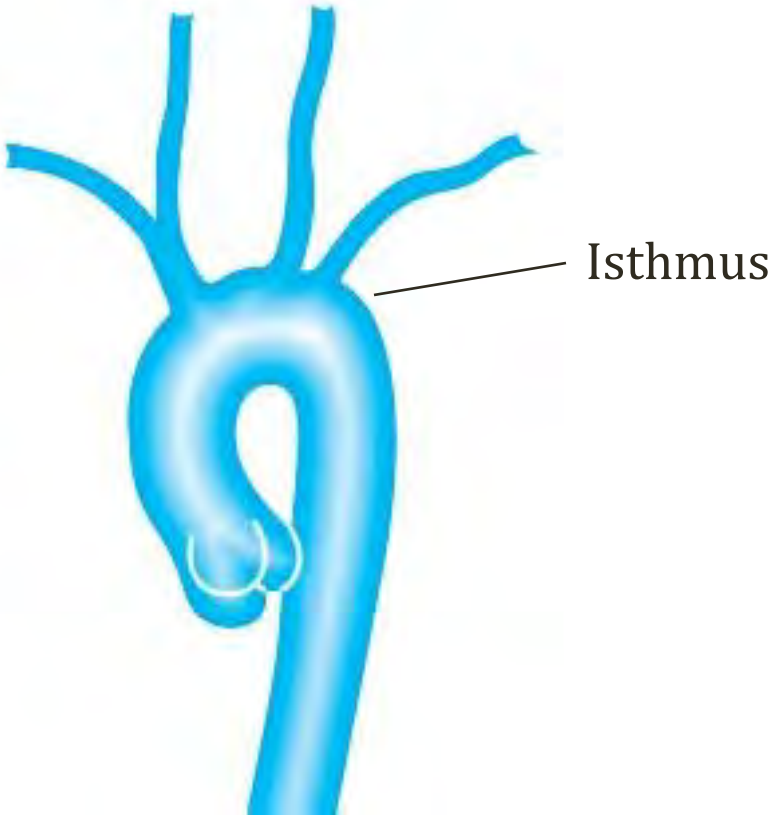
# Abdominal Aortic Aneurysms

- Most are asymptomatic
- Some detected on physical exam
- **Pulsatile mass** from xiphoid to umbilicus
- Natural history is enlargement → rupture
- Followed with **ultrasound** or CT scan
- Surgery if >5.0cm



# Aortic Rupture

- Usually from trauma
- Most common site is isthmus



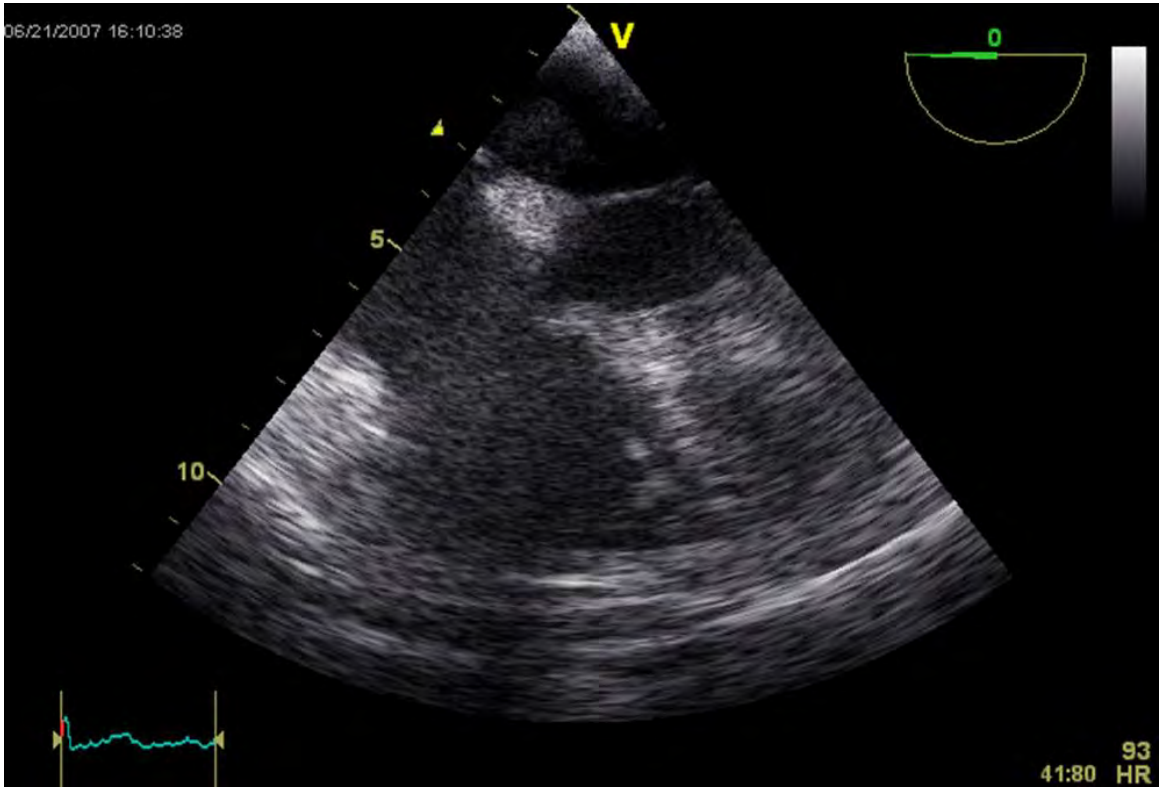
# Cardiac Tumors

Jason Ryan, MD, MPH

# Cardiac Tumors

- Myxoma
  - Most common 1° cardiac tumor
- Rhabdomyomas
  - Most common 1° cardiac tumor children
- Metastatic tumors
  - Most common cardiac tumor overall

# Myxoma



# Myxoma

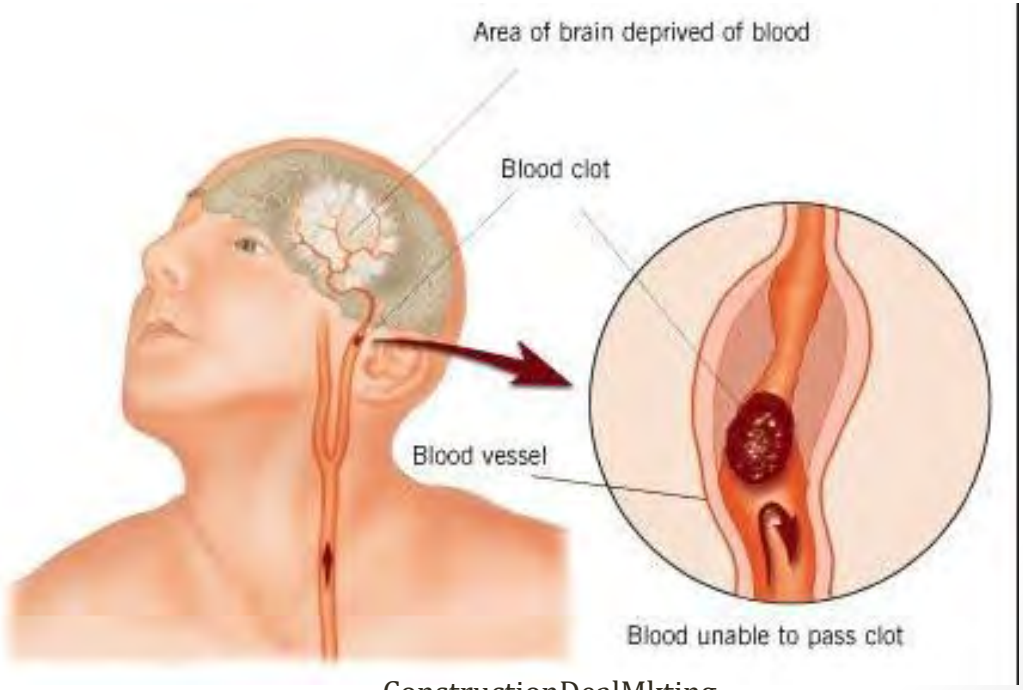
- Common in the **left atrium (80%)**
  - Usually attached to atrial septum
  - Often at the border of fossa ovalis
- Benign (do not metastasize)

# Myxoma

- Mesenchymal cells (undifferentiated cells)
- Endothelial cells
- Thrombus/clot
- Mucopolysaccharides

# Myxoma

- Often cause systemic symptoms
  - "B symptoms"
  - Fevers, chills, sweats
- Can embolize → stroke



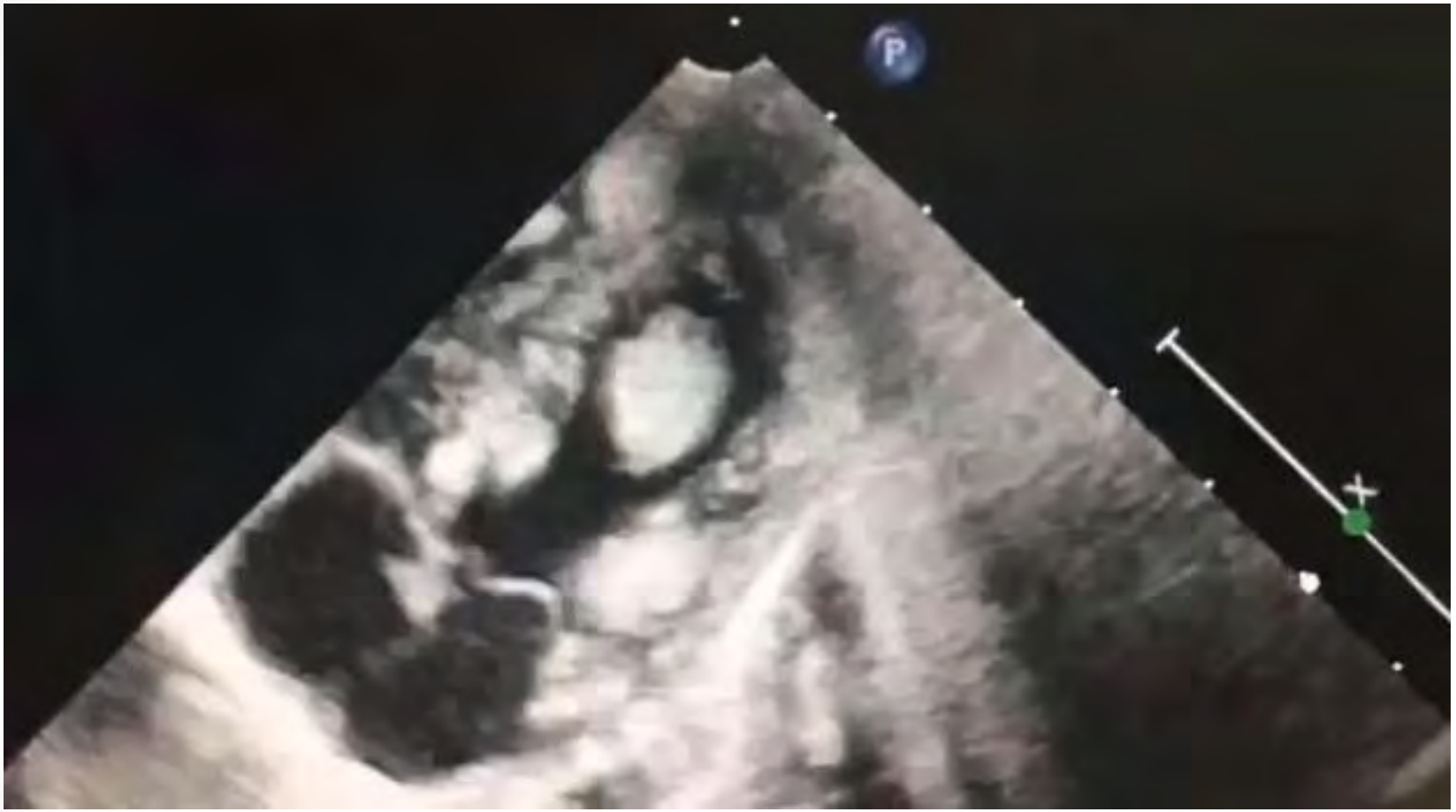

ConstructionDealMkting

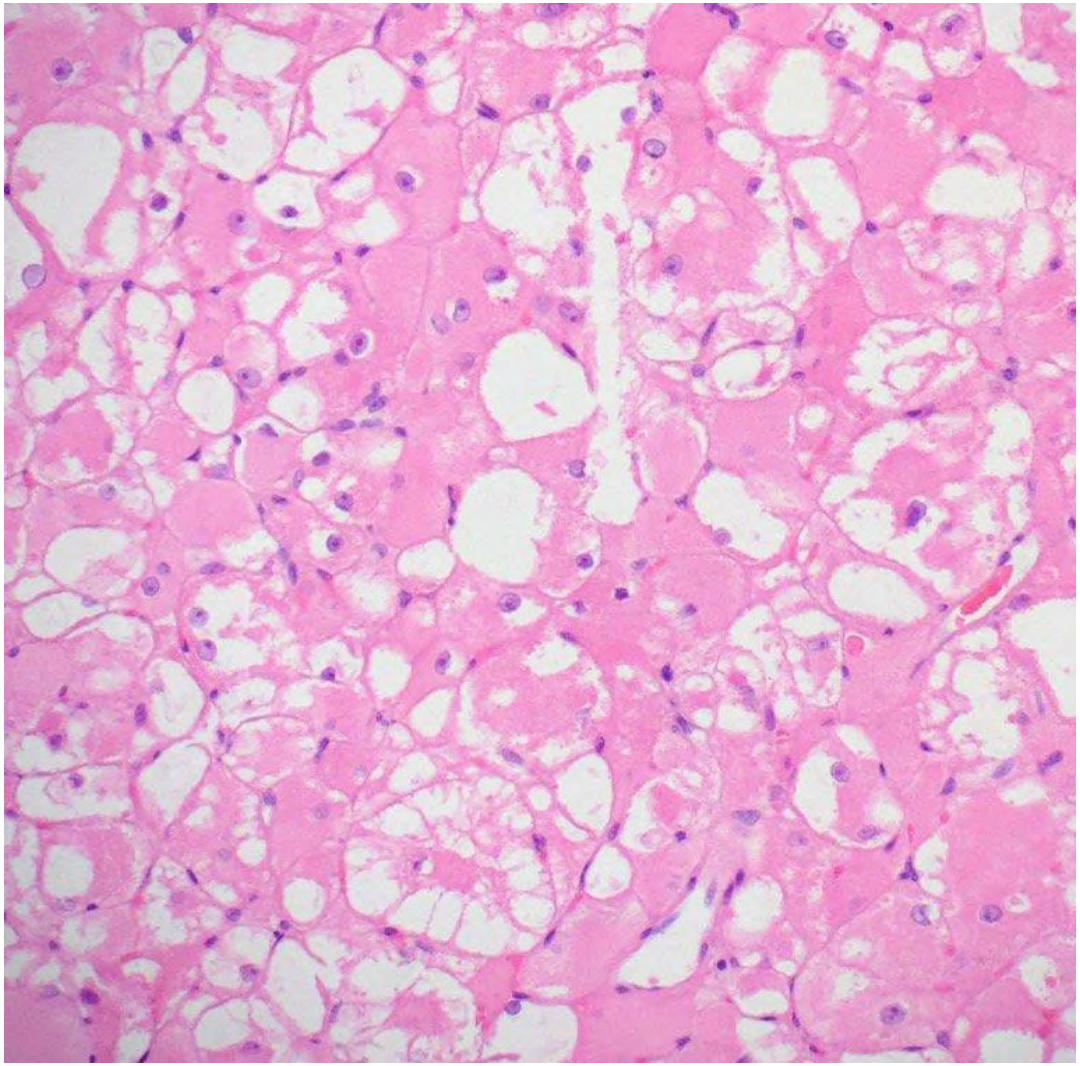
# Myxoma

- May disrupt **mitral valve function**
  - Regurgitation
  - Heart failure
- Can sit in mitral valve
  - “Ball in valve”
  - Mitral stenosis symptoms
  - Syncope or sudden death
- Auscultation: Diastolic “tumor plop”

# Cardiac Rhabdomyomas

- Tumors of muscle cells
- Benign (do not metastasize)
- Usually children (most <1year)
- Sometimes detected prenatal
- Tumor **embedded in ventricular wall**
- Most regress spontaneously
- Rare symptoms from obstruction of blood flow





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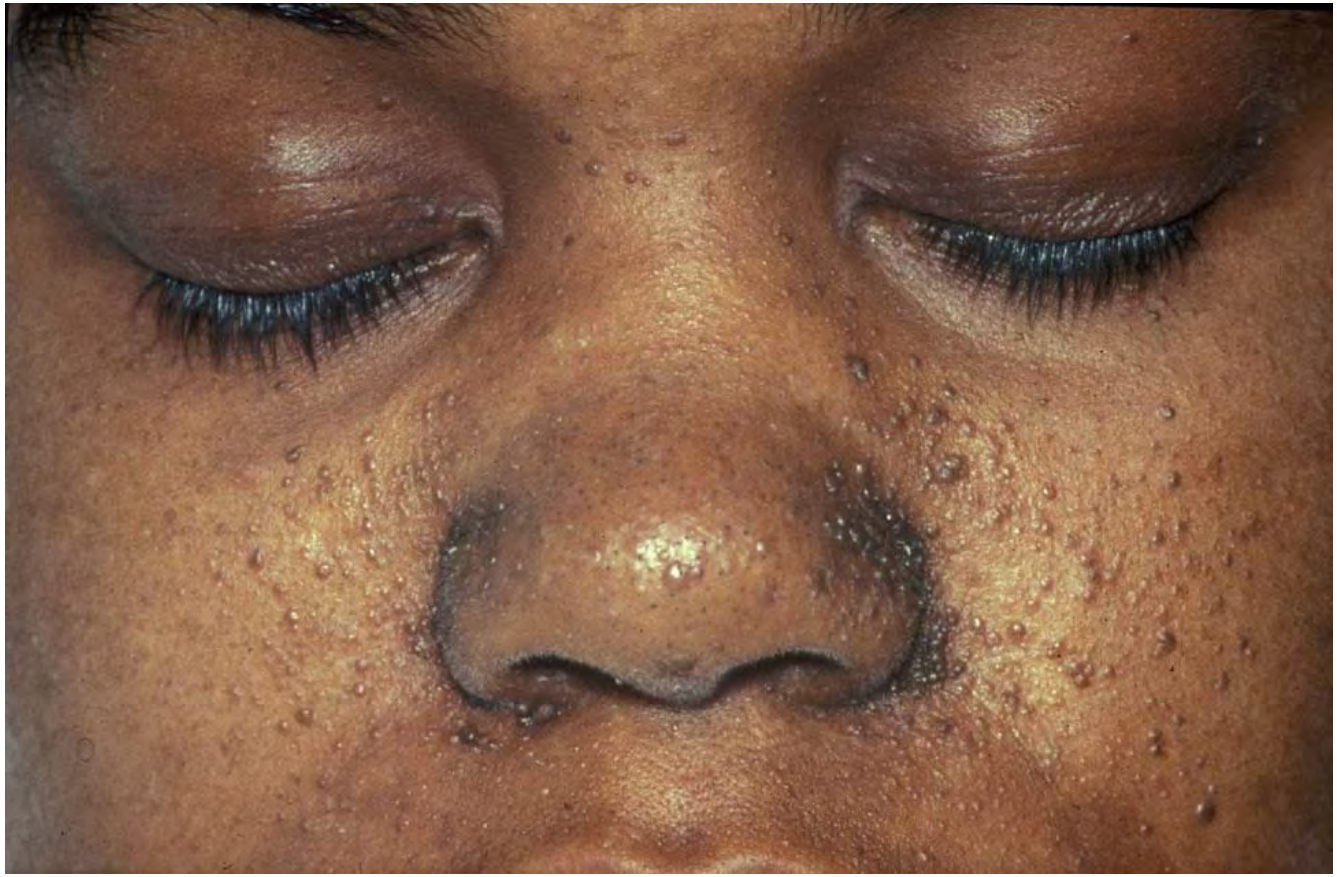
# Cardiac Rhabdomyomas

- Associated with **tuberous sclerosis (90%)**
- Autosomal dominant genetic syndrome
- Mutation in TSC1 or TSC2 gene
- TSC1: Hamartin
- TSC2: Tuberin
- Mutations → widespread tumor formation

# Tuberous Sclerosis

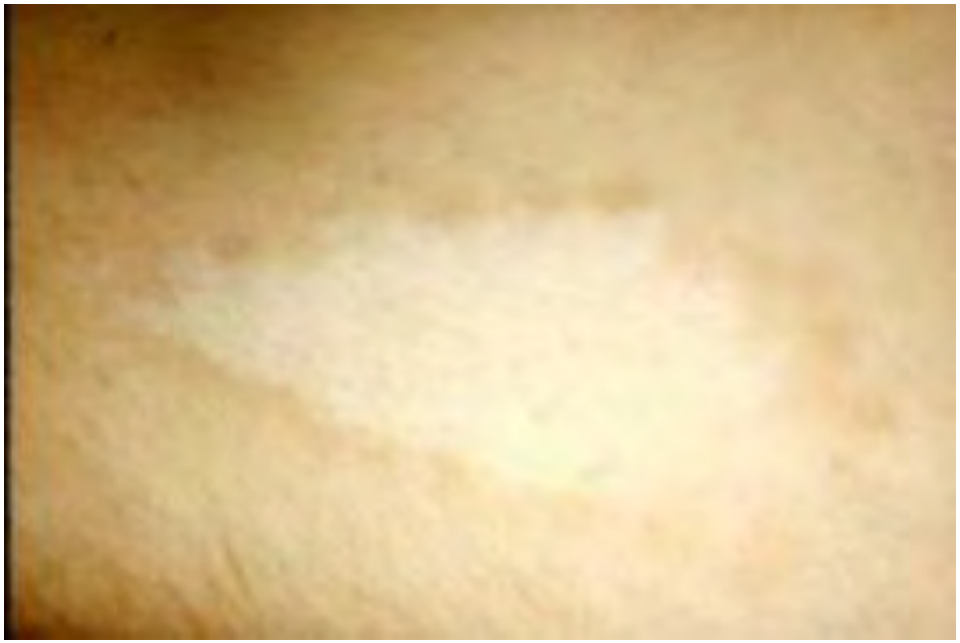
- Involves MULTIPLE organ systems
- Numerous hamartomas and other neoplasms
- **Seizures** – most common presenting feature
- "Ash leaf spots": Pale, hypopigmented skin lesions
- Facial skin spots (angiofibromas)
- Mental retardation

# Tuberous Sclerosis



Herbert L. Fred, MD and Hendrik A. van Dijk

# Tuberous Sclerosis

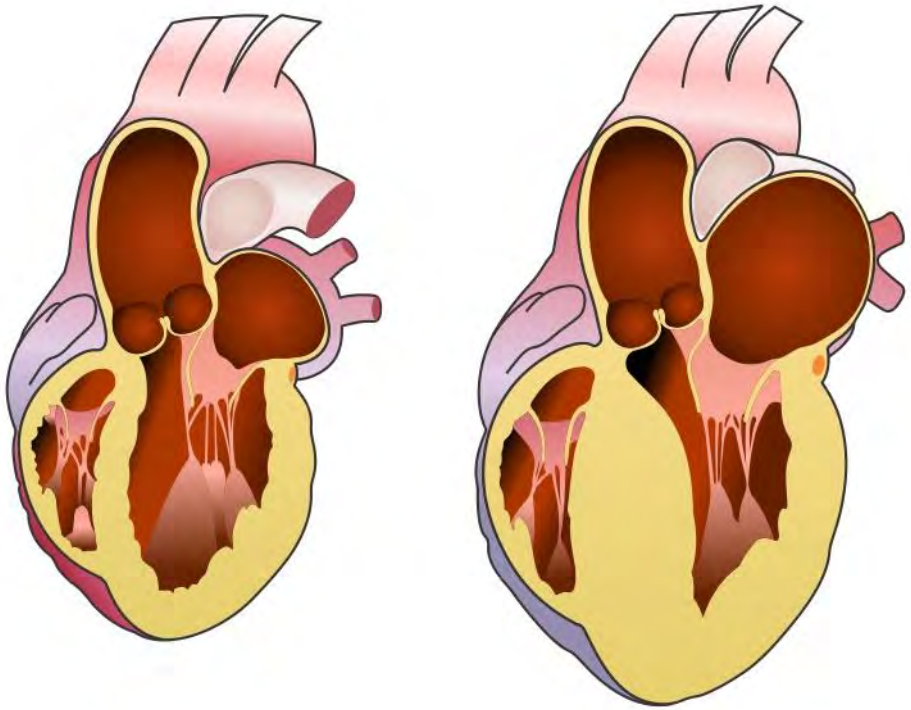


Mohd Hanafi

# Hypertrophic Cardiomyopathy

Jason Ryan, MD, MPH

# Hypertrophic Cardiomyopathy



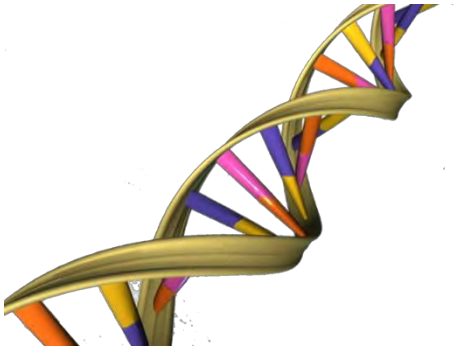
# Hypertrophic Cardiomyopathy

## Names

- Hypertrophic cardiomyopathy (HCM)
- Hypertrophic obstructive cardiomyopathy (HOCM)
- Idiopathic hypertrophic subaortic stenosis (IHSS)

# HCM

- Genetic disorder caused by gene mutations
- About 50% cases familial (50% sporadic)
- **Autosomal dominant**
- Variable expression
  - Significant variation in severity of symptoms
  - Many variations in location/severity of hypertrophy



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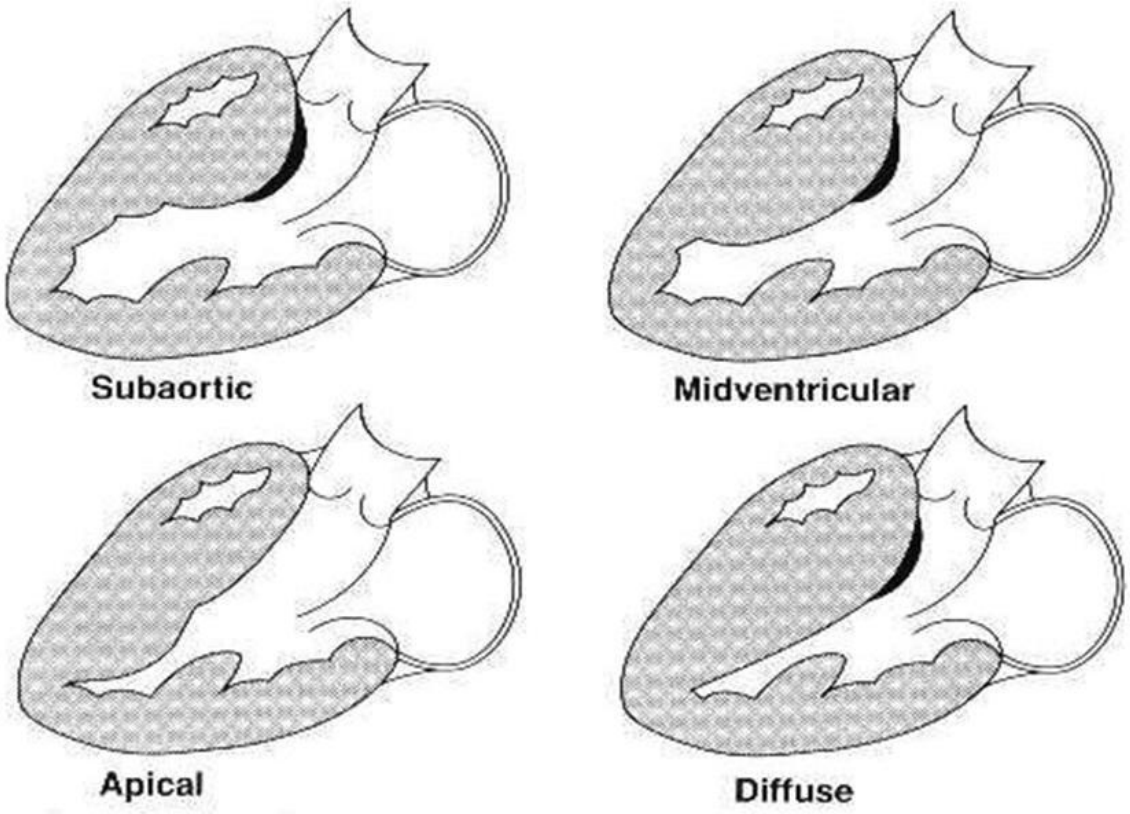
# Morphologic Variants




Zorkun/Wikipedia

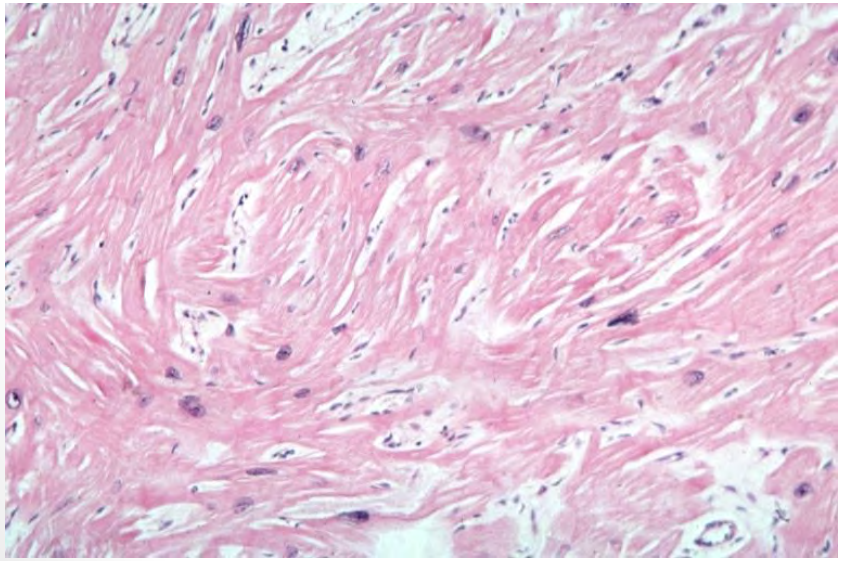
# HCM

- Often **single-point missense mutations**
  - Point mutation → altered amino acid in protein
  - 15+ genes with 1500+ mutations identified
- Often involve genes for **cardiac sarcomere proteins**
  - Beta-myosin heavy chain (40% cases)
  - Myosin binding protein (40% cases)

# HCM

## Histology

- Myocyte disarray (excessive branching)
- Hypertrophy
- Interstitial fibrosis



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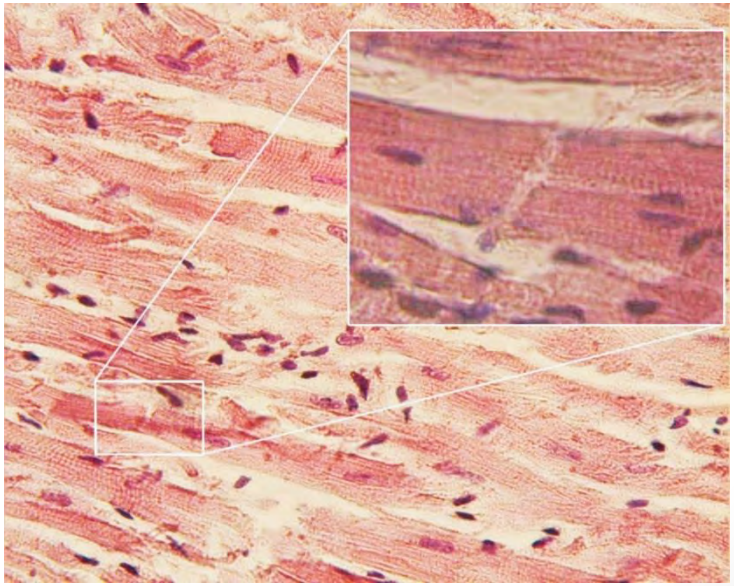


Myokard/Wikipeedia

# HCM

## Clinical Features

- Many patients asymptomatic
- **Heart failure**
  - Diastolic dysfunction
  - Impaired emptying due to LVOT obstruction
- **Chest pain (angina)**
  - Increased O2 demand

# HCM

## Clinical Features

- **Sudden cardiac death**
  - Abnormal myocytes → ventricular arrhythmias
  - Most common cause SCD in young patients
- **Syncope**
  - Arrhythmias may lead to syncope
  - Thickened myocardium → LVOT obstruction
- **Mitral regurgitation**

# HCM

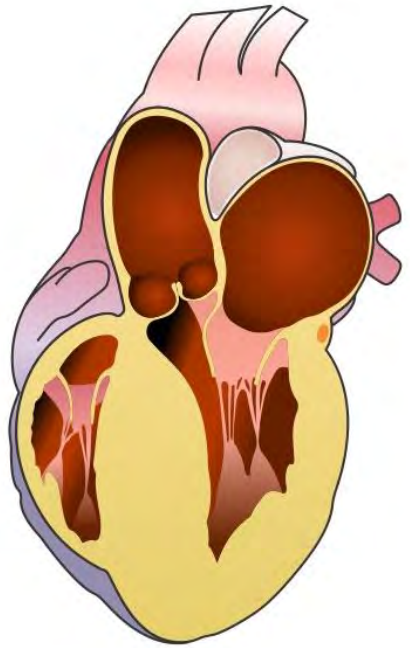
## Clinical Features

- Problem #1: Arrhythmia problem
  - Thick myocardium vulnerable to arrhythmias
  - Most serious is ventricular tachycardia → sudden death
  - Exercise (catecholamines) increase risk SCD
  - **Sudden death in athletes**
  - Defibrillators for high risk patients
  - Avoidance of exercise

# HCM

## Clinical Features

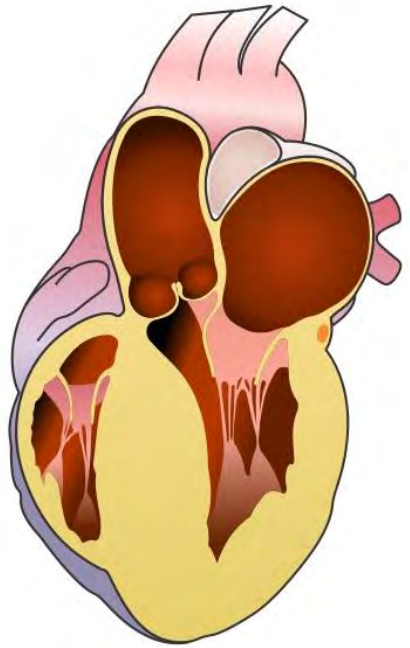
- Problem #2: Outflow obstruction problem
  - Thickened myocardium obstructs blood leaving LV
  - Same physics and symptoms as aortic stenosis
  - Heart failure, chest pain, exercise-induced syncope
  - Treated with surgery
  - Beta blockers (↓ contractility)
  - Ca blockers (verapamil)



# HCM

## Clinical Features

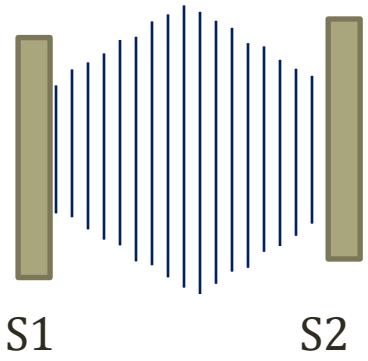
- #3: Mitral valve problem
  - High velocity in LVOT tugs mitral valve chords and leaflets
  - Causes systolic anterior motion (SAM) of mitral valve
  - Over time this leads to **mitral regurgitation**



# HCM

## Clinical Features

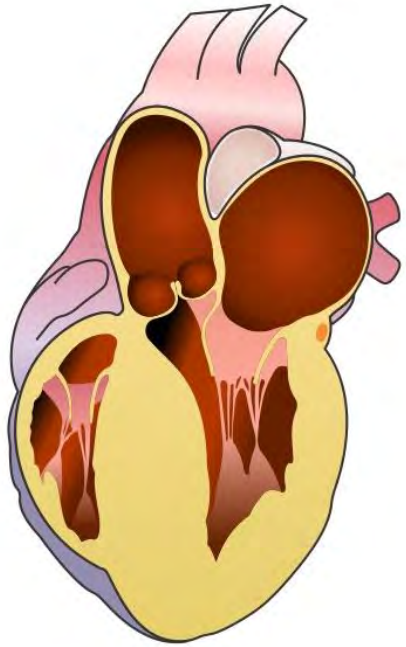
- **Systolic ejection murmur**
- Caused by outflow tract obstruction
- Sounds just like AS unless you do maneuvers
- Lots of associated abnormal heart sounds
  - S4
  - Holosystolic murmur of MR
  - Paradoxical split S2



# HCM

## Maneuvers

- For any HCM maneuver, think about size of LV
- ↑ LV size → ↓ murmur
- ↓ LV size → ↑ murmur



# HCM

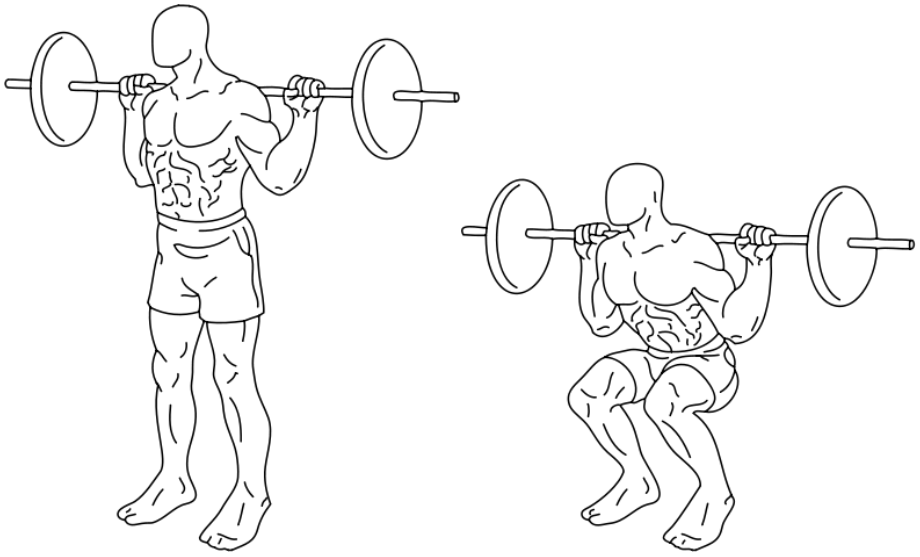
## Maneuvers

- Valsalva
  - Patient bears down as if having a bowel movement
  - Or blows out against closed glottis
  - Increase thoracic pressure → compression of veins → ↓ VR
  - Less VR → Less preload → Smaller LV cavity
  - Obstructing septum moves further into the outflow tract
  - Murmur ***INCREASES*** in intensity

# HCM

## Maneuvers

- Squatting
  - Forces blood volume stored in legs to return to heart
  - Preload rises → size of LV increases → less obstruction
  - Murmur ***DECREASES*** in intensity



Wikipedia

# HCM

## Other maneuvers

- Raising the legs
  - Increases venous return
  - More VR → More preload → Bigger LV cavity
  - This moves the obstructing septum out of the way
  - Murmur ***DECREASES*** in intensity
- Standing
  - Opposite mechanism of leg raise
  - Murmur ***INCREASES*** in intensity

# Aortic Stenosis

- Both HCM and AS cause a systolic ejection murmur
- Less effect of maneuvers on aortic stenosis
  - Fixed obstruction
- Opposite effects of maneuvers in aortic stenosis
  - Less preload → less flow → quieter AS murmur

# HCM

## Maneuver Summary

- Valsalva → INCREASE
- Standing → INCREASE
- Squatting → DECREASE
- Leg Raise → DECREASE

# HCM

## Associations

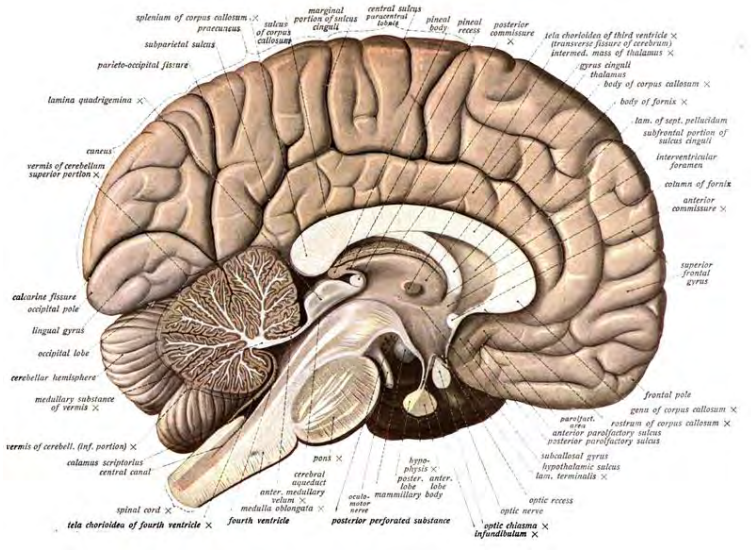
- **Maternal diabetes**
  - Infants: transient hypertrophic cardiomyopathy
  - Usually thickening of interventricular septum
  - May have small LV chamber → obstruction in newborn
  - Resolves by a few months of age

Øyvind Holmstad/Wikipedia

# HCM

## Associations

- **Friedreich Ataxia**
  - Autosomal recessive CNS disease
  - Trinucleotide repeat disorder
  - Spinocerebellar symptoms
  - Often have concentric left ventricular hypertrophy
  - Also septal hypertrophy

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# Cardiac Hypertrophy

## Other Causes

- Hypertension
- Valve disease
- Athlete's heart

Pixabay

# Cardiac Hypertrophy

## Rare Pathologic Causes

- **Fabry Disease**
  - Lysosomal storage disease
  - Deficiency of α-galactosidase A
  - Neuropathy, skin lesions, lack of sweat
  - Left ventricular hypertrophy

# Cardiac Hypertrophy

## Rare Pathologic Causes

- **Pompe Disease**
  - Glycogen storage disease
  - Acid alpha-glucosidase deficiency
  - Enlarged muscles, hypotonia
  - Cardiac enlargement

# Endocarditis

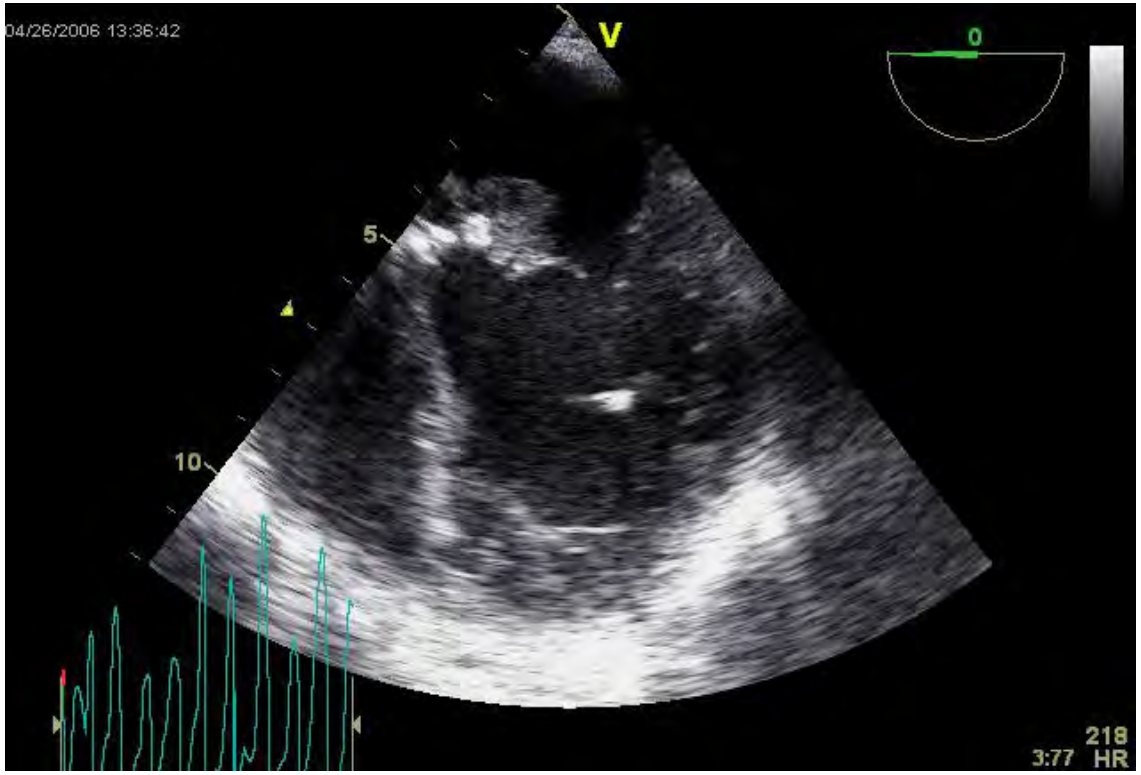
Jason Ryan, MD, MPH

# Endocarditis

- Inflammation of endocardium of heart
- Usually involves **cardiac valves**
- Often causes **new regurgitation murmur**
- Consequence of bacteremia

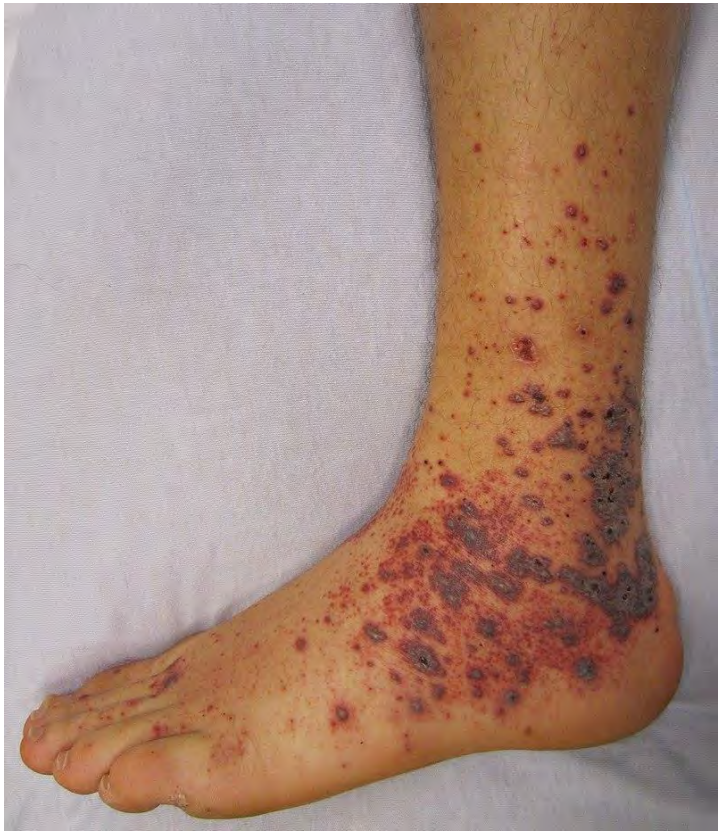
# Endocarditis

## Echocardiogram



# General Symptoms

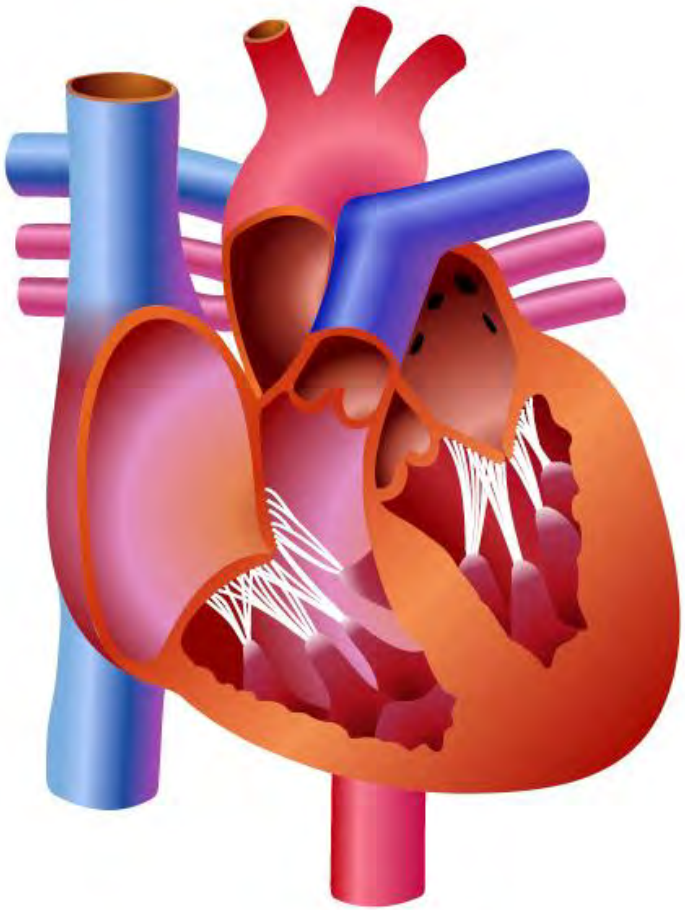
- Fever
- Chills
- Sweats
- Petechiae
  - Small vessel inflammation
  - Leakage of blood



James Heilman, MD

# Regurgitant Valve Disease

- Aortic regurgitation
- Mitral regurgitation
- Tricuspid regurgitation



# Embolic Symptoms

- Brain (stroke)
- Spinal cord (paralysis)
- Eye (blindness)
- Legs (ischemia)
- Splenic or renal infarction
- Pulmonary embolism (tricuspid)
- Coronary artery (acute myocardial infarction)

# Endocarditis Stigmata

- **Physical exam findings** in endocarditis
- Caused by **septic emboli and immune complexes**
- Very rare in modern era

# Endocarditis Stigmata

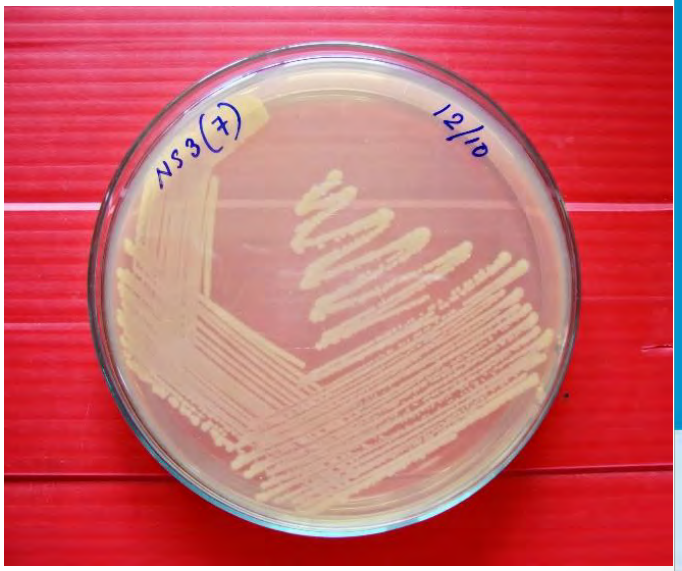
- Roth spots
  - **Retinal lesions**
  - Red with pale center
- Osler nodes
  - **Painful** bumps on pads of fingers and toes
- Janeway lesions
  - **Nontender** red macules on palms and soles
- Splinter hemorrhages
  - Reddish-brown lines under fingernails

# Diagnosis

- Major Duke Criteria
  - Positive blood cultures
  - Vegetation on echocardiogram
- Minor Criteria
  - Fever
  - Risk factors
  - Roth spots, Osler nodes, Janeway lesions, splinters
- 2 major, 1 major 3 minor, or 5 minor

# Microbiology

- Staphylococcus aureus
- Viridans streptococcus
- Streptococcus Bovis
- Enterococcus
- Staphylococcus epidermidis
- Culture negative endocarditis
- Libman-Sacks




Joydeep/Wikipedia

# Staph Aureus

- Gram positive cocci
- Catalase positive
- Coagulase positive
- May infect **tricuspid valve in IV drug users**

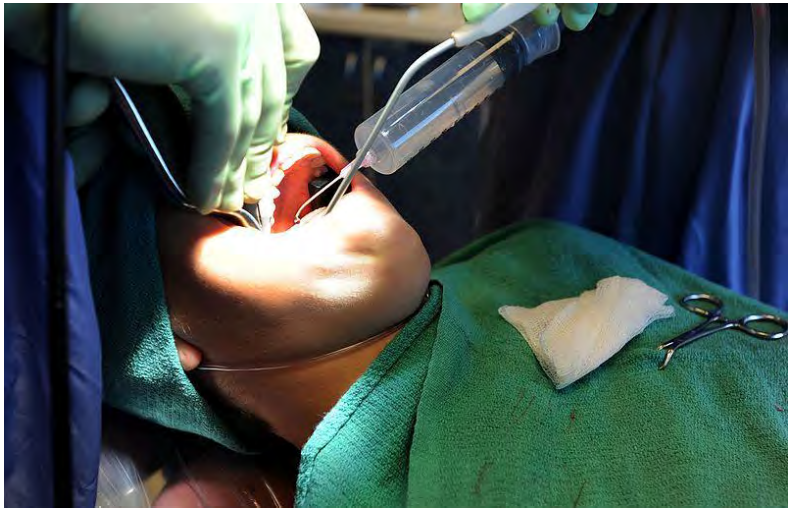
Iqbal Osman/Flikr

# Staph Aureus

- Causes **acute** endocarditis
- Rapid, severe infection
- Symptoms occur over days
- Can occur in patients with **normal heart valves**
  - No pre-disposing valvular heart condition

# Viridans Streptococcus

- Group of gram positive cocci
  - S. mitis, S. mutans, S. sanguinis
- Catalase negative
- Mouth flora
- Endocarditis may occur after **dental procedure**



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# Viridans Streptococcus

- Low virulence bacteria
- Often affect **damaged valves**
  - Bacteria synthesize dextran
  - Dextran adheres to fibrin
  - Fibrin found with endothelial damage
- Classic predisposing condition: **mitral valve prolapse**

# Viridans Streptococcus

- Causes **subacute** endocarditis
- Less severe symptoms
- Symptoms occur over days to weeks

# Streptococcus Bovis

- Gram positive cocci
- Lancefield group D
- Normal gut bacteria
- Associated with **colon cancer**
  - All subtypes associated with cancer
  - Strongest association: **S. gallolyticus** (S. bovis type 1)

# Enterococcus Endocarditis

- Gram positive cocci
- Lancefield group D
- Normal gut bacteria
- Usually a subacute endocarditis course
- Commonly occurs in **older men**
- **Associated with manipulation of GI/GU tract**
  - Abdominal surgery
  - Urinary catheter
  - TURP for treatment of BPH

# Prosthetic Valve Endocarditis

- Occurs with mechanical or biologic valves
- Rarely cured with antibiotics
- Usually requires repeat valve surgery
- Similar bacteria to native valve endocarditis
- **Staphylococcus epidermidis**
  - Rarely cause endocarditis except in prosthetic valves

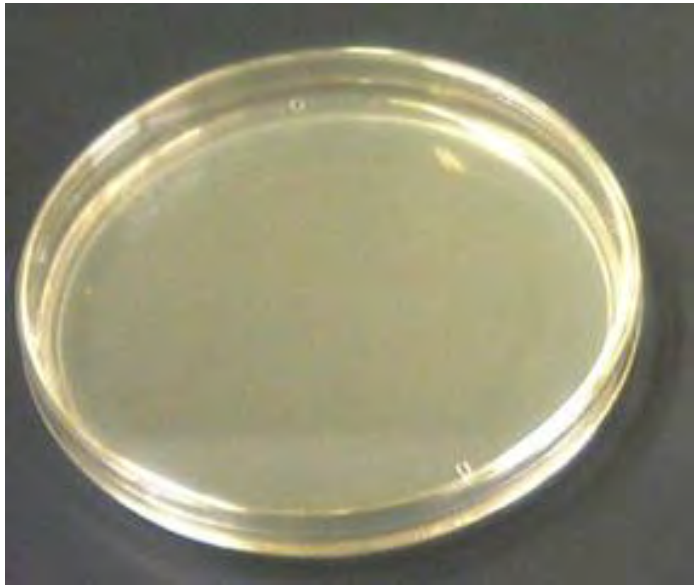
Stif Komar/Wikipedia

# Staphylococcus Epidermidis

- Catalase positive
- Coagulase negative (unlike S. Aureus)
- Most common coagulase negative staphylococcus
- **Normal skin flora**
- Low virulence
- Commonly cause infection of **prosthetic material**
  - Cardiac valves
  - Intravascular catheters
  - Prosthetic joints

# Culture Negative Endocarditis

- Evidence of endocarditis with sterile blood cultures
- Caused by rare bacteria difficult to culture
- Coxiella burnetii
- Bartonella



Y tambe/Wikipedia

# Coxiella Burnetii

- Zoonotic bacteria (transferred from animals)
- Obligate intracellular bacteria
- Found in **farm animals**
- Cattle, sheep and goats
  - Abortions in farm animals: Coxiella **placenta** infection
- Humans **inhale aerosolized bacteria** from animals
- **Causes Q fever**

# Coxiella Burnetii

- Acute Q fever
  - Flu-like illness
  - May present as pneumonia
  - **More than half of cases: no symptoms**
- Chronic Q fever
  - **Most common manifestation is endocarditis**

# Bartonella

- Bartonella quintana
  - Small, gram-negative rod
  - Transmitted by **lice**
  - Patients with poor hygiene
- Bartonella henselae
  - Found in **cats**
  - Causes cat scratch fever

BruceBlaus/Wikipedia

Inge Wallumrød/Pexels.com

# NBTE

## Non-bacterial, thrombotic endocarditis

- Libman-Sacks Endocarditis or Marantic endocarditis
- Lesions on valves that look like endocarditis
- Found on **both sides of valve**
- Mitral valve most common
- Formed by thrombus, immune complexes
- Seen in hypercoagulable states
  - **Advanced malignancy**
  - Systemic lupus erythematosus

# NBTE

## Non-bacterial, thrombotic endocarditis

- **Often asymptomatic** identified at autopsy
- Rarely cause regurgitation or murmurs
- Thrombus easily dislodges → **embolization**
- Most patients asymptomatic until embolism occurs
- May embolize to spleen, kidney, skin, extremities
- May cause stroke
- Can cause myocardial infarction

# Bacterial Endocarditis

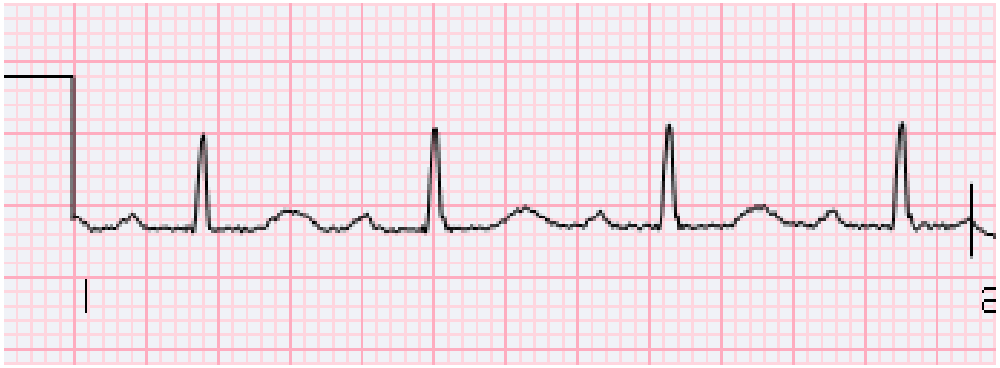
## Treatment

- Several weeks appropriate antibiotics
- Broad spectrum antibiotics initially
- Drug therapy changes when bacteria identified
- Valve surgery sometimes required
  - Large vegetation
  - Severe valve disease → heart failure

# Bacterial Endocarditis

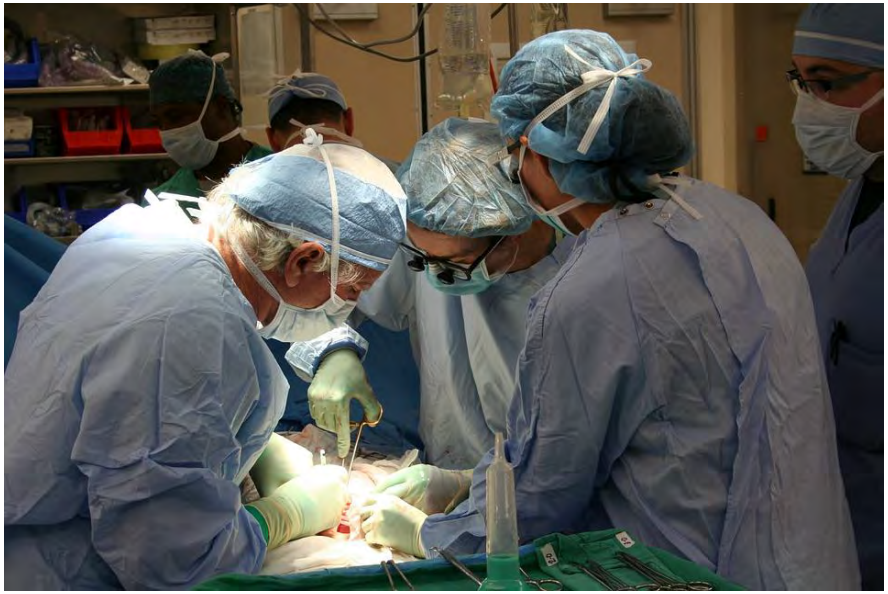
## Complications

- May form abscess beneath valve annulus
- Persistent fever, bacteremia often indicates abscess
- Aortic valve abscess can lead to heart block
  - AV node dysfunction



# Prophylaxis

- Primary prevention for bacterial endocarditis
- **Done before high-risk medical procedures**
- Antibiotics given to some high-risk patients
- New guidelines restrict to highest risk circumstances



Scotth23/Pixabay

# Prophylaxis

| Conditions | Procedures |
| --- | --- |
| Prosthetic valves<br>Prior endocarditis<br>Cyanotic congenital heart disease<br>Heart transplants | Dental work<br>Respiratory procedures<br>Skin surgery |

**Amoxicillin**
**Clindamycin**