



TYPES OF SHOCK

Hypovolemic, Cardiogenic & Obstructive Shock

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OUTLINE

- I) DEFINITION
- II) TYPES OF SHOCK
- III) APPENDIX
- IV) REVIEW QUESTIONS
- V) REFERENCES

I) DEFINITION

- Shock is any situation in which there is inadequate tissue perfusion (not enough blood flow going to the tissues) → ↓ oxygen delivery to the tissues → ischemia → over a long period of time, necrosis:
 - Recall: *Tissues make up organs*
 - ↓ oxygen delivery to the tissues → organ failure (if not reversed)
- Shock is a progressive process:
 - Beginning compensatory stage in ↓ BP
 - Refractory component of shock wherein BP CANNOT be restored despite exhaustive efforts → deadly if not reversed
- Shock is when ↓ BP, which is due to:
 - ↓ CO → $HR \times SVR$
 - ↓ SVR or TPR

II) TYPES OF SHOCK

(A) HYPOVOLEMIC

- Hypo = low, below the normal volume range → lose blood volume

(1) Causes

- **Blood loss**
 - GI bleed (very common)
 - Severe peptic ulcer or perforated duodenal ulcer
→ empties into actual peritoneal cavity
 - Abdominal aortic aneurysm → when ruptured, spill blood into abdominal cavity
 - Trauma (i.e. hit or shot on the head)
 - Postpartum hemorrhage
 - ~24 hours after childbirth, woman starts losing significant volumes of blood (500-1000 mL)
 - Ectopic pregnancy

Recall:

- ovary ejects ovum → fallopian tubes (ampulla) → (+) fertilization with sperm → cilia transports → implanted in the endometrium where the uterine cavity

- Implanted in the actual fallopian tubes → fetal abortion

- **Sequela: Pelvic Inflammatory Disease**

- Hemoptysis or coughing off blood
 - Ruptured esophageal varices
 - Goodpasture's syndrome: collagen connective tissue disorder
 - Pulmonary embolism
- **Non-blood Fluid loss**
 - Severe 3rd degree burn: prevent from getting dehydrated
 - Excessive vomiting, diarrhea
 - Bowel obstruction: affects absorption, food coming down
 - Effect: Pulls fluid from your body into the GI tract

- Acute pancreatitis

Recall:

- Pancreatic proteases ↑ activated → digesting the pancreatic tissue → pancreatic fluid leaking out into the abdominal cavity

- Diabetic ketoacidosis

Recall:

- Kidney has a transport maximum: ~375 mg/min filtration of glucose → reabsorb it back into the blood
- Hyperglycemia (↑ blood glucose level) EXCEEDS transport maximum → **CAN'T REABSORB glucose into the blood** → glucosuria (urine) + water follows → ↑ Urine output (sugar and water)

(2) Pathophysiology of compensation

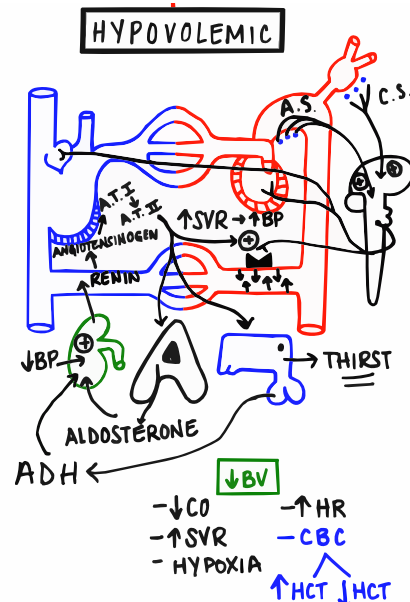


Figure 1. Hypovolemic shock.

Table 1. Pathophysiology of compensation in hypovolemic shock.

Event	Response
↓ Blood volume	Baroreceptors in the aortic and carotid sinus stimulate medullary center ↓ Medulla sends out action potentials ↓
	1) Vasomotor center: Goes to smooth muscle within the tunica media ↓ Release epinephrine ↓ Vasoconstriction ↓ ↑ SVR → ↑ BP
	2) Goes to the heart ↓ ↑ HR • Recall: $CO = SV \times HR$ • $SV = EDV - ESV$ ↓ EDV (filling) due to ↓ BV - ESV (how much it pushes out) • Problem: - Even if ↑ contractility to ↑ CO - BUT ↓↓ EDV so blood pumped out (CO) is NOT INCREASED • ↓ Blood volume, EDV → ↓ SV → ↓ CO
	3) Stimulate the kidneys to ↑ BV ↓ ↑ Renin → Angiotensinogen into Angiotensin I → Angiotensin II ↓ a) a1 receptors on renal vessels: vasoconstriction → ↑ SVR b) adrenal cortex: produce aldosterone → ↑ sodium & water reabsorption from the kidneys c) pituitary gland: ADH → ↑ water reabsorption d) ↑ thirst center
	• Tachycardia • CBC ↑ HCT: NOT ↑ RBC BUT ↑ plasma loss = ↑ RBC/plasma composition → hemoconcentration = non-blood fluid loss ↓ HCT: i.e. blood loss causes • Cyanosis - Bluish cast on fingertips, toes, lips, tongue, mucous membranes - Due to ↓ Blood volume → ↓ tissue perfusion • Hypoxia - Due to ↓ Blood volume → ↓ tissue perfusion - If not resuscitated → ischemia → necrosis → multisystem organ failure

(3) Treatment

● Resuscitate blood volume

- Central line IV OR
- Large bore IV: bigger gauge needle to infuse fluid faster
- Fluid selection:
 - Crystalloids: administer right away
 - Normal Saline
 - Lactated Ringer
 - Plasma volume expanders
 - Stabilizes colloid osmotic pressure → controls the amount of water leaving the bloodstream into the tissue spaces
 - Albumin
 - HetaStarch

● Prevent hypothermia

- ↓ Blood volume → ↓ internal body temperature regulation

● Control hemorrhage → transfusion



(B) CARDIOGENIC

(1) Causes

- **Myocarditis:** inflammation of the myocardium
 - Coxsackie B virus: one of the most common causes, this is like an enterovirus
- **Massive / Multiple / Severe myocardial infarction**
- **Aortic valve stenosis and Mitral valve stenosis**
 - ↑ workload on the heart → heart becomes very weak
- **Arrhythmias**
 - Tachyarrhythmia: ↑ HR, but NOT enough time for filling → ↓ ejection
 - Bradyarrhythmia: ↓ CO (blood being pumped out of the heart)
- **Dilated cardiomyopathy**
 - Ventricular muscles become very weak, flabby → ↓ pump
- **Congenital heart disease**
 - Ventricular septal defect
 - Truncus arteriosus

(2) Pathophysiology

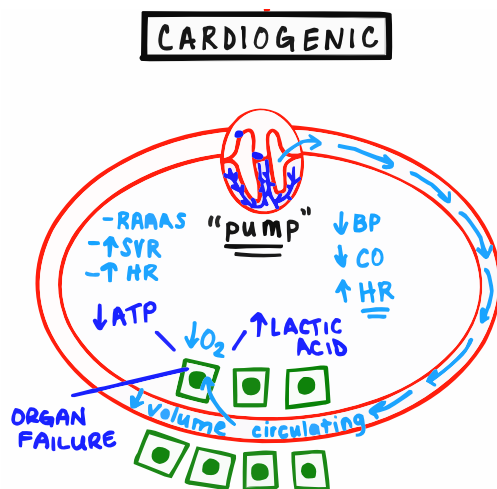


Figure 2. Pathophysiology of cardiogenic shock.

- Problem is due to the heart not being able to generate a certain amount of power → ↓ adequate volume of blood into the circulation

Table 2. Pathophysiology of cardiogenic shock.

Event	Response
Pump "ventricular" failure	↓ contraction ↓ propel blood into the systemic, peripheral & pulmonary circulation ↓ Volume of blood circulating ↓ systemic hypotension (↓BP),
	↓ CO: congestion of blood within the heart ↓ oxygen delivery to tissues ↓ ATP, ↑ Lactic Acid Over time, ischemia > necrosis > organ failure
↓CO Compensation	● ↑ HR: tachycardia but is not going to be enough ● ↑ Renin-Angiotensin-Aldosterone-ADH system ● ↑ SVR

Recall:

- A lot of metabolic pathways in the body depend upon oxygen to produce ATP by cellular respiration → ↓ activities within the cell
 - ↓ protein synthesis
 - ↓ transport pumps
 - ↓ muscular contraction
 - ↓ neuron transmission
- ↓ ATP shifts aerobic cellular respiration to anaerobic respiration → ↑ Lactic acid
 - ↑ Lactic acid dissociating → give up ↑ protons → ↑ acidity = metabolic acidosis
 - ↓ Heart contractility
 - ↓ Heart rate

(3) Treatment

- Treat the underlying disease
 - Myocardial infarction
 - Angioplasty: remove the embolus within the coronary vessels
 - Thrombolytics: breaks the clot
 - Tissue plasminogen activator
 - Heparin
- Administer oxygen: important and main management
- Small amount of isotonic fluids
 - Not losing blood volume, just not able to circulate the blood from the heart → ↓ volume of blood pushed out into the circulation
- Vasopressors
 - Have a hard time being able to get the heart to contract very powerfully
 - Epinephrine:
 - ↑ inotropy (contractility of the heart)
 - ↑ SVR (constricting blood vessels)
 - Dobutamine
 - ↑ inotropy (contractility of the heart) by binding to B1 adrenergic receptors of the heart
 - Amrinone
 - ↑ inotropy (contractility of the heart)
 - Phosphodiesterase-3-inhibitor (PDE3)
 - PDE3: breaks down cAMP → ↓ PKA levels → ↓ Calcium coming into the cell → ↓ contractility
 - Inhibits PDE3 → ↓ breaking down of cAMP → ↑ PKA levels → ↑ Calcium coming into the cell → ↑ contractility
 - At refractory period (point of irreversibility, nonresponse from repeated revival of blood pressure)
 - Atropine
 - ↓ muscarinic receptors
- Intra-aortic balloon pump
 - Device situated in the abdominal aorta →
 - whenever the heart contracts, it stays deflated
 - whenever the heart relaxes, it inflates and expands
 - Purpose: in cardiogenic shock, myocardium isn't getting much oxygen so with this, **the balloon spreads out whenever the heart's relaxed to push the blood into the coronary vessels → save myocardium from irreversible damage**



(C) OBSTRUCTIVE

- There is some type of internal or external obstruction that affects the:
 - heart
 - chambers of the heart, or
 - blood flow going out of or into the heart great vessels

(1) Causes

Recall:

- Atmospheric air (P_{atm}): 760 mmHg
 - Area of higher pressure $\rightarrow$ lower pressure
 - Ex: P_{atm} goes into the pleural cavity which is normally contained with fluid $\rightarrow \uparrow$ air accumulated in the cavity $\rightarrow \uparrow P_{IP}$ from -4 mmHg to 0 to +1 mmHg
- 2 types of pressures:
 - Intrapulmonary pressure (P_{pul}): 0 mmHg
 - Intrapleural pressure (P_{IP}): -4 mmHg
 - You never want $P_{IP} \geq P_{pul}$

OBSTRUCTIVE

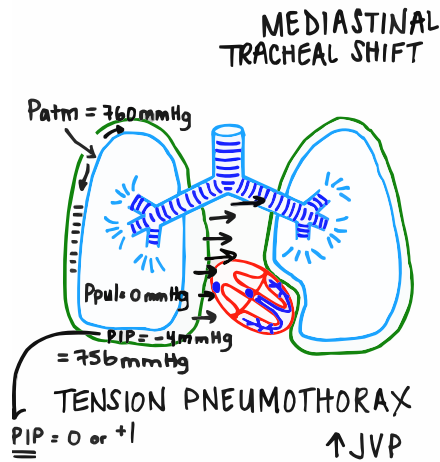
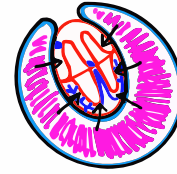


Figure 3. Tension pneumothorax.

- **Tension pneumothorax**
 - Damage to actual parietal pleura due to a stab wound $\rightarrow$ atmospheric pressure
 - Dangerous because $\uparrow P_{IP} >$ Pressure inside the actual lungs $\rightarrow$
 - pushes the lungs $\rightarrow$ **shifts mediastinum contralaterally $\rightarrow$ compress the heart and blood vessels**
 - Compress both SVC and IVC
 - $\downarrow$ blood going into and out of the heart
 - **shifts trachea contralaterally**
 - **Physical exam:**
 - Upon percussion, you will hear a tympanic tap
 - louder, low pitched, hyperresonance
 - Means there's some type of gas or air within that cavity
 - Decreased breath sounds on the affected side due to lung collapse
 - $\uparrow$ JVP, distended neck veins: due to compressed SVC ($\downarrow$ blood going into the heart)
 - X-ray: confirmatory



PERICARDIAL TAMPONADE

Figure 4. Pericardial tamponade.

• Pericardial tamponade

Recall:

- 2 types: visceral and parietal (outer) layer
- In between those layers, it contains serous pericardial fluid
 - Due to a situation where fluid starts developing inside of pericardial cavity
 - If diseased, $\uparrow$ pericardial fluid accumulation which strangulates the heart
 - Effect:
 - $\downarrow$ volume of heart chambers
 - $\downarrow$ filling of blood into the heart
 - $\uparrow$ restriction, harder to contract

○ Beck's triad

Table 3. Beck's triad.

Sign	Pathophysiology
Jugular vein distention or $\uparrow$ JVP	due to compressed SVC ($\downarrow$ blood going into the heart)
Hypotension or $\downarrow$ BP	due to $\downarrow$ filling of blood into the heart and $\uparrow$ restriction, harder to contract
Distant heart sounds	$\uparrow$ Fluid = $\uparrow$ sound moves from a farther distance



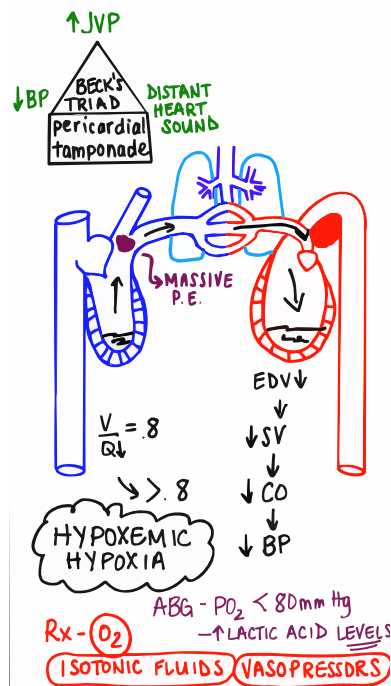


Figure 5. Massive pulmonary embolism.

• Massive pulmonary embolism (PE)

- Saddle embolism: PE in the pulmonary trunk
 - Blocks the pulmonary artery = ↓ blood flow passing through the area →
 - ↓ fluid going into the right ventricle
 - ↓ fluid going into the left ventricle
 - ↓ EDV → ↓ SV → ↓ CO → ↓ BP or hypotension
 - ↑ pressure accumulates beyond the embolus = ↑ PCWP (pressure that's trying to push blood back into the left atrium) → can rupture some capillaries = **Hemoptysis**
 - Note: not that important for obstructive shock, more for cardiogenic shock

Recall:

- V/Q ratio = 0.8
- V/↓Q:
 - overall number will be > 0.8
 - Ventilation decreases → bronchioles constrict = **Respiratory distress**
- ↓ Oxygenation = hypoxemic hypoxia
 - ↓ oxygen delivery to tissue → ischemia → necrotic → organ failure
- ↓ ABG
 - Partial pressure Oxygen < 80 mmHg
 - ↑ Lactic acid (aerobic respiration shifts to anaerobic respiration) → not treated, may go to multiple organ system failure

• Proximal Aortic Dissection

- If it starts dissecting → squeeze the vessels supplying the heart
 - ↓ Filling of the heart
 - ↓ Ejection of blood into the aorta

(2) Treatment

- Treat the underlying disease
 - Pneumothorax:
 - needle decompression to equalize the pressure
 - get the air out of the actual pleural cavity
 - Pericardial tamponade
 - Pericardiocentesis to drain the fluid out of the pericardial cavity
 - Massive pulmonary embolism
 - Thrombolytics
 - Heparin
 - Embolectomy
 - Proximal Aortic Dissection
 - Surgical intervention
- Administer oxygen: important and main management
- Isotonic fluids
- Vasopressors:
 - ↑ inotropy of the heart
 - Drugs that can ↑ vasoconstrict → ↑ resistance ↑ BP



III) APPENDIX

Table 4. Abbreviations.

ABG	Arterial blood gas
BP	Blood pressure
CO	Cardiac output
EDV	End diastolic volume
ESV	End systolic volume
JVP	Jugular venous pressure
HCT	Hematocrit
HR	Heart rate
IVC	Inferior vena cava
PCWP	Pulmonary capillary wedge pressure
PKA	Protein kinase A
SV	Stroke volume
SVC	Superior vena cava
SVR	Systemic vascular resistance
V/Q	Ventilation / perfusion

IV) REVIEW QUESTIONS

1) 75/F consulted for shortness of breath of 5 days duration. Upon history taking, the resident elicited a history of cancer. Her physical examination findings showed tachypnea, hypoxia, and hypotension. Auscultation revealed muffled heart tones and breath sounds. Her jugular vein distension is at 8 cm H₂O. What is the most probable cause of her shock?

- Aortic dissection
- Massive pulmonary embolism
- Pericardial tamponade
- Dilated cardiomyopathy

2) Which of the following defines Cardiogenic Shock?

- Elevated Filling pressure or PCWP
- Atrial failure
- Systolic dysfunction
- None of the above

3) What is the mechanism behind multi-organ hypoxia in patients who go into shock?

- Increased O₂ utilization
- Low cardiac output
- Reduced O₂ consumption
- Severe peripheral vasodilation

4) In the previous question, what treatment should you administer?

- Epinephrine
- Increased IV fluids to compensate for the low cardiac output
- Treat the underlying disease and administer oxygen
- A & C
- All of the above

CHECK YOUR ANSWERS

V) REFERENCES

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TYPES OF SHOCK

Types of Shock: Septic, Anaphylactic & Neurogenic Shock

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OUTLINE

- I) PHYSIOLOGIC CHARACTERISTICS OF THE VARIOUS FORMS OF SHOCK
- II) TYPES OF SHOCK
- III) APPENDIX
- IV) REVIEW QUESTIONS

I) PHYSIOLOGIC CHARACTERISTICS OF THE VARIOUS FORMS OF SHOCK

RECALL:

- ↓ BP can be either due to:
 - ↓ CO
 - Hypovolemic, cardiogenic, obstructive shock
 - ↓ SVR
 - Distributive shock

GUIDE:

Table 1. Types of shock. [Morozowich, & Ramakrishna, 2015]

Type of Shock	CO	SVR	CVP, PCWP
Hypovolemic	↓	↑	↓
Cardiogenic	↓	↑	↑
Obstructive	↓	↑→	↑ / ↑→
Distributive	↑	↓	↑
Neurogenic	↓	↓	↓

- Hypovolemic: ↑ SVR due to constrictor response
- Cardiogenic: ↑ CVP/ PCWP due to impaired myocardium
- Distributive: ↓ SVR due to ↑ expansion/dilation

II) TYPES OF SHOCK

(A) DISTRIBUTIVE

- Pathophysiology:
 - Blood vessel ↑ expansion/dilation → ↓ SVR → ↓ tissue perfusion → ↓ oxygen delivery "hypoxia" → hypoxia progresses to ischemia → necrosis of tissue → tissue death → organ failure

(1) Septic

- Gram positive bacteria mostly release exotoxins
- Fungi also release certain chemical modulators that act like endotoxins but are NOT endotoxins
- Gram positive bacteria + Fungi can induce the similar septic shock just like in Gram negative bacteria, but the latter is more common.
- Gram negative bacteria release endotoxins
 - Endotoxins: like lipopolysaccharides, part of their membrane [Popoff, 2018]

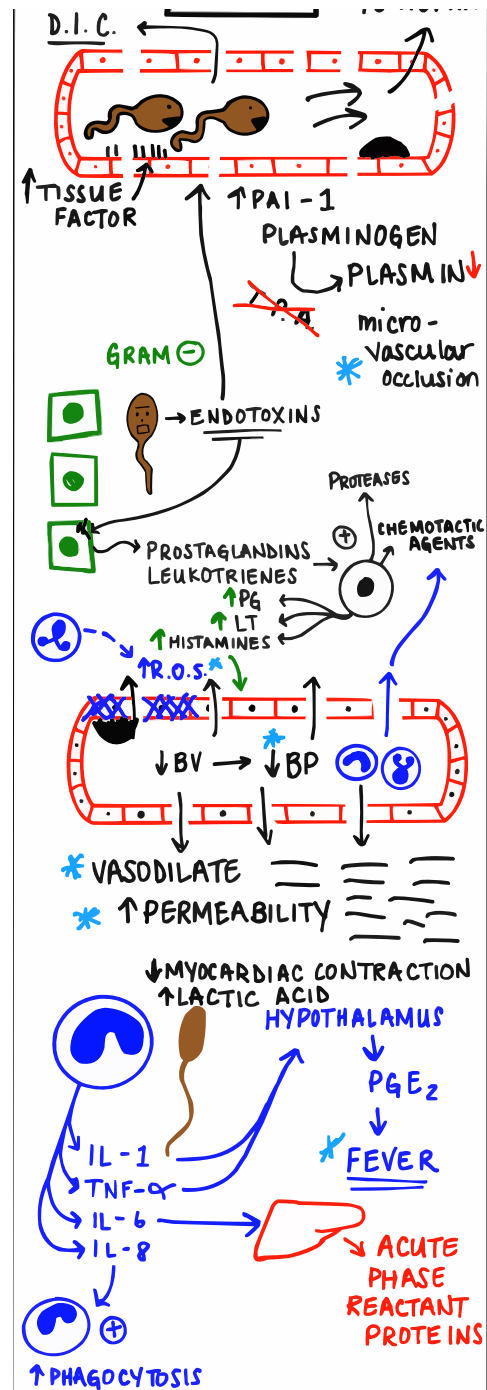


Figure 1. Pathophysiology of septic shock.



Table 2. Septic shock pathophysiology.

Event	Effect
Endotoxins damage the tissues	tissues release chemical mediators: prostaglandins, leukotrienes, lipid mediators like messenger molecules that are broken down from arachidonic acid ↓
	Stimulate mast cells → Mast cells release chemical mediators: histamine, leukotrienes, prostaglandins, proteases (to activate complements C3 & C5 to C3a, C5a), chemotactic agents ↓
	↑ Agents in the blood vessel → ↑ vasodilation + ↑ vascular permeability (leakiness out into the interstitial space) → ↓ vascular resistance ↓
	↑ fluid accumulation in tissues ↓ blood volume = ↓ BP
Complement protein activation	Monocytes, neutrophils recruited from the blood vessel and into the area where infection should be killed
	C3a & C5a: ● stimulate endothelial cells to ↑ endothelial cell dilation & ↑ permeability ● ↑ chemotaxis
Monocyte	● Fights off gram-negative bacteria ● Releases chemicals ○ ↑ IL-1 + ↑ TNF-α: ▪ goes to hypothalamus → reset hypothalamic temperature system → releases PGE-2 w/c change body's thermometer reading → ↑ body temperature = fever ▪ ↑ vasodilation ○ IL-6: goes to liver → ↑ Acute phase reactant proteins (c-peptide, haptoglobin, ceruloplasmin) = ↑ inflammation ○ IL-8: ↑ phagocytosis, ↑ chemotaxis ○ Other ILs, TNF-α: ↓ myocardial contraction ▪ ↓ O ₂ delivery to tissues → ↑ lactic acid
	● Fights off the bacteria ● Release chemicals: ○ ↑↑ ROS: starts damaging endothelial cells → ↑ clots, micro-vascular occlusions (thrombus) ○ Recall: Virchow's triad states that endothelial dysfunction → ↑ clots ○ Extracellular traps: histone proteins + DNA → bind to bacteria to tag them
Neutrophils	
Endotoxins go into endothelial cells	● ↑ Plasminogen Activator Inhibitor-1: ○ Bad because this also ↓ TPA which converts plasminogen → plasmin (↑ fibrinolysis) ○ General effect: ▪ ↓ fibrinolysis ▪ ↑ clots, microvascular occlusions (thrombus) ▪ ↓ blood flow beyond the occlusion = ischemia
	● ↑ Tissue Factor ○ Important to generate coagulation cascade ○ General effect: ↑ clots, microvascular occlusions ● Disseminated intravascular coagulation (DIC): when microvascular occlusions appear in various parts of the body ○ Bleeding due to ↑ consumption of clotting proteins ○ By the time you need to clot, ↓ clotting proteins → bleed from the eyes, mouth, etc

In summary, the event of septic shock:

- ↓ BP due to:
 - ↑ vasodilation → ↓ SVR
 - ↑ vascular permeability
- Septic shock in early stages: ↑ CO
 - Ventricular compensation for ↓ blood volume & ↓ contractility = walls become thinner
- ↑ Fever
- ↑ Acute phase reactant proteins production
- ↑ Clots, Microvascular occlusion → DIC, ischemia

Treatment

- **IV Antibiotics**
 - Request for culture to know the kind of bacteria
 - Use broad spectrum antibiotics so you can treat even if you don't know the bacteria yet
 - 3rd generation cephalosporin (Ceftriaxone) +
 - Penicillin (Piperacillin) + B-lactamase inhibitor (tazobactam) = Zosyn
 - Metronidazole/Clindamycin: intra-abdominal infection
 - Ceftriaxone: no spleen (↑ risk for encapsulated bacteria like N. meningitidis, S. pneumoniae, H. influenzae)
 - Vancomycin: if MRSA
 - Gentamycin: if Pseudomonas aeruginosa
- **Fluids**
 - Crystalloid: Normal Saline/ Lactated Ringer
- **Vasopressors**
 - If not responsive to fluids over a certain amount of time
 - To constrict the blood vessels → get the blood circulating again

(2) Anaphylactic

- Severe systemic allergic reaction, due to first exposure

(i) Causes:

- Drug allergy (Penicillin, Morphine, etc.)
- Bee/ bug stings
- Food allergy
- IV contrast allergy

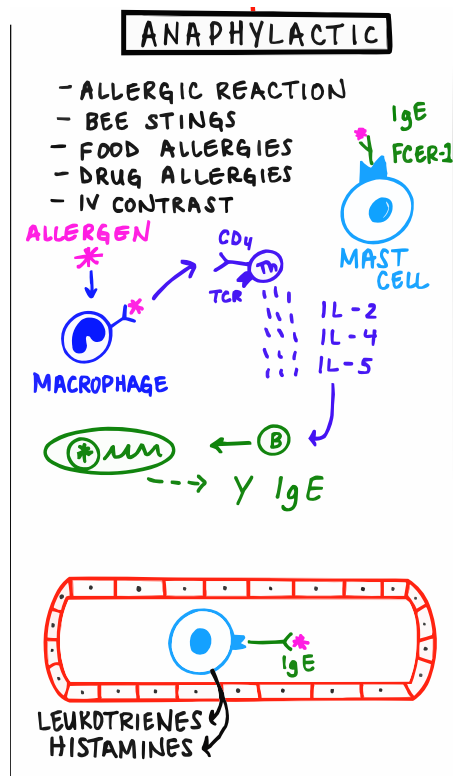


Figure 2. Pathophysiology of anaphylactic shock.



Pathophysiology:

Table 3. Anaphylactic shock pathophysiology.

Event	Response	
Exposure to allergen the first time	macrophages encounter the allergen → express allergen on its membrane with the MHC-II complex ↓	
Antigen + MHC-II complex	takes it to a T-helper cell via its TCR (receptor on the membrane) ↓ T-helper cell produces mediators: IL-2, IL-4, IL-5	
T-helper cell cytokines (IL-2, IL-4, IL-5)	Stimulate B-cell ↓ Convert to Plasma cell → secrete antibodies	IL-5: makes B-cell produce a special type of antibody (IgE)
Mast cell (location: perivascular tissue)	IgE antibody + Mast cell via its FcεRI receptor	
	Anytime the person is exposed to the allergen → ● may produce small amount of histamine OR ● have a hyperactive immune response (↑ inflammatory mediators)	
Mast cell activation	Mast cells degranulate → ↑↑↑ chemical mediators	
	● ↑Leukotrienes	
	● ↑Histamines	
	○ Usually affect the airways & skin	
	○ Go to blood vessels → bind on receptors → ↑ vasodilate + vascular permeability →	
	▪ fluid buildup	
	▪ ↓ SVR, BP, O2 delivery	
	Location	Effect
	airway	restricting airway
	bronchial smooth muscle	constrict, ↓ air = severe respiratory distress
larynx	↑ edema, ↓ air	
lips, eyes	angioedema	
skin	↑ itch, rash, hives	
Blood vessel	↓ Fluid = ↓ blood volume, ↓ BP, systemic hypotension	
	↓ oxygen delivery to tissues → ischemia → necrotic, organ failure	

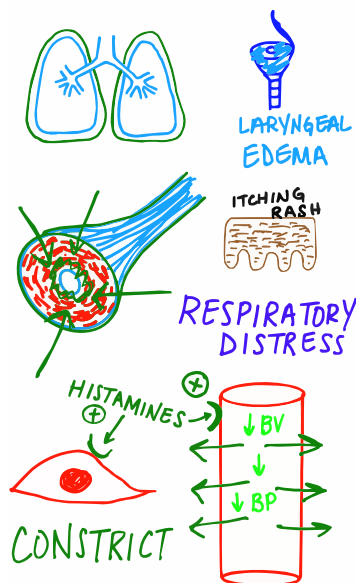


Figure 3. Clinical correlations of anaphylactic shock.

Treatment

- Epinephrine (IM injection)
 - Constricts the blood vessel to retain BP
 - If not working, try IV line at the hospital
- Antihistamines
 - Diphenhydramine (Benadryl)
 - H2-receptor blocker (Ranitidine)
- Monitor for a couple of hours
 - Biphasic phenomenon: 3-4 hours later attack might happen again

(3) Neurogenic

- Nervous system is the problem

Causes:

- Acute spinal cord injury (most common)
- Regional anesthesia

RECALL:

- Vasomotor center activates the neurons in the spinal cord (T1-L2) →
 - takes information to the heart (SA node, AV node, etc) → ↑ HR (chronotropy), contractility (inotropy)
 - takes information to the blood vessel
 - vasoconstriction → ↑ BP

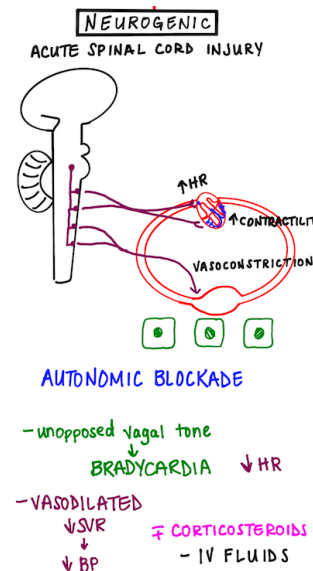


Figure 4. Pathophysiology of neurogenic shock.

Pathophysiology:

Table 4. Neurogenic shock pathophysiology.

Event	Response
↓ Vasomotor center activation or Autonomic blockade	↓ HR (chronotropy) ↓ contractility (inotropy) Vagus nerve (which also controls HR) becomes UNOPPOSED → bradycardia (↓ HR) Blood vessel vasodilation: ↓ SVR, BP, ↓ O2 to tissues, hypoxia, ischemia → necrotic, organ failure

Treatment

- Vasopressors
 - Dobutamine
 - Isoprenaline
 - Epinephrine
 - Atropine
- IV fluids to stabilize blood volume
- Corticosteroid: sometimes used



III) APPENDIX

Table 5. Abbreviations.

CO	Cardiac output
CVP	Central venous pressure
DIC	Disseminated intravascular coagulation
FcεR1	Fc epsilon R1 receptor
MRSA	Methicillin resistant Staphylococcus aureus
O2	Oxygen
PAI-1	Plasminogen activator inhibitor-1
PCWP	Pulmonary capillary wedge pressure
ROS	Reactive oxygen species
SVR	Systemic vascular resistance
TCR	T-helper cell receptor

IV) REVIEW QUESTIONS

- 1) Which of the following is the next choice of treatment for a patient in septic shock, unresponsive to fluids?
 - a. Ceftriaxone
 - b. Norepinephrine/ Epinephrine
 - c. Crystalloid
 - d. Both b & c
- 2) Select the correct pairing of shock: pathophysiology statement/s.
 - a. Neurogenic shock: ↓ SVR
 - b. Septic shock: ↑ vasodilation, ↓ SVR, ↓ BP
 - c. Anaphylactic shock: ↑ histamine
 - d. All of the above
- 3) Which of the following are common causative agents of an anaphylactic shock?
 - a. IV contrast
 - b. Regional Anesthesia
 - c. Encapsulated bacteria
 - d. Endotoxins
- 4) Which mechanism of shock describes the uncontrolled diabetic patient who develops nosocomial pneumonia associated with a palpable systolic BP of 70?
 - a. Distributive shock
 - b. Cardiogenic shock
 - c. Hypovolemic shock
 - d. None of the above

CHECK YOUR ANSWERS

V) REFERENCES

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CARDIOVASCULAR PATHOLOGY

CONGESTIVE HEART FAILURE

Pathophysiology of Congestive Heart Failure

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OUTLINE

- I) TYPES OF HEART FAILURE
- II) COMPENSATORY MECHANISMS
- III) SYMPTOMS AND PE FINDINGS
- IV) APPENDIX
- V) REVIEW QUESTIONS
- VI) REFERENCES

I) TYPES OF HEART FAILURE

(A) SYSTOLIC HEART FAILURE

Pathophysiology

- **Definition:** complex clinical syndrome either due to structural or functional impairment of ventricular filling or ejection of blood [Jameson, & Loscalzo, 2019]
- **Clinical manifestation:** dyspnea, fatigue, signs of HF such as edema and rales [Jameson, & Loscalzo, 2019]
- Myocardium is unable to generate enough stroke volume (SV) or the blood which can be ejected out of the ventricle in 1 heartbeat

Recall:

- $HR \times SV = CO \rightarrow \downarrow SV = \text{directly proportional } \downarrow CO$
- Normal BP: 120/80 with a pulse pressure of 40 mmHg
- Increased BP: 120/100 with a pulse pressure of 20 mmHg $\rightarrow \downarrow$ volume of blood (mL) pushed out
- Factors that affect or $\uparrow$ SV:

Table 1. Factors that affect or increase SV.

Parameter	Effect
Preload ($\uparrow$ myocardial stretch)	$\uparrow$ filling, $\uparrow$ blood volume in the heart before contracting $\uparrow$ VR
Contractility ($\uparrow$ force generated)	$\uparrow$ blood volume leaving the ventricle
Afterload ($\downarrow$ pressure or load the heart pumps against with)	only one with an inversely proportional effect $\downarrow$ afterload $\rightarrow \downarrow$ diastolic pressure (pressure you must overcome to pump blood from the ventricles to aorta) $\rightarrow \uparrow$ SV Ex: Hypertension LV pressure must $\gg \uparrow$ pressure in aorta • Normal BP 120/80 + pulse pressure 40 mmHg • $\uparrow$ BP of 120/100 + pulse pressure 20 mmHg $\rightarrow \uparrow$ diastolic pressure to overcome $\rightarrow \downarrow$ volume of blood (mL) pushed out or SV

Diseases

- **$\downarrow$ Contractility $\rightarrow \downarrow SV \rightarrow \downarrow CO$**
 - **Anterior Myocardial Infarction:** anterior portion of left ventricle controls 60-70% of pumping of heart
 - Lateral Myocardial Infarction
 - **Dilated cardiomyopathy "floppy heart":** ventricles are thin, weak, chambers are globular $\rightarrow \downarrow$ strength to pump out blood)
 - Causes:
 - Bacterial and viral infection
 - Idiopathic
 - Autoimmune

- infiltrative disorders (cancer, sarcoidosis, hemochromatosis)
- alcohol (holiday heart syndrome)

- **$\uparrow$ Preload $\rightarrow \uparrow SV$ WITH $\downarrow$ Contractility**

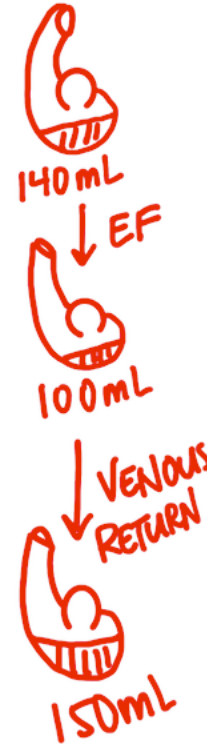


Figure 1. Increased preload, decreased contractility.

Explanation:

- Normal: EDV is 140 mL + contraction $\rightarrow$ Ejection Fraction 70 mL
- Diseased: EDV is 140 mL + $\downarrow$ or weak contraction $\rightarrow$ Ejection Fraction 100 mL $\rightarrow \uparrow$ filling and venous return at 150 mL
- In the long run, even if $\uparrow$ preload and $\uparrow$ SV $\rightarrow$ overtime heart becomes damaged and weak $\rightarrow \downarrow$ contractility $\rightarrow \downarrow$ SV

Mitral regurgitation

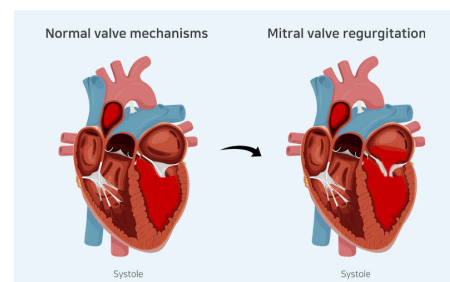


Figure 2. Mitral regurgitation.

- Diseased: LV contraction into aorta $\rightarrow$ Blood leaks and pumps back into LA due to damaged valve $\rightarrow$ bidirectional flow



○ Aortic regurgitation

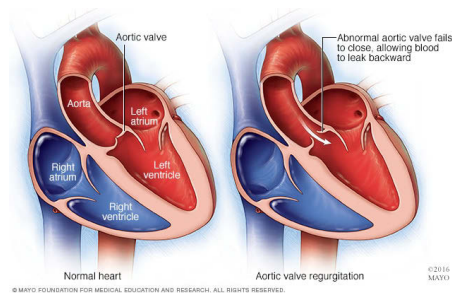


Figure 3. Aortic regurgitation.

- Diseased: LV contraction into aorta → Blood leaks pumps back into LV due to damaged valve → bidirectional flow
- Heart rate
 - Tachyarrhythmia: ↑ HR → ↓ diastolic time period, filling → ↓ preload to ventricles → ↓ SV, ↓ CO
 - Causes:
 - Atrial fibrillation
 - Atrial flutter
 - Wolff Parkinson White syndrome
 - Supraventricular tachycardia
 - Ventricular tachycardia
 - Bradyarrhythmia: ↓ HR → ↓ CO → over time, ↓ BP and perfusion to tissues → congestive HF
 - Cause: Severe heart block

(B) DIASTOLIC HEART FAILURE

Pathophysiology

- **Definition:** Stiff LV/ Fibrotic/ Noncompliant + ↓ compliance + impaired relaxation → ↑ End diastolic pressure [American Family Physician, 2004]
- **Clinical manifestation:** dyspnea, fatigue, signs of HF such as edema and rales [Jameson, & Loscalzo, 2019]
- May progress into Systolic HF

Diseases

- **↓ Preload:**
 - **Myocardial infarction:** fibrous tissues replace the heart muscles
 - **Restrictive cardiomyopathy:** muscle is infiltrated with a lot of substances → ↓ stretchability
 - Amyloidosis: ↑ light chains deposited in heart tissues → ↓ stretchability
 - Cancer → radiation therapy
 - Hemochromatosis: ↑ iron deposited in tissues
 - Sarcoidosis: noncaseating granulomas in different areas of the body
 - **Constrictive pericarditis:** fibrotic/ inelastic pericardium → ↓ filling → ↓ heart movement into pericardial cavity
 - Cardiac tamponade: acute, ↑ fluid accumulating in the pericardial cavity → ↓ filling
- **↑ Afterload:**
 - **Hypertension**
 - ↑ BP, ventricular work →
 - acute adaptation in ↑ BP with hypertrophy (↑ sarcomeres)
 - chronic adaptation: myocardium becomes weak, flabby → diastolic HF → systolic HF

○ Aortic Stenosis

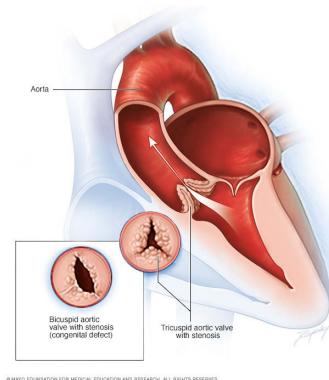


Figure 4. Aortic stenosis.

- May be fibrotic → ↑ BP, ventricular work to open up aortic valve
- Causes:
 - Rheumatic heart disease
 - Bicuspid aortic valve – inborn
- **Coarctation of the aorta**
 - Narrowed aorta → proximal to narrowing: ↑ resistance, ↑ BP
 - Causes: Turner's syndrome
- **Hypertrophic obstructive cardiomyopathy:** congenital
 - Thickened myocardium + bulging interventricular septum → ↑ pressure to push blood against bulging area, ↓ aortic outlet → ↓ blood into aorta



(C) RIGHT SIDED HEART FAILURE

- Not as common to develop on its own, more commonly caused by Left sided HF
- Can develop acutely and chronically

Diseases

- **↑ Afterload**
 - **Pulmonary hypertension:** constricted vessels → ↑ pulmonary circulation pressure
 - Causes:
 - Idiopathic
 - Pulmonary embolism
 - Underlying lung disease
 - **Pulmonary Embolism:** clot ↑ pressure proximal to clot → shunt it to other arteries
 - **Pulmonic stenosis:** ↑ pulmonary valve stiffness
 - Cause: Rheumatic heart disease
 - **Cor pulmonale:**
 - Causes:
 - COPD
 - severe bronchiectasis
 - chronic bronchitis
 - emphysema
 - Normal V/Q ratio: 0.8
 - Diseased:
 - ↓ V/Q → ↓ hypoventilated alveoli ↑ constrict vessels going to it → shunt to other ↑ well ventilated alveoli
 - If ↑↑ Damaged alveoli >> vasculature constriction from the hypoventilated alveoli → too much vasoconstriction → ↑ pressure proximal to vasoconstricted area
- **↑ Preload (chronic) → hypertrophies → overtime muscle weakens → ↓ contractility**
 - **Pulmonary regurgitation:** RV contraction → blood goes back into RV → ↑ RV expansion
 - **Tricuspid regurgitation:** RV contraction → backflows into RA → blood moves back down to RV, ↑ RV expansion
 - Cause: IV drug users: s. aureus → infective endocarditis
- **↓ Contractility**
 - Inferior Myocardial infarction: damages RV
 - Infiltrative diseases
 - Autoimmune disease
 - Myocarditis: myocardium is inflamed
- **Left sided Heart Failure:** ↑ Backflow of blood into pulmonary circulation → pulmonary hypertension → right sided HF

(D) LEFT SIDED HEART FAILURE

- More commonly leads to Right sided HF

(E) HIGH OUTPUT CARDIAC HEART FAILURE

- Usually occurs with an underlying cardiovascular disease
 - Diabetes, sleep apnea, smoke, hypertension, CAD, etc

Pathophysiology

- **↑ Oxygen demand >>> ↓ oxygen supply to the heart due to underlying cardiovascular disease**

Diseases

- **↑ Oxygen demand**
 - **Very severe anemia:** ↑ hypoxia → compensatory ↑ CO
 - **Thiamine deficiency “Wet Beri Beri”** in chronic alcoholics: no PDH → ↓ nutrients, thiamine → altered mental status, ataxia (loss of balance), ophthalmoplegia
 - Normal synthesis: Glucose → pyruvate via PDH → Acetyl CoA
 - If ↓ to no PDH → ↑ PDH buildup → lactic acid → ↑ vasodilation → ↑ arterial to venous (AV) shunting fast → ↓ time to oxygenate tissues → ↑ heart pumps harder
 - **Thyrotoxicosis** (↑ thyroid levels): ↑ metabolic rate, ↑ oxygen usage and demand → ↑ heart pumps harder, ↑ oxygenation for: caloric breakdown, muscle contraction, heat generation
 - **Pregnancy “Peripartum cardiomyopathy”:** ↑ metabolic rate
 - **AV fistula:** fistula ↑ blood shunting to venous side → ↓ SVR
 - Recall:
 - $CO \times TPR = BP$
 - $CO \times \downarrow TPR = \downarrow BP$
 - Compensation: ↑ CO by ↑ HR × ↑ SV

SUMMARY

Table 2. Summary of Types of Heart Failures.

Heart Failure	Pathophysio	Diseases
Systolic ↓ CO, ↓ EF “Compliant”	↓ Contractility ↓ SV → ↓ CO	Anterior & Lateral Myocardial Infarction Dilated cardiomyopathy
	↑ Preload → ↑ SV BUT ↓ Contractility	Mitral Regurgitation Aortic Regurgitation
	↑ HR	Atrial fibrillation Atrial flutter Wolff Parkinson White syndrome Supraventricular tachycardia Ventricular tachycardia
	↓ HR	Heart Block
Diastolic ↓ Preload Preserved EF ↑ Afterload “Non-compliant”	↓ Preload	Myocardial Infarction Restrictive cardiomyopathy Causes: Amyloidosis, Cancer, Hemochromatosis, Sarcoidosis
	↑ Afterload	Constrictive pericarditis Cause: Cardiac tamponade
		Hypertension
		Aortic Stenosis
		Coarctation of Aorta Hypertrophic obstructive cardiomyopathy
Right Sided	↓ Contractility	Inferior Myocardial infarction Infiltrative, Autoimmune diseases Myocarditis
	↓ Preload	Pulmonary regurgitation Tricuspid regurgitation
	↑ Afterload	Pulmonary hypertension
		Pulmonary embolism
		Pulmonic stenosis
		Cor pulmonale
	Left Sided Heart Failure	
High Output Cardiac HF	↑ Oxygen demand	Very severe anemia
		Thiamine deficiency “Wet Beri Beri”
		Thyrotoxicosis
		Pregnancy “Peripartum cardiomyopathy”
		AV fistula



II) COMPENSATORY MECHANISMS

(A) LEFT SIDED HEART FAILURE

Recall:

- $HR \times SV = CO$
- $CO \times TPR = BP$

- $\downarrow CO \rightarrow \downarrow$ volume of blood $\rightarrow \downarrow BP \rightarrow$ Tissue perfusion $\rightarrow$ hypoxia/ ischemia/ necrosis
 - $\downarrow BP$ stimulates carotid sinus and aortic sinus $\rightarrow$ send signals via glossopharyngeal nerve and vagus nerve to the medulla $\rightarrow$ stimulates cardioaccelerator and vasomotor sensor in medulla, part of sympathetic nervous system:
- Compensation within the sympathetic nervous system:

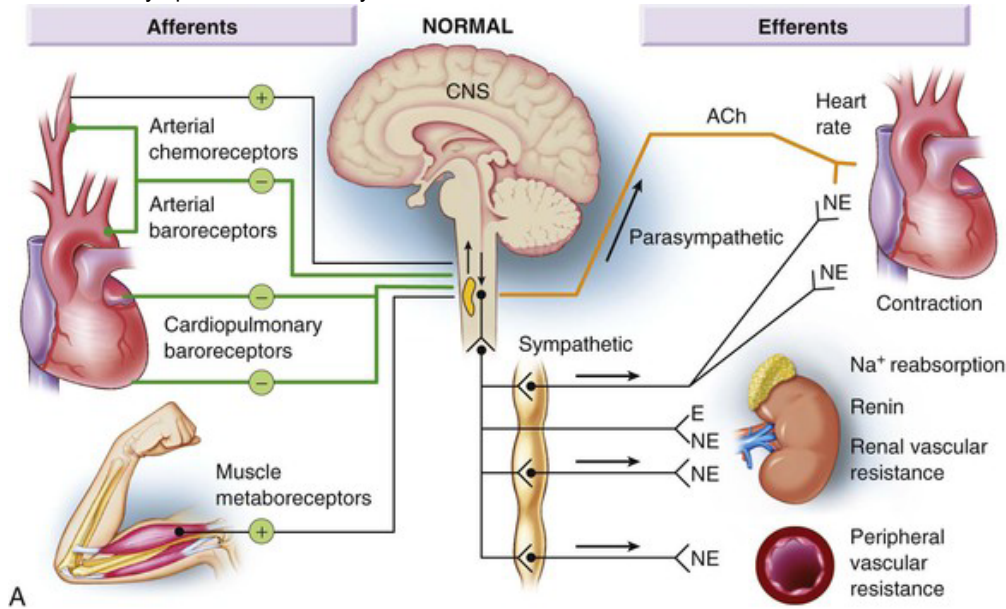


Figure 6. Compensated heart failure.

Table 3. Compensation within the sympathetic nervous system:

Location	Receptor	Effect
$\uparrow$ SA node stimulation	B1	$\uparrow CO$
$\uparrow$ Myocardial stimulation	B1 (nor-epinephrine, epinephrine)	$\uparrow$ myocardial contractility $\rightarrow$ $\uparrow SV, \uparrow CO, \uparrow BP$
Venous and arterial system	a1 (nor-epinephrine)	$\uparrow$ vasoconstriction, $\downarrow$ circumference, $\uparrow TPR \rightarrow \uparrow BP$ <u>$\uparrow$ vasoconstriction in veins:</u> $\uparrow VR \rightarrow \uparrow$ preload $\rightarrow$ $\uparrow SV, \uparrow CO, \uparrow BP$ <u>$\uparrow$ vasoconstriction in kidney vessels:</u> $\downarrow$ blood flow to kidney $\rightarrow$ $\downarrow GFR \rightarrow \downarrow$ urine output $\rightarrow$ $\uparrow$ fluid retention $\rightarrow \uparrow VR, \uparrow$ preload, $\uparrow SV$
JG cells	B1 (nor-epinephrine) secretes renin	RAAS <u>Renin:</u> Angiotensinogen (liver) into Angiotensin I in the venous system $\rightarrow$ heart $\rightarrow$ lungs (ACE) <u>ACE:</u> Angiotensin I into Angiotensin II $\rightarrow$ 1) <u>$\uparrow ADH$ (water reabsorption)</u> $\rightarrow$ $\uparrow BV, VR, \text{preload}, SV$

		2) <u>vasoconstrict arterial system:</u> $\uparrow TPR, BP$ 3) <u>adrenal gland (zona glomerulosa):</u> $\uparrow$ aldosterone in DCT (kidney) $\rightarrow$ $\uparrow Na \& H_2O$ reabsorption $\rightarrow \uparrow BV, VR, \text{preload}, SV$
--	--	---

- Caveat of $\uparrow HR$ as a compensation for $\downarrow CO$:

- $\uparrow HR$ + underlying heart disease = $\downarrow$ filling time
- $\uparrow$ vasoconstriction of both arterial and venous system: $\uparrow$ afterload
 - Arterial vasoconstriction: $\uparrow$ pressure proximal to it $\rightarrow \uparrow$ aortic pressure $\gg$ LV pressure (must overcome it)
 - Venous vasoconstriction: $\uparrow$ preload + already weak heart = $\uparrow$ filling, $VR \gg$ ability to push the blood out
- Compensatory mechanisms further exacerbate the situation

Drugs

- Beta blockers
- ACE inhibitors
- Diuretics: for fluid and volume overload
- Vasodilators (arteriodilators, venodilators)



III) SYMPTOMS AND PE FINDINGS

(A) BACKWARD FLOW / FAILURE

Left Sided Heart Failure

- ↑ Filled up blood → Unable to eject all the blood out → Backflows into different circulations
- 1) ↓ LV pump blood into aorta →
- 2) ↑ blood accumulation in LV → ↑ backs up into LA → backs up into pulmonary veins
- 3) ↑ pressure in pulmonary veins, capillaries
- 4) ↑ fluid leakage into interstitial fluid → **pulmonary edema**

Symptoms and Physical Examination Findings from LSHF

- Lungs become thick and boggy: thickened respiratory membrane
- ↓ Ventilation → ↓ oxygenation of blood → **hypoxemia** → dyspnea or shortness of breath
- ↑ Fluid → ↑ irritation of bronchioles, airways → **dry cough**
- ↑ Fluid + gravity (lying flat) = **Orthopnea**
- **Paroxysmal nocturnal dyspnea**
- ↑ Fluid pops open upon ventilation of bronchioles: **Inspiratory Rales or crackles**

Sequela

- Pulmonary hypertension: due to ↑ pressure in pulmonary veins, capillaries and eventually arteries
- Right sided heart failure

(B) FORWARD FLOW / FAILURE

- Not able to generate enough CO from LV to aorta → ↓ BF to systemic circulation → multisystem organ failure

Right Sided Heart Failure

- 1) Blood backs up into SVC → right and left brachiocephalic vein → internal jugular vein → ↑ pressure in IJV → ↑ **Jugular venous distention**
- 2) Blood backs up into IVC or SVC

Symptoms and Physical Examination Findings from RSHF

- ↑ Pressure in IJV → ↑ **Jugular venous distention**
- Blood backs up into IVC → apply pressure onto the liver → ↓ blood flow into the portovenous circulation, ↑ **Hepatjugular reflux** (≥0.3cm rise in Jugular venous distention pressure)
- Blood backs up into IVC → ↑ fluid accumulates inside the liver (**Hepatomegaly**) + outside of the liver (**Ascites**)
- Blood backs up into portovenous circulation → ↑ spleen size → **Splenomegaly**, Ascites
- Blood backs up into the mesenteric circulation → ↑ fluid in GI system → **Ascites** + substances difficulty passing through/down + pushes through the small and large bowel → substances back up → **Nausea, vomit, abdominal pain**
- **Protuberant abdomen**
 - Dull to percussion
 - Lie to their side → **(+) Fluid wave test**
- Blood backs up into lower extremities → **Calf Edema**

- Bilateral edema, (+) pitting of skin
- Pitting grade depends on how long it stays and retracts, and its depth

- ↓ Blood flow into extremities → ↑ sympathetic nervous system compensation → **Cool, pale, sweaty and clammy extremities**
- If not enough blood flow into organs → multiorgan system failure

(C) SYSTOLIC HEART FAILURE

- ↑ Compliance and filling of heart → heart sound just before systolic contraction
 - Atria: putting blood from the atria into ventricles
 - Ventricles: diastole, filling → extra sound when it hits the ventricular wall → **S3 heart sound** heard with the bell of stethoscope and left lateral decubitus position (PMI shifts or is displaced)

(D) DIASTOLIC HEART FAILURE

- ↑ Thick, fibrotic, noncompliant heart → point at which the heart is unable to fill and stops → **S4 heart sound**

SUMMARY

Table 4. Comparison of symptoms.

Pathophysiology	Symptomatology
↓ Effective pumping blood from LV to systemic circulation ↓ ↑ Blood accumulates (left side of heart) ↓ ↑ LV EDP ↓ Venous Congestion ↓ Pulmonary Congestion/Edema ↓ Impaired gas exchange	• Dyspnea • Orthopnea • Paroxysmal nocturnal dyspnea (PND) • Cyanosis • Signs of hypoxia
↑ Blood accumulates (right side of heart) ↓ Portal vein congestion Hepatic congestion GI system congestion	• Elevated JVP • Hepatjugular reflux • Ascites • Hepatomegaly • Splenomegaly • Protuberant abdomen • (+) Fluid wave test • Nausea, vomit, abdominal pain
↑ Blood accumulates (right side of heart) ↓ Increased Hydrostatic pressure in IVC ↓ Extravasation of blood in peripheral tissue	• Bipedal edema
↓ Blood flow into extremities ↑ sympathetic nervous system compensation	• Cool, pale, sweaty and clammy extremities

IV) APPENDIX

Table 5. Abbreviations.

ACE	Angiotensin-converting enzyme
BV	Blood volume
BP	Blood pressure
CO	Cardiac output
DCT	Distal convoluted tubule in the kidney
EDV	End diastolic volume
HF	Heart failure
HR	Heart rate
VR	Venous return

IVC	Inferior vena cava
LA	Left atrium
LV	Left ventricle
PDH	Pyruvate dehydrogenase
SV	Stroke volume
SVC	Superior vena cava
SVR	Systemic vascular resistance



V) REVIEW QUESTIONS

- 1) **What causes the increase in heart rate as a compensatory mechanism in heart failure?**
 - a. Release of mineralocorticoid from the kidneys B
 - b. Secretion of renin
 - c. Sympathetic nervous system activity
 - d. Vasopressin secretion
- 2) **Which derangement is commonly found in heart failure WITH preserved ejection fraction?**
 - a. Dilatation of ventricular cavity
 - b. Myocyte hypertrophy
 - c. Systolic dysfunction
 - d. Thinning of the ventricular wall
- 3) **Which of the following symptomatology is correctly paired?**
 - a. Systolic heart failure: S4 sound
 - b. Heart failure with reduced ejection fraction: S3 heart sound
 - c. Forward heart failure: dyspnea, pale extremities
 - d. Backward heart failure: cough, hepatojugular reflex, abdominal pain
- 4) **The symptoms and signs of cough, shortness of breath, with positive crackles on both lungs are hemodynamically due to:**
 - a. Pressure overload of the left ventricle
 - b. Impaired filling of the left ventricle
 - c. Volume overload of the left ventricle
 - d. Cardiomegaly (cardiac remodeling)
- 5) **A 45 year old male patient with known pulmonary tuberculosis consulted due to pedal edema and ascites. Initially, transthoracic echocardiogram revealed a thickened pericardium with septal bounce. Cardiac MRI was done and confirmed the presence of pericardial fluid or thickening. Which of the following diagnosis may suggest the presence of signs of volume overload?**
 - a. Aortic regurgitation
 - b. Restrictive cardiomyopathy
 - c. Pulmonary regurgitation
 - d. Tuberculous pericarditis

CHECK YOUR ANSWERS

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CARDIOVASCULAR PATHOLOGY

CONGESTIVE HEART FAILURE

Treatment of Congestive Heart Failure

Last edited: 8/11/2021

Medical Editor: Maxine Abigale R. Bunao



OUTLINE

- I) DIAGNOSTICS
- II) APPROACH TO TREATMENT
- III) DRUGS THAT ALTER RAAS
- IV) DRUGS THAT ALTER THE SYMPATHETIC NERVOUS SYSTEM
- V) MANAGEMENT OF DECOMPENSATED HEART FAILURE
- VI) APPENDIX
- VII) REVIEW QUESTIONS
- VIII) REFERENCES

I) DIAGNOSTICS

- Primarily clinical diagnosis

Table 1. Diagnostic tests.

Tests	Indication and Results
Chest X-ray <i>Note: MUST be supplemented with clinical symptoms</i>	Cardiomegaly: enlarged heart
	Pulmonary Edema: if left heart is failing → fluid backs up to the pulmonary circulation
	Bilateral pleural effusions: fluid in the pleural cavity
BNP <i>Made by ventricles under extreme stress</i>	↑ BNP: >400 pg/mL ↑ likelihood of CHF, not diagnostic ↑ effectiveness of treatment
Echocardiogram <i>Gold standard</i>	Determines types of pathologies: Systolic HF: dilated ventricles Diastolic HF: stiff ventricles Wall motion abnormality Contractility problems Myocardial infarction Cardiomyopathy Valvular problem
Cardiac catheterization	Determine underlying etiology of HF

II) APPROACH TO TREATMENT

- Based upon the severity of patient according to NYHA classification.
- NYHA developed a four-class system

Table 2. NYHA Classification.

NYHA	Interpretation
I	Shortness of breath & chest pain ONLY at
II	EXTREME exertion
III	MILD exertion
IV	MODERATE exertion
	AT REST

- Regardless of class, underlying disease **MUST be treated!**
 - If with diabetes: (+) insulin / diabetic medications / lifestyle management
 - If with hypertension: (+) antihypertensive medications
 - If with hyperlipidemia: (+) statins
 - If with myocardial infarction: (+) cardiac catheterization or CABG
 - If with obstructive sleep apnea: (+) CPAP
 - If obese: (+) lose weight
 - Restrict sodium intake because this holds on to water: <2g / day
 - Restrict water intake: <2L / day

Recall:

Formula:

- $HR \times SV = CO$
- $CO \times TPR = BP$

RAAS axis

Renin-angiotensin-aldosterone system

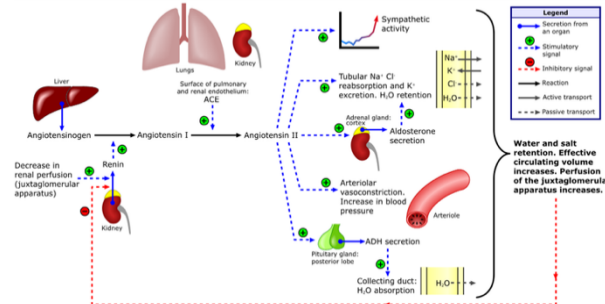


Figure 1. Renin-Angiotensin-Aldosterone System.

Table 2. RAAS.

Stimulus	Response
Failing heart = ↓ CO	JG cells release an enzyme "Renin" which converts Angiotensinogen → Angiotensin I
↓ perfusion to the kidneys OR ↓ blood volume	Enzyme "ACE" at the pulmonary vasculature which converts Angiotensin I → Angiotensin II
Angiotensin II	Binds with receptors on arterioles = ↑ vasoconstriction as compensation ↓ diameter ↑ TPR → ↑ afterload ↑ BP
	Stimulates posterior pituitary gland (CNS) → ADH → kidneys ↓ Urine output, ↑ Water reabsorption ↑ Blood volume → ↑ EDV → ↑ preload ↑ BP
	Stimulate adrenal gland → Aldosterone → kidneys ↓ ↑ Na+/H2O reabsorption ↓ ↑ BV → ↑ EDV → ↑ preload ↑ BP

- Caveat of ↑ vasoconstriction as a compensation for ↓ CO = ↑ afterload (amount of pressure that ventricles must overcome in order to push blood into the aorta)
 - ↑ afterload + underlying heart disease = not helpful
- Caveat of ↑ preload, EDV + weak ventricle = ↑ stress on the heart, cannot keep on pumping the amount of blood wanted



III) DRUGS THAT ALTER RAAS

(A) CLASS I

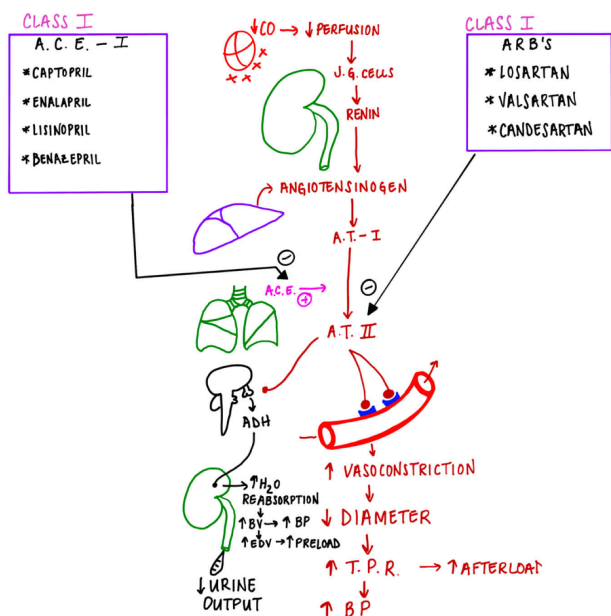


Figure 2. Class I drugs that alter RAAS.

(1) Angiotensin Converting Enzyme Inhibitor (ACE-i)

Table 3. ACE-i drugs and mechanism of action.

ACEi	MOA
Captopril Enalapril Lisinopril Benazepril	Inhibits ACE → ↓ ACE → ↓ Angiotensin II ↓ Angiotensin = total effect is ↓ stress on the heart • ↓ TPR → ↓ afterload • ↓ ADH → ↓ H₂O reabsorption, ↓ BV, ↓ preload • ↓ Aldosterone → ↓ Na/H₂O reabsorption → ↓ EDV, ↓ preload

- Best to start with this
- Side effects: dry cough, angioedema
- If ACE-i can't be tolerated, use ARBs or another drug group

(2) Angiotensin II Receptor Blockers (ARBs)

Table 4. ACE-i drugs and mechanism of action.

ARBs	MOA
Losartan Valsartan Candesartan	Inhibits Angiotensin II ↓ Angiotensin = total effect is ↓ stress on the heart • ↓ TPR → ↓ afterload • ↓ ADH → ↓ H₂O reabsorption, ↓ BV, ↓ preload • ↓ Aldosterone → ↓ Na/H₂O reabsorption → ↓ EDV, ↓ preload

(B) CLASS III

- Benefits
 - ↓ Remodeling of the heart:
 - i.e. you want ↓ fibrosis after a myocardial infarction event)
 - Potassium sparing
 - i.e. for patients with hypokalemia

(1) Aldosterone Antagonists

- Indication: history of myocardial infarction, use if aiming to ↓ remodeling of the heart

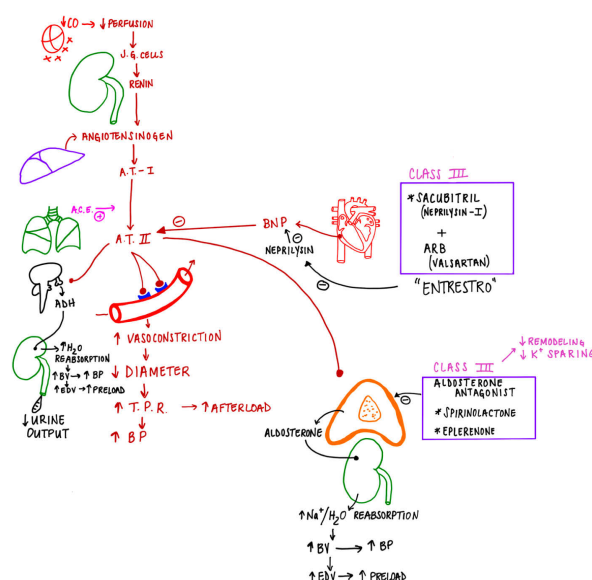


Figure 3. Class III drugs that alter RAAS.

Table 5. AA drugs and mechanism of action.

AAs	MOA
Spironolactone Eplerenone	Inhibit Aldosterone • ↓ Aldosterone → ↓ Na/H₂O reabsorption → ↓ EDV, ↓ preload → ↓ stress on the heart

(2) Neprilysin inhibitor + ARB

- Indication: if the other medications are not working (ACEi, ARBs, AAs)
- Benefits of Entresto:
 - undergone 2 trials, has some evidence that ↓ mortality & morbidity in patients with heart failure

Table 6. Neprilysin inhibitor + ARB and mechanism of action.

	MOA
Entresto	If there is stress on myocardium → ↑ release BNP → Inhibits Angiotensin II • Angiotensin II → ↓ TPR, afterload, stress on the heart • ↓ Aldosterone → ↓ Na/H₂O reabsorption → ↓ EDV, ↓ preload • ↓ ADH → ↓ H₂O reabsorption, ↓ BV, ↓ preload
Combination of neprilysin inhibitor (Sacubitril) + ARB (Valsartan)	Inhibits neprilysin (enzyme) which breaks down or decreases amount of BNP in the blood Valsartan enhances ↑ release BNP → Inhibits Angiotensin II



IV) DRUGS THAT ALTER THE SYMPATHETIC NERVOUS SYSTEM

Recall:

Table 7. SNS Compensation.

Stimulus	Response
↓ CO or blood flow	Carotid sinus and Aortic sinus ↓ Activates sympathetic nervous system
	↑ norepinephrine to B1 receptors on the SA node + contractile myocardium ↓ ↑ HR → ↑ CO Caveat: • ↑ HR BUT ↓ filling time (diastole) for ventricles (to relax and eject enough blood) is NOT enough • ↓ Oxygen delivery to myocardium = ↑ stress
	↑ norepinephrine to B1 receptors on the SA node + contractile myocardium ↓ ↑ contractility → ↑ CO → ↑ BP ↑ contractility → myocardium needs ↑ oxygen consumption Caveat: • ↑ oxygen demand BUT myocardium only has ↓ oxygen supply & ↓ blood flow due to ↑ HR BUT ↓ filling time
	↑ norepinephrine to α1 receptors on renal arterioles ↓ ↑ vasoconstriction of renal vessels → ↑ TPR, ↑ BP, ↑ afterload → ↑ stress on heart

(A) CLASS I

- First line drugs: ACEi/ARB + B-blocker
- Contraindication: Decompensated HF

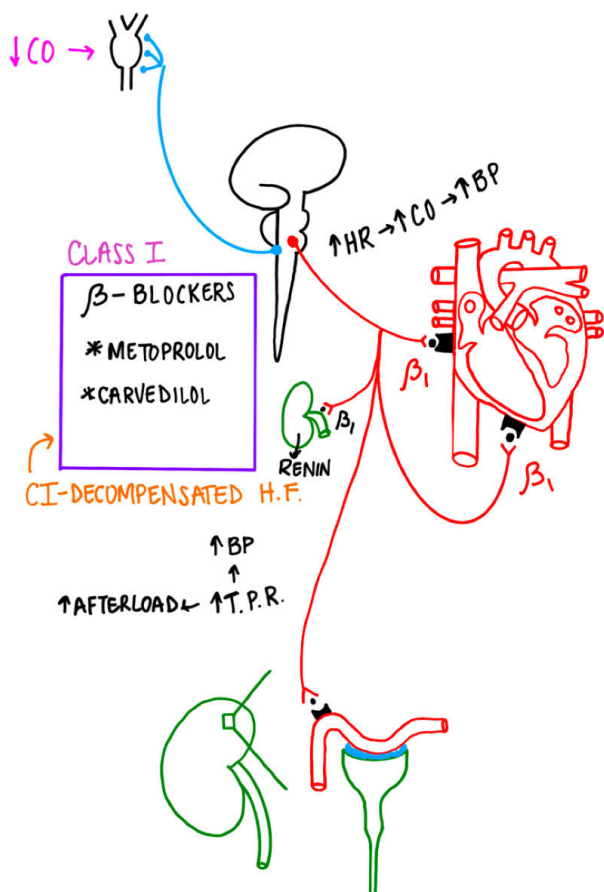


Figure 4. Class I drugs that alter the SNS.

(1) Beta-Blockers

- First line drugs: ACEi/ARB + B-blocker
- Contraindication: Decompensated HF (unable to generate enough CO)

Table 8. B-blocker drugs and mechanism of action.

B-Blockers	MOA
Metoprolol (B1 activity, cardioselective)	↓ HR (negative chronotropy, B1 activity) ↓ contractility (negative inotropy, B1 activity)
Carvedilol (α, B1 activity)	↑ vasoconstriction (↑ norepinephrine to α1 receptors on renal arterioles) ↓ RAAS (B1 activity), ↓ TPR → ↓ afterload

(B) CLASS IV

(1) Cardiac Glycosides

Table 9. Glycoside drug and mechanism of action.

Glycoside	MOA
Digoxin (last line of drug)	↓ HR (negative chronotropy, B1 activity) ↑ contractility (positive inotropy, B1 activity)
Indication: Atrial fibrillation	Block AV node

(2) Inotropic agent

Table 10. Inotropic drug and mechanism of action.

± Dobutamine	MOA
Indication: Decompensated HF	If ↑ heart failure → ↓↓ CO → ↓↓ BP = remains uncompensated = CARDIOGENIC SHOCK ↑ contractility (positive inotropy, B1 activity) ↑ BP

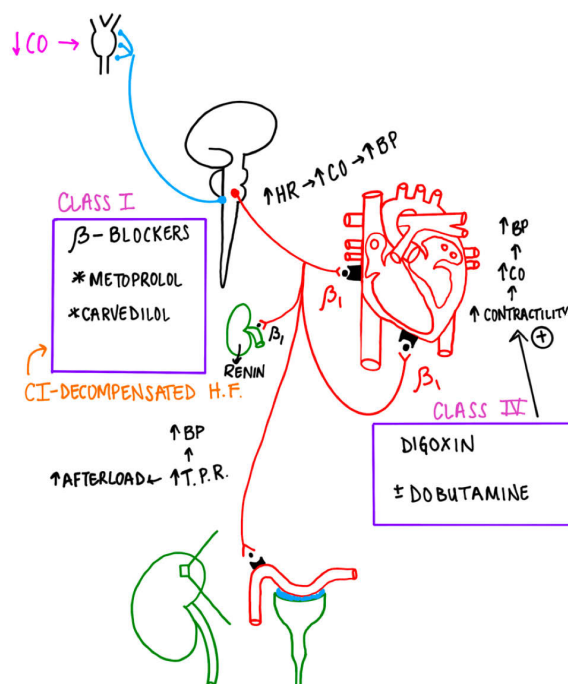


Figure 5. Class IV drugs that alter the SNS.



(C) CLASS II

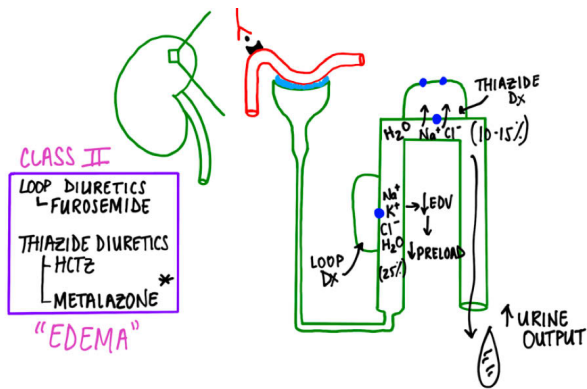


Figure 6. Class II drugs that alter the SNS.

(1) Diuretics

- Indication:
 - If not responding as well as you want them to ACEi/ARB + B-blocker
 - ↑ Fluid in body (↑ peripheral edema, ascites, JVP, pulmonary edema) or significant edema, especially if symptomatic
- The kind of diuretic given depends on the GFR.

Table 11. Loop diuretics and mechanism of action.

Loop Diuretics	MOA
Furosemide	Inhibits (Na ⁺ /K ⁺ /2Cl ⁻) co-transporter at the loop of Henle
Primarily given Start 20mg	↓ Na, K, Cl reabsorption ↑ Na, K, Cl buildup in the tubule + water follows
Note: Increase as needed OR add metolazone	Urinate out 25% of whatever filtered out of GFR → ↑ Urine output ↓ EDV, preload, stress on the heart

Table 12. Thiazide drugs and mechanism of action.

Thiazide Diuretics	MOA
Hydrochlorothiazide Metolazone	Inhibit NaCl transporter at the distal convoluted tubule ↓ Na, Cl reabsorption ↑ Na, Cl buildup in the tubule + water follows Urinate out 10-15% of whatever filtered out of GFR → ↑ Urine output → ↓ total blood volume, EDV, preload, stress on the heart

(D) CLASS III

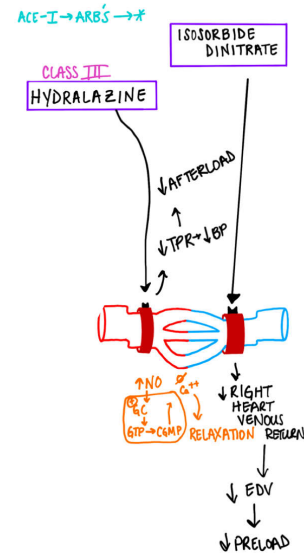


Figure 7. Class III drugs that alter the SNS.

(1) Vasodilators

- Indication:
 - If ACE-I is not tolerated /failed → ARB still not tolerated /failed → Vasodilators

Table 13. Vasodilators and mechanism of action.

Hydralazine	MOA
Indication: Well tolerated in African-American patients and safe in pregnant patients Downside: taken 3x/day	↑ Nitric oxide into smooth muscle of arterioles ↓ ↑ Guanylyl cyclase activation → converts GTP into cGMP ↓ Through protein kinase regulation, ↓ Calcium entry = ↓ contraction ↓ Relaxation of smooth muscle cells ↓ ↓TPR, ↓vasoconstriction → ↓afterload, stress on the heart
Isosorbide Dinitrate	MOA
	↑ Nitric oxide into smooth muscle of venules ↓ ↑ Guanylyl cyclase activation → converts GTP into cGMP ↓ Through protein kinase regulation, ↓ Calcium entry = ↓ contraction ↓ Relaxation of smooth muscle cells Through protein kinase regulation, ↓ Calcium entry = ↓ contraction ↓ Relaxation of smooth muscle cells ↓ ↓Right heart venous return ↓ EDV → ↓preload + weak heart = ↓stress of weakened heart



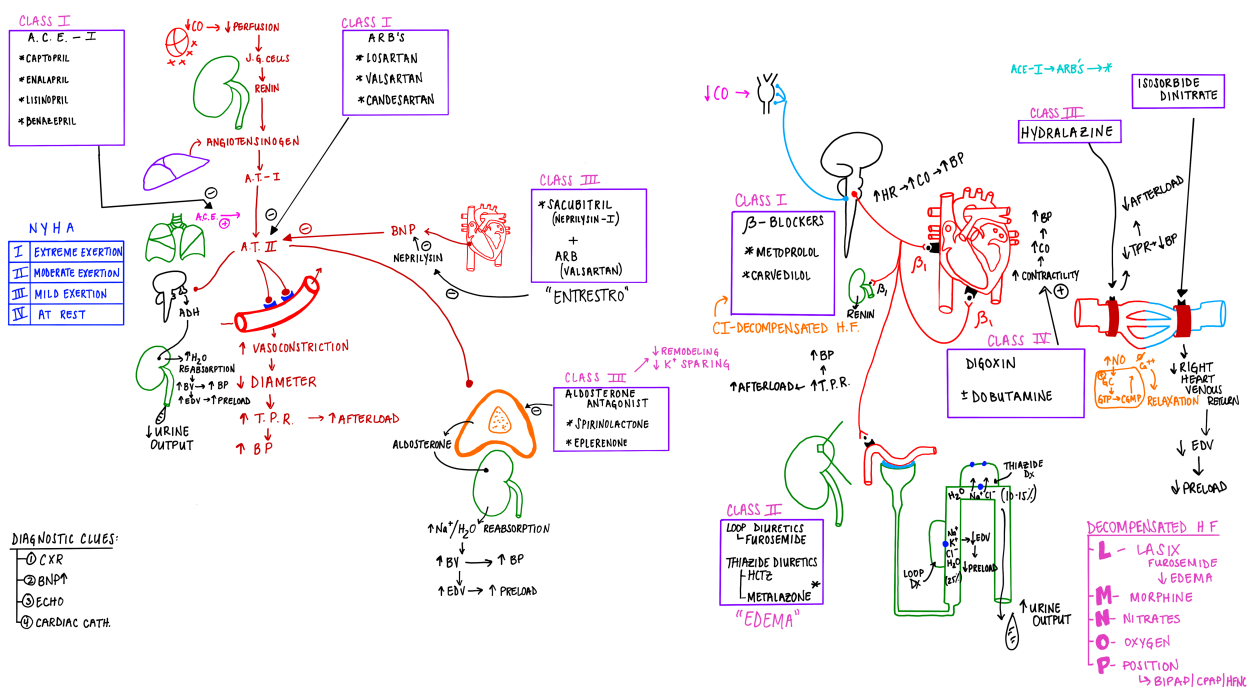
V) MANAGEMENT OF DECOMPENSATED HEART FAILURE

Drug & Indication		Effect
L	Lasix/Furosemide (diuretic)	↓ edema (↑ in left sided HF)
M	2-5 mg Morphine	↓ pain
N	Nitrates (hydralazine, isosorbide dinitrate)	↓ afterload, ↓ ischemic chest pain
O	Oxygen Indication: in CHF fluid can back up into the lungs, if in flash pulmonary edema	BIPAP/CPAP/ High flow nasal cannula to ↓ respiratory work
P	Position (don't position in supine, incline them)	↓ fluid overload Can cause edema but ↓ stress on lungs

Table 14. Acronyms.

ACEi	Angiotensin converting enzyme inhibitor
BNP	Brain natriuretic peptide
BP	Blood pressure
BV	Blood volume
CABG	Coronary artery bypass graft
CPAP	Continuous positive airway pressure
cGMP	Cyclic guanosine monophosphate
EDV	End diastolic volume
GTP	Guanosine triphosphate
NYHA	New York Heart Association
RAAS	Renin-Angiotensin-ADH system

VI) APPENDIX



Treatment of CHF

KRISTIN

NINJA NERD LECTURES

Figure 8. Summary of treatment of CHF.



VII) REVIEW QUESTIONS

- 1) A 75/M came in due to chest pain and shortness of breath for three hours. Physical examination showed 90/60 mmHg, HR 48 bpm, distended neck veins, bilateral crackles mid to basal lung fields. ECG showed ST elevation and troponin was elevated. Which drug should not be given?
- Atorvastatin
 - Aspirin
 - Metoprolol
 - None of the above
- 2) Which of the following drug combinations may be given for patients in heart failure with contraindications to ACEI and ARB?
- Amlodipine + Carvedilol
 - Hydralazine + Isosorbide dinitrate
 - Metoprolol + Furosemide
 - Verapamil + Digoxin
- 3) Jose is a 30-year old male tricycle driver. At age 12 he suffered rheumatic fever and developed mitral regurgitation. Two months ago he developed gradual but progressive shortness of breath on moderate exertion with cough productive of minimal clear sputum. He also had to use two pillows to prop him up to be able to sleep at night. A week later he noticed swelling of his legs after working the whole day. Physical examination showed distended neck veins, crackles at both lung bases and the apical beat was at the 6th intercostal space left anterior axillary line. 2Decho showed enlarged left ventricle and severe mitral regurgitation with an ejection fraction of 35 percent. ECG showed atrial fibrillation. He was diagnosed to have congestive heart failure due to valvular heart disease. Which New York Heart Association (NYHA) functional category best describes him?
- 1
 - 2
 - 3
 - 4

CHECK YOUR ANSWERS

VIII) REFERENCES

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OUTLINE

- I) OVERVIEW
- II) TYPES OF TACHYARRHYTHMIAS
- III) TYPES OF BRADYARRHYTHMIAS
- IV) SICK SINUS SYNDROME
- V) EKG DIFFERENCES & TREATMENT PLAN
- VI) APPENDIX
- VII) REVIEW QUESTIONS
- VIII) REFERENCES

I) OVERVIEW

- Arrhythmia
 - Abnormal electrical activity in the heart:
 - Rate
 - Rhythm
 - sequence of conduction
 - origin of conduction)
 - Easiest way to define is by abnormalities in rate
 - As set by SA node: 60-100 bpm (normal heart rate)
 - >100 bpm: tachyarrhythmia
 - ≥300 bpm: fibrillation
 - <60 bpm: bradyarrhythmia

Guide:

- 0.04 s = small box
 - 5 small boxes = 1 big box
 - 5 small boxes x 0.04 s = 0.20 s
- 0.20 s = 1 big box

Table 1. Classifications of arrhythmias.

Tachyarrhythmia		Bradyarrhythmia
Supraventricular (SVT)	Sinus	Sinus bradycardia
	Atrial	
	Paroxysmal SVT	Heart blocks (1 st , 2 nd , 3 rd degree)
Ventricular	Tachycardia	
	Fibrillation	

II) TYPES OF TACHYARRHYTHMIAS

(A) SUPRAVENTRICULAR TACHYCARDIA

- Any arrhythmia occurring above the ventricles

(1) Sinus

- SA firing too fast

(2) Atrial

- Irritable atrial firing to the AV node before SA node fires towards the AV node
- Types:
 - Focal Atrial Tachycardia: 1 area firing consistently, ectopic focus
 - Multifocal Atrial Tachycardia: 3 areas
 - Atrial fibrillation: faster than multifocal
 - Atrial flutter: Near tricuspid valve, creates re-entry circuit

(3) Paroxysmal SVT

- Refer to AVNRT and AVRT, sometimes with Focal atrial tachycardia as well
- Atrioventricular nodal reentrant tachycardia:
 - reentry circuit in AV node at fast rates
- Atrioventricular reentrant tachycardia:
 - reentry circuit in accessory pathways between atria and ventricles

(B) VENTRICULAR TACHYCARDIA

- Irritable area in the ventricle that generates abnormal activity

(1) Ventricular Tachycardia

- Ventricular tachycardia:
 - irritable area w/c fires w/in ventricle
 - Types:
 - Monomorphic: most common; 1 location of irritable area that's firing
 - Polymorphic: multiple locations of irritable area that's firing
 - With a normal QT-Interval
 - Prolonged QT-Interval (Torsades de Pointes) HIGH YIELD → twisting of the points

(2) Ventricular Fibrillation

- Multiple ectopic foci within the ventricles that are firing
- Presence of reentry circuits



(C) PATHOPHYSIOLOGY

RECALL:

- Conduction Pathway:
 - SA node has funny channels → (+) intrinsically depolarize its own → action potentials → heart contracts on its own
 - SA node > Bundle of His > Bundle branches > Purkinje System
- Normal automaticity rate: 60-100 bpm
- Parasympathetic Nervous system
 - CN 10 or Vagus nerve
 - ↑ Acetylcholine release to the conduction system
 - ↑ potassium leaving the cell
 - hyperpolarizes and relaxes it
 - ↓ conduction from SA node to AV node
 - ↓ HR (bradycardia if <60 bpm)

(1) ↑ Automaticity

Table 2. Increased automaticity in tachyarrhythmias.

Pathophysiology	Response
↑ Automaticity Affects Sympathetic Nervous System (T1-L2)	Recall: Stimulate T1-T5 to heart, innervate contractile myocardial cells ↓ Releases (+) Norepinephrine, Epinephrine ↓ ↑ Conduction: SA node > AV node > down ↓ ↑ HR > 100 bpm = tachyarrhythmia
	Hypovolemia ↑ Vasoconstriction ↑ HR (reflex tachycardia)
	Hypoxia - Anemia - lung disease i.e. COPD - pulmonary embolism (PE) → clot lodged in the vessel alters the blood going into the lungs to oxygenate - sinus tachycardia: one of the most common arrhythmias associated with PE, NOT S1Q1T3
	Sympathomimetic drugs - cocaine - methamphetamines ↑ HR drugs
	Pain/Anxiety: activates hypothalamus which is part of limbic system → ↑ SNS ↑ Metabolic activity fever, hyperthyroidism
	Associated: - Sinus tachycardia (most common) - Others: atrial and ventricular arrhythmias

(2) Triggered Activity

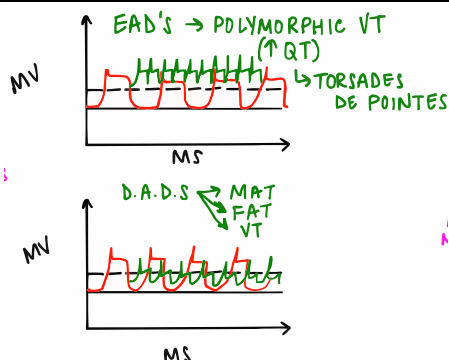


Figure 1. Triggered activity in tachyarrhythmias.

Table 3. Triggered activity in tachyarrhythmias.

Pathophysiology	Response
Triggered activity: Irritable area in myocardium (atrium/ventricle) → conduction starts at ectopic area instead of SA - AV node	Normal waveform: Depolarization: Na-ion influx Plateau: Ca influx, K leaving Repolarization: K leaving ↓ Irritable cell due to causes stated in Table 3 ↓ Abnormal Early After Depolarization: Agitated cell at repolarization ↓ uncontrollable firing ↓ Early depolarization comes just after the previous depolarization
EAD vs DAD differentiation on Table 3	Irritable cell due to causes stated in Table 3 ↓ Delayed After Depolarization ↓ uncontrollable firing of atrial / ventricular myocardial cell right about the latter phase of repolarization

Table 4. Differentiation of EADs and DADs.

	Causes / Etiology	Associated with:
EAD	Electrolyte imbalances: - Hypokalemia - Hypocalcemia - Hypomagnesemia Drugs (ABCDE): - Anti-arrhythmics: Ia, Ic, III - Antibiotics Macrolides - Antipsychotics (c): Haloperidol, Risperidone - Antidepressants: TCA, SSRIs - Antiemetics: Ondansetron	Polymorphic ventricular tachycardia with prolonged QT-interval or Torsades de pointes
DAD	- Underlying ischemia (MI, CAD) - Underlying hypoxia (Lung Dx) - Inflammation (myocarditis) - Stretched out myocardium (Dilated cardiomyopathy, mitral regurgitation) ↑ SNS tone - Digoxin toxicity	- multifocal atrial tachycardia - focal atrial tachycardia - monomorphic or polymorphic ventricular tachycardia with normal QT-Intervals



(3) Re-entry Circuit

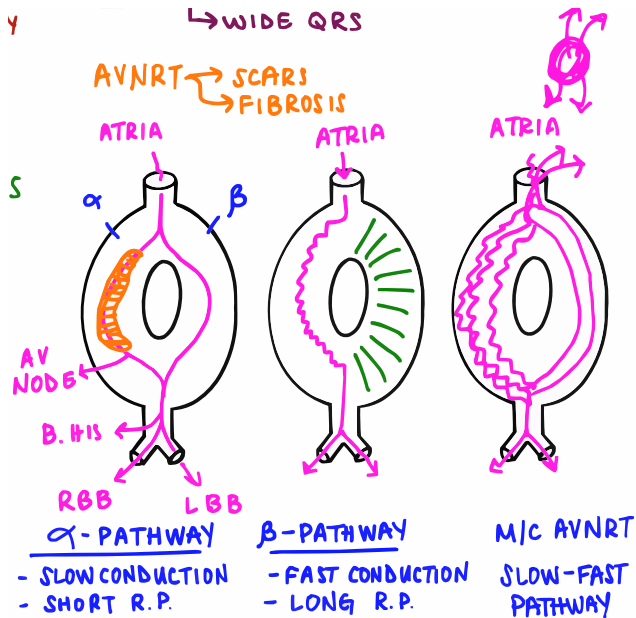


Figure 2. Alpha and Beta Pathway.

Table 5. Re-entry circuits in tachyarrhythmias.

Pathophysiology	Response
Re-entry Circuit	underlying accessory pathway between AV = bundle of Kent (most common, seen in WPW syndrome) ↓ Bi-directional electrical channel (Atria to ventricles or vice versa)
	Others Pathways: Bundle of James, associated with Lown Ganong Levine Syndrome
	Orthodromic AVRT type: most common ↓ Conduction starts at AV node ↓ Doesn't stop at ventricles & continues to go up the atria via Bundle of Kent → AV node = loop Note: AV node to bundle of Kent → depolarizes the left and right ventricles at the same time → Narrow QRS
1) AVRT (Abnormal accessory pathway between AV)	Antidromic AVRT type (less common but more lethal) ↓ Conduction starts at SA node ↓ Atria > Bundle of Kent > ventricles > bundle branches > bundle of his > AV node > atria Note: • Every atrial fibrillation firing goes through the accessory pathway completely unregulated = atrial + ventricular rate can equal on another • Bundle of Kent: fast, unregulated conduction, unlike AV node • Bundle of Kent: back to AV node → Wide QRS

2) AVNRT or proximal SVT (Abnormal pathway within AV node)	- Possible causes - scarring in AV node (MI, heart surgery) - idiopathic fibrosis (elder) - produces 2 abnormal pathways: Alpha pathway Slow conduction ↓ during its downward pathway, beta pathway repolarizes and alpha pathways joins with beta to form a cycle ↓ goes out into the atria > back down into the alpha pathway ↓ short refractory period = quicker repolarization ↓ Note: while beta pathway is repolarizing, alpha fires and circles around just in time beta has finished repolarizing → atria → repeat cycle Beta pathway Fast conduction going to the bundle of His > bundle branches > ventricles ↓ circles around to go up to the beta pathway, while the alpha pathway cancels it going down ↓ AV depolarization stops ↓ long refractory period = slower repolarization ↓ Note: due to slow repolarization, next firing goes down the alpha pathway
	Atrial flutter & Atrial fibrillation - Abnormal re-entry circuit at Tricuspid Valve - Atrial flutter: Cavotricuspid isthmus - Atrial fibrillation: multiple irritable areas within ventricles → own circuits → fire down into AV node > ventricles Ventricular tachycardia, fibrillation - V tach: 1 area in ventricle - V fib: multiple area in ventricle

- Slow-Fast pathway or Alpha-Beta pathway
 - The most common type of AVNRT

- Fast-Slow pathway or Beta-Alpha pathway
 - Not common



III) TYPES OF BRADYARRHYTHMIAS

(1) Sinus bradycardia

- SA node firing too slow
 - Slowed down sending of action potentials
 - (+) Blocked: not received → totally no relaying of action potentials down the pathway

(2) Heart blocks

- conduction blocks in the AV node
- loss of electrical activity connection between atria and ventricles
- Types:
 - 1st degree: not severe
 - 2nd degree
 - Mobitz 1 (Wenckebach)
 - Mobitz 2
 - 3rd degree

(A) PATHOPHYSIOLOGY

(1) ↓ Automaticity

Table 6. Decreased automaticity in bradyarrhythmias.

Pathophysiology	Response
↓ Automaticity	↑ PSNS or Vagal Tone ↓ Stimulate Ach to SA node = ↑ K to hyperpolarize ↓ ↓ Conduction to AV node, down ↓ ↓ HR
	Physiological in: - sleeping, resting & digesting - athlete (powerful myocardium with lower resting HR)
	Pathological: inferior wall MI due to right coronary artery occlusion
	Drugs: slow AV conduction through the AV node → BB, CCB, Digoxin
	↓ metabolic activity → slow depolarizations - Hypothermia (Low body temperature) - Hypothyroid (Myxedema coma)
	Electrolyte imbalance Hyperkalemia (alters membrane potential)
	High ICP (stroke, tumor, hematoma, mass) - brain herniation - Cushing's Triad: ↓ HR, Hypertension, Irregular respiration rate
	Associated: Sinus bradycardia

(2) Conduction block

Table 7. Conduction block in bradyarrhythmias.

Pathophysiology	Response
Conduction block Shut down AV conduction	Etiology: Inferior wall MI due to Right coronary artery occlusion Fibrotic AV node Hyperkalemia BB, CCB, Digoxin Infiltrative diseases: Amyloidosis, Sarcoidosis Lyme's disease: bacteria d/t borrelia burgdorferi

IV) SICK SINUS SYNDROME

Fast and slow firing → Tachybrady syndrome

SA node dysfunctional:

- Due to:
 - Fibrosis
 - myocardial scarring
 - intrinsic problem of the SA node
- Doesn't fire as fast → sinus bradycardia
- Some part of the atria compensate for SA node dysfunction →
 - SVT (atrial flutter, fibrillation, premature atrial contraction) → compensatory tachycardia

V) EKG DIFFERENCES & TREATMENT PLAN

STEPS:

- Determine if tachyarrhythmia (too fast) or bradyarrhythmia (too slow)
 - If Tachy → proceed to A**
 - If Brady → proceed to B**
- Check QRS width
 - Narrow
 - Wide
 - Presence / absence / dropping out of nowhere
- Check Rhythm
 - Regular
 - Irregular
- Check P waves
 - Regular
 - Irregular
- Check PR-interval length
 - Normal
 - Prolonged
- Differential diagnosis

(A) TACHYARRHYTHMIA

REC ALL:

- 0.04 s = small box
 - 5 small boxes = 1 big box
 - 5 small boxes x 0.04 s = 0.20 s
- 0.20 s = 1 big box

Steps

Check QRS width

- <0.12 or 3 little boxes = normal width, narrow
 - 3 small boxes x 0.04 s/small box = 0.12 s
 - Normal means normal conduction pathway from AV node > Bundle of His > Bundle branches
- >0.12 or 3 little boxes = wide width
 - Conduction pathway is NOT normal there is a block OR
 - Origin of conduction is focal / coming from somewhere else

Check if Irregular / Regular

- Measure R-R interval (distance)
 - Exact same distance, constant = regular rhythm
 - Abnormal, inconsistent = irregular rhythm

TIP

When reading an ECG, put a piece of paper and line 1 set of both the Rs in the R-R interval. Use that to match other pairs of R-R interval to see if it matches.

- If it matches = regular
- If it does not match = irregular

Refer to **Table 10 (Appendix)** for completion.

- Even if you can't identify the difference, you may treat them **EMPIRICALLY** and see which of them improves.
 - Helps differentiate which **RHYTHM** it is



(B) BRADYARRHYTHMIA

Steps

Refer to **Table 10 (Appendix)** for completion.

Look at the presence of P-Waves

Look at the **presence, absence, and timing:**

- If regularly present every after P wave
 - 1st degree Heart block
- If irregularly present every after P wave
 - 2nd degree Heart Block Mobitz Type I
- If present and absent, look at the pattern:
 - 2nd degree Heart Block Mobitz Type II
 - 2nd degree Heart Block Mobitz Type II (2:1 variant)

- If dropped/none + produce a wider QRS

- 3rd degree Heart Block

Look at the **timing of PR-interval**

- Prolonged:

- 1st degree Heart block
- Progressively prolonged + dropped QRS:
 - 2nd degree Heart Block Mobitz Type I

- Normal:

- 2nd degree Heart Block Mobitz Type II
- 2nd degree Heart Block Mobitz Type II (2:1 variant)
- 3rd degree Heart Block

VI) APPENDIX

Table 8. Tachyarrhythmia differentials, ECG reading and treatment.

Tachyarrhythmias		ECG reading	Treatment
Narrow QRS	Regular Rhythm	S. TACH  Figure 3. Sinus tachycardia. MUST fulfill all criteria below for sinus rhythm ○ Visible P-waves every QRS? ○ Is P-wave upright (↑), Lead II? ○ Is P-wave inverted (↓), Lead aVR? ○ Make sure the chronology: P wave > QRS > T wave Usually ≤ 150 bpm	Improves with fluid due to usual underlying cause of. ○ ↑ Automaticity, Sympathetic NS which is strongly triggered by hypovolemia ○ Others usually don't respond Treat underlying cause (+) Fever – Tylenol Hypoxic – Oxygen Check urine output Other drugs: Heparin, Tissue plasminogen activator
		FAT  Figure 4. Focal atrial tachycardia. Sinus rhythm BUT with ○ Visible P-waves every QRS? ○ inverted P-wave in Lead II? ○ Explanation: If there is focal area from LA firing & moving away from the usual direction of inferior, downwards towards (+) electrode of Lead II, and instead right, upwards = INVERTED P-WAVE ○ P-wave upright (↑), Lead aVR? ○ Make sure the chronology: P wave > QRS > T wave ○ NOTE: Before diagnosing this, make sure it's not misplaced.	Order of administration ○ STABILIZE FIRST ○ Fluids will NOT improve / work ○ Proceed to the next line of drug if it doesn't work ○ Long term treatment Start Vagal maneuver → ○ ↑ Vagal tone → slows down AV node conduction ○ Valsalva maneuver (like a pooping position) ○ Blow into a plunger maneuver → ↑ intrathoracic pressure → ↑ vagal tone as well Next line of drugs to obliterate SVT > AFL, FAT: ○ Adenosine 6 mg (short acting) which blocks the AV node Next line of drugs to obliterate AFL, FAT if adenosine doesn't work: ○ BB or CCB (consider contraindications)
		AFL  Figure 5. Atrial flutter. Jacked-up sawtooth waves identifiable as atrial flutter ○ This is due to the re-entry circuits (counterclockwise) ○ N (1/2/3 etc) sawtooth waves: 1 QRS ratio the entire ECG strip Most visible in Leads II/ III/ aVF ○ If not seen, also check Lead V1	Electrical cardioversion: ○ IF UNSTABLE: hypotensive, altered mental status, chest pain/pulmonary edema → DO THIS FIRST Long term treatment: ○ Radiofrequency ablation of abnormal tissue ▪ Burn the re-entry circuits so they don't generate abnormal activities ▪ AFL: circuit in Tricuspid isthmus ▪ FAT: circuit in Ectopic foci
		AVRT/AVN RT (SVT)  Figure 6. Atrioventricular reentrant tachycardia. None: ○ P waves, flutter waves, T waves ○ P waves are hidden within the QRS complexes Sometimes a retrograde P wave after the QRS in Leads II, III, aVF	



	Irregular Rhythm	A. FIB (most common)	 Figure 7. Atrial fibrillation. Fibrillation waves "squiggly lines" - NO Visible P-waves every QRS - Squiggly lines due to multiple ectopic foci / re-entry firing - Most visible: Lead V1 Irregularly Irregular R-R intervals	Vagal maneuver - Can try but doesn't generally work Next line of drugs: - Adenosine: doesn't generally work - BB or CCB: may/not work Electrical cardioversion: - To restart the heart, generate a new rhythm - If UNSTABLE: hypotensive, altered mental status, chest pain/pulmonary edema → DO THIS FIRST Long term treatment: Radiofrequency ablation of abnormal tissue - Burn the re-entry circuits / multiple foci so they don't generate abnormal activities - BB may also be needed CHAD-VASC Score - Done to predict A. FIB - Score >2 → ↑ need for anticoagulation → ↓ risk for thromboembolism, reach the brain (stroke)
		AFL w/ VARIABLE BLOCK	 Figure 8. Atrial fibrillation with variable block. Sawtooth waves identifiable as atrial flutter 2 sawtooth waves: 1 QRS: 1 sawtooth wave: 1 QRS ratio the entire ECG strip This is why we call it the variable block (2-1-1-1) Most visible in Leads II/ III/ aVF If not seen, also check Lead V1	
		MAT	 Figure 9. Multifocal atrial tachycardia. NONE - Fibrillation waves - Flutter waves ≥3 Variable, morphologically odd-looking P waves - Inverted / pointed / jacked-up looks like "M" - Difference is due to firing coming from different atrial foci Variable R-R intervals - Due to the variable ectopic foci in the atria, some are closer to or farther from the AV node >100 bpm to differentiate from wandering atrial pacemaker Due to an underlying disease - COPD - Pulmonary embolism - Heart failure	
Wide QRS	Regular Rhythm	V. TACH (monomorphic) Most common	 Figure 10. Ventricular tachycardia. Similar morphology Wide complex tachycardia difficult to differentiate between: V. TACH - WIDER QRS >0.14 s - Look for AV dissociation: inverted P-waves snuck within the QRS Extreme RAD CVD History (structural origin), >35 y/o	If a patient is treated as V. TACH, but actually has SVT w/ BBB → - Can improve the arrhythmia OR - Not be affected at all Drug of choices: Amiodarone (antiarrhythmic): Regenerates, resets normal rhythm Procainamide Next line of management: Cardioversion: Put pads; V. Tach is very unstable and can easily progress into V. Fib Defibrillate: can be done in worst case scenario Synchronized cardioversion: you're timing the electrical jolt given with the R wave; difficult for irregular rhythms Long term treatment: Radiofrequency ablation of abnormal tissue - Burn the re-entry circuits / multiple foci so they don't generate abnormal activities - Ischemia (most common cause) in V. Tach → look for underlying myocardial infarction - Stabilize - Generate normal rhythm - Check for ST elevation/ depression - Check troponin - If positive, request for PCI - May need Automatic Implantable Cardiac Defibrillator - To regenerate normal rhythm even if not at the hospital - Indication: recurrent/ malignant



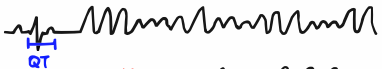
Irregular Rhythm	SVT w/ BBB	Wide complex tachycardia difficult to differentiate between: - SVT with BBB - WIDE QRS <0.14 s - No AV dissociation - No extreme RAD - No significant CVD history (structural origin), <35 y/o	If a patient is treated as SVT w/ BBB but actually has V. TACH and gets treated, it could worsen the scenario/kill the patient. ONLY treat it as SVT w/ BBB if you've fulfilled the criteria. If not you treat it as V TACH. Drug of choices: Adenosine (administer with caution): usually used first in algorithms because if it's SVT w/ BBB, then it goes away and if not it's monomorphic V. Tach Long term treatment: - Radiofrequency ablation of abnormal tissue
	ANTIDROM IC AVRT (least common)	-	Can be treated as V. Tach (Amiodarone, Procainamide, Cardioversion) Do not give AV Nodal blockers (Adenosine, BB, CCB, Digoxin) to patient with Antidromic AVRT especially if they have pre-excitation disease: - A FIB OR Antidromic AVRT Long term treatment: - Radiofrequency ablation of abnormal tissue
	PMVT Type 1: Normal QT Type 2: Long QT-interval (Torsades de Pointes)	 Figure 11. Polymorphic ventricular tachycardia. Look first for the QT-interval before they developed the irregular arrhythmia - Normal QT-interval vs AF with WPW - Prolonged QT-interval: ≥ 500 ms Have different morphologies of QRS complexes	For PMVT with Normal QT Management of choice: - Drugs first: Amiodarone OR Procainamide - Synchronized Cardioversion: sometimes it's hard to sync with the R waves → shift to Defibrillation Long term treatment: - Radiofrequency ablation of abnormal tissue - May need Automatic Implantable Cardiac Defibrillator for recurrent V. Tach or V. Fib For PMVT with Prolonged QT, suspecting Torsades de Pointes TDP is due to big causes of EADs - Hypokalemia, hypomagnesemia, hypocalcemia - Offending drugs (ABCDE) Give Magnesium sulfate - Check potassium levels → if low, replete the potassium levels Discontinue the offending drugs or decrease them: - Antiarrhythmics - Antibiotics - Antipsychotics - Antidepressants - Antiemetics Overdrive pacing or give them Isoproterenol ↑ HR a little → ↓ QT-interval → ↓ incidence of going back to TDP
	A. FIB with WPW	 Figure 12. Atrial fibrillation with WPW syndrome. Differentiating criteria ↑↑↑ Rates - Because the most common kind of WPW is Antidromic AVRT - Electrical activity from A. Fib → bundle of Kent → ventricles - Atrial + ventricular rate can almost equal one another	Can be treated like PMVT with normal QT-interval Do not give AV Nodal blockers (Adenosine, BB, CCB, Digoxin) - Electrical activity from A. Fib won't go to the AV node (highly regulated), only go through Bundle of Kent - Can quickly lead to V. Fib
	AF + BBB (one of the most common in this category)	 Figure 13. Atrial fibrillation with bundle branch block. Differentiating criteria ↑ Rates are not as fast - QRS morphology is relatively the same: - Recall: A. FIB has multiple foci firing and going down the bundle branch system → irregular R-R interval - Due to the block, will not go down the normal conduction pathway → widens QRS complex	Management of choice: - Drugs first: BB OR CCB - Cardioversion Long term treatment: - Radiofrequency ablation of abnormal tissue
	V. FIB Due to breakdown of PMVT & AF with WPW	 Figure 14. Ventricular fibrillation. Produces NO PULSE → very dangerous	Need to immediately administer CPR - Chest compressions - Epinephrine - Defibrillate



Table 9. Bradyarrhythmia differentials, ECG reading and treatment.

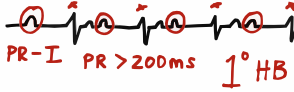
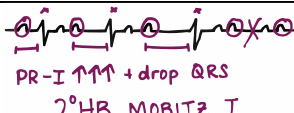
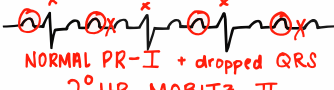
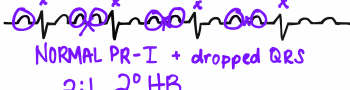
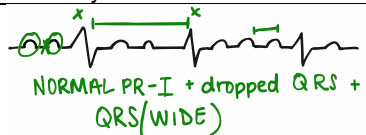
Bradyarrhythmias		ECG reading	Treatment
SINUS BRADYCARDIA		 SINUS BRADYCARDIA Figure 15. Sinus bradycardia. Look for P-waves → QRS every after it ○ Sinus rhythm but just at a slower rate	Monitor since relatively benign
HEART BLOCK	1st degree	 PR-I PR > 200ms 1° HB Figure 16. 1st degree heart block. Look for P-waves → QRS every after it Look for PR-interval ○ > 200 ms = prolonged	
	2nd degree Mobitz I (Wenckebach Phenomenon)	 PR-I ↑↑↑ + drop QRS 2° HB MOBITZ I Figure 17. 2nd degree heart block type I. Look for P-waves → but no QRS every after it (irregular) PR-interval: Prolonged progressively each time every after QRS QRS: drops Tip to memorize: ○ Longer longer drop, you have a winky bock (Wenckebach) ○ ↑↑↑ PR-interval + drop QRS	Need to pay attention to these ○ HR can drop really low because the conduction through AV node ○ Recall: ▪ CO = HR x SV → if HR drops, CO drops ▪ BP = CO x TPR → if CO drops, BP drops ▪ Hypotension → altered mental status or chest pain or pulmonary edema → UNSTABLE and treat them IF UNSTABLE: ○ Atropine: ▪ Recall: Acetylcholine → ↓ automaticity, slow conduction ▪ ↓ PS effect on AV node → block acetylcholine -AV node binding → ↑ Automaticity, nothing blocks conduction = ↑ conduction ○ Epinephrine ▪ ↑ Sympathetic = ↑ AV conduction = ↑ HR ▪ If HR doesn't increase → PACING ○ Pacing ▪ Transcutaneous ▪ Transvenous: slow down the venous circulation ▪ Permanent pacemaker (for 3rd degree heart block)
	2nd degree Mobitz II	 NORMAL PR-I + dropped QRS 2° HB MOBITZ II Figure 18. 2nd degree heart block type II. Look for P-waves → but no QRS every after it (irregular) PR-interval: Normal QRS: drops Pattern: ○ P wave – QRS – P wave – Drop QRS ○ QRS drops out of nowhere	
	2nd degree Mobitz II (2:1 variant)	 NORMAL PR-I + dropped QRS 2:1 2° HB Figure 19. 2nd degree heart block type II, variant 2:1. Look for P-waves → but no QRS every after it (irregular) PR-interval: Normal QRS: drops Pattern: ○ P wave – QRS – P wave – Drop QRS – P wave – QRS ○ QRS drops out of nowhere ○ For every 2 P waves: 1 QRS	
	3rd degree	 NORMAL PR-I + dropped QRS + QRS(WIDE) 3° HB Figure 20. 3rd degree heart block. P wave: SA node rate = 60-80 bpm PR-interval: Normal QRS: drop/ none + produce a wider one ○ Wider because conduction stops at the AV node → ventricles are depolarizing on their own ○ AV dissociation ○ QRS = ventricular rate (20-40 bpm)	Treat underlying disease ○ Conduction block: Inferior wall myocardial infarction due to right coronary artery occlusion ▪ One of the most common causes ▪ Look for signs of STEMI/NSTEMI ▪ Look out for positive troponins ▪ CATHLAB → PCI (stent) ○ Hyperkalemia ▪ Ca chloride or gluconate stabilizes cardiac membranes ▪ Insulin: shunt potassium into the cells ▪ D50: so their sugar doesn't drop ▪ Albuterol: shunt potassium into the cells → ↓ circulating potassium levels ▪ HCO3 to address the acidosis ▪ Lasix: to excrete the excess potassium ○ Overdose from ↑↑↑ BB or CCB or Digoxin which blocks the AV node ▪ BB: Glucagon ▪ CCB: Calcium ▪ Digoxin: Digibind ○ Lyme's disease due to borrelia burgdorferi ▪ Ceftriaxone ○ Hypothermia ▪ Rewarm ○ Hypothyroidism ▪ Levothyroxine if with Myxedema



Table 10. Abbreviations.

AFL	Atrial flutter
A. FIB	Atrial fibrillation
AVRT/ AVNRT	Atrioventricular (nodal) reentrant tachycardia
BBB	Bundle branch block
DADs	Delayed after depolarizations
EADs	Early after depolarizations
FAT	Focal atrial tachycardia
MAT	Multifocal atrial tachycardia
PCI	Percutaneous coronary intervention
PMVT	Polymorphic ventricular tachycardia
S. TACH	Sinus tachycardia
V. TACH	Ventricular tachycardia
WPW	Wolff-Parkinson-White syndrome

VII) REVIEW QUESTIONS

1) What is the diagnosis shown below?



- 1st degree AV block
- 2nd degree AV block Mobitz type 2
- Atrial fibrillation
- Ventricular tachycardia

2) What is the first line of management for the above-mentioned case?

- Amiodarone to reset to the normal rhythm
- Procainamide
- Beta-blocker
- A & B

3) A 60/F presents to the emergency room with a chief complaint of lethargy and unsteady gait of 1 day duration. Patient is a known hypertensive and diabetic maintained on insulin, and amlodipine. When probed, she revealed to have started taking her amitriptyline, an antipsychotic, without her doctor's orders. During the consult, the patient experiences loss of consciousness lasting for 30 seconds.

Her ECG reading showed: prolonged QT interval at 600 ms. Metabolic panel showed hypokalemia, and hypomagnesemia.



- Consider Torsades de pointes
- Consider 1st degree Heart block
- Consider Atrial fibrillation
- None of the above

4) Which pathway or underlying mechanism of AVNRT does fast conduction going to the bundle of His > bundle branches > ventricles describe?

- Alpha pathway
- Beta pathway
- Fast-slow pathway
- Slow-fast pathway

5) If found to have a 3rd degree heart block, how do you administer treatment?

- Treat underlying inferior wall myocardial infarction through PCI.
- Administer Ca chloride to stabilize cardiac membranes in cases of hyperkalemia.
- Add HCO₃ to address the acidosis.
- All of the above

CHECK YOUR ANSWERS

VIII) REFERENCES

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OUTLINE

- I) INTRODUCTION
- II) HYPERTENSIVE CRISIS
- III) APPENDIX
- IV) REVIEW QUESTIONS
- V) REFERENCES

I) INTRODUCTION

- Hypertension is $\uparrow$ systolic or diastolic BP.
- Categorization according to American Heart Association:**
 - Note: May have isolated systolic or diastolic HTN, or both.

Table 1. AHA definition of high blood pressure.

Category	Systolic	Diastolic
Normal	<120 mmHg (LV pressure)	<80 mmHg (pressure at rest of aorta)
Pre-HTN	120-129 mmHg	<80 mmHg
Stage 1 HTN	130-139 mmHg	80-89 mmHg
Stage 2 HTN	≥ 140 mmHg	≥ 90 mmHg

- Diagnosis:
 - Take 2 separate blood pressure measurements on 2 separate office visits.
 - If any point in time, they are $>130/80$ mmHg, can be considered as Stage 1 HTN and be given treatment, depending on their cardiovascular risk factors.
 - Note: *White Coat Hypertension*
 - Outside of the office: Normal BP
 - Inside the office: elevated BP due to stress/anxiety
 - Diagnose with ambulatory blood pressure monitoring (ABPM) which is a 24-hour monitoring $\rightarrow$ gives the entire average BP of the day (morning, night).

(A) CAUSES OF PRIMARY HYPERTENSION

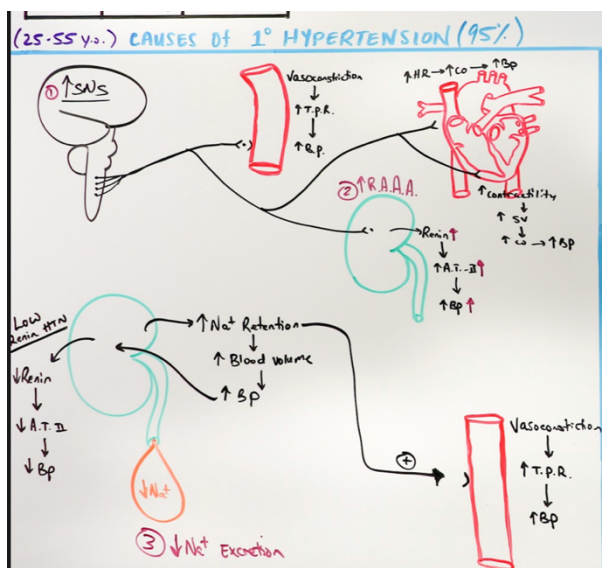


Figure 1. Causes of primary hypertension.

- Most of the time, causes are of primary type
- 95% of the cases are due to essential hypertension.
- Essential hypertension: exact reason or etiology is unknown.
- Age range: 25-55 years old
- Risk factors that increase primary hypertension
 - Diabetic: hyperinsulinemia $\rightarrow \uparrow$ BP
 - Obesity
 - Obstructive sleep apnea
 - Type A personality: very excited or neurotic
 - Vitamin D deficiency
 - Family history
 - Smoke and alcohol history
 - Ethnicity

(1) Hypersensitive sympathetic nervous system

Recall:

- SNS is important in regulating blood vessel tone.
- SNS neurons from the thoracolumbar region $\rightarrow$ go to arterials $\rightarrow$ act on different receptors

Table 2. Hypersensitive sympathetic nervous system.

Event	Effect
$\uparrow$ Norepinephrine on smooth muscle	$\uparrow$ vasoconstriction $\rightarrow \uparrow$ TPR $\rightarrow \uparrow$ BP
$\uparrow$ JG cell activation	$\uparrow$ Renin $\rightarrow \uparrow$ Angiotensin II $\rightarrow \uparrow$ BP (via $\uparrow$ Aldosterone, ADH)
$\uparrow$ SA node stimulation	$\uparrow$ HR $\rightarrow \uparrow$ CO $\rightarrow \uparrow$ BP
$\uparrow$ Contractility of myocardium	$\uparrow$ SV $\rightarrow \uparrow$ CO $\rightarrow \uparrow$ BP

(2) $\uparrow$ RAAS

Table 3. RAAS.

Event	Effect
$\uparrow$ RAAS	$\uparrow$ Renin $\rightarrow \uparrow$ Angiotensin II $\rightarrow \uparrow$ BP (via $\uparrow$ Aldosterone, ADH)

(3) $\downarrow$ Sodium Excretion

- Common in African-American and elderly individuals who have **low renin hypertension** because the cause is due to increased sodium retention.

Table 4. Low sodium excretion.

Event	Effect
$\downarrow$ Sodium excretion in urine $\rightarrow \uparrow$ Sodium retention	$\uparrow$ Blood volume due to water $\rightarrow \uparrow$ BP
	inhibits RAAS $\rightarrow \downarrow$ renin production $\rightarrow \downarrow$ Angiotensin II
$\uparrow$ Sodium retention can also cause	$\uparrow$ vasoconstriction $\rightarrow \uparrow$ TPR $\rightarrow \uparrow$ BP

(B) CAUSES OF SECONDARY HYPERTENSION

- Not as common, only 5% of the cases are due to secondary hypertension
- Age range: <25 years old
- Risk factors that increase secondary hypertension:



(1) Renal Parenchymal Diseases

- Renal parenchymal disease
 - kidney tubules are located here which are for reabsorption and excretion
 - ↑ Sodium retention → ↑ water retention → ↑ BP
- Glomerular disease
 - Damaged glomeruli → ↓ filtration of plasma
 - Glomerulonephritis
 - IgA Nephropathy
 - Post-streptococcal glomerulonephritis
 - Lupus nephritis
 - Diabetic nephropathy → End stage renal disease
- Tubular disease
 - Polycystic kidney disease (PKD)

(2) Renovascular Diseases

- Damaged blood vessels going to the kidneys
- Renal artery Stenosis
 - Atherosclerotic plaque accumulating in the renal artery wall → ↓ Blood flow → ↓ urinary excretion → ↑ blood plasma, salts
- Vasculitis
 - Inflammation due to antibody deposition in vascular wall → narrowing → ↓ Blood flow → ↓ urinary excretion → ↑ blood plasma, salts
 - Polyarteritis Nodosa
 - Wegener's granulomatosis
- Fibromuscular dysplasia
 - 20–30-year-old females
 - Proteinaceous deposits within the vessel wall → dysplastic → narrow lumen → ↓ Blood flow → ↓ urinary excretion → ↑ blood plasma, salts

Note:

- Underlying kidney disease → ↑ BUN, Creatinine, ↓ GFR, ↑ proteinuria

(3) Adrenal gland diseases

Table 5. Adrenal gland diseases.

Location	Disease	Effect
Zona glomerulosa	Conn syndrome	↑↑↑ Aldosterone → ↑ Sodium & water reabsorption → ↑ Blood volume → ↑ BP
		May have electrolyte abnormalities (↑ Na, ↓ K)
Zona fasciculata	Cushing's Syndrome	↑↑↑ Cortisol → ↑ Nor/epinephrine receptor sensitivity → ↑ vasoconstriction → ↑ BP
		Pendular obesity, buffalo hump, moon facies, hyperglycemia, abdominal striae
Adrenal medulla	Pheo-chromocytoma	↑↑↑ Nor/epinephrine → ↑ contractility, HR, SV, RAAS → ↑ BP
		Headaches, diaphoresis, episodic palpitation

(4) Thyroid diseases

Table 6. Adrenal gland diseases.

Disease	Effect	
Hyperthyroidism	↑ T3, ↑ T4, ↓ TSH (if disease comes from the thyroid) ↓	
	↑ HR	↑ BP
	↑ Nor/epinephrine receptor sensitivity → ↑ contractility, vasoconstriction	
Hypothyroidism	↓ T3, ↓ T4, ↑ TSH (if disease comes from the thyroid) ↓	
	↑ Sodium retention → ↑ Blood volume → ↑ BP	↑ Diastolic BP
Hyper-parathyroidism	↑ PTH → ↑ Ca in blood: ↑ osteoclastic activity/ ↑ Ca reabsorption in kidneys/ (+) Vit D to ↑ Ca reabsorption in gut ↓	
	Acts on smooth muscle → ↑ Vasoconstriction	
	↑ TPR → ↑ BP	

(5) Coarctation of the Aorta

- Turner's syndrome
 - Coarctation of the aorta: narrowing portion of the aorta → ↑ BP proximal the narrowing → ↑ TPR → ↑ diastolic BP → ↑ ventricles working harder to pump against the high pressure in the aorta

(6) Head trauma

- ↑ ICP + nausea/vomiting/papilledema/focal neural deficits + history of head trauma → Cushing's triad
 - Hypertension (↑ BP)
 - Bradycardic
 - Irregular respiration

(7) Pregnancy

- Preeclampsia
 - Risks and signs and symptoms:
 - (+) >20 weeks age of gestation
 - (+) Hypertension
 - (+) Proteinuria: determined by 24-hour urine test or protein-creatinine ratio
 - ↑ Fetal distress
 - Complication: Eclampsia
 - (+) Hypertension
 - (+) Proteinuria
 - Possible seizures
 - Prevention of eclampsia: Magnesium sulfate
 - Control of BP: Methyldopa, Hydralazine, Labetalol, Nifedipine



(8) Medications

Table 7. Medications.

Medications	Effect
Combined Oral Contraceptives	↑ Estradiol (E2) ↑ Angiotensinogen (liver) ↑ Angiotensin II → ↑ BP
Sympathomimetic (Amphetamine/ Adderall, Ritalin/ Methylphenidate, Vyvanse/ Lisdexamfetamine; Cocaine)	↑ Vasoconstriction ↑ HR ↑ contractility
Serotonin Syndrome (↑↑ SSRIs, SNRIs)	↑ Hyperthermia ↑ Rigidity ↑ Hyperreflexia ↑ Pupillary changes
MAO inhibitors (Resagiline, Selegiline for refractory and resistant depression) + Tyramine (cheese)	Hypertensive crisis

II) HYPERTENSIVE CRISIS

- Any blood pressure $\geq 180/120$ mmHg
- Organs to pay attention to:

Table 8. Possible end-organ damage.

Organ	Disease	Manifestations
Eye	Hypertensive Retinopathy	Visual changes Blurring/ Losing of vision Dot hemorrhages Flame hemorrhages Cotton wool spots (protein & lipid) Hard exudates Thickened vessels through the central retinal artery → AV nicking, copper wiring Watch out: Papilledema!
Heart	LV Hypertrophy → diastolic HF	↑ LV stress
	Left Bundle branch block	-
	Ischemic heart disease → possible M.I.	↑ hypertrophy → ↑ oxygen demand
	Arrhythmia	↑ hypertrophic ventricles → altered electrical pathways
Blood vessel	Aortic dissection	↑ BP → tear through the endothelial lining → blood vessel develops 2 nd lumen → blood travels through tunica media + normal lumen → rupture
	Abdominal aortic aneurysm	↑ atherosclerotic plaque → dilation of arteries (i.e. abdominal aorta) → ↑ rupture (if people smoke, have CVD risk factors) → massive bleeding
	Atherosclerotic plaques	Hypertensive risk + Endothelial injury → ↑ risk of clots + atherosclerotic plaques
Kidneys	Hyaline arteriosclerosis <i>Hypertension is the 2nd most common cause CKD</i>	Proteinaceous deposit in the glomerular vessel → kidney damage → overtime ↑ CKD → ↑ BUN, creatinine, proteinuria, Na
Brain	Lacunar infarcts due to hypertension	↑ BP → infarcts in small vessels, particularly near basal nuclei → ataxia, hemiparesis, sensory deficits
	Charcot-Bouchard Aneurysm	Intracranial bleed
	Subarachnoid hemorrhage	Vertebral + basilar + internal carotid arteries → can form berry aneurysms → rupture → ↑ accumulate in the subarachnoid space

(A) TYPES OF CRISES

Table 9. Types of crises.

Type	BP	End organ damage
Urgency	$\geq 180/120$ mmHg	None
Emergency		Present



III) APPENDIX

Table 10. Abbreviations.

ABPM	Ambulatory blood pressure monitoring
AV	Arteriovenous
BP	Blood pressure
CKD	Chronic kidney disease
CVD	Cardiovascular diseases
HR	Heart rate
HTN	Hypertension
ICP	Intracranial pressure
MI	Myocardial infarction
PTH	Parathyroid hormone
RAAS	Renin Angiotensin Aldosterone System
SV	Stroke volume
TSH	Thyroid stimulating hormone
TPR	Total peripheral resistance

IV) REVIEW QUESTIONS

- 1) What differentiates primary causes of hypertension from secondary causes?
 - a. Underlying kidney disease
 - b. Essential hypertension which occurs mostly in 25–55-year-old patient.
 - c. Risk factors including diabetes, obesity, and obstructive sleep apnea.
 - d. Both b & c
- 2) Billy, 35/M, complains of a lump developing on his neck area. Apart from this, he noted excessive sweating even right after showering. He usually showers 4x a day. His movements are notably jerky as well. His PE results showed the following: HR: 110 bpm, RR 15 and 36.5 degrees Celsius. Which of the following is the correct pathophysiological mechanism underlying the patient's clinical manifestation?
 - a. Increased blood pressure through increased sodium retention
 - b. Increased blood pressure through ↑ nor/epinephrine receptor sensitivity
 - c. Increased PTH → increased calcium reabsorption
 - d. None of the above
- 3) How can you differentiate hypertensive urgency from hypertensive emergency?
 - a. BP of ≥180/120 mmHg but without end-organ damage.
 - b. BP of ≥180/120 mmHg but with end-organ damage.
 - c. BP of ≥140/120 mmHg but without end-organ damage.
 - d. BP of ≥140/120 mmHg but with end-organ damage.

- 4) Max, 5/F, presents to the emergency room with tea colored urine. Upon conducting the physical examination, results showed that she was febrile (38 degrees Celsius), breathless (RR 30) and had edematous lower extremities. History revealed that she developed pharyngitis 10 weeks ago and was prescribed with antibiotics. However, her mother stopped her treatment midway because she appeared to be "well already and asymptomatic." What is the most probable secondary cause of hypertension with the patient?
 - a. Vasculitis
 - b. Tubular disease
 - c. Glomerular disease, specifically PSGN
 - d. Fibromuscular dysplasia

CHECK YOUR ANSWERS

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OUTLINE

- I) OVERVIEW
- II) ETIOLOGY
- III) PATHOPHYSIOLOGY
- IV) CLINICAL FEATURES
- V) DIAGNOSIS
- VI) TREATMENT
- VII) APPENDIX
- VIII) REVIEW QUESTIONS
- IX) REFERENCES

I) OVERVIEW

Blood vessel Layers from the lumen outward:

- Tunica Intima (Interna)
- Tunica Media
- Tunica Externa (Adventitia)

What is an Aortic Dissection?

- A tear through the Tunica Intima (Between Tunica Intima and Tunica Media)
 - Most common site is Aorta
- Tear in the intima
 - Blood entering the media
 - create false lumen
 - lead to progressively growing hematoma

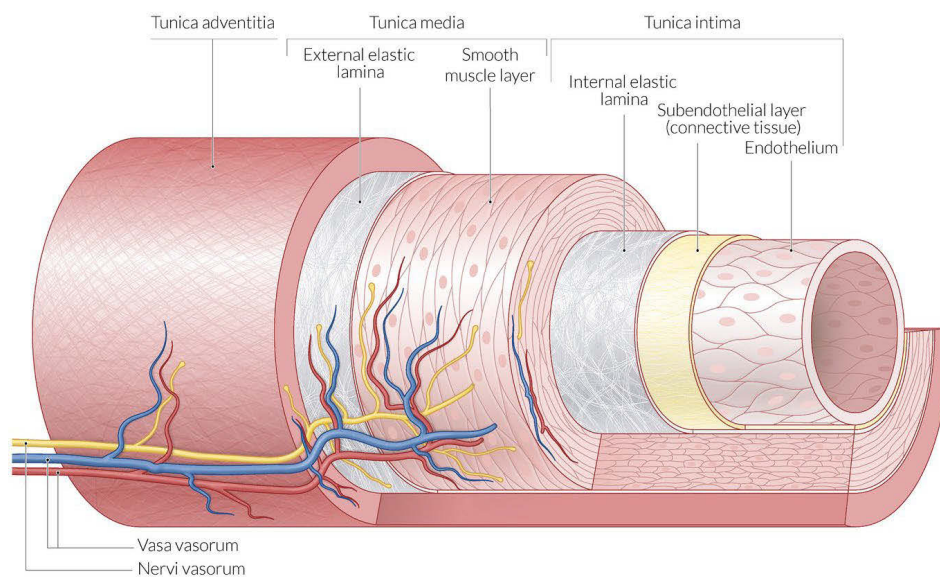


Figure 1. Artery Structure (AMBOSS).

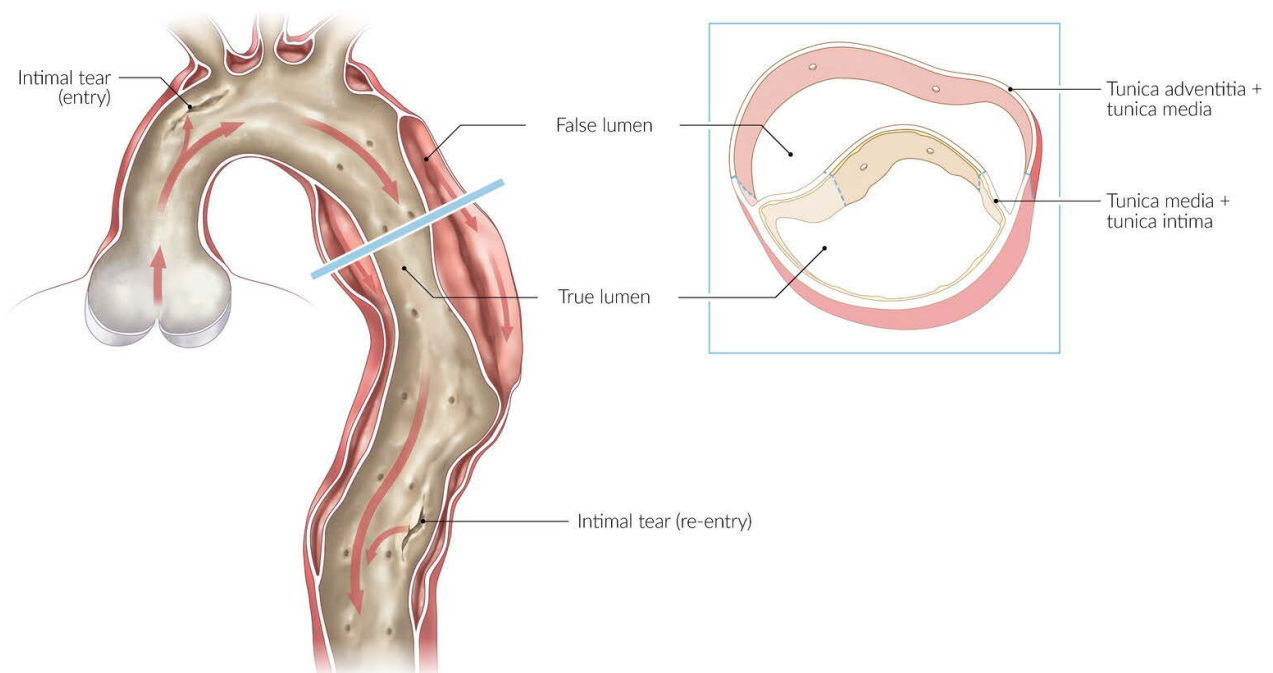


Figure 2 Aortic Dissection (AMBOSS)



II) ETIOLOGY

(A) ACQUIRED CAUSES

(1) Hypertension

- **Most Common cause**
- High risk Hypertensive patients for Aortic Dissection are patients with:
 - Age > 40-60
 - Tobacco Use
 - Hyperlipidemia
- Secondary Hypertension
 - Transient elevation in blood pressure
 - **Cocaine or Amphetamines Use**
 - High intensity weightlifting → Heavy Valsalva maneuver → Brief rise of Blood Pressure
- Mechanism:
 - ↑ Shear Forces on the vessel wall → Tear in the Tunica Intima → Blood tracks in between Tunica Intima and Tunica Media Layer
 - Arteriosclerosis of the Vasa Vasorum
 - In HTN patients → Atherosclerosis of the Vasa Vasorum → ↓ Blood Flow to the Tunica Media → necrotic processes → Weak Vessel walls → ↑ Risk of having a tear → ↑ Risk of Dissection

Blood Supply of the Blood Vessels

- Tunica Intima → directly from blood in the lumen
- Tunica Media and Tunica Externa → Vasa Vasorum

Vasa vasorum

- small blood vessels supply oxygen and nutrients to the outer layers of the arterial wall

- Blood Supply of the Blood Vessels**
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- Vasa vasorum**
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- Vasa vasorum**
- small blood vessels supply oxygen and nutrients to the outer layers of the arterial wall

(2) Trauma

Motor Vehicle Collision

- Motor Vehicle Collision
- Secondary to Deceleration type of Injury

Iatrogenic Injuries

- Catheterization
- Valve Repairs

(3) Vasculitis

- = Inflammation of the blood Vessel wall
- Triggers :
 - Tertiary **Syphilis**
 - Inflammation of the Vasa vasorum caused by Treponema pallidum → ↓ Blood Supply to the arterial walls → Cystic Medial Degeneration of the Tunica Media → Weak wall → ↑ Risk of Dissection
 - **Takayasu Arthritis**
 - Inflammatory granulomas deposit in the vessel walls → Medial Degeneration of the Tunica Media → Weak wall → ↑ Risk of Dissection
 - Age < 50
 - Usually, Aorta is Involved
 - Less Facial and Ocular involvement compared to Giant cell. Arthritis

Giant Cell Arthritis

- =Temporal Arthritis
- Autoimmune Vasculitis
- chronic inflammatory disease involving large- and medium-sized arteries
 - Most Common→ Involvement of the cranial branches of the carotid arteries
- Age >50

Table 1. Takayasu vs Giant Cell Arthritis.

	Takayasu Arthritis	Giant Cell Arthritis
Age	<50	>50
Affected Vessels	Mostly Aorta and its branches	Mostly Temporal Vessels
Clinical Features	● Constitutional symptoms: Weight loss, Fever, Fatigue. ● Absent or weak Peripheral Pulse ● Discrepant blood pressure between arms	● Constitutional symptoms: Weight loss, Fever, Fatigue. ● Headache ● Ocular Involvement ● Jaw Claudication

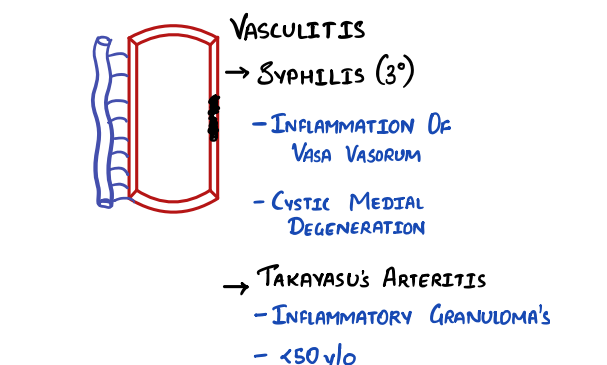
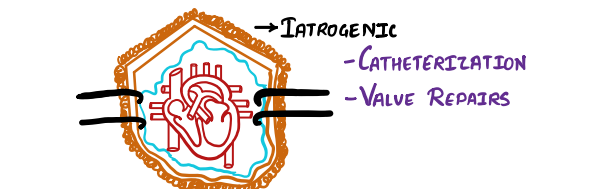
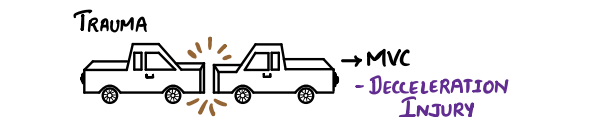
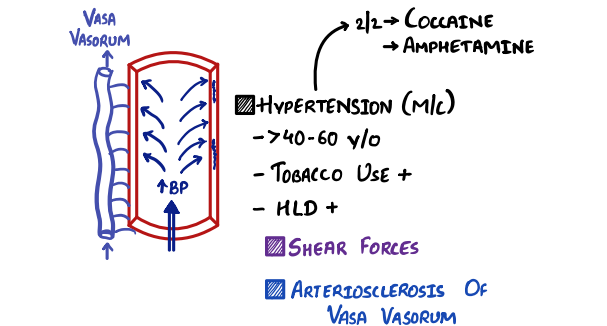


Figure 3. Acquired Causes of Aortic Dissection



(B) CONGENITAL CAUSES

(1) Connective Tissue Diseases

- Defect in the connective tissues of the blood vessels
→ Weak vessel wall → ↑ Risk of having a tear, ↑ Risk Aneurysm → ↑ Risk of Dissection
- Connective tissues of the blood vessels **Figure 1**
 - Subendothelial Layer
 - Elastic Laminas
 - Tunica Externa

Aneurysm

- True Aneurysm
 - abnormal dilation of an artery due to a weakened vessel wall, ≥50% dilation of all 3 layers of aorta
- False Aneurysm
 - external hematomas with a persistent communication to a leaking artery, rupture within adventitia

Aneurysm → ↑ **Risk of Dissection**
Dissection → ↑ **Risk of Aneurysm**

Marfan Syndrome

- Etiology
 - Mutation of Fibrillin Gene → ↓ Elasticity of the vessel walls → ↑ Risk Aneurysm and ↑ Risk of Dissection
- Clinical Features
 - Cardiovascular Disorders: mitral valve prolapse, aortic aneurysm, and dissection
 - Musculoskeletal Disorders: tall stature with disproportionately long extremities, joint hypermobility
 - Eyes Disorders: subluxation of the lens of the eye

Fibrillin= A glycoprotein that forms a supportive sheath around Elastin

Ehlers-Danlos Syndrome(EDS)

- Etiology
 - Mutation of Collagen Gene → ↓ Resilience of the blood vessels → ↑ Risk Aneurysm and ↑ Risk of Dissection
- Clinical Features
 - Cardiovascular Disorders: mitral valve prolapse, aortic aneurysm, and dissection
 - Musculoskeletal Disorders: Joint Hypermobility
 - Skin Disorders : Skin hyperextensibility, Easy Bleeding , Tendency to bruise easily

(2) Bicuspid Aortic Valve

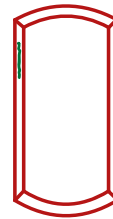
- One of the most common types of congenital heart disease
- Genetic Disorder → 2 valve cusps fuse together → Bicuspid Aortic Valve
- ↑ Risk of
 - Aortic Stenosis (Most Common)
 - Aortic Regurgitation
 - Hypertension
 - Aortic Aneurysms (unknown Mechanism)
 - Aortic Dissections (unknown Mechanism)
- (Potential) Mechanism
 - Bicuspid aortic Valve → Left Ventricle Hypertrophy → HTN → Work harder to push blood out → ↑ Risk Aortic Dissection , ↑ Risk Aneurysm

(3) Coarctation of Aorta

- A narrowing of the descending aorta (after aortic arch), at the level of **Left Subclavian artery** , near **Ductus Arteriosus**
- Mechanism: Narrowing cause a lot of resistance → ↑ Blood pressure proximal to the affected area → HTN → ↑ Risk Aortic Dissection , ↑ Risk Aneurysm
- Patients with Coarctation of Aorta probably have
 - History of Turner Syndrome
 - Associated Bicuspid aortic Valve

ANEURYSMS ⇌ DISSECTIONS

CONNECTIVE TISSUE DISORDERS



MARFAN SYNDROME

- MUTATION → FIBRILLIN ↓ → ↓ ELASTICITY

EHLERS DANLOS SYNDROME (E.D.S)

- MUTATION → COLLAGEN ↓ → ↓ RESILIENCY

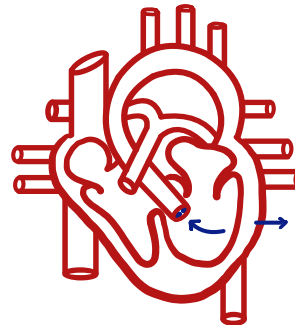


BICUSPID AORTIC VALVE

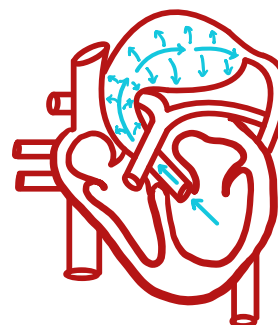
- ↑ RISK → AORTIC STENOSIS (M/C)
→ AORTIC REGURGITATION

- ↑ RISK OF HYPERTENSION

- ↑ RISK OF AORTIC ANEURYSMS
↓
AORTIC DISSECTION



COARCTATION OF AORTA



- NARROW AORTA AT
L. SUBCLAVIAN

- HTN → ANEURYSMS

↑
→ DISSECTION

- H/O TURNERS SYNDROME
- BICUSPID AORTIC VALVE

Figure 4. Congenital Causes of Aortic Dissection



III) PATHOPHYSIOLOGY

Tear in the aortic intima → blood enters the media of the aorta and forms a false lumen in the intima-media space → 4 Possible Scenarios:

- 1) **Reentry** of the blood into the True lumen
- 2) ↑ pressure within the aortic wall → **Rupture**

3) Narrowing / **Occlusion** of a branching vessel (due to forming Hematoma) → Malperfusion Syndromes

4) **Intramural (Intraluminal) Thrombosis** → Forming hematoma at the tear site

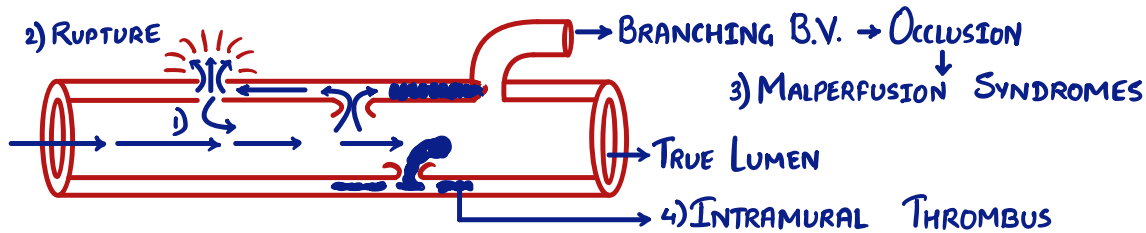
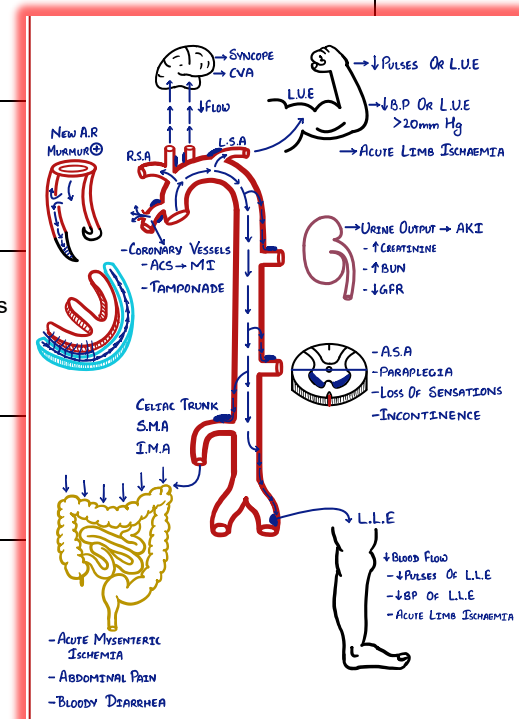


Figure 5. Pathophysiology of Aortic Dissection

IV) CLINICAL FEATURES

Table 2. Clinical Features of Aortic Dissection

Affected Structure	Mechanism	Clinical Features
Aortic Valve	Blood moves between the intima and media into the valve leaflet	New Aortic Regurgitation murmur
Coronary Arteries	Malperfusion of Coronary arteries (mostly right)	• Acute Coronary Syndrome • MI (STEMI, NSTEMI)
Pericardium	Coronary arteries rupture into the pericardium → Hemopericardium (Blood Accumulation in the pericardial space) → compression of the Heart	• Cardiac Tamponade (Classic signs of Beck's triad: low blood pressure, distension of the jugular veins and decreased or muffled heart sounds)
Brachiocephalic, common carotid, or left subclavian arteries	Occlusion → ↓ blood flow to the brain	• Syncope • Cerebral Vascular incidents (Stroke)
Left Subclavian Artery	Occlusion of the Left Subclavian Artery and <u>no</u> occlusion of the Right Subclavian Artery	• Upper extremity pulselessness • ↓ BP on the Left upper Extremities (A considerable variation (>20 mmHg) in systolic blood pressure may be seen when comparing the blood pressure in the arms.) • Acute limb Ischemia ○ Pulselessness ○ Pain ○ Losing color (Pallor) ○ Weak muscle → Paralysis ○ Cold (Poikilothermia)
Renal artery	Dynamic Obstruction and Malperfusion of the Renal Artery	• ↓ Urine output • Acute kidney Injury ○ ↑ Creatinine ○ ↑ BUN ○ ↓ GFR
Artery of Adamkiewicz	Occlusion → ↓ Blood flow of Anterior Spinal Artery → Damage to the anterior two-thirds of the spinal cord	• Anterior Spinal Artery Syndrome ○ Paraplegia of lower extremities ○ Loss of Sensations ○ Incontinence
Celiac or mesenteric arteries	Dynamic Obstruction → ↓ Blood flow to GI Tract	• Acute Mesenteric Ischemia • Abdominal pain • Bloody Diarrhea • Nausea and vomiting
Common iliac artery	If Occlusion of the Left Common Iliac artery → ↓ Blood flow to the Left Lower Extremities LLE	• Pulselessness of LLE • ↓ BP compared to RLE • Weakness • Acute Limb Ischemia ○ Pulselessness ○ Pain ○ Losing color (Pallor) ○ Weak muscle → Paralysis ○ Cold (Poikilothermia)



V) DIAGNOSIS

(1) Aortic Involvement

- Tearing Ripping pain →
 - Anterior chest pain → Dissections **involving** the Ascending Aorta
 - Neck and Jaw Pain → Dissections **involving** the Aortic Arch and its branches → e.g., Carotid arteries
 - Interscapular Pain → Dissections **involving** the Descending Aorta (Beyond Left Subclavian artery)
- **Most Common Location for Aortic Dissection = Ascending Aorta (2.2cm of Aortic Valve)**

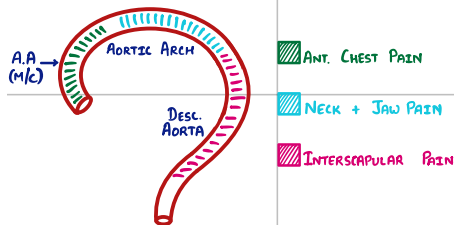


Figure 6. Aortic Involved site Associated Pain

(2) EKG

- Indication:
 - Initial evaluation of patients with chest pain
 - Rule Out → Acute MI
 - less helpful in dissection leads to coronary ischemia
- Findings may include:
 - Normal
 - ST Elevation (Coronary Artery Occlusion)
 - ST Depression
- **Troponin** may be POSITIVE



ST-ELEVATION

- 1mm ST-E IN 2 CONTIGUOUS LEADS EXCEPT V₂-V₃ WHERE 2mm ST-E IS REQUIRED

DDX OF ST-ELEVATION

1. STEMI
2. BENIGN EARLY REPOLARIZATIC
3. PERICARDITIS
4. VASOSPASM
5. PULMONARY EMBOLISM
6. L.V. ANEURYSM
7. L.V. HYPERTROPHY
8. L.B.B.B.

Figure 7 ST-Elevation [from the 12 leads of EKG lecture]

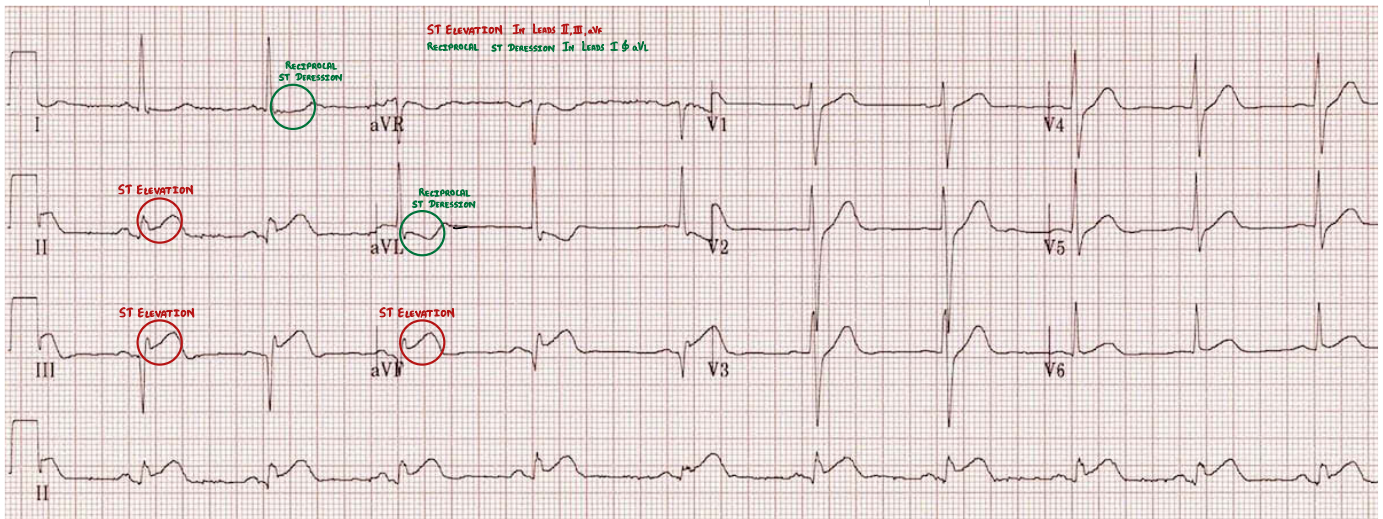


Figure 8. EKG of STEMI

(3) Chest Xray

- Advantage → Rapid
- To Rule Out
 - Pneumothorax
 - pleural effusion
 - Pneumonia
- Finding:
 - Mediastinal widening → $\geq 8\text{cm}$ → **Suspicious** for Aortic Dissection (Suspicious not Diagnostic!)

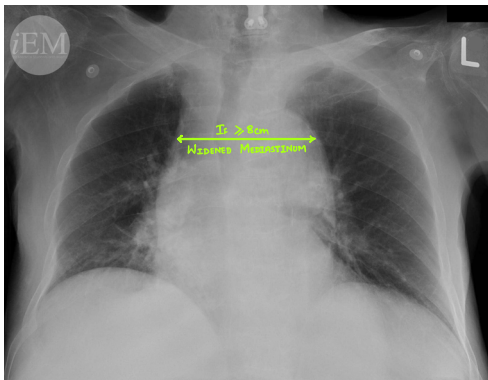


Figure 9. Widened Mediastinum on a Chest Xray

(4) TEE, Trans Esophageal Echocardiography

- **TEE**
- Can be Performed at the bedside
- Indications:
 - Hemodynamically **unstable** patients
 - Severely low GFR
 - Contrast Induced Nephropathy
- Rule out → Cardiac Tamponade
- Findings:
 - Intimal Flap
 - False Lumen

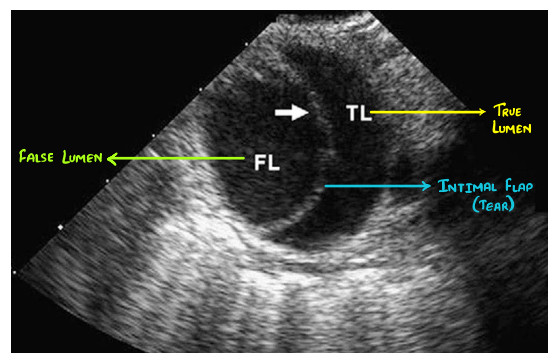


Figure 10. Aortic Dissection TEE.



(5) CTA; CT Angiography

- CTA → **GOLD STANDARD**
- Indications:
 - Hemodynamically **Stable** patients
 - Surgical Planning
- Findings:
 - Intimal Flap
 - False lumen
 - Leak / rupture
 - Aortic Hematoma

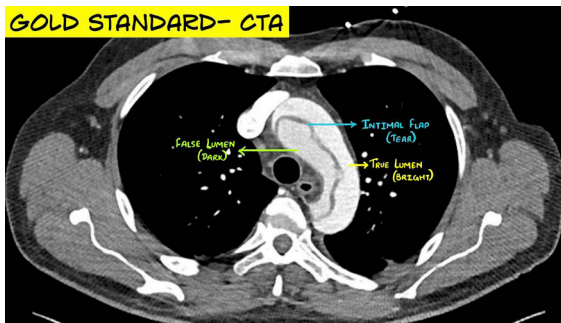


Figure 11. Aortic Dissection CTA.

(6) MRA; Magnetic Resonance Angiography

- Time Consuming
- Indications:
 - Hemodynamically Stable patients
 - Contradiction to CTA
- Findings:
 - Similar to CTA

Table 3. Imaging Techniques Comparison

Imaging Modalities	Advantages	Disadvantages
CXR	• Rapid, Bedside	• Poor Sensitivity
TEE	• Rapid, Bedside • No radiation exposure • Sensitive and Specific	• Invasive • May not be readily available
CTA	• Gold standard: Very high sensitivity and specificity • Operative Planning	• Cannot be performed at the bedside • Radiation exposure • Contrast exposure
MRA	• Very high sensitivity and specificity • No radiation exposure	• Cannot be performed at the bedside • Time Consuming

VI) TREATMENT

Type of Dissection Determination

- Aortic dissection classification systems
 - The DeBakey System
 - The Stanford System (Preferred)
- Stanford Classification
 - Stanford **A**
 - Involves **A**scending Aorta
 - Emergency → Surgical Therapy
 - Stanford **B**
 - **B**eyond Left Subclavian Artery → Involves **D**escending Aorta
 - Medical Therapy BUT you may need Surgical Intervention
 - Complications → may need Surgery
 - Medical Treatment Failure
 - Rupture
 - Propagation of dissection
 - Expanding intramural Hematoma

(A) SURGICAL TREATMENT

- 1) Open Surgery → replacement of the dissection with a polyester graft implantation
 - a. Type A Dissections
- 2) Endovascular Stent Placement
 - a. Type B Dissections

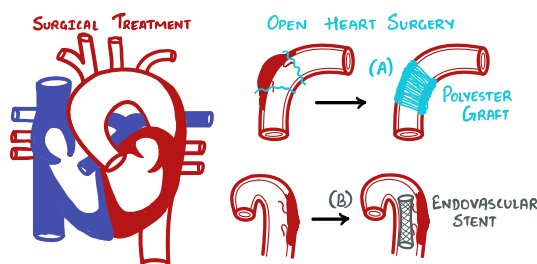


Figure 12. Aortic Dissection Surgical Treatment.

(B) MEDICAL TREATMENT

(1) Hypotensive Patients

- Goal → **Mean Arterial Pressure ≥ 70 mmhg**
- IV Fluid
 - IV Fluid → $\uparrow$ Blood Volume → $\uparrow$ Blood Pressure
- Vasopressor
 - $\rightarrow \uparrow$ SVR $\rightarrow \uparrow$ Blood Pressure
 - **Norepinephrine**
 - **Phenylephrine** (Pure Alpha-1 vasoconstrictor)
- Blood Transfusion
 - $\rightarrow \uparrow$ Blood Volume $\rightarrow \uparrow$ Blood Pressure
- Evaluate 3 Scenarios and fix them
 - Rupture → repair the rupture
 - Cardiac Tamponade → Pericardial Fluid Drainage
 - Severe Aortic insufficiency → Valve Repair

(2) Hypertensive Patients

- Goal:
 - **Systolic Blood Pressure 100-120mmhg**
 - **Heart Rate < 60 bpm**
- 1) Beta Blockers (Alpha and Beta blocker activity)
 - **Esmolol**
 - **Labetalol**
 - Mechanism:
 - Blocking Beta receptors on AV/SA nodes → $\downarrow$ Heart Rate
 - Blocking Alpha-1 → Vasodilation → $\downarrow$ SVR → $\downarrow$ BP
 - Beta Blockers are given first to **prevent Reflex Tachycardia**
- 2) Vasodilators
 - Vasodilators → Low Blood Pressure → Stimulate Cardiac Acceleratory Center in the brain → $\uparrow$ Heart rate and contractility (Reflex tachycardia)
 - Sodium Nitroprusside
 - Vasodilation → $\downarrow$ SVR → $\downarrow$ BP



VIII) REVIEW QUESTIONS

1) Best Diagnostic test in Hemodynamically stable patients with suspected aortic dissection:

- a) ECG
- b) CTA
- c) CXR
- d) TEE

2) Best Diagnostic test in Hemodynamically unstable patients with suspected aortic dissection:

- a) ECG
- b) CTA
- c) MRA
- d) TEE

3) Which Statement is True?

- a) Type B dissections involves the ascending aorta.
- b) Type A dissections can be treated medically.
- c) Type A dissections are surgical emergencies, Type B are still emergencies but can often be treated medically.
- d) All patients with Type B dissections should have surgery.

4) Which one is not a High-Risk condition associate with Aortic Dissection?

- a) Athletic Lifestyle
- b) Cocaine Use
- c) Hypertension
- d) Preexisting Aortic Aneurysm

5) Acute Mesenteric Ischemia may happen as a result of

- a) Dynamic Obstruction of common Iliac Artery
- b) Dynamic Obstruction of Celiac and mesenteric arteries
- c) Dynamic Obstruction of Anterior Spinal Artery
- d) Dynamic Obstruction of Renal Artery

6) Treatment of Type B Aortic Dissection in a patient with Hypertension:

- a) Sodium Nitroprusside → Esmolol
- b) Polyester Graft Implantation → Norepinephrine
- c) Labetalol → Sodium Nitroprusside
- d) IV Fluids → Phenylephrine

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ATRIAL FIBRILLATION

Atrial Fibrillation

Medical Editor: May Perez

OUTLINE

- I) ATRIAL FIBRILLATION
- II) RISK FACTORS FOR ATRIAL FIBRILLATION
- III) PATHOPHYSIOLOGY
- IV) CLINICAL MANIFESTATIONS
- V) DIAGNOSIS
- VI) TREATMENT
- VII) REVIEW QUESTIONS
- VIII) REFERENCES

I) ATRIAL FIBRILLATION

- Atrial Fibrillation (A-fib) is a supraventricular arrhythmia that originates above the ventricles
- Causes irregularly irregular rhythm and many other complications
- There is **no absolute identifiable cause** for A-fib, but there are risk factors which will be referred to as "cardiac causes" and "non-cardiac causes" in this lecture

(A) MECHANISMS

(1) Stretching of the myocardium

- Causes myocardium to dilate and hypertrophy

(2) Ischemia: Decreased oxygen

- To myocardium of atria

(3) Inflammation

- Of the atria itself or anywhere near the atria

(4) Increase in sympathetic nervous system (SNS) stimulation on the atria

- Causes a lot of calcium loading and agitation to the atria

(5) Electrolyte Imbalance

- Particularly Ca^{2+} and K^+

II) RISK FACTORS FOR ATRIAL FIBRILLATION

(A) CARDIAC CAUSES

(1) Congestive Heart Failure (CHF)

- **Mechanism: Increased Stretch**
- Condition wherein the heart's muscles are floppy and flabby causing the stretching and distention of the myocardium of both the ventricles and the atria
- ↑stretch of myocardium → atrial dilation → atrial hypertrophy
- Changes the morphology of the atria

(2) Dilated cardiomyopathy

- **Mechanism: Increased Stretch**
- The ventricles get thin, floppy, and ballooned, affecting the atria

(3) Valvular Diseases

- **Mechanism: Increased Stretch**
- Conditions wherein the mitral valve isn't working very well
- With a normal mitral valve, the atria contracts to push blood into the ventricles

(i) Mitral Stenosis

- Stenotic mitral valve (valvular narrowing) allows less blood to flow from the atria into the ventricles → some volume is retained in the atria → atria will balloon up to accommodate the extra volume

(ii) Mitral Regurgitation

- Can have the same effect as mitral stenosis, but is less common

(4) Coronary Artery Disease or Myocardial Infarction

- **Mechanism: Ischemia** (decreased O_2)
 - Ischemia can trigger atria to develop ectopic foci and reentry circuits nearby, causing an atrial arrhythmia.
- Severe coronary artery disease or history of myocardial infarction
- If there's an ischemic or infarcted area, tissue in the atria near the area must undergo remodeling

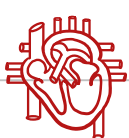
(5) Rheumatic Heart Disease

- **Mechanism: Inflammation**
 - The valves, atria, endocardium, or myocardium may be inflamed
- May be due to Rheumatic fever
- May lead to Mitral Stenosis, ultimately leading to A-fib
- May also generate enough inflammation and atrial agitation to directly cause the A-fib

Note: There is a separate lecture on Rheumatic Fever: Etiology, Pathophysiology, & Diagnosis.

(6) Hypertension

- **Mechanism: Increased Stretch**
- Due to high blood pressure, left ventricle contracts more → left ventricular hypertrophy
- Overtime, there is enough hypertrophy to cause atrial hypertrophy or atrial remodeling
- Cause the atria to generate abnormal electrical activities



CHF
- STRETCH



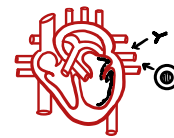
DILATED CMP
- STRETCH



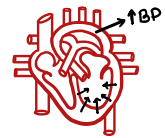
VALVULAR D/O's
- MITRAL STENOSIS
↑ DILATION
- MITRAL REGURGITATION
(L/C)



CAD/M.I.
- ISCHEMIA (↓ O_2)



RHEUMATIC HEART DS.
- INFLAMMATION



HYPERTENSION
- L.V.H
- ATRIAL HYPERTROPHY

Figure 1 Cardiac causes of Atrial fibrillation



(B) NON-CARDIAC CAUSES

(1) Lung Pathologies

- **Mechanism: Ischemia**
 - $\downarrow O_2 \rightarrow$ Hypoxemia $\rightarrow$ May trigger atria to be irritable $\rightarrow$ abnormal foci or reentrance circuits $\rightarrow$ Ischemia
- In a normal lung: takes in O_2 , bring it into the alveoli, push it into the blood, and get rid of CO_2
- In a pathological process of the lung parenchyma,
 - **COPD** and **pneumonia**: Ventilation Problem
 - Decreased ability to get O_2 to the blood
 - **Acute onset pulmonary embolism**: Perfusion Problem
 - A clot in the vessel may prevent O_2 from getting pass the occlusion
 - Either mechanisms will lead to low O_2

(2) Thyrotoxicosis or Hyperthyroidism

- **Mechanism: Increased SNS activity**
- Releases plenty of FT3 and FT4
 - T3 and T4 increases the β -adrenergic stimulation
 - Increased sensitivity of the β_1 -adrenergic receptors to epinephrine and norepinephrine

(3) Holiday Heart Syndrome

- **Mechanisms: Inflammation, Electrolyte Imbalance, and Increased SNS activity**
- In **excessive alcohol intake** (e.g., *acute alcohol binge-drinking*), ethanol causes a cytotoxic effect on the body
 - $\uparrow$ ROS (reactive oxygen species) formation $\rightarrow$ inflammation
 - $\uparrow$ SNS effects on the heart
 - Can alter the electrolytes $\rightarrow$ electrolyte abnormalities
 - e.g., K^+ and Mg^{2+} : important cations in the electrical activities of the heart
 - May be due to alcohol-induced vomiting or the alcohol content itself not having enough micronutrients we need

(4) Pheochromocytoma

- **Mechanism: Increased SNS activity**
- Tumor in adrenal medulla
- Releases catecholamines (epinephrine & norepinephrine) that bind to β_1 -adrenergic receptors $\rightarrow \uparrow Ca^{2+}$ influx and cation loading $\rightarrow \uparrow$ SNS activity $\rightarrow$ agitates atria $\rightarrow$ A-fib

(5) Drugs (Cocaine and Methamphetamines)

- **Mechanism: Increased SNS activity**
- Act as sympathomimetics
- Bind to the same receptors that epinephrine and norepinephrine bind to $\rightarrow \uparrow$ SNS activity $\rightarrow$ increased cation loading $\rightarrow$ irritation of the atria $\rightarrow$ atrial fibrillation
- Can be an acute onset

(6) Sepsis

- **Mechanism: Increased SNS activity**
- Can also be an acute onset
- When in sepsis, the blood pressure drops (may lead to a hypotensive state), patient becomes febrile, and has other body complications
- In a septic response, there's vasodilation, capillary permeability, fever
- Since sepsis is a stressful event, the body's protective response is to go into a "**Fight or Flight**" mode by **hyperactivating the SNS**.
 - This increases the heart rate and blood pressure, counteracting the negative effects of sepsis

(7) Surgical Procedures

- An invasive surgical procedure can cause **significant post op stress** on the body $\rightarrow$ trigger a **catecholamine response** $\rightarrow$ hyperactive SNS $\rightarrow$ atrial fibrillation

(8) Electrolyte Abnormalities

- **Mechanism: Electrolyte Imbalance**
- Hypokalemia ($\downarrow [K^+]$) and hypomagnesemia ($\downarrow [Mg^{2+}]$) in the body can alter the heart's electrical activity, causing the body to undergo an atrial fibrillation or supraventricular tachyarrhythmia.

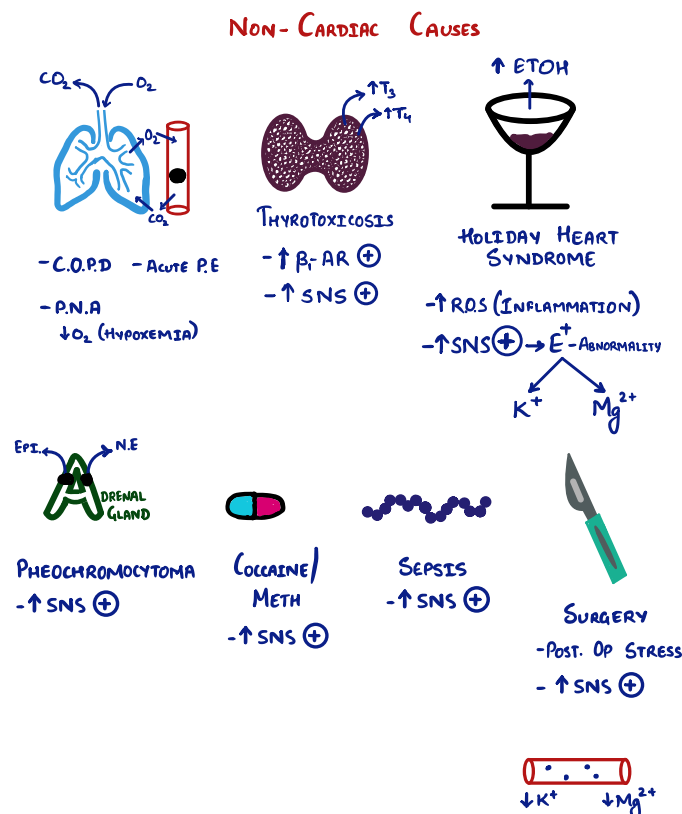


Figure 2 Non-Cardiac Causes of Atrial Fibrillation



III) PATHOPHYSIOLOGY

- How do these risk factors lead to the pathophysiological and clinical features & complications associated with atrial fibrillation?

(A) RECALL: WHAT ARE THE FIVE MECHANISMS BY WHICH ATRIAL FIBRILLATION OCCURS?

(1) Increased stretch on the heart

- CHF,
- dilated cardiomyopathy,
- mitral stenosis,

(2) Inflammation of the myocardium

- Rheumatic heart disease,
- Holiday heart syndrome,
- increased ROS production

(3) Low Oxygen Delivery to the Myocardium

- Coronary artery disease,
- myocardial infarction,
- COPD,
- pneumonia,
- acute pulmonary embolism,

(4) Increased sympathetic activity

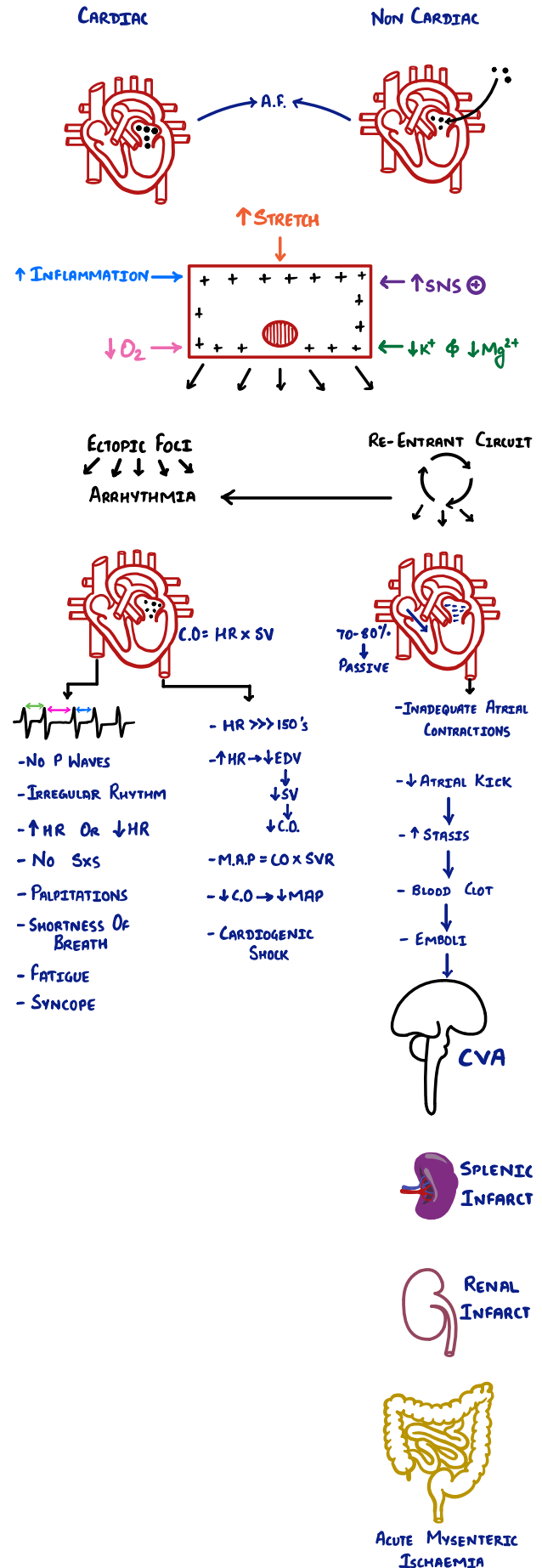
- Thyrotoxicosis,
- Pheochromocytoma,
- excessive alcohol intake,
- cocaine & methamphetamine consumption,
- septic reaction,
- post-op

(5) Electrolyte imbalance,

- particularly hypokalemia and hypomagnesemia

- If there's significant agitation to the myocardium to the point that it needs to undergo remodeling, it can start generating abnormal electrical activity via 2 ways
 - Formation of ectopic foci in multiple areas in myocardium of the atria
 - Development of re-entrant circuits
Alpha and beta pathways (check out overview of arrhythmia lecture)

PATHOPHYSIOLOGY



IV) CLINICAL MANIFESTATIONS

● SA Node

- Pacemaker of the heart
- Generates sinus rhythm
- Send electrical activities to the AV node to be sent to the ventricles via the bundles of His, bundle branches, and Purkinje fibers

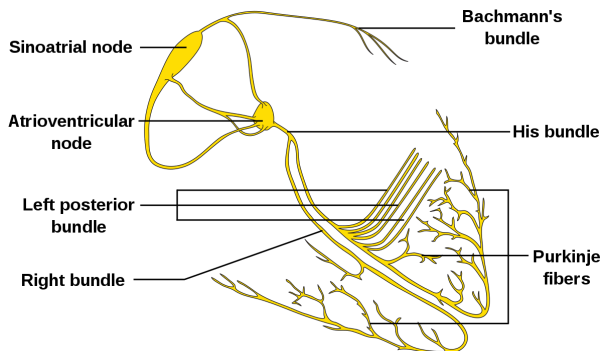


Figure 3. Bundles of His

(1) Heart Rhythm

- If there are areas other than the SA node that are actively firing due to the previously mentioned triggers, they're going to interfere with the normal sinus pathway
- For example, if there are different ectopic foci firing and they get to the AV node before the SA node, they will trigger QRS complexes with noted rhythm variations.

(i) Observable Changes from normal rhythm

- **No visible p waves**
- **Irregular rhythm**
 - Variations in R-R intervals due to different ectopic foci sending signals to the AV node → ventricles
- **Variations in HR**
 - Can be fast (↑HR) or slow (↓HR)
 - It's also possible to be asymptomatic for atrial fibrillation

(ii) Common Symptoms

- Palpitations
- Shortness of breath
- Fatigue
- Episodes of syncope

(iii) Asymptomatic for atrial fibrillation

- It's also possible for a patient to be completely asymptomatic for atrial fibrillation.

(2) Cardiogenic Shock

- Summary of Mechanism: ↑↑↑HR → ↓ventricular filling time → ↓ end-diastolic volume → ↓SV → ↓CO → ↓MAP → hypotension → cardiogenic shock
- If there is tachycardia: HR >>> 150
 - Recall: $CO = HR \times SV$
 - Technically, increase in HR should increase CO
 - But in this case, the HR is so fast → there's not enough time for the ventricles to fill → lowers end-diastolic volume → lowers SV → lowers CO
 - $MAP = CO \times SVR$
 - MAP: Mean Arterial Pressure
 - SVR: Systemic Vascular Resistance
 - ↓CO → ↓MAP → hypotension
 - Since it's coming from the heart, it can lead to cardiogenic shock

(3) Emboli

- Sometimes, patients may not have any symptoms
- If there's an ectopic foci or re-entrant circuits causing depolarization and contractions, the abnormal electrical activity produces inadequate atrial contractions

● Recall: Cardiac Cycle

- 70-80% of the blood from the atria passively flows down to the ventricles
- 20-30% blood volume comes from the **atrial kick**
 - Phenomenon where the atria contracts end-diastole to squeeze the remaining volume out

(i) Summary of Mechanism:

- Atrial fibrillation → atrial quivering → inadequate electrical activity → inadequate atrial contraction → ↓atrial kick → ↓blood volume stays in the atria and doesn't flow to the ventricle → ↑Stasis → clot
- **Stasis**: blood stays in an area longer than it should
- **Virchow's Triad**: Stasis, endothelial injury, and hypercoagulability increases the risk of a clot

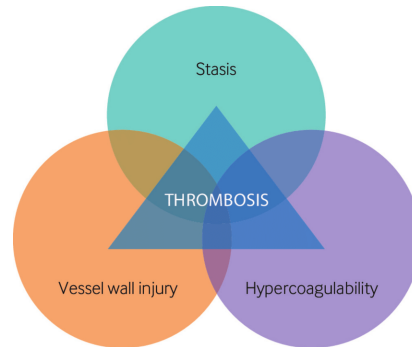


Figure 4. Virchow's Triad [Khan, et al.]

(ii) What happens to the clot?

- When a clot forms on the atria or the valve
 - A patient may undergo cardioversion or the patient's heart may naturally convert
 - **Cardioversion**: medical procedure used to return an abnormal heartbeat to normal.
- **Clot is removed from the atria or valve due to:**
 - The atria contracting strong enough
 - An increased stressful event causes the heart to contract more
- **The removed clot may flow through the systemic circulation** up to the brain, down to the descending aorta, and **embolize in multiple different organs**

(iii) Where can the emboli go?

- (a) Brain
 - One of the first signs is a cerebrovascular accident (CVA)
 - Develops an ischemic stroke
 - May present as neurologic deficits
- (b) Spleen
 - May develop a splenic infarct
 - May present as pain in LUQ and show issues or abnormalities in the CBC
- (c) Kidney
 - May develop a renal infarct
 - May cause increase in BUN and creatinine
- (d) Gut
 - May develop an acute mesenteric ischemia
 - May present as abdominal pain



V) DIAGNOSIS

(A) CLASSIFICATION OF ATRIAL FIBRILLATION

(1) Hemodynamics

(i) Hemodynamically unstable Atrial Fibrillation

- Patient presents with any of the following:
 - ↓BP (hypotensive)
 - Pulmonary edema
 - Especially in a state of cardiogenic shock, wherein the Ejection Volume Fraction is not adequate enough → blood backs up to the pulmonary circulation
 - Altered Mental Status
 - Severe Chest Pain

(ii) Hemodynamically Stable Atrial Fibrillation

- Simply put, patient does not present with any of the symptoms listed above.
- Patient has:
 - Normal BP
 - No pulmonary edema
 - Normal mentation
 - No obvious significant refractory chest pain

(2) Ventricular Rate

(i) Atrial Fibrillation with Rapid Ventricular Rate

- HR > 100 bpm
- HR, particularly the ventricular rate, is really fast
- Ectopic foci are firing really fast; hitting the AV nodes, and going down to the ventricles

(ii) Atrial Fibrillation with Slow Ventricular Rate

- HR < 60 bpm
- Re-entrant circuits or ectopic foci are not firing as fast or as frequent, causing the AV nodes to send conduction down to the ventricles
 - This slows down the ventricular rate

(3) Onset and Duration

(i) New Onset Atrial Fibrillation

- A-fib developed less than 48-72 hours ago.

(ii) Paroxysmal Atrial Fibrillation

- A-fib developed less than 7 days ago

(iii) Persistent Atrial Fibrillation

- A-fib has been present for more than 7 days

(iv) Long-Standing Atrial Fibrillation

- A-fib has been present for more than a year

(v) Permanent Atrial Fibrillation

- Persistent A-fib without any attempt to cardiovert the patient to normal sinus rhythm
- A-fib > 7 days without cardioversion attempt

(4) Mitral Valve Involvement

(i) Valvular Atrial Fibrillation

- Presence of mitral stenosis or a mechanical valve
 - This can determine what type of anti-coagulant the patient needs

(ii) Nonvalvular Atrial Fibrillation

- No involvement of mitral valve or mechanical valve
 - This can determine what type of anti-coagulant the patient needs

DIAGNOSIS

CLASSIFICATION

HEMODYNAMICS

HD UNSTABLE -

☑ ↓BP ☑ PULMONARY EDEMA ☑ AMS ☑ CHEST PAIN

HD STABLE -

NONE OF THE ABOVE ISSUES

VENTRICULAR RATE

RAPID VENTRICULAR RATE: AF ± RVR
HR >>> 100 BPM

SLOW VENTRICULAR RATE: AF ± SVR
HR < 60 BPM

ONSET AND DURATION

NEW: <48-72 HRS LONG STANDING: >1YR

PAROXYSMAL: <7 DAYS PERSISTENT: >7 DAYS

PERMANENT: >7 DAYS WITHOUT ATTEMPTS TO
CARDIOVERT → NORMAL SINUS RHYTHM

MITRAL VALVE INVOLVEMENT

VALVULAR A.F.: MITRAL STENOSIS OR
MECHANICAL VALVE

NONVALVULAR A.F.: NO MITRAL STENOSIS OR
MECHANICAL VALVE



(B) DIAGNOSTIC TESTS

(1) EKG

- The best test that can be used: quick, cheapest, and the most non-invasive procedure
- **Focus on Lead V₁**
 - Shows atrial activity
 - If there's no evidence on V₁, look at V₂, V₃, and aVF

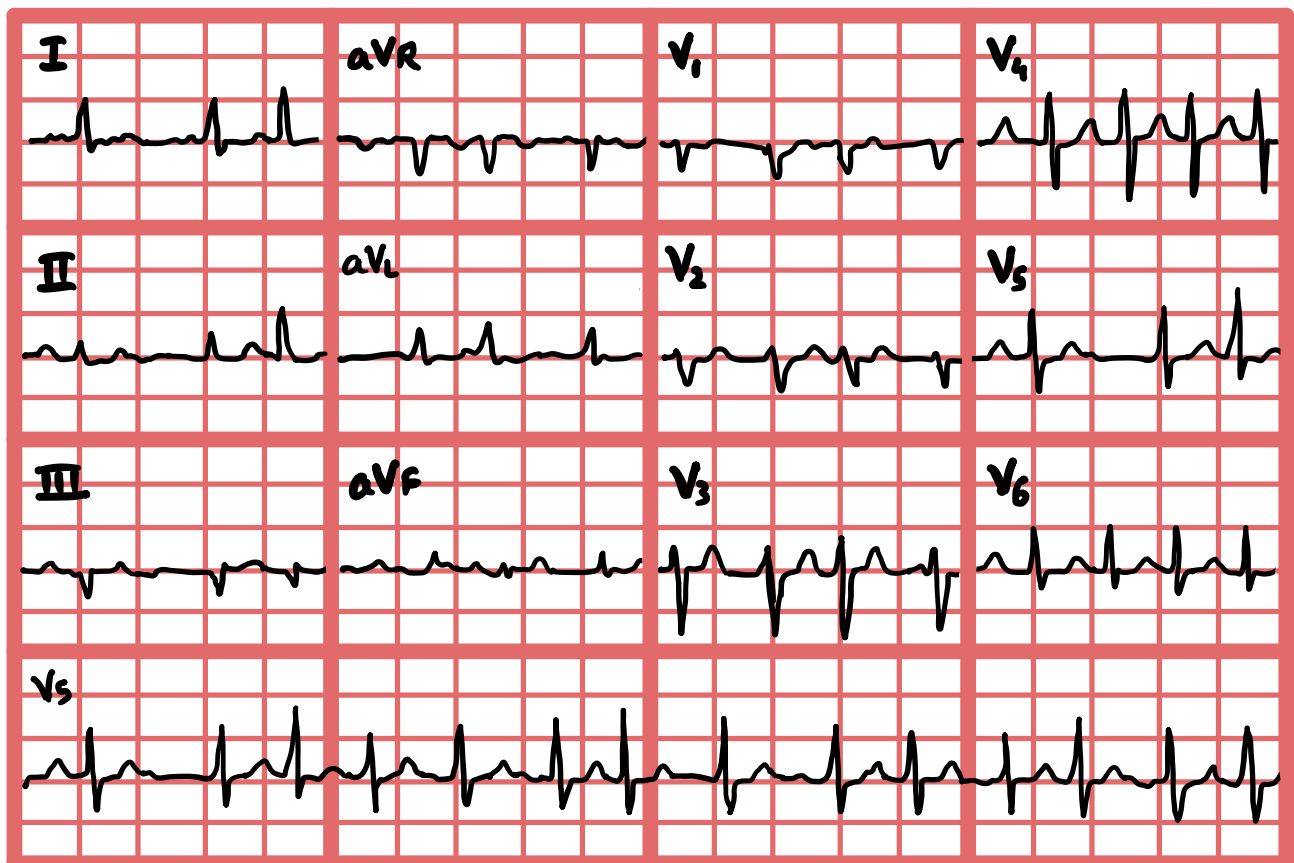
(i) What can be seen on ECG?

- Presence or absence of A-Fib
- Wolff-Parkinson-White (WPW) syndrome
 - Tachycardia (close to 200 bpm)
 - Irregular rhythm
- Potential causes of A-fib
 - E.g., recent MI, coronary artery disease, hypertension
- Rule out ST segment elevation/depression
- Left Ventricular Hypertrophy

Note: A patient may not be in A-fib at the exact moment the ECG is done. A normal ECG does not automatically mean that the patient is fine.

(ii) What can be done other than the ECG?

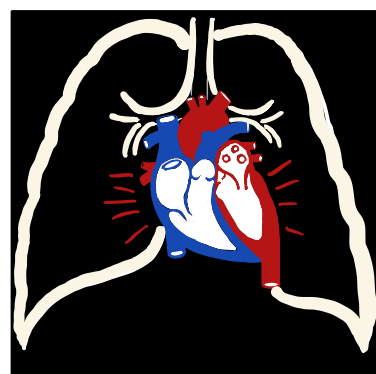
- Holter Monitoring
 - Gold standard
 - Addresses problem with standard ECG wherein electrical activity is only assessed at a particular moment in time
 - Can track a patient's electrical activity over a certain amount of time
 - It's essentially ECG for outpatient monitoring
- Loop Recorder
 - An implantable heart recording device may also be used to monitor outpatient's electrical activity
 - More invasive than Holter monitoring
- Telemetry
 - In-patient continuous monitoring of heart's electrical activity



(2) Chest X-Ray (CXR)

- A key test in determining the trigger/s for A-fib
 - **Pneumonia**
 - **COPD**
 - You may see hyperinflated lungs, hyperlucid lungs, and flattened diaphragm
 - These aren't diagnostic of COPD, but if patient also has a history of tobacco abuse, then COPD is a possible rule in.
 - **Cardiomegaly**
 - May indicate CHF, dilated cardiomyopathy, and other cardiac conditions
- Can also be used to **rule out other conditions** to make sure that the diagnosis is really A-fib

CXR



(3) Ultrasound: Echocardiogram

(i) Types of Echocardiograms

(a) Trans-Esophageal Echocardiogram (TEE)

- **Gold standard**
- May be a little bit better than the TTE at picking up something in the atria
- Invasive type of procedure

(b) Trans-Thoracic Echocardiogram (TTE)

- Non-invasive procedure
- Most used echocardiogram

(ii) What to look for in an echocardiogram

(a) Atrial thrombus

- Indicates presence of a clot
 - Needs urgent treatment (anti-coagulant)
- Recall: If patient goes back into normal sinus rhythm, clot may embolize into other organs

(b) Mitral Valve Issues

- Mitral valve stenosis, mitral regurgitation, or mechanical valve that may not have been indicated on patient's history (*i.e., patient doesn't know*)

(c) Left Ventricular Ejection Fraction (LVEF)

- Useful in determining if patient has heart failure with reduced ejection fraction

(d) Left Ventricular Hypertrophy

- Associated with hypertension

(e) Atrial Dilation

- An enlarged atrial size may be diagnostic for atrial fibrillation, even if it doesn't show on their ECG, Holter monitor, or in-patient Telemetry.

T.E.E Or T.T.E



■ ATRIAL THROMBUS ⊕

■ MITRAL VALVE D/O ⊕

■ LVEF

■ LVH

■ ATRIAL DILATION ⊕

(4) Laboratory Tests

- Not necessarily enough to diagnose A-fib, but can help determine what is triggering or causing the A-fib.

(i) Brain natriuretic peptide (BNP)

- Elevated BNP may point to **CHF**
- Result can be **correlated with ECG reading**
 - Check for signs of LVEF abnormalities and hypertrophic ventricles

(ii) Troponin Levels

- If elevated, may point to **myocardial ischemia**
- Correlate with the ST segment on ECG

(iii) Complete Blood Count (CBC)

- Elevated **WBC count** may indicate **pneumonia**
- Pro-calcitonin levels may also indicate an infection
- Results can be **correlated with CXR**

(iv) TSH with Reflex to FT₄

- If TSH is low, thyroid hormone may be high
- Useful in screening for **hyperthyroidism**
- May also be used for the differential diagnosis of primary, secondary, and tertiary hypothyroidism

(v) Blood alcohol level (etOH)

- Recall: **Holiday Heart Syndrome**

(vi) Urine Metanephrine Test

- To detect or rule out pheochromocytoma
 - Additionally, an **Adrenal CT** can be done to check for a mass within the adrenal gland

(vii) Urine Toxicology Test ("Tox Screen")

To detect the presence of metabolites of cocaine, methamphetamine, or urinary alcohol

LABS



- BNP ↑↑↑ → CHF

- TROPONINS → M.I.

- CBC → ↑WBC

- TSH & REFLEX → ↑T₃ + T₄

- BLOOD ETOH ⊕

- URINE METANEPHRINES ⊕

- URINE TOX ⊕



VI) TREATMENT

(A) TREATMENT ALGORITHM

(1) Determine Patient's Hemodynamic Status

(i) Perform Direct Current Cardioversion

- If patient is **hemodynamically unstable**

(ii) Perform Rate Control

- If patient is **hemodynamically stable**
- Rate control primarily regulates the rapid A-fib.
- The two preferred rate control agents are beta blockers and calcium channel blockers

(2) Determine patient's need for anti-coagulation

- This is done after performing rate control and ideally reaching a target HR of less than 100-110 bpm
- Goal: **to reduce the risk of embolization**
 - Patients getting admitted are usually started on unfractionated or low molecular weight heparin
 - Oral anti-coagulants can also be used
- 50-70% of the time, patients will undergo spontaneous cardioversion within 24 hours of onset
 - A-fib (especially acute onset A-fib) will convert into normal sinus rhythm without intervention with electricity or chemical induction process

(3) Step 3: Consider Cardioversion

- For patients who did not undergo spontaneous cardioversion, determine if it's necessary to cardiovert the patient back to normal sinus rhythm.

(i) Perform Cardioversion

- For patients who are on A-fib for less than 48 hours and have a low risk of ischemic stroke
 - Determine risk via the CHA₂DS₂-VASc system
- Can be done electrically or chemically
- Based on their CHADS-VASc score and other associated risk factors, decide if patient needs to be put on oral anticoagulants for four weeks after cardioversion.

(ii) Perform TEE and Give Oral Anti-Coagulants

- For patients who have been on A-fib for more than 48 hours or for an unknown period, and have an unknown period or for more than 48 hours

(a) Option 1

- **Perform TEE** to check if they have a clot within their atria at that moment
 - (+) Left Atrial Thrombus
 - Oral anti-coagulation for 3 weeks
 - Recheck for clot via TEE
 - (-) Atrial Thrombus
- **Perform cardioversion**
- Give **oral anticoagulants** for 4 weeks
 - It's also possible for these patients to be on long-term anti-coagulants due to their increased risk

(b) Option 2

- Give **oral anticoagulant** for 3 weeks
- **Perform cardioversion**
- Give **oral anticoagulant** for 4 weeks or more

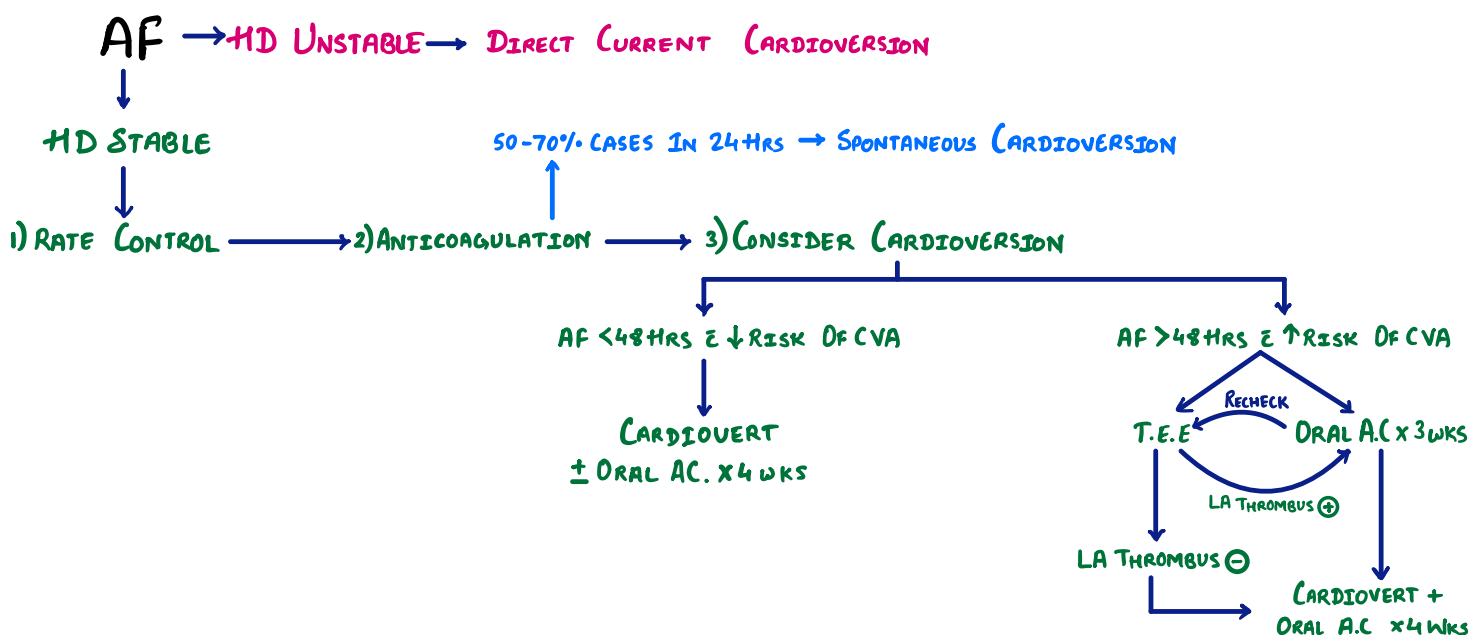


Figure 5 Overview of Atrial Fibrillation Treatment Algorithm



(B) TREATMENT MECHANISMS

(1) Rate Control

- Conduction system
- AV Node

(i) Rate control agents

- **block the electrical activity** coming from the ectopic foci and re-entrant circuits from moving through the AV node and down into the Bundles of His
- Sifts through the excess electrical activity and only allows for certain things to go down to the ventricles
- Slows down the ventricular rate

(a) Beta blockers

- Metoprolol: commonly utilized drug
- Contraindication: reactive airway disease, underlying COPD
 - β -2 receptor in the lungs may exacerbate their condition

(b) Calcium Channel Blockers

- Drugs that block calcium channels in AV cells → block calcium entry → slows down electrical activity being transmitted through AV node
- Contraindication: patients with decompensated heart failure
- Drugs: Diltiazem (most common), Verapamil

(c) Digoxin

- Takes a bit longer for its effects to kick in
- Drug good for hypotension or heart failure
- Targets sodium-potassium-ATPase
 - Alters calcium-sodium exchangers
 - Effect: increases contractility
- AV Node: Stimulates Vagus Nerve (CN X) → stimulates parasympathetic nervous system → increases acetylcholine release → more K^+ leave the cell → slows down HR

(d) Amiodarone

- Third-line agent
- Has effects on both rate and rhythm control
 - Blocks entry of sodium and calcium, and has a little bit of beta blocker effect

(2) Three Ways to Control Rhythm

(i) Chemical Cardioversion: Utilize drugs

(a) Examples of drugs:

- Type 1a (e.g., procainamide)
- Type 1c (e.g., Flecainide, Propafenone)
- Type III (e.g., Ibutilide, Amiodarone)

Note: There will be a separate lecture on the different classes of antiarrhythmic drugs.

(b) Mechanism:

- Alters activity of different type of channels (e.g., Na^+ channels, K^+ channels) → regulates electrical activity within the myocardial cells of the atria → regulates rhythm

(c) Contraindication:

- May potentially affect QT interval → increases risk for Torsades de pointes (TdP)

(ii) Electrical Cardioversion

- Shock the heart to reset all the electrical activity of the myocardium so that it can get back into a normal sinus rhythm

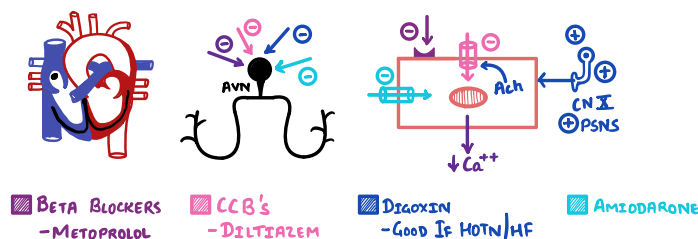
(iii) Radiofrequency Ablation (RFA)

- Utilization of radiofrequency waves to burn and destroy ectopic areas
 - They are usually near the entrances of the pulmonary veins and atria

(iv) Maze procedure

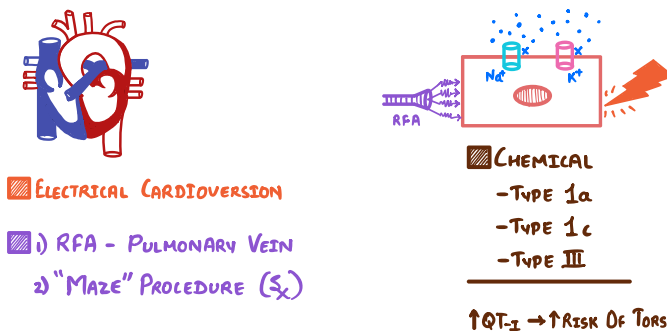
- Surgical procedure
- RFA would still be the first line or option before the maze procedure

RATE CONTROL :



RHYTHM CONTROL :

DRUGS



(3) Anticoagulation

- Patients with A-fib are at high risk for forming clots and embolizing them to different areas in the body

(i) CHA₂DS₂-VASc Score

- Way to risk stratify and determine patient's need for anticoagulation
- Compared with patient's **HAS-BLED score** → Determines the risk of bleeding

Criteria	Poss. Point
C ongestive heart failure Signs/symptoms of heart failure confirmed with objective evidence of cardiac dysfunction	+1
H ypertension Resting BP > 140/90 mmHg on at least 2 occasions <u>or</u> current antihypertensive pharmacologic treatment	+1
A ge 75 years or older	+2
D iabetes mellitus Fasting glucose > 125 mg/dL or treatment with oral hypoglycemic agent and/or insulin	+1
S troke, TIA , or TE Includes any history of cerebral ischemia	+2
V ascular disease Prior MI, peripheral arterial disease, or aortic plaque	+1
A ge 65 to 74 years	+1
S ex Category (female) Female gender confers higher risk	+1

Figure 6. CHA₂DS₂-VASc Criteria for Atrial Fibrillation

(a) Score Assessment

- 0 → Anticoagulation is not needed
- 1 → Anticoagulation *possibly* needed
 - Compute for HAS-BLED score for benefit-risk assessment
 - Also check patient's risk factors and other underlying medical conditions
- ≥ 2 → Anticoagulation is needed
 - If their HAS-BLED score is high, use a **Watchman device**
 - Used to prevent patient from forming clots, if they can't be on anticoagulants
 - The left atrial appendage is occluded so that clots cannot be formed

(ii) Anticoagulant Drugs

(a) Warfarin

- **Drug of choice**, especially for patients with the following conditions:
 - Valvular A-fib
 - Chronic Kidney disease
 - Liver Disease
- **Monitor PT/INR level**
 - PT/INR: prothrombin time international normalized ratio
 - Level must be kept at a range of 2-3
 - < 2 → risk of clots
 - > 3 → risk of bleeding

(b) Direct Oral Anticoagulants (DOACs)

- Generally good for patients with non-valvular A-fib
- Lower risk of bleeding compared to Warfarin

(i) Factor Xa inhibitors

- Rivaroxaban
- Apixaban
- Edoxaban

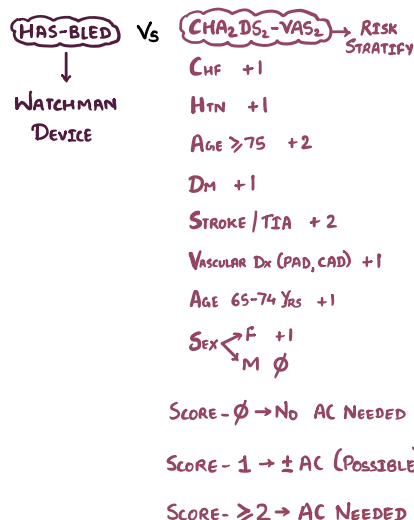
(ii) Factor IIa inhibitors

- Dabigatran

(c) Heparin

- Unfractionated heparin or Low molecular weight heparin
- Easily titratable
- Monitored via the PTT
 - Too high PTT → decrease the dose
 - Too low PTT → increase the dose
- Can be used as a 'bridge'
 - To bridge a patient into DOAC or Warfarin
 - E.g., useful for patient on Warfarin (to be hypercoagulable for a small period of time)

ANTICOAGULATION %



WARFARIN:

- VALVULAR AF
- CKD OR LIVER Dx
- INR = 2-3

DOAC's

- Xa-I**
 - RIVAROXABAN
 - APIXABAN
- IIa-I**
 - DABIGATRAN
 - NON VALVULAR AF

HEPARIN

- UFH OR LMWH
- HOSPITAL
- PTT
- BRIDGE



VII) REVIEW QUESTIONS

1) What type of Atrial Fibrillation developed less than 7 days ago?

- a) New Onset Atrial Fibrillation
- b) Paroxysmal Atrial Fibrillation
- c) Persistent Atrial Fibrillation
- d) Long-Standing Atrial Fibrillation

2) Which test/s is/are considered gold standard in diagnosing Atrial Fibrillation?

- a) Chest X-Ray
- b) Complete Blood Count
- c) Electrocardiogram
- d) Urine Metanephrine Test

3) Which disease is known to be associated with excessive alcohol intake?

- a) Torsades de pointes
- b) Holiday Heart Syndrome
- c) Myocardial Infarction
- d) Acute onset pulmonary embolism

VIII) REFERENCES

- Khan, F., Vaillancourt, C., & Bourjeily, G. (2017). Diagnosis and management of deep vein thrombosis in pregnancy. *BMJ Clinical Research*, 357. <https://doi.org/10.1136/bmj.j2344>





OUTLINE

- I) PATHOPHYSIOLOGY
- II) SIGNS AND SYMPTOMS
- III) DIAGNOSTICS
- IV) REVIEW QUESTIONS
- V) REFERENCES

I) PATHOPHYSIOLOGY

- **Inflammatory condition** that could be in response to streptococcal pharyngitis, particularly group A
 - gram-positive bacteria that grow in culture as pairs or chains of variable length
- **Body's response to strep throat:** produce antibodies against the foreign bacteria to try to destroy it
 - needs antibiotics
 - **97%** of the population respond properly by producing antibodies against the bacteria itself
 - **3%** of the population produce antibodies against the bacteria AND against other tissues that have antigens or proteins that mimic the bacteria's antigens

(A) GROUP A BETA-HEMOLYTICUS STREPTOCOCCI (GABHS)

- Most common etiological bacteria leading to strep throat
 - Specifically, Streptococci pyogenes (*pus-forming*)
- **beta-hemolyticus**
 - RBCs on blood agar
 - After putting and properly incubating GABHS on blood agar, white spots can be seen
 - Bacteria breaks down the RBC by producing enzyme called **streptolysin**
 - Breaks down bacteria via beta-hemolysis
 - Alpha-hemolysis
 - Doesn't completely break bacteria down
- **Has M proteins**
 - Particular antigens on the streptococci pyogenes that activates the immune system

(B) IMMUNE SYSTEM RESPONSE INITIATION

- Bacteria produces tissue damage which triggers inflammatory response
 - Production of leukotrienes, prostaglandins, histamines (from mast cell activation)
 - This increases the inflammatory response and cause blood vessels in the area to dilate and increase their capillary permeability

(1) Increased blood flow

- Allows for more WBCs, complement proteins, and immune system structures

(2) Increased permeability

- Allows for the WBCs, complement proteins, and immune system molecules to leak out of the capillaries and into the tissue spaces to break down the bacteria

(C) MACROPHAGE & NEUTROPHILS

- Macrophage and neutrophils comes into the area

(1) Neutrophils

- Neutrophils love to break down bacteria
- They will phagocytose the bacteria
- When neutrophil phagocytoses bacteria, it will take it in and utilize lysosome
- Lysosomes will break down the cell wall and remaining antigens will undergo exocytosis
 - Antigens freely circulate through the lymphatic circulation towards a regional lymph node

(2) Macrophage

- Macrophage engulfs and then breaks down the bacteria
- Activates the **HLA-2/MCH-2 gene** on chromosome 6 to produce MHC-2 molecules
- Macrophage will present bacteria with MHC-2 molecules to the **T-helper cells**
 - located within the lymph nodes
 - have specific proteins (**CD4**) that can recognize and react with the MHC-2 molecule
 - **T-Cell Receptor (TCR)**
 - Another molecule on T cells that specifically reacts with the foreign antigen
 - **Massive release of cytokines** by T cells
 - IL-4, IL-2, IL5, etc.
 - IL: interleukin
 - Cytokines activate B cells in the lymph nodes
 - ILs stimulate B cells to start proliferating/ clonal expansion
 - ILs trigger B cells to differentiate
 - They turn into plasma cells
 - Protein-production factors
 - Cytokines will also stimulate anti-body production

(3) Antibody are designed to

- attack the antigen
- enhance the phagocytosis of macrophage
- activate the natural killer cells
- enhance the complement proteins
- produce membrane attack complexes
- elicit more inflammation to bring more inflammatory mediators in the area to break down the bacteria
- The above process responds well with 97% of the population



(D) DIFFERENCE WITH 3% OF THE POPULATION

- Reason isn't completely determined
 - Specific in children (5-15 years old)
 - Situations of poverty
 - Areas with overcrowding population
- Antibodies designed to attack proteins on GABHS also attack other tissues in the body due to **Molecular Mimicry**
 - Our body has proteins that mimic or look very similar to GABHS

LOCATION OF PROTEINS

(1) Skin

- Keratin
- Antibodies will keratinize or react with the skin

(2) Central Nervous System

- **Basal ganglia**
 - Coordinate movement
 - Prevent overshooting, undershooting, and dampening of motor movements
 - **Gangliosides** (lysoganglioside proteins)
 - Proteins similar to GBAHS
 - Can produce Sydenham Chorea

(3) Heart Tissue

- Pancarditis:
 - Can affect all the different layers
 - Endocardium, myocardium, pericardium
- Proteins
 - Laminin
 - Tropomyosin (protein of muscle cells)
 - Myosin
 - Actin
 - Troponin

(4) Synovial joint

- Vimentin
 - Produces (migratory) polyarthritis when antibody attaches to the Vimentin



II) SIGNS AND SYMPTOMS

(A) HEART

- When the antibodies are directed to the heart tissue
- 50-60% of symptoms of rheumatic fever that arise usually present to the heart
- Consistent recurrent rheumatic fever can lead to rheumatic heart disease
- Can affect the different layers of the heart

(1) Pericardium

- Visceral Layer
- Parietal Layer
- Serous/pericardial fluid
 - can be found in between the two layers
- **Pericarditis causes inflammation**
 - Leads to pericardial friction rub
 - Felt as an intense stabbing chest pain when there's inflammation of the two layers
 - Heard as a scratchy sound during auscultation

(2) Myocardium

- **Cardiac muscle** tissue responsible for contracting and ejecting blood out of the heart
- When damaged by the antibodies, it produces **fibrinoid necrosis**
 - a specific type of necrosis in the myocardium
- **Aschoff bodies**
 - can be seen in the cell of patient with rheumatic fever
 - a lot of fibrinogen and inflammatory cells are deposited in the area
 - Anitschkow cell
 - Caterpillar-like macrophages
 - T-Cells
 - The more widespread it is, the more it doesn't allow the heart to contract
- ↑Aschoff bodies → ↓preload → loss of myocardial cells → ↓contractility → ↓stroke volume → ↓cardiac output → **congestive heart failure**
 - Recall: *preload is the degree of stretch*

(3) Endocardium

- Inner lining of the heart
- Valves are attacked
- Over time, heart will develop **rheumatic vegetations**
 - Inflammatory infiltration (T cells, macrophages)
 - swollen → edema
- As inflammation occurs, valves activate fibroblasts
 - When stimulated, fibroblasts produce collagen and fibrous tissue → cause valves to thicken
- **Recurrent episodes of rheumatic fever can lead to:**
 - Valve stenosis and regurgitation**
 - Specifically targets the mitral (bicuspid) valve and aortic (semilunar) valve
 - chordae tendineae thickening**
 - Produces commissural fusion**
 - Type of fibrosis wherein the valves start to fuse
 - May lead to the point where the valves don't open anymore
 - Subacute bacterial endocarditis**
 - Valve become so damaged that it leads to septic, bacterial vegetation
 - Can break off and lodge in the pulmonary or cerebral vessels

(B) CENTRAL NERVOUS SYSTEM

- 1) Lentiform nucleus
 - Made up of putamen and globus pallidus interna & externa
- 2) Caudate nucleus
- 3) Subthalamus
 - Right below the thalamus
- **Basal ganglia**
 - Coordinate movement
 - Prevent overshooting, undershooting, and dampening of motor movements
- **Gangliosides (lysoganglioside proteins)**
 - Proteins attacked by the antibodies because they are similar to GBAHS
 - Can produce **Sydenham Chorea**
 - 3% of symptoms caused by rheumatic fever
 - Uncontrolled, rapid, jerky movements in:
 - Face
 - Tongue
 - Upper limbs

(C) SYNOVIAL JOINT

- One of the four signs that usually appear
 - Rheumatic fever can usually appear 1-4 weeks post-streptococcal pharyngitis
 - First sign to arise is the fever and joint pain
- **75% of symptoms that usually develop is polyarthritis**
 - Different from the normal arthralgia
 - Involves particularly the larger synovial joints
 - Hip joint, shoulder joint
 - Migratory
 - Pain over the joint

(D) SKIN

- Can affect the dermis and epidermis
- Can lead to **erythema marginatum**
 - Annular concentric ring-like rash
 - Skin lesion that particularly occurs in the
 - Upper and lower extremities
 - Trunk of the body
- Can lead to development of **Subcutaneous nodules**
 - collagen deposits
 - Particularly around the area of subcutaneous tissue
 - Usually appear on the extensor surfaces of the body
 - Back of the wrist
 - Side of the elbows
 - Knees



III) DIAGNOSTIC'S

(A) JONES CRITERIA

- To make a diagnosis, there has to be **evidence of post-strep infection**, and one of the following options:
 - 2 major criteria
 - 1 major criteria + 2 minor criteria

(1) Major Criteria

- **J**: Joints → **Polyarthriti**s
- **O**: Myocardium → **Pancarditi**s
- **N**: Nodules → **Subcutaneous Nodules**
- **E**: **E**rythema Marginatum
- **S**: **S**ydenhams Chorea

(2) Minor Criteria

- Fever
- Arthralgia: joint pain
- Prolonged PR interval
- Valvular dysfunction
 - Particularly mitral and aortic
- ↑CRP, ↑ESR
 - When there's inflammation, liver responds by producing C-reactive peptide (CRP) and fibrinogen
 - CRP
 - Acute marker for non-specific types of inflammation
 - Fibrinogen
 - Causes RBCs to stick together and form **Rouleaux**
 - Linear clump of RBCs stacked together
 - Cause RBCs to fall faster and hence, have a higher Erythrocytes sedimentation rate (ESR)

(3) Evidence of Post-Strep Infection

- (+) Rapid Antigen Test
- (+) Culture Sensitivity
- Positive/Elevated Anti-streptolysin O titer

IV) REVIEW QUESTIONS

- 1) Which of the following is/are not a major criteria?
 - a) Evidence of post-strep infection
 - b) Arthralgia
 - c) Pancarditis
 - d) Polyarthriti
- 2) Which is not a common site where rheumatic fever symptoms can be observed?
 - a) Heart
 - b) Lungs
 - c) Joints
 - d) Central Nervous System
- 3) Which of the following is NOT used to detect evidence of a post-strep infection?
 - a) High anti-streptolysin O tier
 - b) Rapid antigen test
 - c) RT-PCR
 - d) None of the above

V) REFERENCES

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OUTLINE

- I) CAUSES & PATHOPHYSIOLOGY
- II) CATEGORIES OF ISCHEMIC HEART DISEASE
- III) CLINICAL FEATURE
- IV) COMPLICATIONS
- V) DIAGNOSIS
- VI) 12 LEAD ECG STEMIS

- VII) TREATMENT
- VIII) APPENDIX
- IX) REVIEW QUESTIONS
- X) REFERENCES

I) CAUSES & PATHOPHYSIOLOGY

- Ischemic heart disease is also known as **coronary artery disease (CAD)**
- The underlying mechanism is a reduction in coronary blood flow, which supply oxygenated blood to the myocardium of the heart

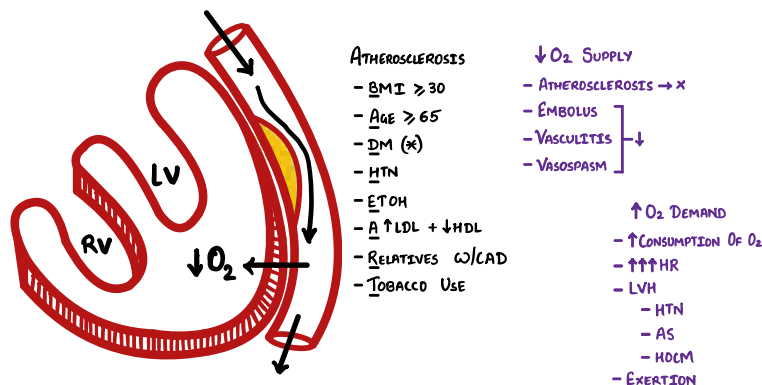


Figure 1. Causes of Ischemic Heart Disease

(A) ATHEROSCLEROSIS

- The most common cause of ischemic heart disease is the reduction or complete loss of coronary blood flow due to **atherosclerosis**
- Recall: Coronary blood vessels deliver oxygen to the myocardium of the heart and pick-up waste products (e.g. carbon dioxide)
- In this disease, atherosclerotic plaques develop within coronary vessels, causing a decrease in blood flow
- The plaques form a "big block" along the coronary vessels, resulting in:
 - Reduced blood flow and oxygen supply
 - Reduced amount of carbon dioxide or waste products being picked up
- When the myocardium has decreased or no oxygen supply,
 - it cannot generate ATP to initiate muscle contraction $\rightarrow$ myocardial failure

(1) Risk Factors for Plaque Formation (Mnemonic: BAD HEART)

- B**MI ≥ 30 (**obesity**; modifiable risk factor)
- A**ge ≥ 65 (non-modifiable risk factor)
- H**ypertension (most common risk factor)
- E**tOH (alcohol abuse)
- A**n increase in LDL and a decrease in HDL (**hyperlipidemia**)
 - LDL – increased deposition of fat and cholesterol on the vessel wall
 - HDL – decreased removal of fat and cholesterol along the vessel wall
- R**elatives with CAD
 - e.g. relatives who passed away due to heart attack/MI
- T**obacco use
 - Smoking increases endothelial injury and plaque formation

(B) OTHER CAUSES

- When there is a mismatch between oxygen supply and demand, this can lead to **ischemia**
 - When ischemia is not reversed, it can lead to cell death or **infarction**

(1) Decreased Oxygen Supply

- Embolus
- Vasculitis
 - Inflammation of vessels can narrow the lumen
- Vasospasm

(2) Increased Oxygen Demand

- Tachycardia
 - Increased heart rate $\rightarrow$ increased myocardial contractility $\rightarrow$ increased oxygen consumption
- Left Ventricular Hypertrophy
 - Seen in patients with hypertension, aortic stenosis, and hypertrophic obstructive cardiomyopathies
- Exercise/Exertion
 - Increases heart rate and myocardial contractility



II) CATEGORIES OF ISCHEMIC HEART DISEASE

(A) STABLE ANGINA

(1) Pathophysiology

- **Stable plaque**, with a strong fibrous cap preventing it from rupturing
- Occludes $\geq 70\%$ of the lumen

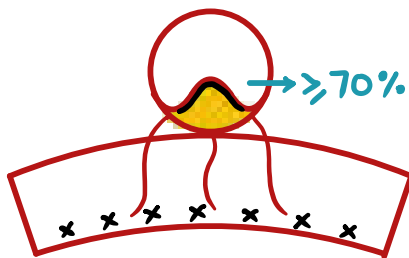
(2) Clinical Features

- Substernal chest pain characterized as "squeezing, tight choking"
- Chest pain occurs with exertion and can disappear with rest
 - there must be increased oxygen demand for the chest pain to manifest

(3) Blood Flow

- Patients with stable angina have **subendocardial ischemia**
 - The endocardial layer is the farthest layer from the coronary blood vessels; thus, it is the most susceptible to ischemia

STABLE ANGINA



- STABLE PLAQUE
- ISCHEMIA
- CP $\geq$ EXERTION

Figure 2. Stable Angina

(B) UNSTABLE ANGINA

(1) Pathophysiology

- **Unstable plaque**, with a weak fibrous cap that is prone to rupture
- Fatty center of the plaque is exposed; platelets attach to the center, leading to thrombus formation
- Occludes $\geq 90\%$ of the lumen (**near total occlusion**)

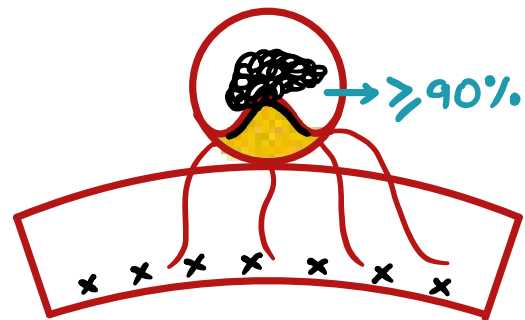
(2) Clinical Features

- Chest pain occurs at rest and worsens with exertion

(3) Blood Flow

- Patients with unstable angina also have **subendocardial ischemia**

UNSTABLE ANGINA



- UNSTABLE PLAQUE
- ISCHEMIA $\geq$ $\uparrow$ O_2 DEMAND
- CP @ REST

Figure 3. Unstable Angina



(C) SUBENDOCARDIAL INFARCTS / NSTEMI

(1) Pathophysiology

- **Unstable plaque**, with a weak fibrous cap that is prone to rupture
- Fatty center of the plaque is exposed; platelets attach to the center, leading to thrombus formation
- Occludes $\geq 90\%$ of the lumen (**near total occlusion**)

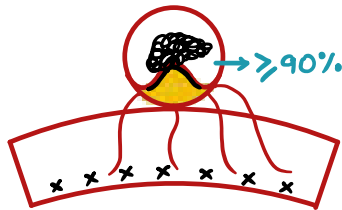
(2) Clinical Features

- Chest pain occurs at rest and worsens with exertion

(3) Blood Flow

- In subendocardial infarction, there is significant reduction of blood flow leading to infarction (cell death)
- Infarction results from at least **30 minutes of unreversed ischemia**

SUBENDOCARDIAL INFARCT (NSTEMI)



- UNSTABLE PLAQUE
- INFARCTION ✓ (≥ 30 MIN)
- CP @ REST

Figure 4. Subendocardial Infarct / NSTEMI

(D) TRANSMURAL INFARCT/STEMI

(1) Pathophysiology

- **Unstable plaque**, with a weak fibrous cap that is prone to rupture
- Fatty center of the plaque is exposed; platelets attach to the center, leading to thrombus formation
- Occludes **100%** of the lumen (**total occlusion**)

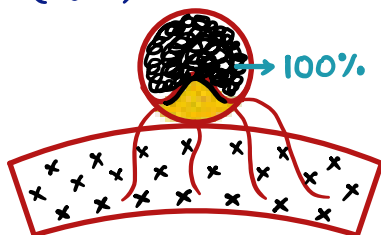
(2) Clinical Features

- Chest pain occurs at rest
- Severe chest pain with exertion

(3) Blood Flow

- There is complete loss of oxygen supply
- The entire myocardium (from the endocardium to the epicardial portion) will infarct ("**transmural**")

TRANSMURAL INFARCT (STEMI)



- UNSTABLE PLAQUE
- INFARCTION
- CP @ REST

Figure 5. Transmural Infarct / STEMI

Acute Coronary Syndrome

- A general term which encompasses:
 - Unstable angina
 - Subendocardial infarction / NSTEMI
 - Transmural infarct / STEMI

(E) VASOSPASTIC ANGINA / PRINZMETAL'S ANGINA

- With vasospastic angina, the chest pain is not related to/caused by atherosclerosis

- Typically occurs in young females with a history of:
 - Using illicit drugs (e.g. cocaine, methamphetamine)
 - Smoking
 - Alcohol abuse
 - Triptan use (for migraines or Reynaud's)
 - No cardiovascular risk factors

- Chest pain occurs at night

(2) Pathophysiology

- Chest pain is due to **vasoconstriction of coronary vessels**, narrowing the lumen and causing ischemia to the entire myocardium ("**transmural**")

(3) Diagnostic Features

- ST elevation on EKG
- Negative troponins
 - Troponins are a marker of destruction/infarction
- Reproduced by acetylcholine or ergonovine

- Reproduced by hyperventilation

(4) Treatment

- Prescribe **calcium channel blockers** or **nitroglycerin** to dilate blood vessels
- Avoid **beta blockers**
 - Recall: Beta receptors facilitate dilation; alpha receptors facilitate constriction
 - If beta receptor activity is blocked, only alpha receptor activity will register, leading to worsening vasoconstriction

PRINZMETAL'S (VASOSPASTIC) ANGINA

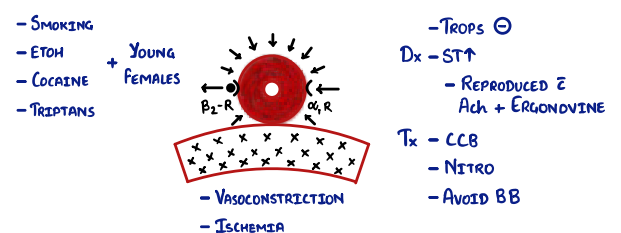


Figure 6. Prinzmetal's Angina / Vasospastic Angina



III) CLINICAL FEATURE

Taking history is important, use the OPQRST approach

Table -1. Presentation of IHD when taking history

History (OPQRST)	Stable Angina
Onset	Stable Angina: 5-10 mins Unstable angina, NSTEMI and STEMI (Acute Coronary Syndrome): >10 mins
Provocation	Worse on exertion, improved on rest, also improves with Nitroglycerin → Suggestive of Stable Angina When it occurs at rest, but can intensify with exertion → Unstable angina, NSTEMI and STEMI (Acute Coronary Syndrome)
Quality	Squeezing / Stabbing/ Pressure "Feeling like an elephant is sitting on your chest"
Radiation	Left Arm, Left Neck, Left Jaw <i>Epigastric pain can be indicative of inferior STEMI</i>
Severity	Variable
Time	Constant

(A) CHEST PAIN:

- Heart has autonomic fibers that synapse on the dorsal grey horn of the spinal cord (cervicothoracic region)
- Sensory fibers from the left arm, left side of the neck and left side of the jaw synapse in the dorsal grey horn too.
 - So when an infarct develops in the heart, neurons traveling to the dorsal grey horn might travel at the same time as the sensory fibers from the left arm, neck and jaw
 - When both of these fibers travel to the brain, the brain interprets the chest pain coming from the left arm, left side of the neck and the left side of the jaw.
- The **autonomic nervous system** can activate in response to this resulting in:
 - Nausea, vomiting, diaphoresis, syncope, sense of impending doom.

Atypical (silent) presentations in:

- Diabetics (neuropathy of particular nerves)
- Elderly
- Post heart transplant (alteration with the nerve signaling)
 - These patients can have MI **without** any chest pain

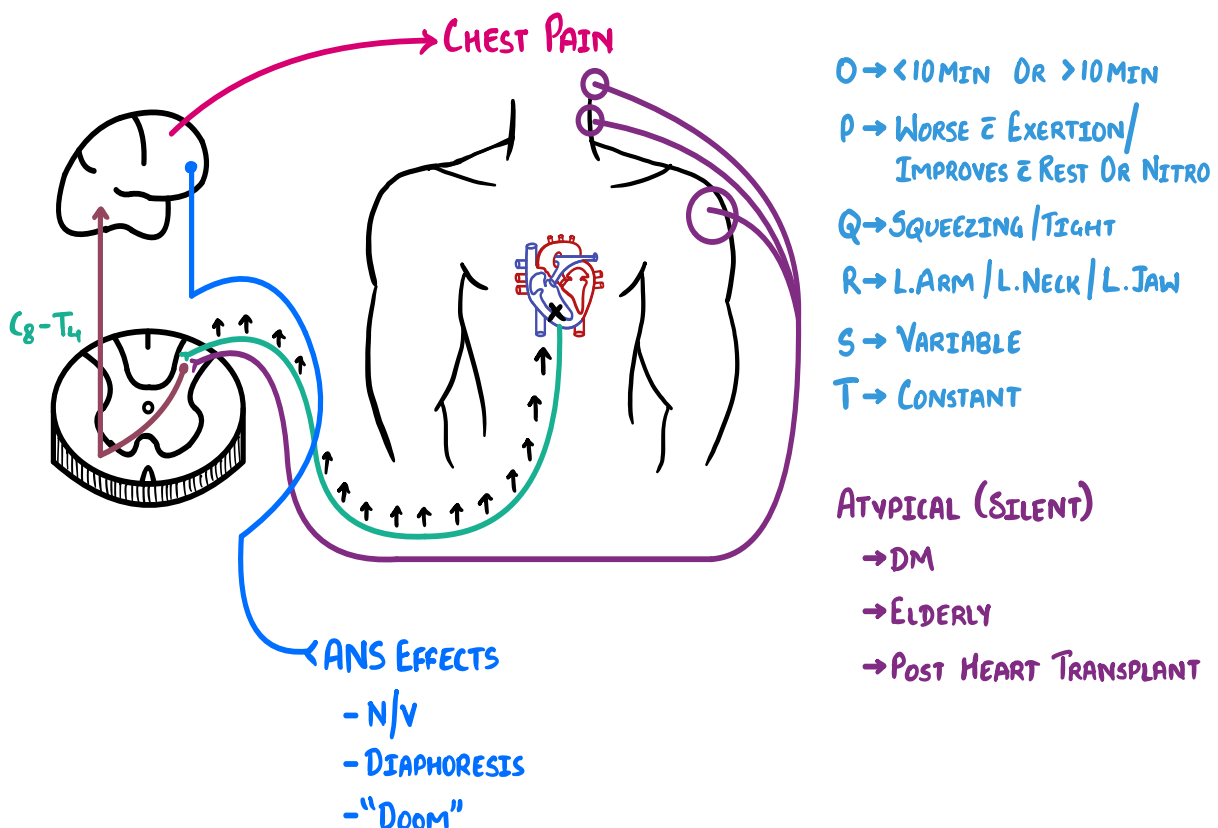
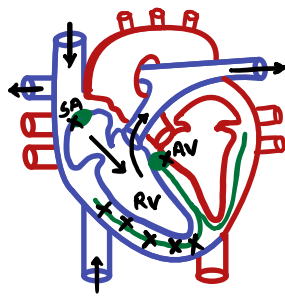


Figure 7. Chest pain radiation to the left arm, left side of the neck and left side of the jaw



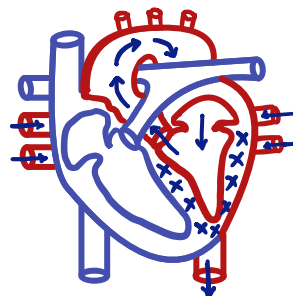
RIGHT VENTRICULAR M.I



- JVD - EDEMA OF L.E's
- HOTN
- LUNGS CLEAR
- ↓HR
- SINUS BRADYCARDIA
- AVB

Vs

LEFT VENTRICULAR M.I



- PULMONARY EDEMA
- HOTN
- "S₄"
- REFLEX ↑HR

Figure 8. Right Ventricular MI Vs Left Ventricular MI

RIGHT VENTRICLE MI:

JVD & Lower Extremities Edema

- Normally, the right ventricle receives blood from the superior/inferior vena cava → right atrium → right ventricle → to the lungs
 - If the right ventricle undergoes ischemia and there is a decrease in the heart's ability to pump blood
 - A back flow of blood into the vena cava occurs
 - If it backs up into the *superior vena cava* it will travel to the brachiocephalic → jugular veins causing **Jugular Venous Distension (JVD)**
 - If it backs up into the *inferior vena cava* it can cause lower extremities edema, hepatomegaly, ascites, etc.

Hypotension

- When there is less blood in the right ventricles, there is less blood being pumped to the lungs
 - Preload decreases = decreases stroke volume = decreases the cardiac output
 - Causing **hypotension**
 - Lungs are clear (no edema)

Decreased Heart Rate

- Right coronary artery supplies the SA and AV node
 - If the right coronary artery is occluded (as in IHD) SA and AV node (especially the AV node) do not receive proper blood supply
 - This affects the conduction through the heart
 - Can lead to **decrease in heart rate**
 - Sinus bradycardia
 - AV block (it can be 1st, 2nd or 3rd degree, it depends on the severity of the AV dysfunction)
 - It is important to avoid giving drugs that ↓ preload

LEFT VENTRICLE MI:

Pulmonary Edema

- Pulmonary Circulation → Left Atrium → Left Ventricle
 - if the left ventricle undergoes ischemia and stops working, it will cause a back flow into the pulmonary circulation and leak out into the pulmonary capillaries
 - Causing **pulmonary edema**
 - Presentation: shortness of breath

Hypotension

- When there is less blood in the left ventricles, there is less blood being pumped to the aorta
 - Decreased ejection fraction leads to **hypotension**
 - Hypotension decreases perfusions to organs
 - Leading to **cold mottled pale extremities**

Reflex Tachycardia

- Hypotension triggers this reflex
 - As there is a ↓ cardiac output, the autonomic nervous system compensates by ↑ heart rate to ↑ cardiac output and blood pressure
 - This is called **reflex tachycardia**

S₄ heart sounds

- Since the ventricles are infarcted they become really stiff
 - When the ventricles fill it produces a **S₄ heart sound**

Right Ventricular MI	Left Ventricular MI
Lungs are clear	Pulmonary Edema
↓Preload → ↓SV → ↓CO → ↓BP (HOTN)	↓EF (Ejection Fraction) → HOTN
Jugular Venous Distension (JVD)	↓Perfusion → Cold, mottled skin, Pallor
Hepatomegaly + Ascites	
Edema in the lower extremities	
Sinus Bradycardia OR	<u>S₄ heart sound</u>
AV block (degree depends on severity)	<u>Reflex Tachycardia</u> (↑HR)



IV) COMPLICATIONS

THE FIRST 24 HOURS

Sudden cardiac death

- If there is an MI, the *cell permeability* ↑ in the area of infarction.
 - high permeability: ↑ cations (calcium, sodium) load into the cells, this depolarizes the cells abnormally, and generates electric potentials causing the ventricles to contract abnormally
 - This can lead to PVC and progress into VT then VF
 - Ventricular fibrillation can result in **Sudden Cardiac Death**

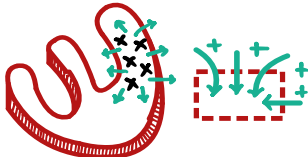
Cardiogenic Shock

- If there is a significant infarct in a major vessel (e.g LAD occlusion) especially in the left ventricle
 - The heart would not be able to push blood into the systemic circulation resulting in **hypotension**
 - Hypotension causes cold extremities due to hypoperfusion
 - This can progress to **cardiogenic shock**

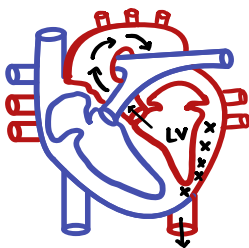
Flash Pulmonary Edema

- Blood backs up into the pulmonary circulation leading to **flash pulmonary edema**
 - Shortness of breath, hypoxia
 - reflex tachycardia to maintain a decent cardiac output

→ **SCD**
→ PVC's → VT → VF



→ **ACUTE HF**



- HOTN → SHOCK
- COLD EXT.

- FLASH PULMONARY
EDEMA

- REFLEX ↑ HR

(A) 24 HOURS - 3DAYS

Rupture syndrome:

• IN SEPTUM:

- When there is an infarction in the septum, the tissue can become weak and susceptible to rupture
 - Since the left ventricle pumps blood at a higher pressure, with a weak septum it would be able to push blood into the right ventricle
 - This is called a **Ventricular Septal Defect** due to an inter-ventricular septal rupture
 - May cause:
 - Murmur (hollow systolic murmur)
 - Mixed venous oxygenation

• IN LEFT VENTRICLE:

- Infarct in the left ventricle can render it weak and if it ruptures, blood can get into the pericardial cavity, this is called a **free wall rupture**.
 - Blood in the pericardial cavity can lead to hemopericardium resulting in **Cardiac Tamponade**.
 - **Recall:** Beck's Triad occurs with cardiac tamponade, this consists of hypotension, JVD, and muffled heart sounds.

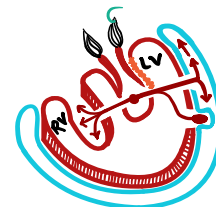
• IN PAPILLARY MUSCLES:

- Papillary muscles are found in the inner walls of the heart, and they attach to the valves via the chordate tendineae to anchor the valves.
 - If an infarct develops in the papillary muscles, the tissue can get weak and rupture.
 - Valves would no longer be anchored and become flail causing regurgitation.
 - If this occurs in the left heart, it causes **Mitral Valve Regurgitation**.
 - Presentation: mitral valve murmur, hypotension, pulmonary edema, etc.

Left Ventricular Pseudo Aneurysm

- In free wall ruptures, blood can accumulate in the pericardium and this can form a pseudoaneurysm
 - Due to blood stasis, clots can form in these areas and increase the **risk of thrombi (mural thrombus)**

→ **RUPTURE SYNDROMES**



1) **VSD**
- MURMUR ⊕
- MIXED VENOUS O₂

2) **FREE WALL RUPTURE**
- TAMPONADE

3) **PAPILLARY RUPTURE**
- MR MURMUR

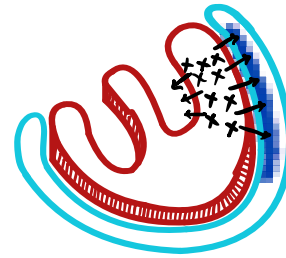
4) **LV PSEUDOANEURYSM**
- ↑ THROMBI



Pericarditis

- If there is an infarct in the left ventricle, an inflammatory reaction can occur to clean up the debris
 - This local inflammatory reaction is called **pericarditis**
 - Presentation: *sharp* and *positional* chest pain, friction rub (via lung sounds)
 - The inflammation can increase the formation of fluid, leading to **pericardial effusion**.

→ PERICARDITIS



→ CP

- SHARP
- POSITIONAL
- FRICTIONAL RUB
- PERICARDIAL EFFUSIONS

Left Ventricular Aneurysm

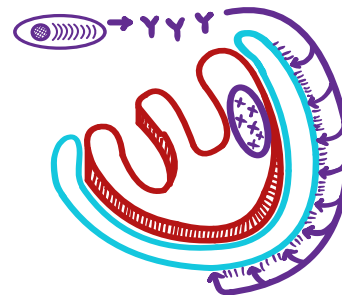
- In an infarction, first there is a soft granulation tissue → fibrous tissue.
 - Fibrous tissue can "bulge out" creating a **left ventricular aneurysm**
 - There is a low risk of rupture since the fibrous tissue is stronger
 - Since the affected area of the ventricle is not contracting, this creates *blood stasis* which increases the risk of clot formation and mural thrombi.
 - **Recall:** Virchow's triad; if there is stasis, hypercoagulability or endothelial injury then there is a higher risk of clot formation
 - Thrombi also increases the risk of **emboli** formation which can occlude different organs (e.g. brain, spleen, kidney, etc.)

Dressler's Syndrome

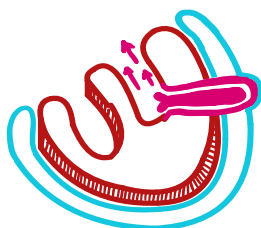
- Infarct in the ventricle can create an underlying immune reaction, however the etiology is unknown
 - The immune system develops antibodies against the pericardium
 - This leads to the inflammation of the pericardium

(This occurs later, unlike the pericarditis that occurs in the 3-14 days time period)

→ DRESSLER SYND.



→ LV ANEURYSM



- MURAL THROMBI
- ↑ EMBOLI

V) DIAGNOSIS

(A) OVERVIEW OF DIAGNOSTICS (EKG AND BIOMARKERS)

- The diagnostics used in ischemic heart disease are:
 - 12-lead EKG
 - Biomarkers such as troponin and CK-MB

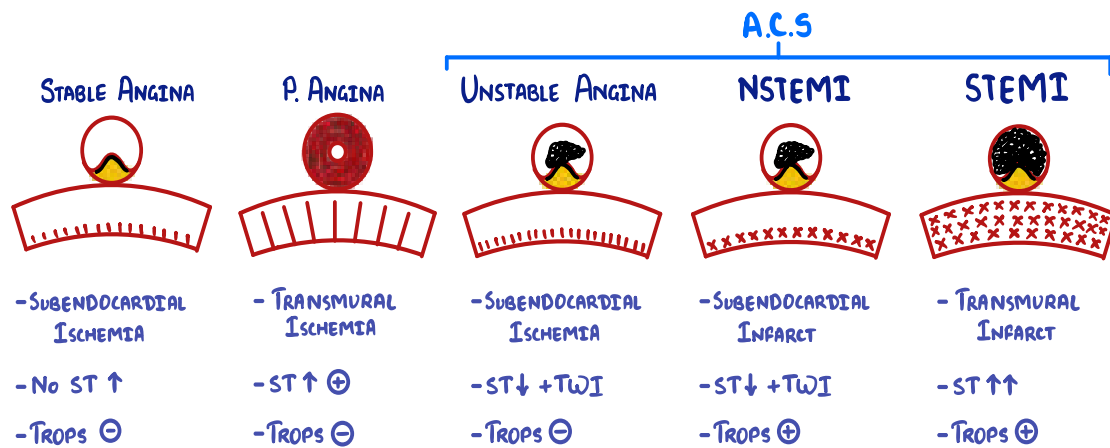


Figure 9. Diagnostic features of different ischemic heart diseases.

(1) Stable Angina

- Subendocardial ischemia
- 12-lead EKG will show **NO ST segment elevation**
 - May have other ST wave changes but it would not be anything obvious such as ST depression, T wave inversions, Q waves
- Stable angina does NOT have infarction but it has **ischemia** → no cell destruction → no leakage of biomarkers = **(-) troponin** and **CK-MB**

- For patients with ischemic chest pain, biomarkers such as **troponin** and sometimes, **CK-MB** should also be ordered (aside from EKG)

(2) Prinzmetal (Vasospastic) Angina

- Transmural ischemia → produce **ST segment elevation** that is transient and can be reproduced by acetylcholine or ergonovine
- (-) troponin** and **CK-MB** since vasospastic angina has ischemia; **NO infarction**

(3) Acute Coronary Syndromes (Unstable Angina, NSTEMI, STEMI)

- Unstable angina, NSTEMI and STEMI are categorized as **acute coronary syndrome (ACS)**
 - Most severe of ischemic heart disease

(i) Unstable Angina

- Subendocardial ischemia → NO infarction → may show signs of **ST depression** and **T wave inversion** but **NO ST segment elevation**
- (-) troponin** and **CK-MB** since there is no infarction

(ii) NSTEMI

- Subendocardial infarct → there is tissue destruction → may show **ST segment depression** and **T wave inversion**; **NO ST segment elevation**
- (+) troponin** and **CK-MB** since there is tissue destruction so these biomarkers can leak

(iii) STEMI

- Transmural infarct
- 12-lead EKG shows **ST segment elevation**
- (+) troponin** and **CK-MB** since it is a transmural infarct = there is tissue destruction and biomarkers can leak

(B) BIOMARKERS

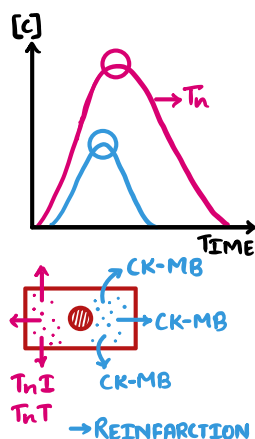


Figure 10. Biomarkers troponin and CK-MB.

- Myocardial cell has special types of molecules called **troponin (TnI and TnT)** and **CK-MB**
 - If there is tissue destruction, these biomarkers will leak out of the cells
 - CK-MB** is more specific for heart tissue destruction
- TnI and TnT usually takes **12-24 hours** before reaching the peak similar to CK-MB; however, **CK-MB normalizes quicker** than TnI and TnT
 - CK-MB can be used to determine **re-infarction**
 - If patients complain of new chest pain after an infarction, **order CK-MB**; troponins will still remain elevated and would not have normalized yet



(C) REVIEW OF CORONARY VESSELS AND THE LEADS INVOLVED IN THE EKG

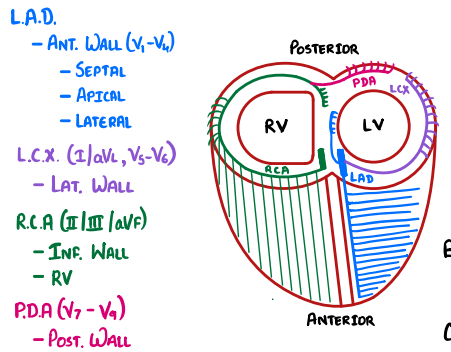


Figure 11. Coronary vessels and their corresponding EKG leads.

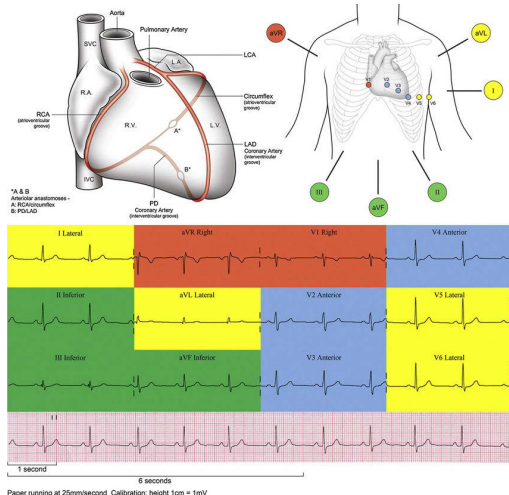


Figure 12. (Top left) Coronary arteries; (Top right) Positioning of EKG leads; (Bottom) Corresponding EKG leads [Blakeway et al. 2012].

(1) Left Anterior Descending Artery (LAD)

- Supplies the **anterior** compartment of the heart (including the septum)
- If there is infarction in the anterior wall of the heart, LAD is involved
- Leads involved: **V₁-V₄**
 - V₅ and V₆ sometimes

(2) Left Circumflex Artery (LCX)

- Branch of the LAD
- Supplies the **lateral** wall of the heart
- Leads involved: **I, aVL, V₅ and V₆**

(3) Right Coronary Artery (RCA)

- Supplies the right ventricle (**marginal branch**) including the apex of the heart and the posterior part of the septum
- If there is infarction in the **inferior part** of the heart, RCA is involved
- Leads involved: **II, III, aVF** and right-sided chest leads

(4) Posterior Descending Artery (PDA)

- Branch of the RCA
- Supplies the **posterior** wall of the heart
- Leads involved: **V₇-V₉**

Table -2. Summary of the coronary vessels and the leads involved when infarction occurs.

ARTERY	HEART PORTION SUPPLIED	LEADS INVOLVED
LAD	Anterior	V ₁ -V ₄
LCX	Lateral	I, aVL, V ₅ , V ₆
RCA	Inferior	II, III, aVF, right-sided leads
PDA	Posterior	V ₇ -V ₉

(D) DIAGNOSTIC FEATURES

(1) EKG

- Sequence of ischemia-infarction (**STEMI**) as seen in EKG:
 - Hyperacute T waves
 - Very particular for MI
 - ST segment elevation
 - Q waves
 - ± T wave inversion (TWI)
 - ST segment normalizes
 - T wave normalizes
- Also look for **ST segment depression** and **T wave inversion** by itself = indicative of unstable angina and NSTEMI

(2) Echo

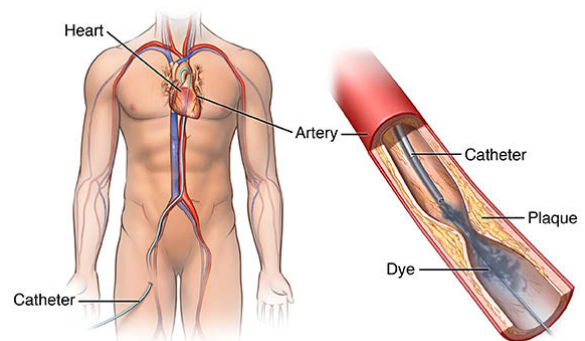
- Important for diagnosing ischemic heart disease
 - Developing an infarct in the LCX territory → left lateral wall became ischemic and infarcted → not contracting

- Can show **wall motion abnormality**

(3) Cath (Cardiac Catheterization)

- Best/most definitive test** for myocardial infarction
- A catheter is taken up from the radial or femoral artery then look into the vessels of the heart and release some contrast
 - Then, flow of the contrast can be visualized
 - If the flow of contrast stops in one area, there might be occlusion in the vessel
- Diagnostic; **AND**
- Therapeutic
 - Percutaneous coronary intervention (PCI)

Coronary angiography



Angiogram

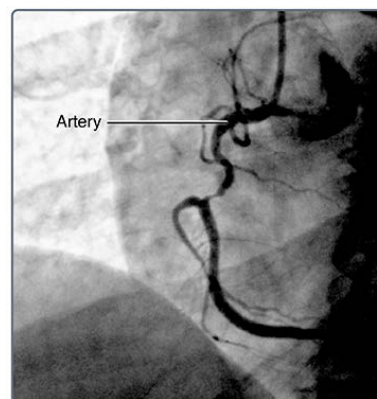


Figure 13. (Top) The process of cardiac catheterization or coronary angiography. (Bottom) Visualization of coronary vessels through injection of dye [Johns Hopkins Medicine, n.d.].



(E) DIAGNOSTIC APPROACH

- Patient complains with ischemic chest pain

(1) 12 Lead ECG

- First test to do if concerned with IHD
 - Shows $ST \uparrow$ → **Cath**
 - No $ST \uparrow$ but there is $ST \downarrow$, TWI and Q waves → **Troponin**

(2) Troponin

- If (+) troponin → patients can be re-stratified through **TIMI Score**
 - TIMI Score re-stratifies patients with NSTEMI or unstable angina and determines the need for catheterization based on the risk of mortality
 - For patients with intermediate probability of coronary artery disease (CAD)
 - TIMI ≥ 2 → **Cath**
 - *!! may be asked in exams*
- If (-) troponin → may be **stable angina**
 - Determine whether they should get a **stress test** → **(+) stress test** → elective **Cath**

(i) TIMI Score

- Re-stratifies patients with NSTEMI or unstable angina and determines the need for catheterization based on the risk of mortality
- For patients with intermediate probability of coronary artery disease (CAD)

NSTE-ACS (TIMI Score) Mnemonic:

- Age ≥ 65
- Marker (Trops are elevated)
- ECG ($ST \downarrow$)
- Risk factors (≥ 3)
 - Diabetes, hypertension, smoking, age
- Ischemic chest pain with at least 2 events within 24-hr period
- CAD $\geq 50\%$ stenosis of one of coronary vessels
- ASA use within the last 7 days

0-1: $\downarrow$ risk = medically managed and reevaluate
 ≥ 2 : $\uparrow$ risk = considered for catheterization

DIAGNOSTIC APPROACH

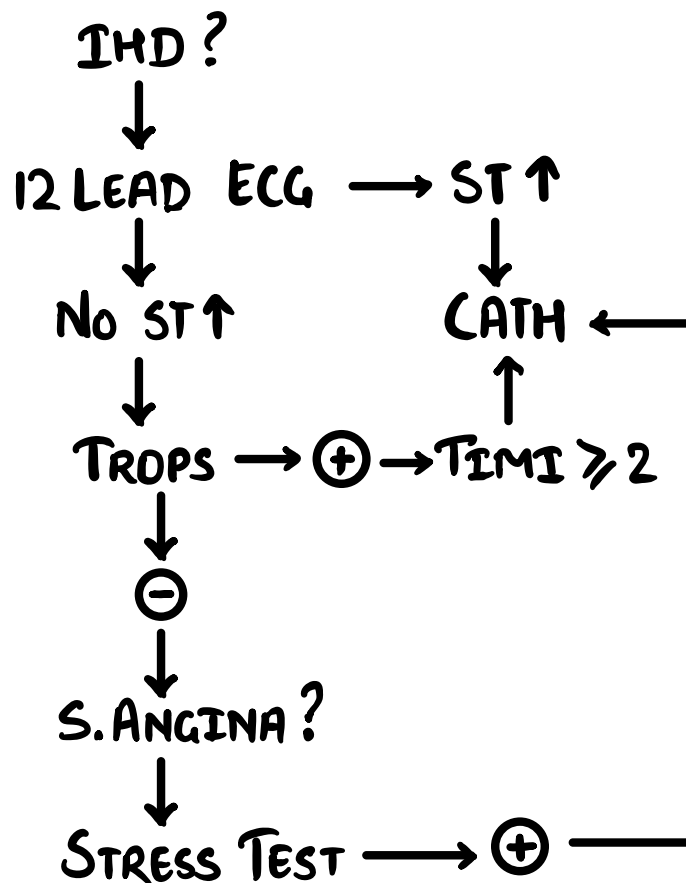


Figure 14. Summary of the diagnostic approach for patients with ischemic chest pain.

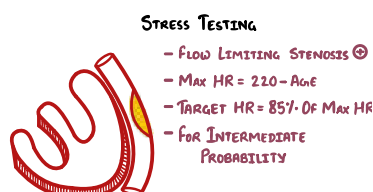


(F) STRESS TESTING

(1) How to determine the need for Stress Testing?

- Look for the Diamond Classification of Chest Pain for **Stable Angina**
 - Anginal chest pain + age/gender
 - Substernal chest pain
 - Worse chest pain with exertion
 - Relieved by nitroglycerin

(2) Stress Testing



EKG → ST↓ Or TWI (+)

ECHO → WALL MOTION ABNORMALITIES (+)

MPI → "COLD SPOTS" (+)

Figure 15. Stress testing and the "positives" for EKG, echo and MPI.

- Only important in **flow limiting stenosis**
 - !! can come up in exams
 - Cannot diagnose MI
- Patients should have an **intermediate** probability of CAD
 - Do not send if the patient has high or low probability of CAD
 - If patient has a **high** probability → Catheterization
- With patients with ↓O₂ supply because of occlusion, an increase in O₂ demand can **worsen** the ischemia → worsen the chest pain
- Patient walk on a treadmill → increase O₂ demand → **ischemic event**

- Max HR = 220-Age
- Target HR = 85% of Max HR
 - Target HR for the patients to work out to reaching a high oxygen demand that can induce an ischemic event

- Baseline EKG, Echo and MPI (myocardial perfusion imaging) are determined and then compared post-workout
 - EKG:** ST↓ or TWI = (+)
 - Uninterpretable EKG due to a pacemaker, left bundle branch block, other abnormalities → go do an Echo
 - Echo:** wall motion abnormality = (+)
 - MPI:** cold spots (areas of poor perfusion) = (+)
 - New imaging modality that uses Technetium to visualize well perfused myocardium

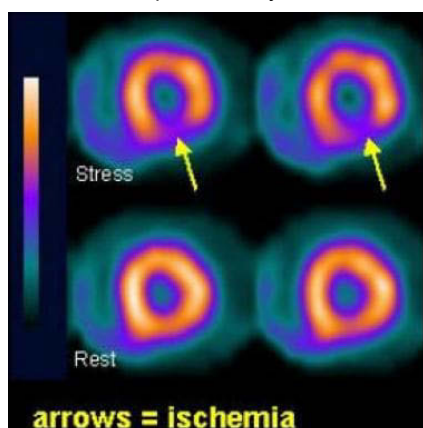


Figure 16. Cold spots (arrow) as seen in MPI [Cardona, 2021].

(3) Pharmacologic Stress Testing

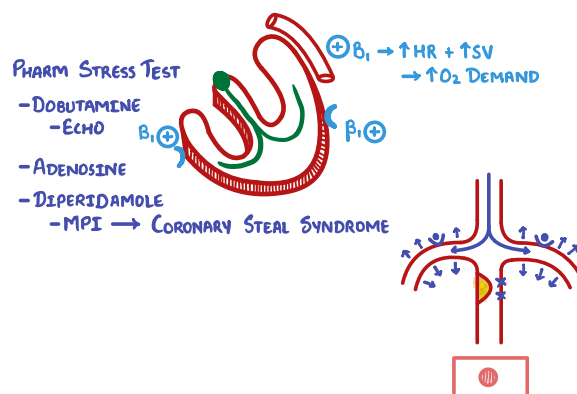


Figure 17. Pharmacologic Stress Testing.

- For patients who are NOT able to do the exercise aspect of stress testing
 - Patients who do not want to exercise; disabled; etc.
- Can replicate stress testing (workout) through certain medications
 - !! They love to ask this on USMLE Step 2
- Medications used: **dobutamine**, **adenosine** and **diperidamole**

(i) Dobutamine

- For Stress Echo
- Dobutamine binds on β₁ receptors on the myocardium and nodal cells → ↑HR, ↑SV → ↑contractility → ↑O₂ demand

(ii) Adenosine and/or Diperidamole

- For MPI
- Vasodilators
 - Both bind on **healthy vessels** and cause them to dilate maximally → allow blood to easily flow on the healthy vessels
 - Do not work on **diseased vessels** → no dilation → blood is "stolen" by healthy vessels (less resistance) → diseased vessels are "starved" and start to get ischemic = **Coronary Steal Syndrome**



VI) 12 LEAD ECG STEMIS

- When looking at an EKG, determine the following:
 - Rate
 - Rhythm
 - Axis
 - ST segments

Larger version of the ECG Strips can be found in the [Error! Reference source not found.](#) section.

(A) CASE 1: ANTERIOR STEMI

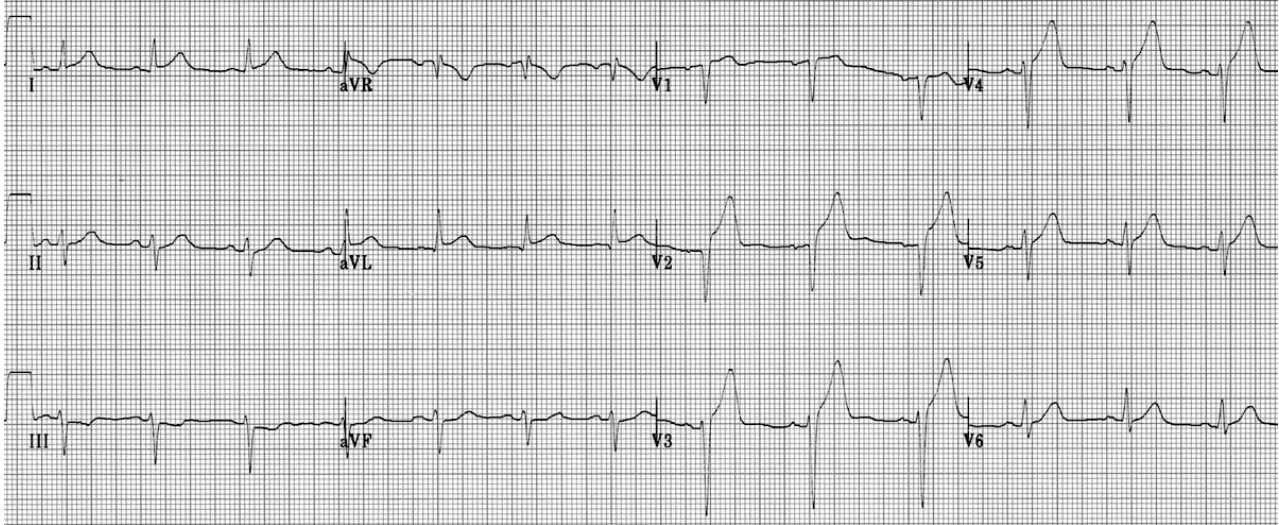


Figure 18. Case 1 ECG Strip.

- In this case, there are no rhythm strips. Therefore, rate-rhythm sequence can be skipped and move on to ST segment deviation
- Check all the limb leads (I, II, III, aVR, aVL, aVF) and then the precordial leads (V1-V6)

Table 3. ST segment deviation in each ECG lead.

ECG LEADS	ST SEGMENT DEVIATION
I	Subtle ST segment elevation
II	Unremarkable
III	Nothing specific – may be an ST-T wave abnormality
aVR	Unremarkable
aVL	ST segment elevation
aVF	Unremarkable
V1	ST segment elevation + pathologic Q wave (deep and wide Q wave)
V2	ST segment elevation + hyperacute T wave (funky and asymmetric T wave)
V3	ST segment elevation + hyperacute T wave
V4	ST segment elevation + hyperacute T wave
V5	Unremarkable
V6	Unremarkable

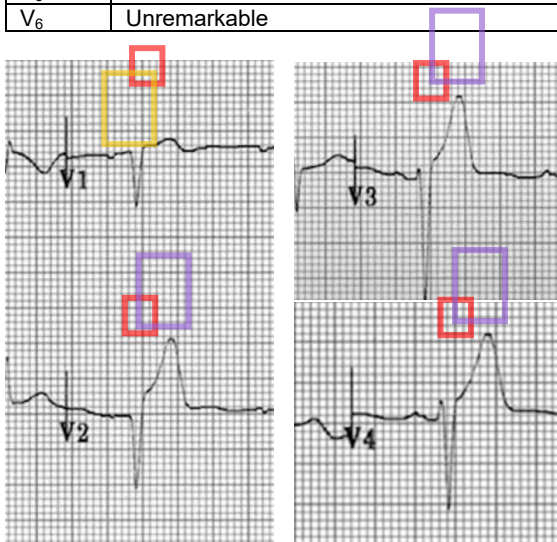


Figure 19. ST segment elevation (red) in V1-V4. Pathologic Q wave (yellow) in V1. Hyperacute T wave (violet) in V2-V4.

- Since there is ST segment elevation in V1-V4, there is occlusion in **LAD** → infarction or ischemia in the anterior heart
 - If it starts affecting some of the lateral part (anterolateral), there can be some changes in V5, V6, I and aVL
 - Suspicion: **anterior MI**

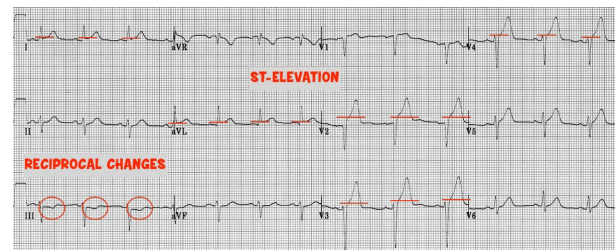


Figure 20. Labeled ECG Strip of Case 1.

- Summary:**
 - There are ST segment elevation in V1-V4, I, and aVL
 - Reciprocal changes (ST segment depression or T wave inversion) in III
 - Very significant in STEMI
 - ST segment depression:** below the TP segment
- The case is a **significant LAD occlusion** causing ischemia in the anterior septal (V2 & V3), apical (V4) and lateral (I & aVL) portion of the heart with reciprocal changes in III = **anterior STEMI**

Anterior STEMI

- ST↑ in V2-V4



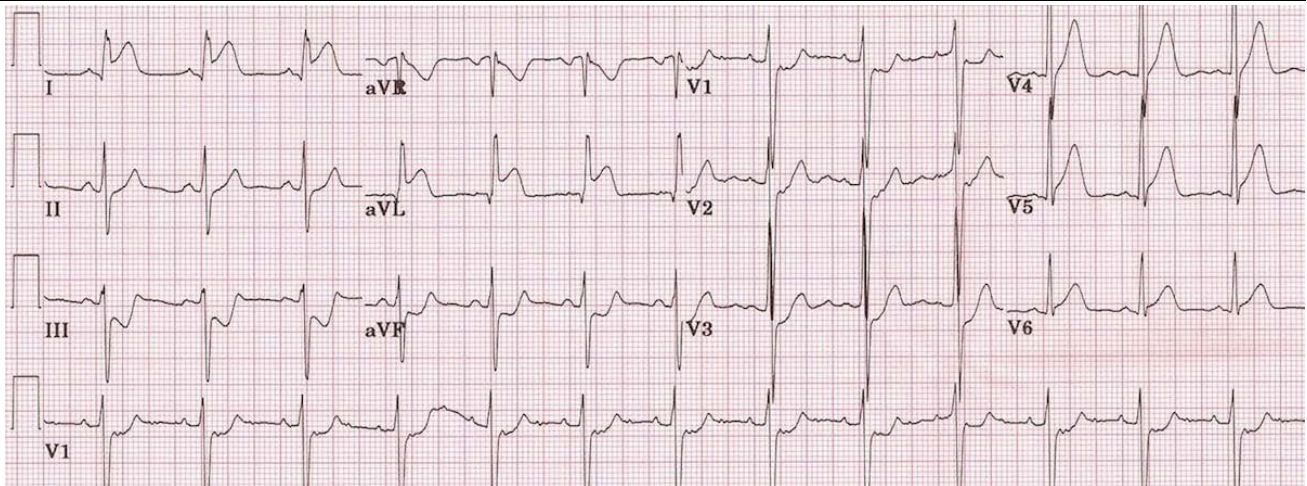
(B) CASE 2: LATERAL STEMI

Figure 21. ECG strip of Case 2.

(1) Rate, Rhythm, Sinus

- **Rate:** regular
 - Not too fast, not too slow
- **Rhythm:** regular
 - Normal sinus rhythm – upright P wave in II and inverted P wave in aVR

(2) ST Segment Deviation

Table 4. ST segment deviation in ECG leads for Case 2.

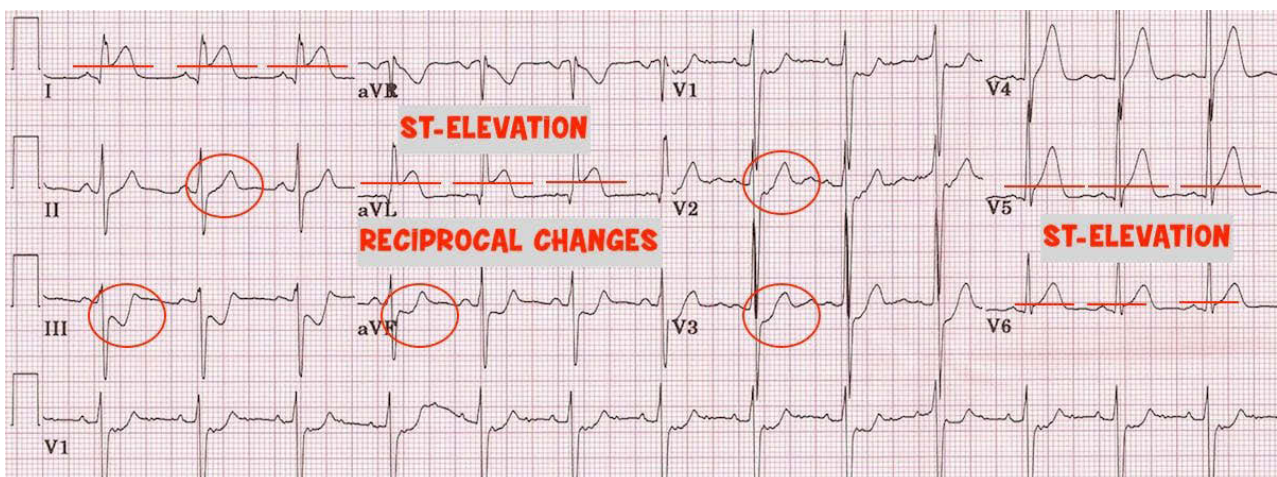
ECG LEADS	ST SEGMENT DEVIATION
I	Large ST↑
II	Unremarkable
III	ST↓ (reciprocal change)
aVR	Unremarkable
aVL	ST↑
aVF	ST↓ (reciprocal change)
V ₁	Small ST↓ (reciprocal change)
V ₂	ST↓ (reciprocal change)
V ₃	ST↓ (reciprocal change)
V ₄	Unremarkable
V ₅	ST↑
V ₆	Subtle ST↑

Mainstem occlusion can be found in **aVR****Summary:**

- ST↑ in leads I and aVL → occlusion in **LCX** or distal LAD → affecting the **high portion of the left ventricle**
- ST↑ in lead V₅ → affect the **anterolateral** portion of the heart
- Subtle ST↑ in lead V₆

• **Diagnosis:** Lateral STEMI**Lateral STEMI**

- ST↑ in I, aVL

Figure 22. Labeled ECG strip of Case 2. ST elevation in leads I, aVL, V₅ and V₆. Reciprocal changes (encircled) in III, aVF, V₂, and V₃.

(C) CASE 3: INFERIOR STEMI

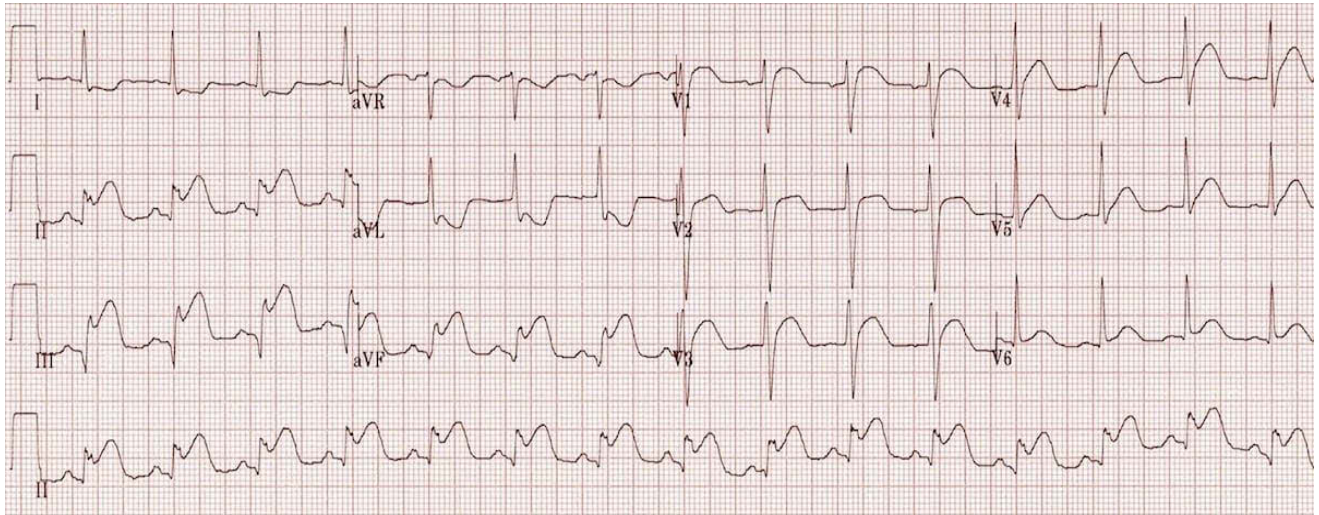


Figure 23. ECG strip of Case 3.

(1) Rate, Rhythm, Sinus

- **Rate:** regular
- **Rhythm:** regular
 - R-R intervals are similar
 - P wave in lead II is upright, inverted in aVR = **sinus** rhythm

(2) ST Segment Deviation

Table 5. ST segment deviation in ECG leads for Case 3.

ECG LEADS	ST SEGMENT DEVIATION
I	ST↓
II	ST↑
III	ST↑
aVR	Unremarkable
aVL	ST↓
aVF	ST↑
V ₁	Subtle ST↑
V ₂	Unremarkable
V ₃	Unremarkable
V ₄	Unremarkable
V ₅	Unremarkable
V ₆	Unremarkable

• **Summary:**

- ST↑ in II, III and aVF = **inferior STEMI** → affects the inferior portion of the heart
- Reciprocal changes in I and aVL
- Inferior STEMI is associated with occlusion of the RCA
 - Occlusion of the RCA will affect the blood flow in the inferior wall of the heart AND the right ventricle developing right ventricular infarction
 - Therefore, **evaluate right-chest leads** to assess for RV infarction

Inferior STEMI

- ST↑ in II, III and aVF

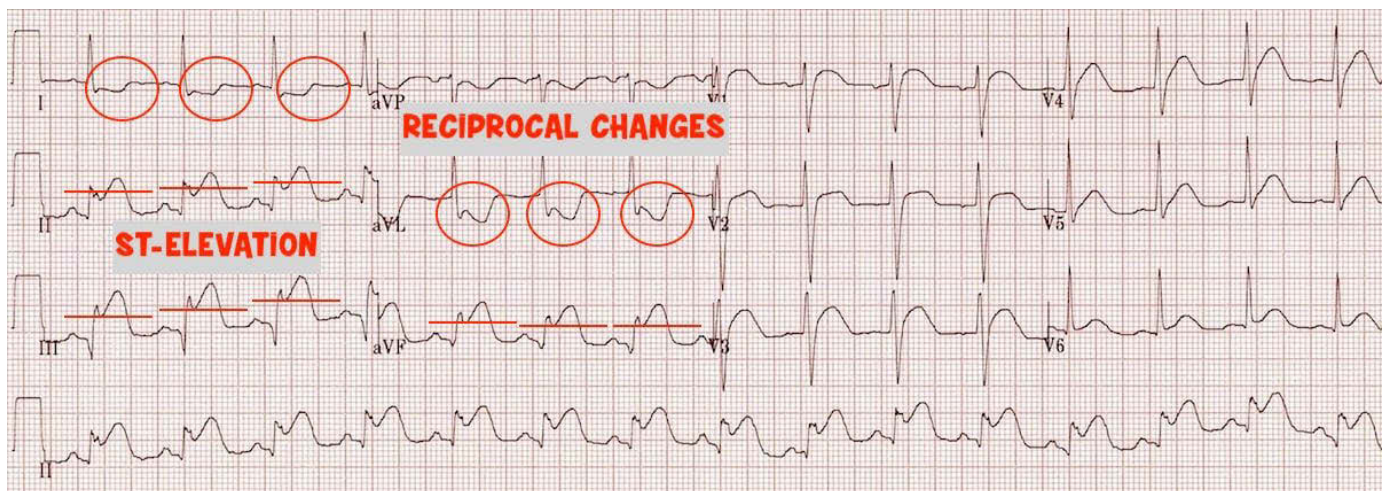


Figure 24. Labeled ECG strip of Case 3. ST elevation (line) in II, III and aVF with reciprocal changes (encircled) in I and aVL



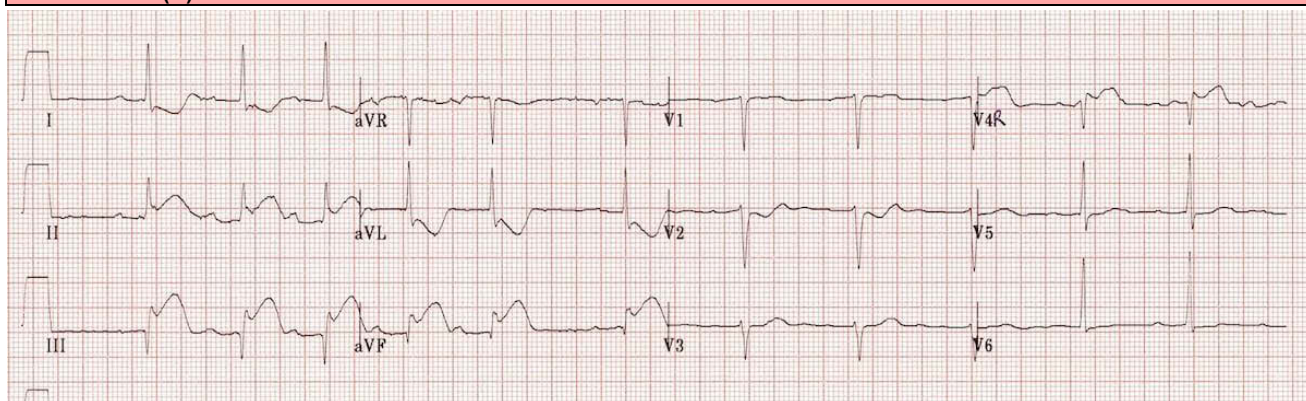
(D) CASE 4: INFERIOR STEMI WITH ASSOCIATED RIGHT-SIDED MYOCARDIAL INFARCTION

Figure 25. ECG strip of Case 4.

Table 6. ST segment deviation in ECG leads for Case 4.

ECG LEADS	ST SEGMENT DEVIATION
I	ST↓
II	ST↑
III	ST↑
aVR	Unremarkable
aVL	ST↓
aVF	ST↑
V ₁	Unremarkable
V ₂	Small ST↓
V ₃	Unremarkable
V ₄	Unremarkable
V _{4R} *	ST↑
V ₅	Unremarkable
V ₆	Unremarkable

*V_{4R}: right-sided V₄

- ST↑ in II, III and aVF with reciprocal changes in I and aVL = **inferior STEMI**
- Remember to have a high degree of suspicion for right ventricular infarction therefore track over the chest leads (V1-V6) into the right side
 - Any ST↑ (V1R-V4R) in the right-sided chest leads = high suspicion for RV infarction or right-sided MI
- **Summary:**
 - ST↑ in II, III and aVF = **inferior STEMI**
 - ST↑ in V4R = **associated right-sided MI**

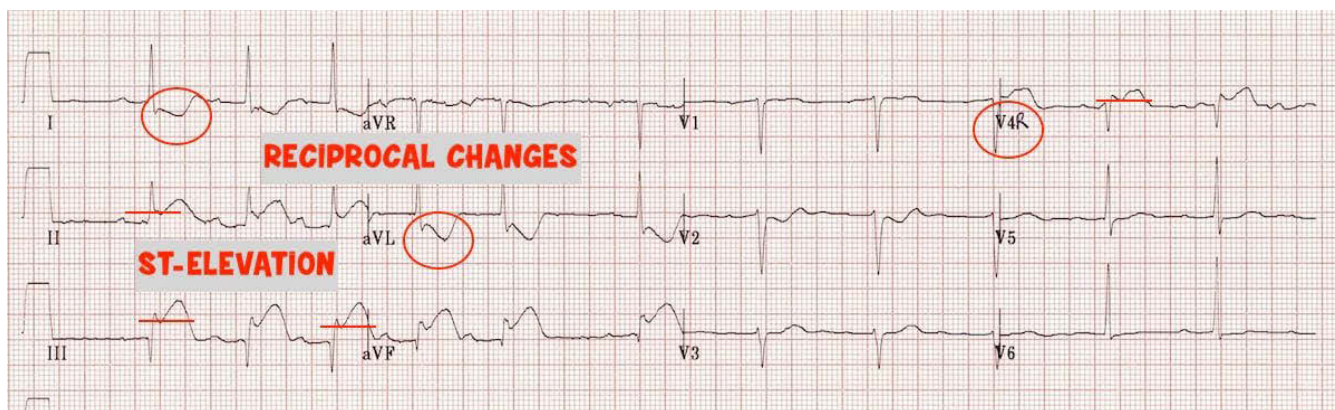


Figure 26. Labeled ECG strip of Case 4. ST elevation in II, III and aVF indicating an inferior STEMI. ST elevation in V4R indicating an associated RV infarction.

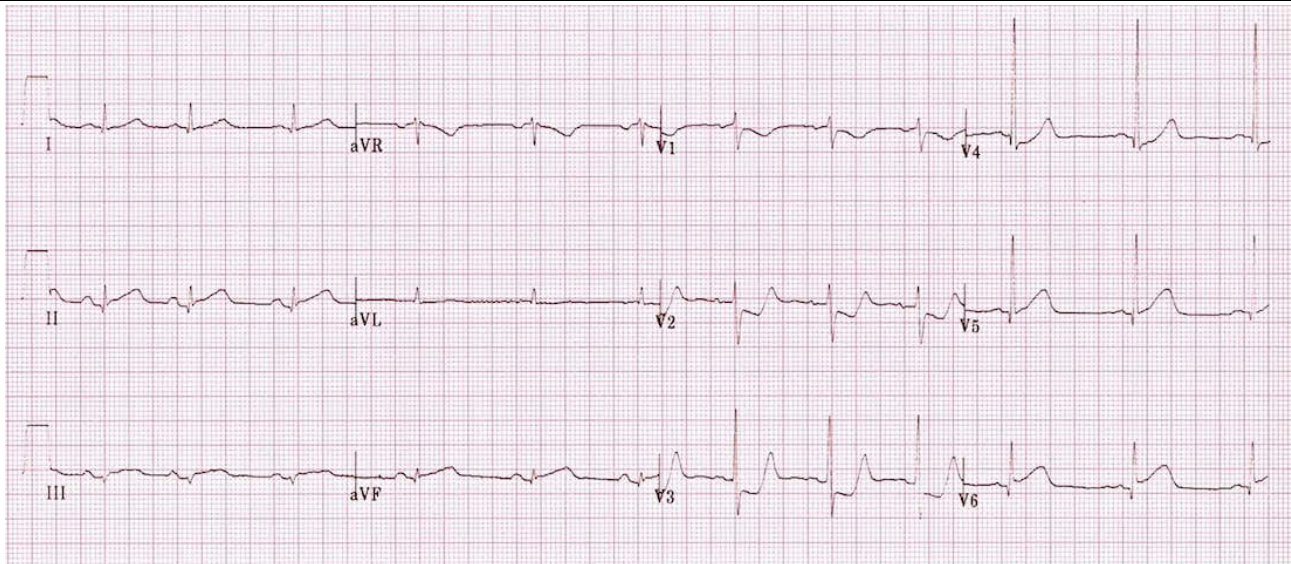
(E) CASE 5: POSTERIOR STEMI WITH INFERIOR WALL INVOLVEMENT

Figure 27. ECG strip of Case 5.

Table 7. ST segment deviation in ECG leads for Case 5.

ECG LEADS	ST SEGMENT DEVIATION
I	Unremarkable
II	Subtle ST↑ (~1 mm)
III	Subtle ST↑
aVR	Unremarkable
aVL	Unremarkable
aVF	Subtle ST↑
V ₁	TWI
V ₂	ST↓
V ₃	ST↓
V ₄	ST↓
V ₅	Unremarkable
V ₆	ST↑

- Subtle ST↑ in II, III and aVF but no reciprocal changes in I and aVL so there may be involvement of the inferior wall
 - Think of the blood supply: RCA supplies the right ventricle and the inferior portion and runs at the posterior portion to branch off as PDA that supplies the posterior heart
 - Is there any involvement of the inferior wall that is posterior related?
- Remember that the PDA gives way to the posterior and inferior portion of the heart
 - It does not pick up ST↑ in precordial V1-V6 chest leads. You would have to put the leads on the posterior part of the chest wall to pick up ST elevation

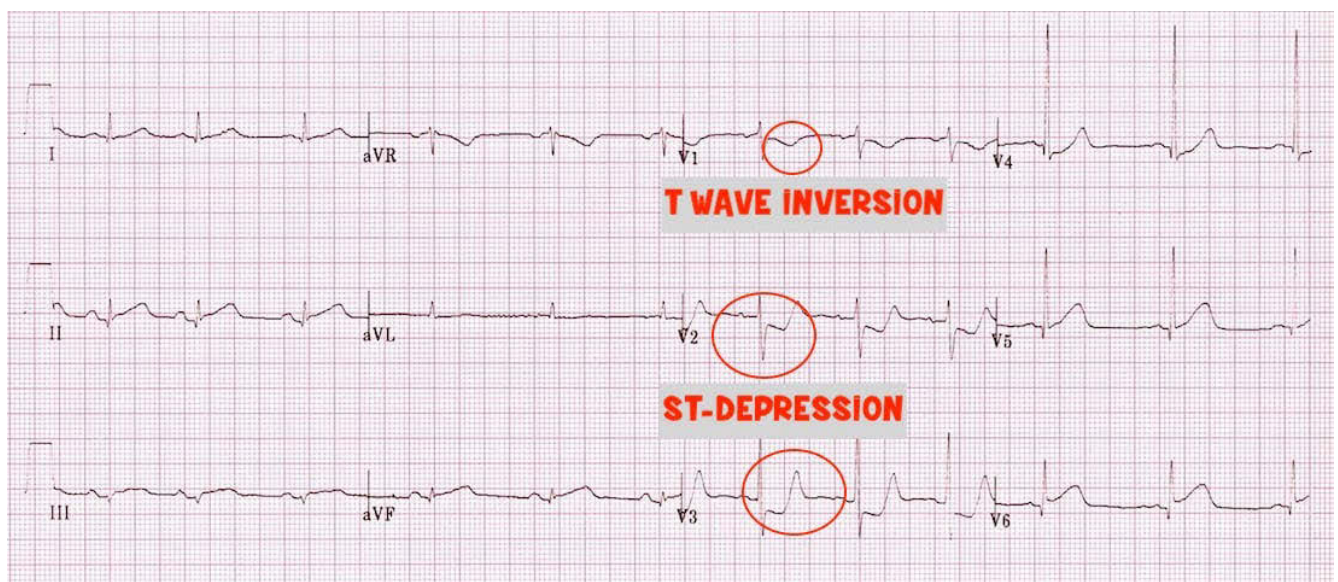


Figure 28. Labeled ECG strip of Case 5.



(1) Posterior Chest Leads (V7-V9)

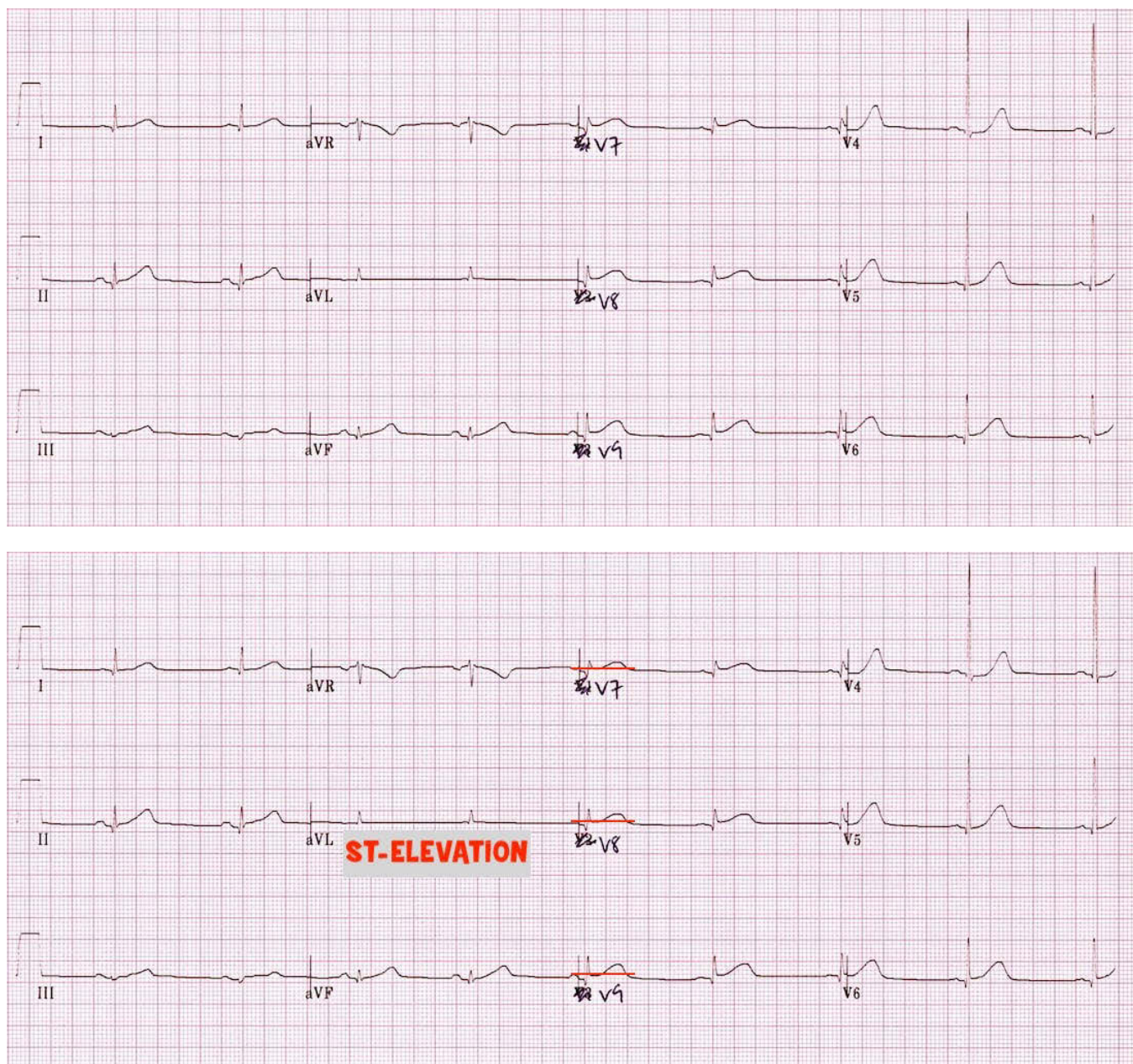


Figure 29. ECG strips (bottom: labeled) of Case 5 with posterior chest leads (V7-V9)

Table 8. ST segment deviation in posterior ECG leads for Case 5.

ECG LEADS	ST SEGMENT DEVIATION
II	Subtle ST $\uparrow$ (~1 mm)
aVF	Subtle ST $\uparrow$
V ₇	ST $\uparrow$
V ₈	ST $\uparrow$
V ₉	ST $\uparrow$

- ST $\uparrow$ in posterior chest leads, II and aVF = **posterior STEMI with inferior wall involvement**
 - There were ST $\uparrow$ in chest leads that had ST $\downarrow$ in the prior figure



VII) TREATMENT

(A) REDUCE RISK OF THROMBOSIS

- Goal:
 - ↓ risk of Plaque formation
 - ↓ risk of thrombosis
- Role of Platelets in forming Thrombosis:
 - Plaque is formed → rupture → exposure the thrombogenic core of fat tissue → platelets adhesion and activation
 - Platelet's granules secrete:
 - ADP
 - TXA_2 = Thromboxane A_2
 - 5-HT
 - These molecules can cause :
 - More platelets to come to the area = **Platelet Aggregation**
 - Increase the **stickiness** (Adhesion)
 - Stimulate the expression of proteins → Glycoproteins on the platelets like GPIIb / IIIa

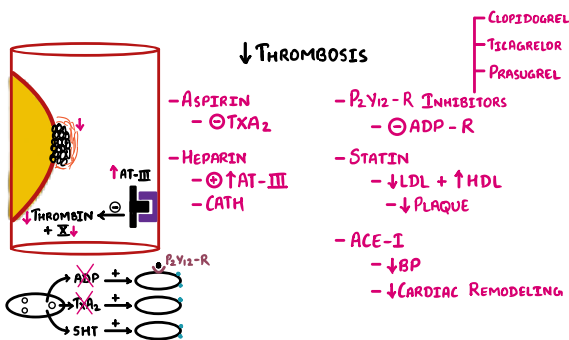


Figure 30. IHD Treatment- Reduce Thrombosis.

(1) Aspirin

- Antiplatelet
- Mechanism:
 - Irreversibly inhibits Cyclooxygenase-1 (COX-1) → Inhibits the production of **Thromboxane A_2 (TXA_2)** → **Inhibits Platelet Aggregation**
 - higher doses Aspirin → Inhibits COX-2 → Blocks prostaglandin production → analgesic and antipyretic effects

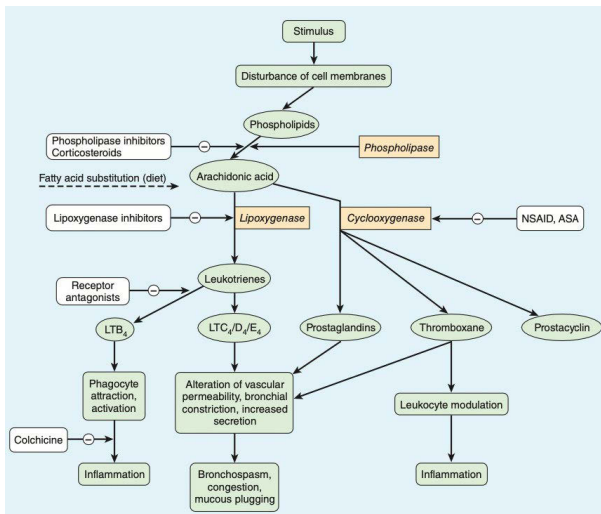


Figure 31. Prostanoid mediators derived from arachidonic acid and sites of drug action. ASA, acetylsalicylic acid (aspirin); LT, leukotriene; NSAID, nonsteroidal anti-inflammatory drug. (Pharmacology Katzung)

(2) P2Y₁₂ Receptor Inhibitors

- Antiplatelet
- ADP (= Adenosine Diphosphate) binds to P2Y₁₂ Receptors
- Medications in this group :
 - Clopidogrel = Plavix
 - Ticagrelor = Brilinta
 - Prasugrel
- Mechanism:
 - binds to the adenosine diphosphate (ADP) P2Y₁₂ receptor on the platelet surface → ↓ platelet aggregation and ↓ Stickiness

(3) Heparin

- Anticoagulant
- Heparin is produced endogenously
- Mechanism:
 - Binds to antithrombin III → enhance the activity of AT-III which is inhibition of **Thrombin and factor X** (These molecules induce coagulation) → decrease coagulation → decrease clot formation → decrease thrombosis
- Types of Heparins
 - Unfractionated Heparin → intravenous or subcutaneous use
 - Low Molecular Weight (LMW) Heparin → Preferred
- Heparin is beneficial in
 - STEMI, NSTEMI, Unstable Angina
 - Especially If you are getting **CATH**

(4) Statins

- Mechanism:
 - They do not necessarily reduce thrombosis, they ↓ Plaque formation
 - HMG-CoA reductase inhibitors → Ideally ↓ LDL & ↑ HDL → ↓ Plaque formation → may ↓ risk of forming future thrombosis

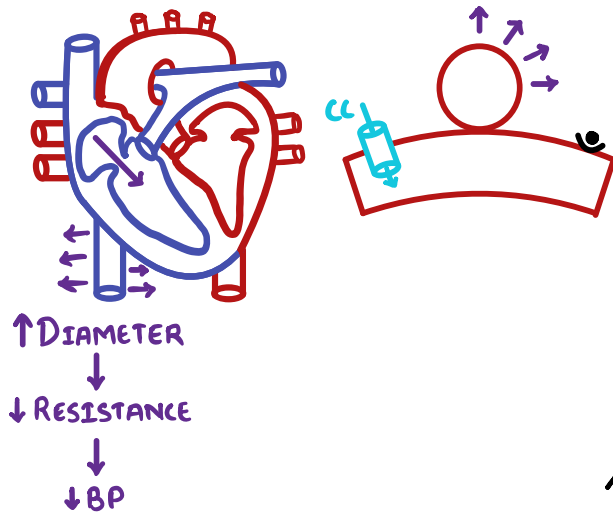
● **Modifiable Risk Factors:** (Reduce the risk of plaque forming)

- Diabetes
 - Glucose control
 - Exercise
 - Diet
- Hypertension
 - Medication
 - Lose weight
 - Exercise
 - Less salt intake
- Obesity
 - Lose weight
 - Exercise
 - Diet
- Smoking
 - Smoking cessation
- Alcohol consumption
 - Reduce Alcohol use

ACE-I

- Is recommended in **long term** treatment of patients if they Blood pressure can tolerate
- Mechanism:
 - ↓ Blood pressure
 - ↓ Cardiac Remodeling (especially in patient who had MI)





↓ O₂ DEMAND / ↑ O₂ SUPPLY

- NITROGLYCERIN → ↓ PRELOAD → ↓ SV
⊖ RV-MI → CORONARY VASODILATOR
- MORPHINE → ↓ PRELOAD → ↓ SV
→ ↓ AFTERLOAD
- BETA BLOCKERS → ↓ CONTRACTILITY
(± CCB) → ↓ HR
- OXYGEN → IF HYPOXIC

↑ REVASCULARISATION

Figure 32. IHD Treatment -Reduce Oxygen demand.

(1) Nitroglycerin

- Mechanism
 - Vasodilator (→ ↑ Diameter → ↓ resistance → ↓ BP)
 - Dilation of the **Venous system** → ↓ Preload → ↓ SV → ↓ O₂ demand
 - Vasodilation of the **coronary vessels** → increase perfusion of the ischemic cardiac tissue
- Contraindication
 - Avoided in patients who are **PRELOAD** dependent such as **Right Ventricular MI**
 - Phosphodiesterase inhibitor
 - Aortic Stenosis

(2) Morphine

- Mechanism
 - Vasodilator
 - Venous Dilation → ↓ Preload → ↓ SV → ↓ O₂ demand
 - Arteries Dilation → ↓ Resistance → ↓ Afterload → ↓ O₂ demand
- Some studies suggest it may have adverse effect on outcome
 - For refractory Ischemic patients
 - Reserved for patients with an unacceptable level of pain

(3) Beta Blockers

- Mechanism
 - Beta-1 receptors locations:
 - SA node, AV nodes and Bundle system

- Contractile unit of the Myocardium
- Beta-Blockers
 - Block Beta-1 receptors on the contractile unit of the myocardium → ↓ contractility → ↓ O₂ demand
 - Inhibit conduction system → ↓ HR → ↓ O₂ demand

(4) Calcium Channel Blockers

- Sometimes can be added to the treatment plan
- Mostly Dihydropyridines such as
 - Amlodipine
 - Nicardipine
 - Nimodipine
 - Nifedipine
- Mechanism
 - Act mainly on Vascular Smooth Muscle → Vasodilation of the arteries → ↓ Afterload → ↓ O₂ demand
 - Vasodilation of the coronary arteries
 - Some of them may block calcium channels on the heart and may reduce HR → ↓ O₂ demand
- Contraindications
 - Decompensated heart failure (Weak Heart)

(5) Oxygen

- In patients with Hypoxia → Supplemental O₂ → ↑ O₂ supply



(C) REVASCULARIZATION

- Overall Indications:
 - Severe chest pain
 - STEMI
 - NSTEMI and Unstable Angina refractory to medical treatment
 - Start developing complications such as :
 - Heart Failure
 - Left Ventricular dysfunction

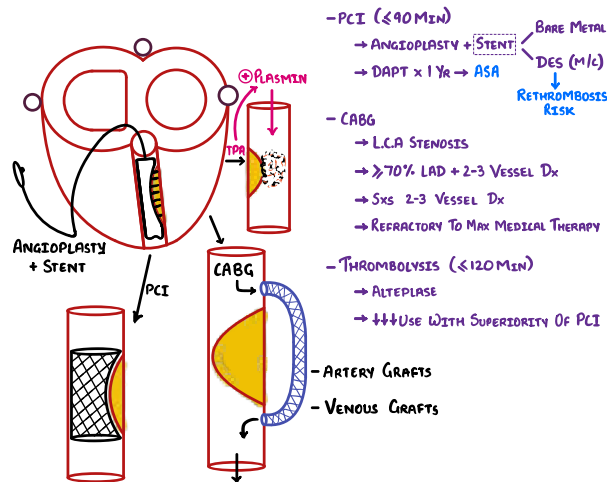


Figure 33. IHD Treatment- Revascularization.

(1) Percutaneous Coronary Intervention (PCI)

- Timeframe ≤ 90 mins
 - door-to-balloon time
 - time from presentation at a percutaneous coronary intervention (PCI) center to first balloon inflation

Indications:

- Preferred for patients with STEMI, NSTEMI, Unstable Angina with elevated troponin and high TIMI score not benefited from medical therapy
- Stable Angina ≥ 70 % stenosis , positive stress test
- Hemodynamically unstable

Mechanism:

- Angioplasty + Stent

Selection of Stent type:

- bare-metal stents (BMS)
- Drug-eluting stents (DES) (Most common, preferred)
 - antirestenotic drug → inhibit growth around the stent → prevent excessive intimal hyperplasia → reduce the risk of restenosis
- Common complication with stents → **Re-thrombosis**
 - Dual Antiplatelet Therapy (DAPT) for at least a year
 - Clopidogrel + ASA
 - Ticagrelor + ASA
 - After a year the risk of restenosis and Re-thrombosis may reduce but should stay on Aspirin

(2) Coronary Artery Bypass Graft surgery (CABG)

Types of graft:

- Arterial grafts
 - Radial Artery
 - Internal Thoracic Artery
- Venous grafts (preferred)
 - Saphenous vein

Indications:

- Left main stem Coronary Artery Stenosis
- Significant stenosis (≥ 70%) of the proximal left anterior descending artery, with 2-vessel or 3-vessel occlusion
- Severe Chest Pain + 2-3 Vessels disease
- NSTEMI, Unstable Angina not responding to maximal medical treatment

(3) Thrombolysis

- Least preferred
- Timeframe ≤ 120 mins
 - patient's presentation and delivery of fibrinolytic therapy (door-to-needle time)

● Alteplase

Mechanism

- TPA=Tissue Plasminogen Activator → plasmin → fibrinolysis

Efficacy

- is inferior to PCI
- if timely primary PCI is not available → TPA → Normally after TPA the patient needs to have angiography and PCI

Contraindications

- Active bleeding
- Prior intracranial hemorrhage
- Recent surgery
- Severe hypertension

Mnemonic for Medical Management of Ischemic Heart Diseases

- MONA BASH-C
 - Morphine
 - Oxygen
 - Nitroglycerin
 - Aspirin
 - Beta Blockers
 - ACE-I
 - Statin
 - Heparin
 - Clopidogrel and other P2Y₁₂ Receptor inhibitors



VIII) APPENDIX

Table -9. Presentation of IHD when taking history

History (OPQRST)	Stable Angina
Onset	Stable Angina: 5-10 mins Unstable angina, NSTEMI and STEMI (Acute Coronary Syndrome): >10 mins
Provocation	Worse on exertion, improved on rest, also improves with Nitroglycerin → Suggestive of Stable Angina When it occurs at rest, but can intensify with exertion → Unstable angina, NSTEMI and STEMI (Acute Coronary Syndrome)
Quality	Squeezing / Stabbing/ Pressure "Feeling like an elephant is sitting on your chest"
Radiation	Left Arm, Left Neck, Left Jaw <i>Epigastric pain can be indicative of inferior STEMI</i>
Severity	Variable
Time	Constant

Table -10 RV vs LV MI clinical features

Right Ventricular MI	Left Ventricular MI
Lungs are clear	Pulmonary Edema
↓Preload → ↓SV → ↓CO → ↓BP (HOTN)	↓EF (Ejection Fraction) → HOTN
Jugular Venous Distension (JVD)	↓Perfusion → Cold, mottled skin, Pallor
Hepatomegaly + Ascites	
Edema in the lower extremities	
Sinus Bradycardia OR	<u>S4 heart sound</u>
AV block (degree depends on severity)	<u>Reflex</u> Tachycardia (↑HR)

Table -11. Summary of the coronary vessels and the leads involved when infarction occurs.

ARTERY	HEART PORTION SUPPLIED	LEADS INVOLVED
LAD	Anterior	V ₁ -V ₄
LCX	Lateral	I, aVL, V ₅ , V ₆
RCA	Inferior	II, III, aVF, right-sided leads
PDA	Posterior	V ₇ -V ₉

Table -12 Wide table sample

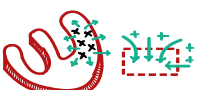
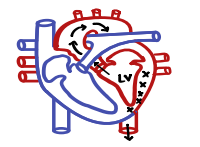
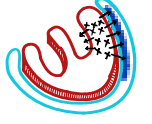
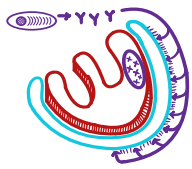
Type of IHD	Ischemia/Infarction	EKG	Troponin, CMB
Stable angina	Subendocardial ischemia	<u>No</u> ST ↑	(-)
Prinzmetal (vasospastic) angina	Transmural ischemia	ST ↑	(-)
Unstable angina	Subendocardial ischemia	ST ↓ + TWI	(-)
NSTEMI	Subendocardial infarction	ST ↓ + TWI	(+)
STEMI	Transmural infarction	ST ↑↑	(+)

Table -13 Categories of Ischemic Heart Disease

	Unstable Angina	Stable Angina	Subendocardial Infarct	Transmural Infarct
Plaque	Stable plaque	Unstable plaque	Unstable plaque	Unstable plaque
Occlusion	≥ 70%	≥ 90% Near total occlusion	≥ 90% Near total occlusion	100% Total occlusion
Clinical Features	Chest pain with exertion	Chest pain at rest; worsens with exertion	Chest pain at rest; worsens with exertion	Chest pain at rest; severe with exertion
Blood Flow	Subendocardial Ischemia	Subendocardial Ischemia	Subendocardial Infarction	Transmural Infarction (entire myocardium is affected)



Table 14. Summary of the Complications of Ischemic Heart Disease

Time	Complication	Mechanism	Clinical Manifestations	
0-24 hours	Sudden Cardiac Death	↑ cell permeability → ↑ cations load → depolarizes cells abnormally → ventricles contract abnormally → PVC → VT → VF → in Sudden Cardiac Death	Death	→ SCD → PVCs → VT → VF  → ACUTE HF  - HOTN → SHOCK - COLD EXT. - FLASH PULMONARY EDEMA - REFLEX ↑ HR
	Cardiogenic Shock	Occlusions of major coronary vessels → ↓ output to the systemic circulation resulting in hypotension → hypoperfusion → cardiogenic Shock	Cold Extremities	
	Flash Pulmonary Edema	Blood backs up into the pulmonary circulation leading to flash pulmonary edema	Shortness of breath, hypoxia Reflex Tachycardia	
24 hours – 3 days	Rupture Syndrome	Infarction in the interventricular septum → Rupture → Ventricular Septal Defect	Murmur (hollow systolic murmur) Mixed venous oxygenation	→ RUPTURE SYNDROMES  1) VSD - MURMUR ⊕ - MIXED VENOUS O₂ 2) FREE WALL RUPTURE - TAMPONADE 3) PAPILLARY RUPTURE - MR MURMUR 4) LV PSEUDOANEURYSM - ↑ THROMBI
		Infarction in the left ventricle → ruptures → blood can get into the pericardial cavity → Cardiac Tamponade	Beck's Triad occurs with cardiac tamponade, this consists of hypotension, JVD, and muffled heart sounds	
		Infarction in the papillary muscles → the tissue can get weak and rupture → valves flail causing Mitral Valve Regurgitation	Mitral valve murmur Hypotension Pulmonary Edema	
	Left Ventricle Pseudoaneurysm	In free wall ruptures, blood can accumulate in the pericardium and this can form a pseudoaneurysm	Mural thrombus	
3 days – 14 days	Pericarditis	Infarction in the left ventricle leads to a local inflammatory reaction to clean up the debris ➢ The inflammation can increase the formation of fluid, leading to pericardial effusion	Sharp & Positional Chest Pain Friction Rub (Via Lung Sounds) Pericardial Effusion	→ PERICARDITIS  → CP - SHARP - POSITIONAL - FRICTIONAL RUB - PERICARDIAL EFFUSIONS
14 days – 1 month	Left Ventricular Aneurysm	In an infarction, soft granulation tissue turns to fibrous tissue. ➢ Fibrous tissue can "bulge out" creating a left ventricular aneurysm ➢ <i>Blood stasis</i> of the affected area increases the risk of mural thrombi and emboli .	Shortness of breath Organ Damage	→ LV ANEURYSM  - MURAL THROMBI - ↑ EMBOLI
	Dressler's Syndrome (Pericarditis)	Infarction in the ventricles can create an underlying immune reaction, however the etiology is unknown ➢ The immune system develops antibodies against the pericardium → inflammation of the pericardium	Chest Pain Pericardial Effusion Dyspnea	→ DRESSLER SYND. 



IX) REVIEW QUESTIONS

- 1) Which of the following patients is at risk for atherosclerosis?
 - a) 58-year-old male with diabetes
 - b) 42-year-old female smoker
 - c) 31-year-old male with a BMI of 35
 - d) All of the Above
- 2) Which of the following characterizes stable angina?
 - a) Squeezing chest pain which occurs at rest
 - b) Plaque with a strong fibrous cap
 - c) ST elevation on EKG
 - d) Near total occlusion of coronary vessel
- 3) Which of the following is incorrect about subendocardial infarct?
 - a) Chest pain can occur at rest
 - b) There is thrombus formation
 - c) There is near total occlusion of coronary vessel
 - d) Unreversed ischemia was present for at least 2 hours
- 4) The following are categorized under Acute Coronary Syndrome except:
 - a) Stable Angina
 - b) Unstable Angina
 - c) NSTEMI
 - d) STEMI
- 5) Which of the following medications should be avoided in patients with Prinzmetal's angina?
 - a) Amlodipine
 - b) Nitroglycerin
 - c) Metoprolol
 - d) Nifedipine
- 6) The EKG of a patient complaining of chest pain shows depression of the ST segment and T wave inversion. Her troponin level is elevated. The patient might have:
 - a) Subendocardial ischemia
 - b) Transmural ischemia
 - c) Subendocardial infarction
 - d) Transmural infarction
- 7) Which of the following should be ordered once a patient who was admitted for MI experiences another chest pain?
 - a) EKG
 - b) Troponin
 - c) CK-MB
 - d) ANP
- 8) If the patient has ischemia on the inferior part of the heart, which of the following coronary vessels is involved?
 - a) LAD
 - b) LCX
 - c) RCA
 - d) PDA
- 9) A patient undergoing stress test has a baseline myocardial perfusion scan. Which of the following drugs should NOT be used to replicate stress?
 - a) Adenosine
 - b) Dobutamine
 - c) Dipyridamole
 - d) None of the above

10) An ECG shows ST elevation in II, III and aVF. What STEMI is indicated?

- a) Posterior STEMI
- b) Inferior STEMI
- c) Lateral STEMI
- d) Anterior STEMI

11) Aspirin is effective in ischemic heart disease treatment because:

- a) Inhibition of ADP production
- b) Analgesic effect
- c) Inhibition of TXA2 production
- d) Antipyretic effect

12) Which statement is false about the medications used in ischemic heart disease?

- a) Beta blockers decrease the Oxygen demand
- b) Morphine is contraindicated in Right Ventricular MI patients
- c) Nitroglycerin increase the perfusion to the Ischemic tissue
- d) Calcium Channel Blockers should be avoided in Decompensated Heart Failure patients

13) If a patient is presented with severe chest pain and occlusion of 3 vessels, which Revascularization approach is recommended?

- a) PCI
- b) CABG
- c) TPA+ PCI
- d) TPA

X) REFERENCES

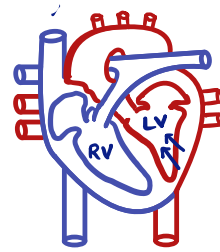
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OUTLINE

- I) OVERVIEW
- II) CAUSES
- III) PATHOPHYSIOLOGY
- IV) COMPLICATION
- V) DIAGNOSIS
- VI) TREATMENT
- VII) APPENDIX
- VIII) REVIEW QUESTIONS
- IX) REFERENCES



I) OVERVIEW

(A) DEFINITION

- **Cardiomyopathy** is there some type of disease or there is something that is **causing problems with the myocardium of the heart**
 - There are issues where there's **decreased function of the myocardium** of the heart
 - Usually, it's not due to ischemic cause or valvular disease

(B) TYPES

- **Types of cardiomyopathies** [Brieler, Jay et al., 2017]
 - Arrhythmogenic (ARVD/C)
 - Dilated
 - Hypertrophic
 - Restrictive

(C) CAUSES

- The most common cause of someone developing dilated cardiomyopathy is **idiopathic**
 - We don't really know why
- There may be some suspicion that there's genetic involvement
 - 50% of cases that have dilated cardiomyopathy is usually due to idiopathic
 - Maybe there's some kind of familial relationship

II) CAUSES

OVERVIEW

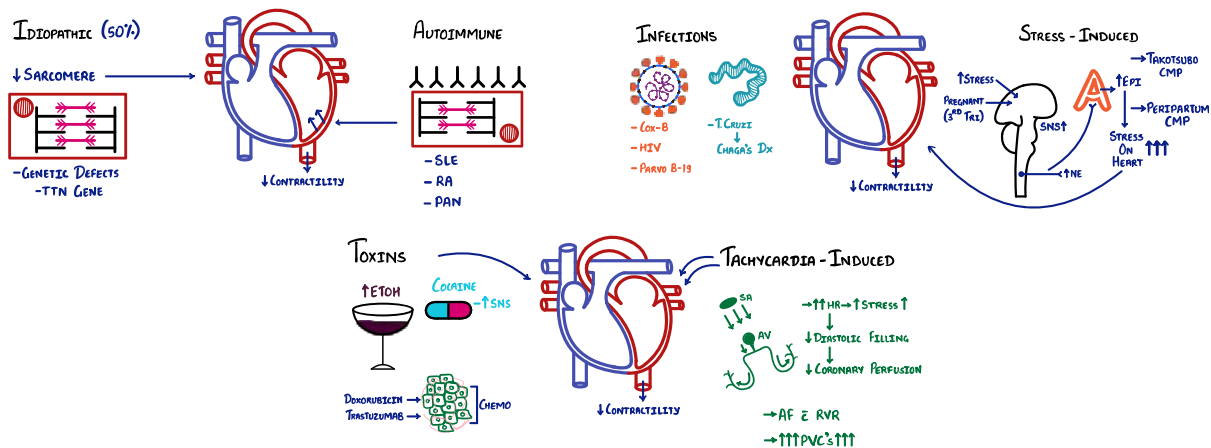


Figure 1. Causes of dilated cardiomyopathy

Causes of dilated cardiomyopathy

- **Idiopathic**
 - TTN gene
- **Autoimmune**
 - Systemic lupus erythematosus
- **Infection**
 - Cox-B
 - HIV
 - Parvo B-19
 - *Trypanosoma cruzi*
- **Stress-induced**
 - High emotional stress
 - Pregnancy
- **Toxins**
 - Cocaine or methamphetamine
 - Doxorubicin, trastuzumab
- **Tachycardia-induced**
 - Atrial fibrillation (AFib)
 - High PVC burden
- **Metabolic**
 - Adrenal medulla cancer (pheochromocytoma)
 - Vitamin B₁ deficiency
 - Thyroid gland cause



(A) GENETIC DEFECTS

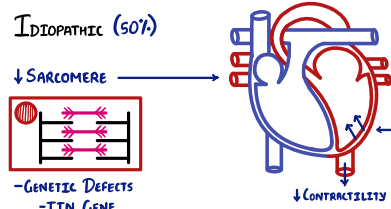


Figure 2. Genetic defect

Most common (50% of the cases)

Etiology

- Probably affects **TTN gene**
 - Controls different proteins that are **connecting different parts of the sarcomere proteins**
 - Sarcomere is the structural and functional unit of the actual muscle
- Remember sarcomere is the structural and functional unit of the actual muscle

Pathophysiology

- If there's genetic defect in the sarcomere
 - Decrease in the sarcomere function → **decrease ventricular contractility**
 - Reduction in cardiac output**
- Reduction in cardiac output causes ventricles trying to come up with
 - Dilating** the ventricles
 - Trying to make their ventricles a little bit **thinner**

(B) AUTOIMMUNE

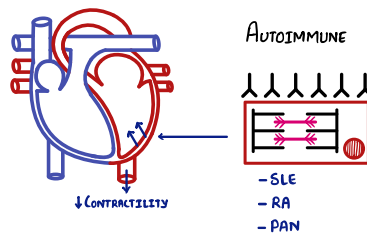


Figure 3. Autoimmune

Etiology

- Systemic lupus erythematosus (SLE)
- Polyarteritis nodosa (PAN)

Pathophysiology

- Develop certain types of autoantibodies** and cause particular destruction of the actual myocyte
 - Destroy myocyte → destroy functional unit of the cardiac muscle
 - Decrease in the contractility** of the muscle → **reduction in cardiac output**

(C) INFECTIONS

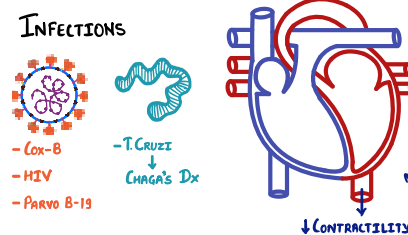


Figure 4. Infections

Etiology

- Coxsackie B virus (Cox-B)
- HIV
- Parvovirus B19
- Trypanosoma cruzi**

Pathophysiology

- May actually cause myocarditis
 - Inflammation of the myocardium** → decrease the function of the myocardium
 - Decrease in contractility**

Trypanosoma cruzi

- High yield material**
- Nasty bug that leads to the disease called **Chagas disease**

Clinical vignette that may present

- Patient went traveling maybe in **South America** or **Africa** and came back
- Having these conditions**
 - Low-grade fever
 - Periorbital swelling
 - Having difficulty swallowing
 - Mega esophagus
 - Had difficulty being able to eliminate feces
 - Because they have a mega colon
 - Chest pain or cardiomyopathy



(D) STRESS-INDUCED

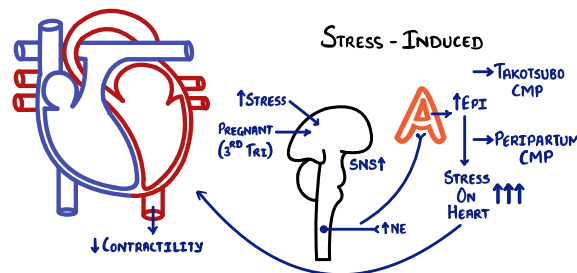


Figure 5. Stress-induced

Etiology

- **High emotional stress** → **Takotsubo cardiomyopathy**
 - E.g., due to emotional stressor or loss of a loved one
- **Pregnancy** → **Peripartum cardiomyopathy**
 - Particularly **third trimester** up to about **six months postpartum**

Takotsubo cardiomyopathy

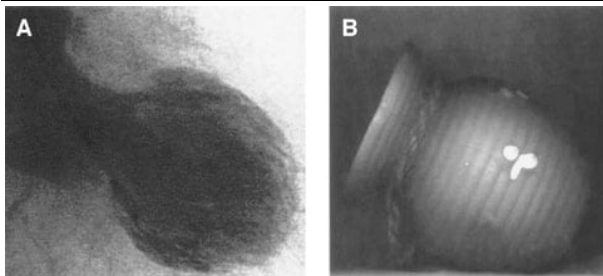


Figure 6. Takotsubo cardiomyopathy
(A) ventriculogram (B) takotsubo pot [Buttner, R., & Burns, E., 2021]

- This cardiomyopathy is named after the takotsubo pot due to LV appearance like this pot [Buttner, R., & Burns, E., 2021]

Peripartum cardiomyopathy

- Around the time periods of pregnancy can put a lot high degrees of stress on the body
 - Particularly **third trimester** up to about **six months postpartum**

Pathophysiology

- Put a lot of stressors on **sympathetic nervous system**
 - Sympathetic nervous system on **high activation** due to high stress state
 - **Increase the release of norepinephrine**
- Norepinephrine **stimulates adrenal medulla** to increase the secretion of epinephrine that works on the heart
 - Puts tons of stress on the heart
 - Increase the contractility of the heart and heart rate
- Overtime increase stress on the heart for a long time (**acute intense stress on the heart**)
 - Heart starts to go into a failure state

(E) CARDIOTOXINS

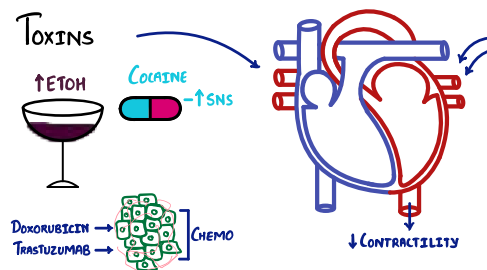


Figure 7. Cardiotoxins

Etiology

- Cocaine or methamphetamine usage
- Doxorubicin / daunorubicin /trastuzumab

Alcohol abuse

- Too much alcohol can put a lot of stress on the heart
- Those toxins can put a lot of **destruction to the actual cardiac cells**
 - Less cardiac tissues to maintain enough contractility
 - Decrease in contractility
 - Decrease in the cardiac performance overall

Cocaine or methamphetamine

- Similar effect to **sympathomimetic surge**
- Lots of norepinephrine and epinephrine causes
 - Vasoconstriction
 - Increase contractility
 - Increase heart rate
- These puts lots of stress for the heart

Doxorubicin / daunorubicin / trastuzumab

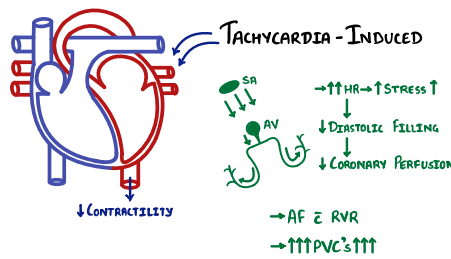
- Chemotherapeutic agent → kill cancer cells
- Trastuzumab is a breast cancer drug

Clinical vignette

- Taking some type of medication for their chemo and start developing dilated cardiomyopathy
- **Think about these agents**



(F) TACHYCARDIA-INDUCED



Etiology

- **SA node firing excessively** or there's some type of **ectopic focus**
 - Regardless there's lots of electrical activity going on throughout this conduction system

Pathophysiology

- **Super high heart rate put a lot of stress on the heart**
 - **Reduce diastolic filling**
 - Less time for the myocardium to get perfusion
- **Reduction in coronary perfusion** causes
 - Reduce O₂ delivery to the myocardium
 - This gives lots of stress on the myocardium
- Stress over long periods of time
 - Cause myocardium to just tuck up and give up

"Hey, I can't maintain this high degree of stress that you're continually requiring of me. I'm gonna have to start slowing down"

- This tachycardia overtime can lead to tachycardia-induced cardiomyopathy

May see this condition in patients with

- **Atrial fibrillation**
 - With a rapid ventricular rate
- **High PVC burden**
 - If someone has tons of PVCs over a long period of time
 - Put lots of stress on myocardium
 - Over time reduce contractility

(G) METABOLIC

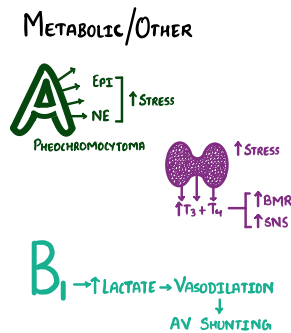


Figure 8. Metabolic cause

Etiology

- Adrenal medulla cancer → pheochromocytoma
- Thyroid gland cause

Adrenal medulla cancer (Pheochromocytoma)

- Adrenal medulla cancer that pumping out tons of **epinephrine and norepinephrine**
 - High amount of epinephrine and norepinephrine increase the stress on myocardium
- **Effects**
 - Increase contractility
 - Increase afterload
- These causes lots of stress → heart will tuck out
 - Reduced contractility

Vitamin B₁ (Thiamine) deficiency

- Remember thiamine is needed to **stimulate pyruvate dehydrogenase**
 - Convert pyruvate to Acetyl-CoA
- **No pyruvate dehydrogenase → can't generate Acetyl-CoA**
 - Pyruvate starts shunting into **making lots of lactate**
 - **Lactate causes vasodilation**
- Vasodilating vessels leads to **AV shunting**
 - Remember blood flowing from arteriole to venule has to go through capillary bed
 - **If we vasodilate them → blood runs through those capillary bed really fast**
 - Doesn't get enough time to be able to dribble off some O₂
- Heart has to work harder to be able to pump more blood to those tissue
 - Because we're just **shunting the blood so quickly**
 - **We're not giving enough time for O₂ delivery**
- Heart doesn't know that → keeps working harder and harder → eventually tuck out

Thyroid gland

- Pumping tons of thyroid hormone → **increases basal metabolic rate**
 - Increase sympathetic nervous system
 - This gives more stress to heart
 - Long period of stress → dilated cardiomyopathy

(H) MNEMONIC

A ALCOHOL ABUSE
BUNCH OF STUFF **B**ERI BERI (WET)
CAN COXSACKIE B MYOCARDITIS
CAUSE CHRONIC COCAINE USE
CARDIAL CHAGA'S DISEASE
DILATION DOXORUBICIN TOXICITY

Figure 9. Dilated cardiomyopathy causes mnemonic

- **A** Bunch of stuffs **C**an **C**ause **C**ardiac **D**ilation
 - Alcohol abuse
 - Beri-beri (wet)
 - Vitamin B₁ deficiency
 - Coxsackie B myocarditis
 - Chronic cocaine use
 - Chagas disease
 - Caused by *Trypanosoma cruzi*
 - Doxorubicin & daunorubicin



III) PATHOPHYSIOLOGY

OVERVIEW

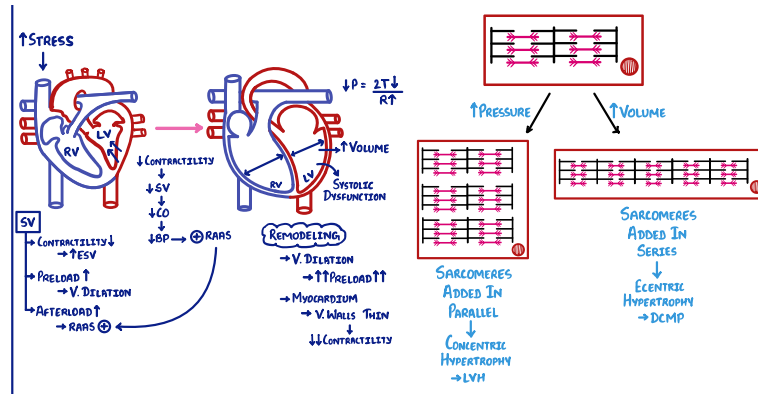


Figure 10. Pathophysiology of dilated cardiomyopathy

- When we have a patient who has this issue
 - They have **reduced contractility**
- This is due to putting lots of stress onto the heart from the different things mentioned earlier
 - Work harder overtime → heart isn't able to maintain that demand → cardiac contractility drops
 - Reduction in contractility** → potentially **reduce stroke volume** → **reduce cardiac output** → **drops blood pressure**
 - Remember that

$$CO = HR \times SV$$

$$BP = CO \times TPR$$

- This causes heart compensation → compensates in a way we don't like it → dilated cardiomyopathy

(A) FACTORS AFFECTING STROKE VOLUME

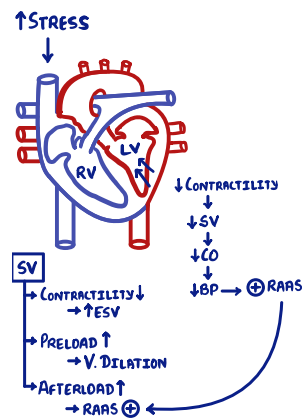


Figure 11. Factors affecting stroke volume

Contractility

- Patient with dilated cardiomyopathy **won't be able to pump much blood out of ventricle** → **high systolic volume**
 - More blood that's staying within the ventricles** even after the ventricles contract
- Ventricles are starting to get filled with blood** because can't pump enough it out

Preload

- Preload** is amount of **blood that gets into the heart** during the **diastolic process**
 - Whenever heart is relaxing → more blood coming it → more preload
- If we need to **increase preload** → need to **make ventricles bigger**
 - Bigger lumen diameter of the ventricle
 - Causes **ventricular** and possibly atrial **dilation**

Afterload

- Afterload is altered by **renin-angiotensin-aldosterone system (RAAS)**
 - Low cardiac output → **drops blood pressure**
 - Low BP stimulate RAAS → **increase afterload**
- One thing that heart tries to fix
- Heart does this stuff
 - "Okay, I'm gonna try to increase my preload. So in order for me to be able to increase my preload, I'm going to dilate my ventricle"
- Right and left ventricles are dilated
 - Whole point of being dilated is to **accommodate more volume**
 - This increase preload
 - Then increase stroke volume
- Unfortunately, this can work to disadvantage



(B) CARDIAC REMODELING

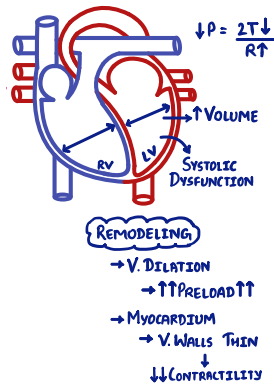


Figure 12. Cardiac remodeling – eccentric hypertrophy

- What happens next is, we go through a process called **remodeling process**
 - Causes ventricular dilation

The thought

- Increase the actual ventricle
 - Increase preload → increase stroke volume

Problem

- Increase preload a little bit too much
- Remember **Frank Starling's law**
 - "As you stretch the sarcomere, if you get it to the **optimal stretching point**, the contraction increases"
 - Basically
 - Increase stretch → increase contraction**
- If you stretch the sarcomere **too much beyond their point of optimal contractility**
 - Contractility goes down
- Because ventricles dilate, myocardium has to go through remodeling process
 - Myocardium has to actually accommodate all of these higher volume
 - The actual ventricular walls will actually start to be thinner
 - This drops the actual contractility even more

Cardiac remodeling type

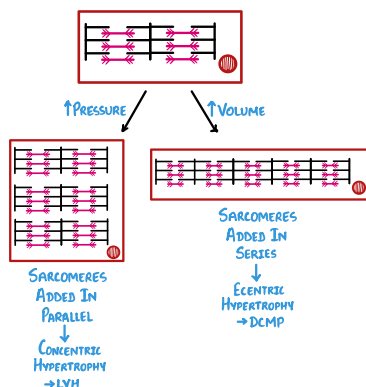


Figure 13. Cardiac remodeling type

- Put the myocardium cells under a high degree stress because of these two situations
 - High **volume** state
 - High **pressure** state
- We have two of these sarcomeres in a line

(i) High volume stress

- If we put the actual muscle cells under high degree of **volume stress**
 - Sarcomeres are added in **series**



Figure 14. Sarcomeres are added in series

- This causes them to go through a special type of hypertrophy → **eccentric hypertrophy**
 - Causes the ventricles to become **thin**
 - And allow for the actual lumen of the left ventricle to dilate to accommodate these high volume

- Disease**
 - Dilated cardiomyopathy

(ii) High pressure stress

- If we put the actual muscle cells under high degree of **pressure stress**
 - They have to be able to work hard against a high degree of pressure
 - Sarcomeres are added in **parallel**

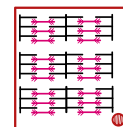


Figure 15. Sarcomeres are added in parallel

- This causes them to go through a special type of hypertrophy → **concentric hypertrophy**
 - In this condition, causes the ventricle to get **thicker** → myocardium thickness will increase

- Disease**
 - Left ventricular hypertrophy in condition due to
 - Hypertension
 - Aortic stenosis

Quick recap – Dilated cardiomyopathy

- Reduction in contractility
 - Ventricles trying to remodel by **increasing preload**
 - Get **volume overloaded**
 - Dilate the lumen** of the ventricle
- Ventricle walls get thin due to **eccentric hypertrophy** → **contractility drops**



(C) LAPLACE'S LAW

• Formula

$$P = \frac{2T}{R}$$

Symbol	Explanation
P	Collapsing pressure of ventricle • Pressure to pump the blood out
T	Tension • Represents contractility (force that the myocardium generate)
R	Ventricle lumen diameter

Problem within this patient

- Diameter of the ventricle really increased
- Because the ventricular walls get really thin → contractility and the tension, the force that they can generate drops

Interpretation

- If the **tension** drops → **collapsing pressure drops**
 - Imagine this ventricle had to **collapse and push blood out**
 - This is the pressure and a way to think about this
- If the **radius** goes up → **collapsing pressure drops**
- These put a person into a situation where they aren't able to eject enough blood → **systolic dysfunction**

IV) COMPLICATION

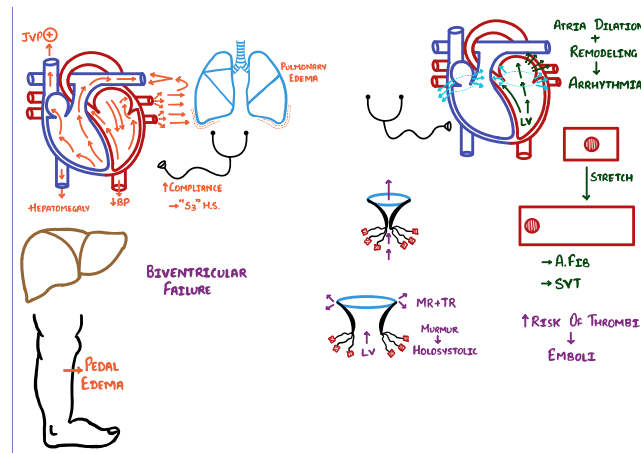


Figure 16. Complications of dilated cardiomyopathy

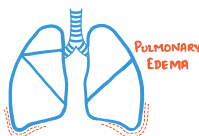
(A) BIVENTRICULAR FAILURE

Overview

- Dilated cardiomyopathy can cause biventricular failure
 - Often starts with the left ventricular failure
 - Produces right ventricular failure
- Left ventricle failing because now it is unable to generate enough pressure
 - To eject the blood out to the systemic circulation

Pathophysiology

- Blood starts accumulating in the left ventricle
 - Backs up into the left arteria
 - Backs up into the pulmonary circulation
 - Backs up into the pulmonary capillary area



- This causes fluid to start accumulating in the interstitial spaces → **pulmonary edema**

Common symptoms

- Difficulty of breathing
- Dyspnea
- Crackles or rales
 - Via auscultation
- Hypoxia
- Maybe even cough
- Low blood pressure
 - Small degree of hypotension

- These puts a lot of actual stress on the pulmonary circulation
 - **Right ventricle has to work harder** → over time right ventricle starts to fail
- **Can't pump blood outward to the pulmonary circulation**
 - Causes blood back up to the atria
 - Then down to inferior vena cava
 - Or up into superior vena cava

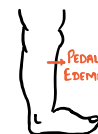
(i) Superior vena cava

- Up to the superior vena cava → brachiocephalic → jugular vein plumps
 - Causes **jugular venous distension**

(ii) Inferior vena cava



- Accumulate fluid around the liver → **hepatomegaly**



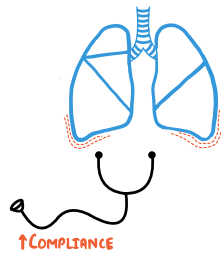
- Back up into the lower extremities → **pedal edema**

Table 1. Quick recap for right and left-sided heart failure

Right-sided failure	Left-sided failure
Jugular vein distension	Hypotension
Hepatomegaly	Pulmonary edema
Pedal edema	



S3 heart sound



- Whenever we have **systolic dysfunction**
 - Imagine left ventricle is very stretchy
 - Because it's very stretchy → **high amount of compliance**
- Whenever blood is coming from the atria into ventricle through the **diastolic filling process**
 - It can fill until whenever we get to that **maximum filling process** → **boom!**
- It causes pathological heart sound because of the **maximum compliance** of the ventricle → S3 sound
 - High yield for patients with dilated cardiomyopathy
- So, we have biventricular failure
 - With additional S3 heart sound

(B) HOLOSYSTOLIC MURMUR

Anulus rings and valves structure

- We have particular ring where our valves are → anulus type of ring
 - It's kind of a fibrous skeleton that's a kind of separation structure between the atria and ventricle
- When our **ventricle stretches**, anulus ring also **stretches**
 - Remember **tricuspid** and **mitral valve** hangs off the anulus rings

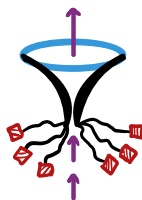


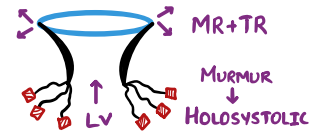
Figure 17. Anulus ring and valve structure

- Structures when we zoom in
 - Anulus
 - Valve flaps
 - Chordae tendinea connected to the papillary muscle

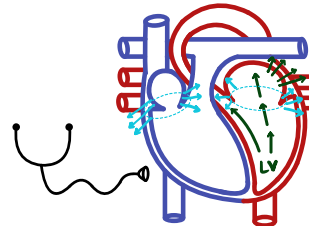
Normal physiology

- If the left ventricle is accumulating blood
 - Ventricle contracts → underwent systole process
 - Valves close and block blood from coming back into the atria
 - **No type of regurgitation**

Pathophysiology

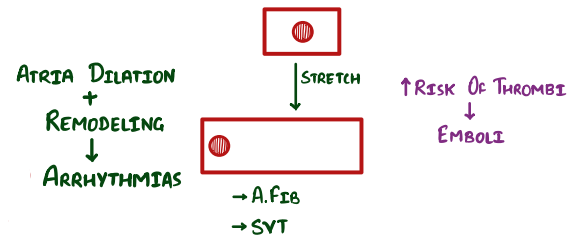


- Now whenever left ventricle tries to go through the systolic process and pump blood up
 - But the anulus is stretched
- The blood will kind of like regurgitate back into the atria on both places
 - Mitral regurgitation murmur (MR)
 - Tricuspid regurgitation murmur (TR)
- We give the term **holosystolic murmur (MR + TR)**



- Whenever the person is through the **systolic period/contractile phase**
 - From the S1 and the way to S2
 - We'll be able to hear the **whooshing sound**
 - Where blood is going through the actual valves back into the atria

(C) ELECTRICAL REMODELING



- With these actual atria and ventricle
 - They're both stretching
- Whenever this all remodeling process occur because blood is backing up into the atria
 - Atria undergo a remodeling process to accommodate larger volume
 - Atria also can undergo dilation process
- Atria undergo **electrical remodeling**

"Atria don't like being stretched"

- When we stretch those atria cells
 - They get ticked off and **alter the electrical activity** →
 - This lead to atrial arrhythmia

Atrial arrhythmia

- **Atrial fibrillation**
 - More common
 - High risk of forming thrombi in the **left ventricle**
 - **Because of decreased systolic function**
 - They form thrombus in their left atrium because ventricle isn't contracting
 - While blood's sitting within that area → increased risk of embolizing
- **Supraventricular tachycardia**



V) DIAGNOSIS

OVERVIEW

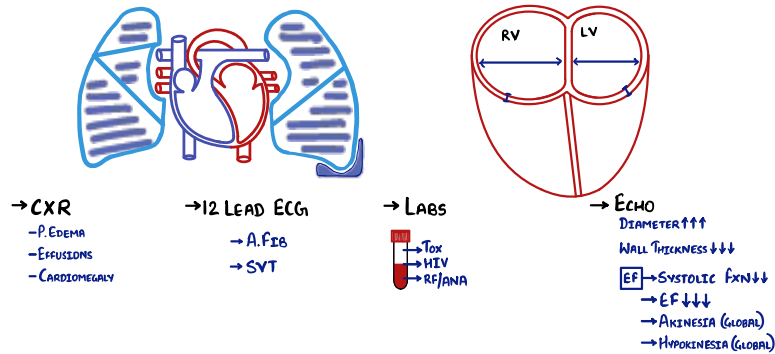


Figure 18. Diagnosis of dilated cardiomyopathy

- **Things to diagnose dilated cardiomyopathy**
 - Echocardiogram
 - Chest X-Ray
 - 12-lead EKG
 - Lab
 - Medical history
- Anytime a patient comes in and they see us
 - We don't automatically think of "Oh, this is dilated cardiomyopathy for sure"
 - They present with symptoms that **we want to rule out the more significant fatal deadly causes**

- They may present with
 - Chest pain
 - Dyspnea / shortness of breath
 - Palpitation
- We want to **rule out** certain type of **cardiopulmonary causes** such as
 - Full blown
 - Acute decompensated heart failure
 - Myocardial infarction (MI)
 - Pulmonary process going on

(A) CHEST X-RAY

- Get chest X-ray if the patient present with
 - Short of breath
 - Crackles or rales on auscultation

Findings from CXR

- **Pulmonary edema**
 - They got fluid all up in the lung
 - Because **left ventricular systolic failure** is causing fluid to back up
- **Pleural effusion**
- **Cardiomegaly**
 - **Nonspecific signs**
 - This sometimes would make us think "Oh, they got a heart failure"
 - Sometimes this is the common symptom of patients with dilated cardiomyopathy

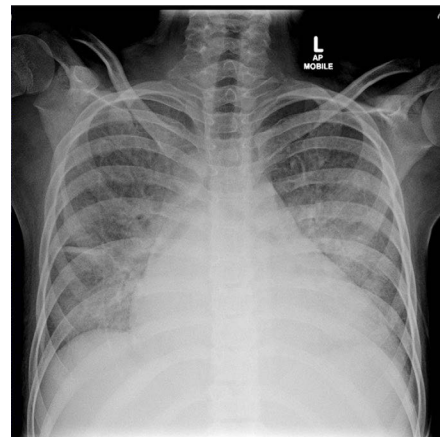


Figure 19. Chest X-Ray findings (nonspecific) [Dixon, 2010]

(B) 12-LEAD EKG

- We should always get 12-lead EKG if patients are having
 - Shortness of breath
 - Chest pain
 - Palpitation

Findings from 12-lead EKG

- Dilating atria → shows atrial fibrillation
- Shows some type of supraventricular tachycardia
 - These are not tests that are going to tell me anything about dilated cardiomyopathy
 - It's just helping to rule out other particular causes

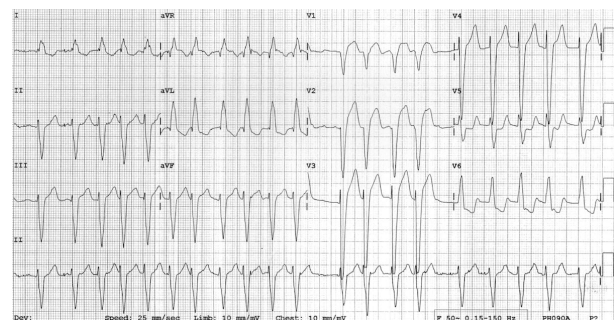


Figure 20. Example of dilated cardiomyopathy 12-lead EKG

[Buttner, R., & Burns, E., 2021]

Table 2. Diseases that Chest X-Ray and 12-lead EKG rule out on diagnosing dilated cardiomyopathy

Chest X-Ray rules out	12-lead EKG rules out
• Pneumonia • ARDS • Pneumothorax	Any type of ischemia • ST segment elevation • MI



(C) ECHOCARDIOGRAM

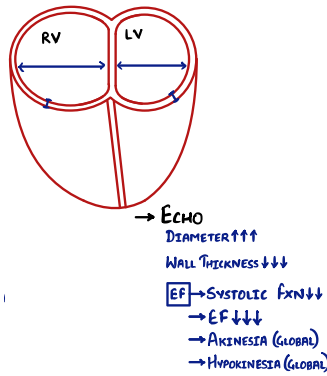


Figure 21. Echocardiogram

- Parameters that we check with echo
- Definitive test

Diameter

- Increased diameter of the left ventricle**
 - Or also potentially right ventricle if they have biventricular failure

Wall thickness

- Really thin/decreased wall thickness**
 - Because of the ventricular dilation → myocardium had to go undergo the eccentric hypertrophy
 - To allow for the volume overload state

Ejection fraction

- Systolic function is decreased**
- Expect ejection fraction would be reduced → HFrEF
 - Heart failure reduced ejection fraction
- They may have **akinesia or hypokinesia** (global)
 - Entire left ventricle would just not produce a lot of contractility
 - Because all of their left ventricle is super thinned

(D) LABS

→ LABS



Figure 22. Labs

- Rule out the etiology/cause of someone having a dilated cardiomyopathy
- Most common cause → idiopathic
 - We're not doing any genetic testing in this patient
 - It's not going to really going to yield a lot of information

Toxicology screening

- Rule out any type of alcohol abuse or cocaine, methamphetamine usage

Viral panel

- Coxsackie B virus not really necessary
- HIV test necessary

Autoimmune disease

- Check for
 - ANA
 - Rheumatoid factor (RF)

(E) PATIENT HISTORY

- Stress states**
 - Takotsubo cardiomyopathy** → ask about any kind of emotional stressor
 - Postpartum cardiomyopathy**
 - Pregnant
 - Within their third trimester at least less than 6 months postpartum

- We might not need labs to really determine this
 - Sometimes it's looking through the medical history
- If we want to test for certain disease
 - Think about those causes and things that we could order to determine those causes



VI) TREATMENT

OVERVIEW

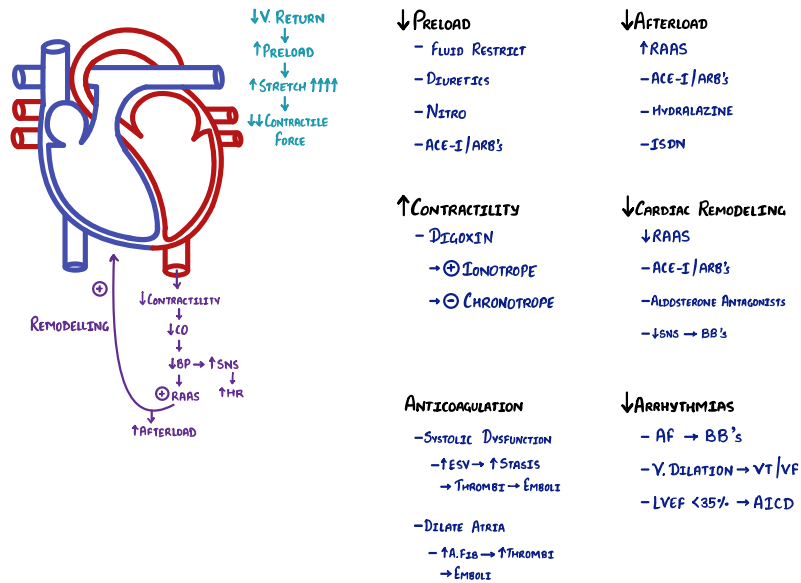


Figure 23. Treatment for dilated cardiomyopathy

Quick recap

- **Reduction in cardiac contractility**
 - Lead to reduction in cardiac output → reduction in blood pressure
 - Stimulate RAAS → lead to increase in cardiac remodeling → left ventricular dilation
 - Ventricle walls super thin → ejection fraction drops
 - RAAS also leads to increase in afterload → angiotensin II causes vasoconstriction of the arterial
 - If we constrict the arteriole → increase the pressure within the arteries → puts lots of stress on left ventricle
 - Heart tries to increase preload → dilate the ventricle too much
- **Frank Starling's law**
 - Increased preload → increased stretch → increased contractile force at optimal length
 - Stretch out the ventricle beyond optimal length → **drop contractile force**

Treatment

Table 3. General condition and treatment for dilated cardiomyopathy

Condition	Treatment
Increased preload • Will cause ventricles to stretch way too much • Reduce contractile force	Give drugs to reduce preload and lifestyle change
High afterload	Give drugs to reduce afterload
Decreased contractility	Give drugs to increase the contractility of the ventricles
Remodeling	Give drugs to reduce cardiac remodeling
Atrial fibrillation and systolic function drops • High risk of clots	Give anticoagulants
Thinning atria and ventricles • Put them at risk for ventricular tachycardia, ventricular fibrillation	Give antiarrhythmic drugs or AICD

(A) REDUCE PRELOAD

- **This also reduces venous return**
- **Achieve less fluid/less volume within the blood**
 - Fluid and sodium restriction
 - Get rid of the fluid → diuretics
 - Treatment is similar with heart failure
- **Nitroglycerin**
 - It causes vasodilation → less pressure to push up blood into atria and ventricle → less venous return
- **Inhibit angiotensin II**
 - Remember angiotensin II causes arterial vasoconstriction, venoconstriction
 - Give them **ACE-I and ARB**

(B) REDUCE AFTERLOAD

- High afterload due to **high amount of RAAS activity**
 - Give drugs that **inhibit** this → **ACE-I and ARB**
- **Vasodilate arteries** and reduce afterload
 - Hydralazine
 - Isosorbide dinitrate

(C) INCREASE CONTRACTILITY

- Increase the **inotropic** action → **digoxin**
 - Positive inotropic → **increase contractility**
- **Negative chronotropic**
 - **Reduce heart rate**
 - Useful in patient with atrial fibrillation



(D) INHIBIT CARDIAC REMODELING

- Dependent upon **RAAS** and **sympathetic nervous system**

Reduce activity of RAAS

- **ACE-I** and **ARB**
- **Aldosterone antagonist**
 - Spironolactone, eplerenone

Reduce activity of sympathetic nervous system

- Remember high sympathetic nervous system activity → increase heart rate to increase blood pressure
- **β-blockers**
 - Metoprolol, esmolol
- Consider **calcium channel blocker**
 - Not the best thing to do
 - **Avoid especially if they have very decompensated heart failure**

(E) ANTICOAGULANT

Forming of clots

(i) Systolic dysfunction

- Due to **systolic dysfunction** → reduction in contractility
 - Not able to push as much blood out of the heart
- Remember volume of blood that sits in the heart after systolic → **systolic volume**
- More blood sitting in the heart → blood not moving →
 - Increases risk of stasis of blood flow
- **Virchow's triad**
 - Increase stasis → increase the risk of clots
 - Increase the risk of forming thrombi → can quickly break off and form emboli

(ii) Atrial fibrillation

- Dilate the atria → causes them to electrical remodeling process
 - Increase risk of AFib → increase the risk of thrombi
- Because they **don't have very good contractility in the atria** → **blood starts accumulating**
 - **Same process as previous**

Consider anticoagulants

- **Warfarin**
 - If they have valvular issue like they have mechanical heart valve
- **DOAC**
 - Rivaroxaban, apixaban, dabigatran
- These will **prevent them from developing embolic stroke**

(F) REDUCE RISK OF ARRHYTHMIA

- Consider **β-blocker**
 - Atrial fibrillation benefit from this
- Consider **calcium channel blocker**
 - With the ventricular dilation
 - Can also stretch those ventricles → become irritated → electrically remodeled → lead to VTac, VFib
 - Can cause someone to go into sudden cardiac death
- **AICD**
 - Automatic implantable cardiac defibrillator
 - **Certain situation where patient is having**
 - Arrhythmia that are **high risk of ventricular tachycardia, ventricular fibrillation**
 - **Left ventricular ejection fraction < 35%**
 - We don't want to waste any time
 - Reduce the risk of going into VTac, VFib and actually having a sudden cardiac death
 - Whenever they go into VTac or VFib
 - It will shock them to prevent them from going into a sudden cardiac that type of issue

VII) APPENDIX

Table 4. Summary of causes of dilated cardiomyopathy

Causes		Pathophysiology
Idiopathic	• TTN gene	• Decrease in the sarcomere function → decrease ventricular contractility ◦ Reduction in cardiac output ◦ Dilating the ventricles ◦ Trying to make their ventricles a little bit thinner
Autoimmune	• Systemic lupus erythematosus • Rheumatoid arthritis • Polyarteritis nodosa	• Develop certain types of autoantibodies and cause particular destruction of the actual myocyte ◦ Destroy myocyte → destroy functional unit of the cardiac muscle ◦ Decrease in the contractility of the muscle → reduction in cardiac output
Infection	• Coxsackie B virus (Cox-B) • HIV • Parvovirus B19 • <i>Trypanosoma cruzi</i>	• Inflammation of the myocardium → decrease the function of the myocardium • Decrease in contractility
Stress—induced	• High emotional stress → Takotsubo cardiomyopathy • Pregnancy → Peripartum cardiomyopathy	• Put a lot of stressors on sympathetic nervous system ◦ Sympathetic nervous system on high activation due to high stress ◦ Increase the release of norepinephrine • Norepinephrine stimulates adrenal medulla to increase the secretion of epinephrine that works on the heart ◦ Puts tons of stress on the heart ◦ Increase the contractility of the heart and heart rate • Overtime increase stress on the heart for a long time (acute intense stress on the heart) ◦ Heart starts to go into a failure state ◦ Decrease in contractility



Cardiotoxic	● Alcohol abuse ● Cocaine or methamphetamine usage ● Doxorubicin / daunorubicin / trastuzumab	Alcohol abuse ● Put a lot of destruction to the actual cardiac cells ○ Less cardiac tissues to maintain enough contractility ○ Decrease in contractility ○ Decrease in the cardiac performance overall Cocaine or methamphetamine ● Similar effect to sympathomimetic surge ● Lots of norepinephrine and epinephrine causes ○ Vasoconstriction ○ Increase contractility ○ Increase heart rate ● These puts lots of stress for the heart
Tachycardia-induced	● Atrial fibrillation ● High PVC burden	● Super high heart rate put a lot of stress on the heart ○ Reduce diastolic filling ○ Less time for the myocardium to get perfusion ● Reduction in coronary perfusion causes ○ Reduce O₂ delivery to the myocardium ○ Gives lots of stress on the myocardium ● Stress over long periods of time ○ Cause myocardium to just tuck up and give up
Metabolic	● Adrenal medulla cancer (pheochromocytoma) ● Vitamin B₁ deficiency ● Thyroid gland cause	Adrenal medulla cancer (Pheochromocytoma) ● Adrenal medulla cancer that pumping out tons of epinephrine and norepinephrine ○ High amount of epinephrine and norepinephrine increase the stress on myocardium ● Effects ○ Increase contractility ○ Increase afterload ● These causes lots of stress → heart will tuck out ○ Reduced contractility Vitamin B₁ (Thiamine) deficiency ● Pyruvate starts shunting into making lots of lactate ○ Lactate causes vasodilation ● Vasodilating vessels leads to AV shunting ● Heart has to work harder to be able to pump more blood to those tissue ○ Because we're just shunting the blood so quickly ○ We're not giving enough time for O₂ delivery ● Heart keeps working harder and harder → eventually tuck out Thyroid gland ● Pumping tons of thyroid hormone → increases basal metabolic rate ○ Cells have to work harder ○ Increase sympathetic nervous system ○ This gives more stress to heart ○ Long period of stress → dilated cardiomyopathy



Table 5. Condition, pathophysiology, and treatment for dilated cardiomyopathy

Condition	Pathophysiology	Treatment
Increased preload	→ Increased preload → Cause ventricles to stretch way too much → Reduce contractile force	Drugs to reduce preload and lifestyle change • ACE-I • ARB • Diuretics • Nitroglycerin • Restrict fluid and sodium intake
Increased afterload	→ Increased afterload → High arterial pressure → Puts stress to heart	Drugs to reduce afterload • ACE-I • ARB • Hydralazine • Isosorbide dinitrate
Decreased contractility	→ Decreased contractility → Decreased cardiac output	Drugs to increase the contractility of the ventricles • Digoxin
Remodeling	→ Low cardiac output and blood pressure → Activation of RAAS → Cardiac remodeling	Reduce cardiac remodeling • ACE-I • ARB • Aldosterone antagonist ◦ Spironolactone ◦ Eplerenone • β-blockers ◦ Metoprolol ◦ Esmolol • Calcium channel blockers
High risk of atrial fibrillation and systolic function drop	→ Decreased contractility → Increased systolic volume → Stasis of blood → High risk of clots	Anticoagulants • Warfarin • DOAC ◦ Rivaroxaban ◦ Apixaban ◦ Dabigatran
Thinning atria and ventricle	→ Electrical remodeling → Put them at risk for ventricular tachycardia, ventricular fibrillation	Antiarrhythmic drugs, IACD • β-blockers • Calcium channel blockers

• Formulas

◦ Cardiac output

$$CO = HR \times SV$$

Symbol	Explanation
CO	Cardiac output • Amount of blood that's being pumped out from the heart per minute
HR	Heart rate • Beats per minute
SV	Stroke volume • Amount of blood that's being pumped out from the heart per beat • Equals venous return/preload ◦ Amount of blood that comes back to the heart per beat

◦ LaPlace's Law – With wall thickness [Nadruz, 2015]

$$P = \frac{2T \times h}{R}$$

Symbol	Explanation
P	Collapsing pressure of ventricle • Pressure to pump the blood out
T	Tension • Represents contractility (force that the myocardium generates)
R	Ventricle lumen diameter
h	Ventricle wall thickness

◦ Blood pressure

$$BP = CO \times TPR$$

Symbol	Explanation
BP	Blood pressure • Pressure exerted by blood to artery wall
CO	Cardiac output • Amount of blood that's being pumped out from the heart per minute
TPR	Total peripheral resistance • Affects afterload



VIII) REVIEW QUESTIONS

- 1) What is the most common cause of dilated cardiomyopathy?
 - a) Autoimmune
 - b) Coxsackie B virus
 - c) Idiopathic
 - d) Pregnancy
- 2) Which option below that contributes to stress-induced dilated cardiomyopathy?
 - a) Destruction of the cardiomyocytes
 - b) Ischemia due to coronary blood vessel occlusion
 - c) Renin-angiotensin aldosterone system
 - d) Sympathetic nervous system activation
- 3) Biventricular failure can be found in patient with dilated cardiomyopathy because left ventricle failure that causes pulmonary edema and eventually causes right ventricular failure
 - a) True
 - b) False

This scenario is used to answer question no. 4-9

A 35-year-old female patient present with chest pain and palpitation. She also has difficulty of breathing. She reported to have difficulty swallowing and eliminating feces. She denies contacting person with similar situation as her. She studied abroad in an African country around 10 years ago and came back 6 years ago. During physical examination, S3 heart sound, holosystolic murmur, and crackles were heard with auscultation. The other physical examination findings are unremarkable. 12-lead EKG shows atrial fibrillation and signs of LV hypertrophy based on Sokolow-Lyon criteria with no ST-elevation. Lab result shows no elevation in troponin and unremarkable toxicology screening result. CXR shows signs of enlarged heart with pulmonary edema.

- 4) What are the more probable causes this condition in this patient? (May choose more than 1)
 - a) Adrenal medulla cancer
 - b) Alcohol abuse
 - c) Autoimmune
 - d) Emotional stressor
 - e) Endurance exercise
 - f) Infection by *Trypanosoma cruzi*
 - g) Total occlusion of coronary artery vessels
 - h) Resistance exercise
- 5) Based on the information given, what are the differential diagnosis for this patient? (May choose more than 1)
 - a) Heart failure with preserved ejection fraction
 - b) Heart failure with reduced ejection fraction
 - c) Myocardial infarction
 - d) Pneumonia
 - e) Dilated cardiomyopathy
 - f) Hypertrophic cardiomyopathy
 - g) Myocarditis
 - h) Rheumatoid arthritis-associated cardiomyopathy

- 6) What other signs that you expect to find in this patient with further examination? (May choose more than 1)
 - a) Reduced ejection fraction
 - b) Increased thyroid hormone
 - c) Hypotension
 - d) Jugular venous distension
 - e) Hepatomegaly
 - f) Thinning of the ventricle wall
 - g) Hypokinesia of ventricle
- 7) What would you like to do next in order to ensure your diagnosis or decide treatment plan for this patient?
 - a) Activate cath lab
 - b) Ask question about previous emotional stressors
 - c) Ask question about past medication
 - d) Ask question about syncope history
 - e) Echocardiogram
 - f) MRI
 - g) *Trypanosoma cruzi* serology
 - h) HIV screening
 - i) 24-h Holter monitoring

- 8) In order to ensure the condition of the patient, you want to order echocardiogram. Echocardiogram shows increased diameter of the left ventricle with thinning of the ventricular wall. The patient's ejection fraction was 45%. What is your now current differential diagnosis?
 - a) Heart failure with preserved ejection fraction
 - b) Heart failure with reduced ejection fraction
 - c) Myocardial infarction
 - d) Pneumonia
 - e) Dilated cardiomyopathy
 - f) Hypertrophic cardiomyopathy
 - g) Myocarditis
 - h) Rheumatoid arthritis-associated cardiomyopathy
- 9) Assume that we've treated the underlying cause, what is another treatment plan for this patient? (May choose more than 1)
 - a) To reduce preload → lifestyle change by restricting fluid and sodium intake
 - b) To increase afterload → administer epinephrine via IV
 - c) To inhibit cardiac remodeling → prescribe ARB
 - d) Reduce risk of thromboembolism events → prescribe rivaroxaban
 - e) Reduce the risk of VTach and VFib → Implant AICD

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HYPERTROPHIC CARDIOMYOPATHY

Hypertrophic Cardiomyopathy

Medical Editor: Sohani Kashi Puranic

OUTLINE

- I) INTRODUCTION
- II) CAUSES
- III) CONSEQUENCES
- IV) PATHOPHYSIOLOGY, COMPLICATIONS, CLINICAL FEATURES
- V) MANEUVERS
- VI) DIAGNOSIS
- VII) TREATMENT
- VIII) SUMMARY
- IX) APPENDIX
- X) REVIEW QUESTIONS
- XI) REFERENCES

I) INTRODUCTION

(A) CARDIOMYOPATHY

Cardiomyopathy is a disease process affecting the heart where there is dysfunction of **myocardium**.
 → More commonly affects **left ventricle**
 → Cardiomyopathies are a heterogenous group of **disease of the myocardium** associated with **mechanical and/ electrical dysfunction** that usually exhibit inappropriate **ventricular hypertrophy or dilatation** and are due to a variety of causes that are frequently **genetic** [Robbins]

(B) TYPES

There are 3 distinct pathological patterns:

- (1) Dilated Cardiomyopathy
- (2) Hypertrophic Cardiomyopathy
- (3) Restrictive Cardiomyopathy

Among the 3 major patterns, DCM is most common (90% of cases), and Restrictive Cardiomyopathy is least frequent

(C) HYPERTROPHIC CARDIOMYOPATHY

HCM is a common (1 in 500 prevalence), clinically heterogenous, genetic disorder characterized by **myocardial hypertrophy**, **poorly compliant** left ventricular myocardium leading to **abnormal diastolic filling** and intermittent ventricular outflow obstruction.

[Robbins]

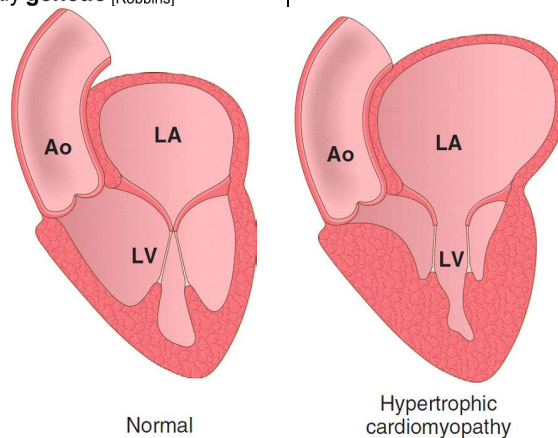


Figure 1. Normal Morphology of Heart & in HCM

[Robbins Pg. 568; Fig 12.28]

II) CAUSES

(A) GENETIC CAUSES

(1) Mutation in proteins in the sarcomere

- (i) Inheritance
 - **AUTOSOMAL DOMINANT** disorder
 - 50% familial
 - 50% sporadic
- (ii) Mutation
 - Heavy chain of **β subunit of myosin**
 - Single- point missense mutation
- (iii) Consequences
 - ↓ **sarcomere function**
 - ↓ cardiac function

(B) SECONDARY CAUSES

(1) Friedreich's ataxia

- (i) Inheritance
 - **AUTOSOMAL RECESSIVE** disorder
- (ii) Defect
 - Tri nucleotide repeat disorder (GAA)
 - Alterations in proteins of:

Tissue/ Cell Affected	Consequence
Myocytes	Hypertrophic Cardiomyopathy
CNS	Ataxia
Pancreas	Diabetes Mellitus

Table 1. Tissues affected in Friedreich's Ataxia

(2) Other Causes

- (i) Chronic Hypertension
- (ii) Aortic Stenosis
- (iii) Amyloidosis
- (iv) Fabry disease, Pompe disease

These causes ultimately lead to decreased sarcomere function



III) CONSEQUENCES

→ Decreased Sarcomere function puts the heart under stress. To overcome this, the following events occur:

- (1) Stimulation of myocytes to improve function
- (2) Myocytes secrete growth factors
- (3) Increased myocyte growth and thickness

(i) Macroscopically

- Asymmetric growth/ hypertrophy
→ Increased thickness of left ventricle, more in interventricular septum

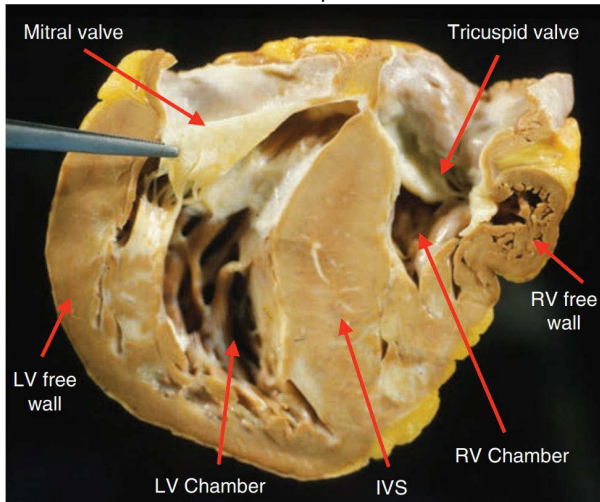
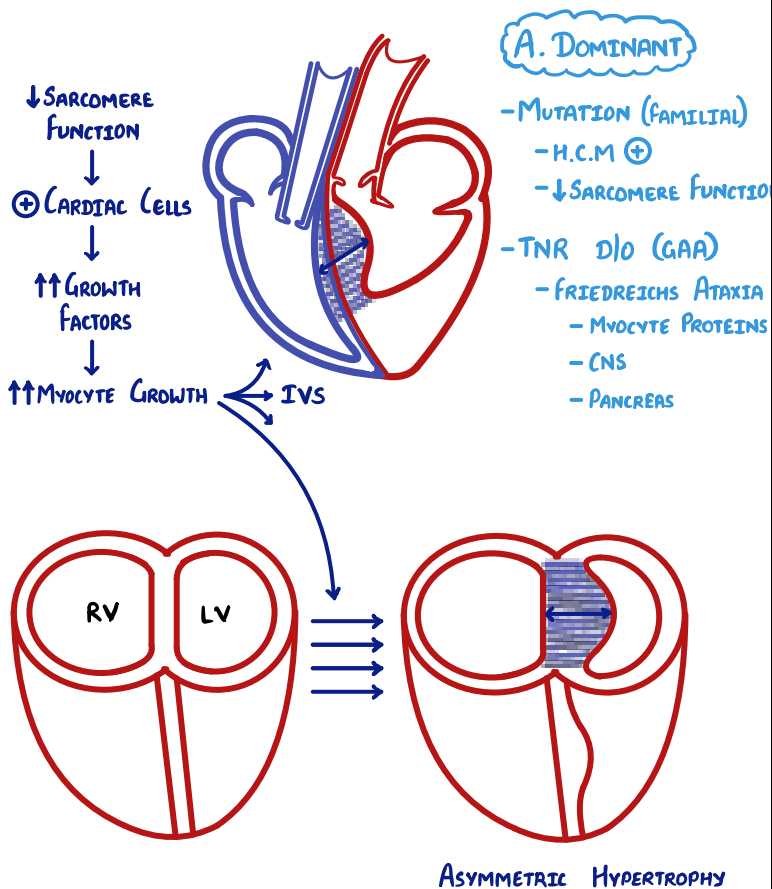


Figure 2. Asymmetrical Hypertrophy

[Harrisons Pg. 1794; Fig 254-15]



(ii) Microscopically

(a) Myocyte disarray

→ Haphazard growth

(b) Concentric hypertrophy

→ Sarcomeres added in **parallel arrangement**
→ Ventricular septum gets thicker, narrows the lumen
→ Also seen in other diseases:

- (i) Aortic stenosis
- (ii) Hypertension
- (iii) Ischemic Cardiomyopathy

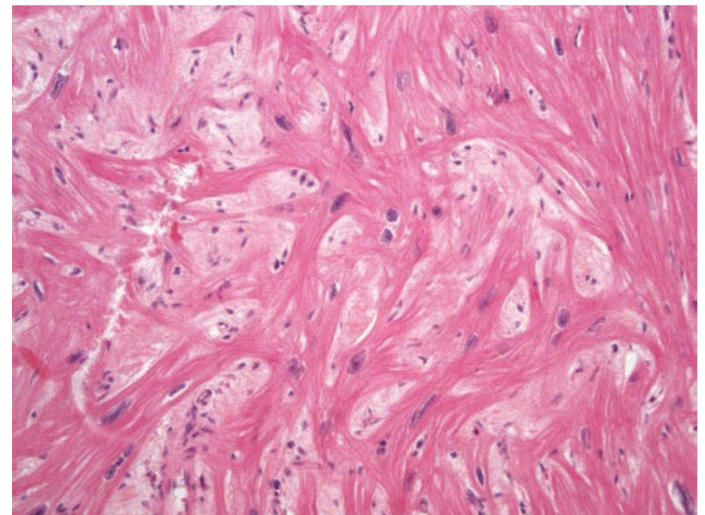
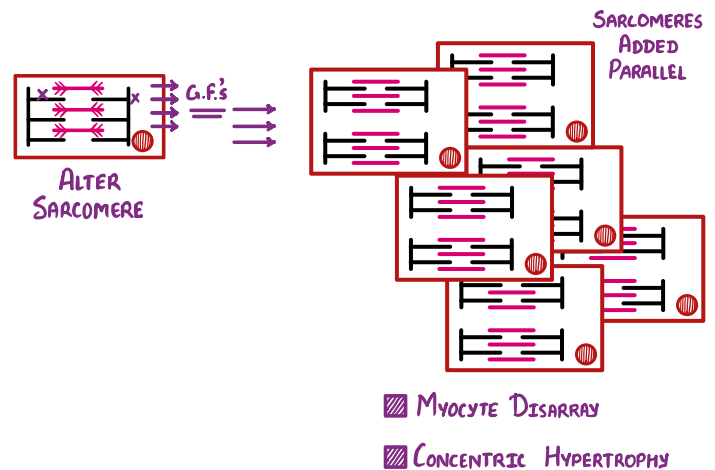


Figure 3. Myocyte disarray, hypertrophy, exaggerated branching

[Harrisons Pg. 1794; Fig 254-17]



Table 2. Hypertrophy & Hyperplasia

	Hypertrophy	Hyperplasia
Definition	Increase in size of cells, resulting in increase in the size of the affected organ	Increase in number of cells in an organ/ tissue in response to a stimulus
Mechanism	Increased cellular protein production	Growth factor driven proliferation of mature cells/ increased output of new cells from tissue stem cells
Examples		
Physiological	Uterus during pregnancy, Muscles of bodybuilders	Female breast at puberty, Liver regeneration
Pathological	Enlargement of heart due to pressure overload (Hypertension/ Valvular disease)	Benign Prostatic Hyperplasia, Endometrial Hyperplasia
Diagram		

IV) PATHOPHYSIOLOGY, COMPLICATIONS, CLINICAL FEATURES

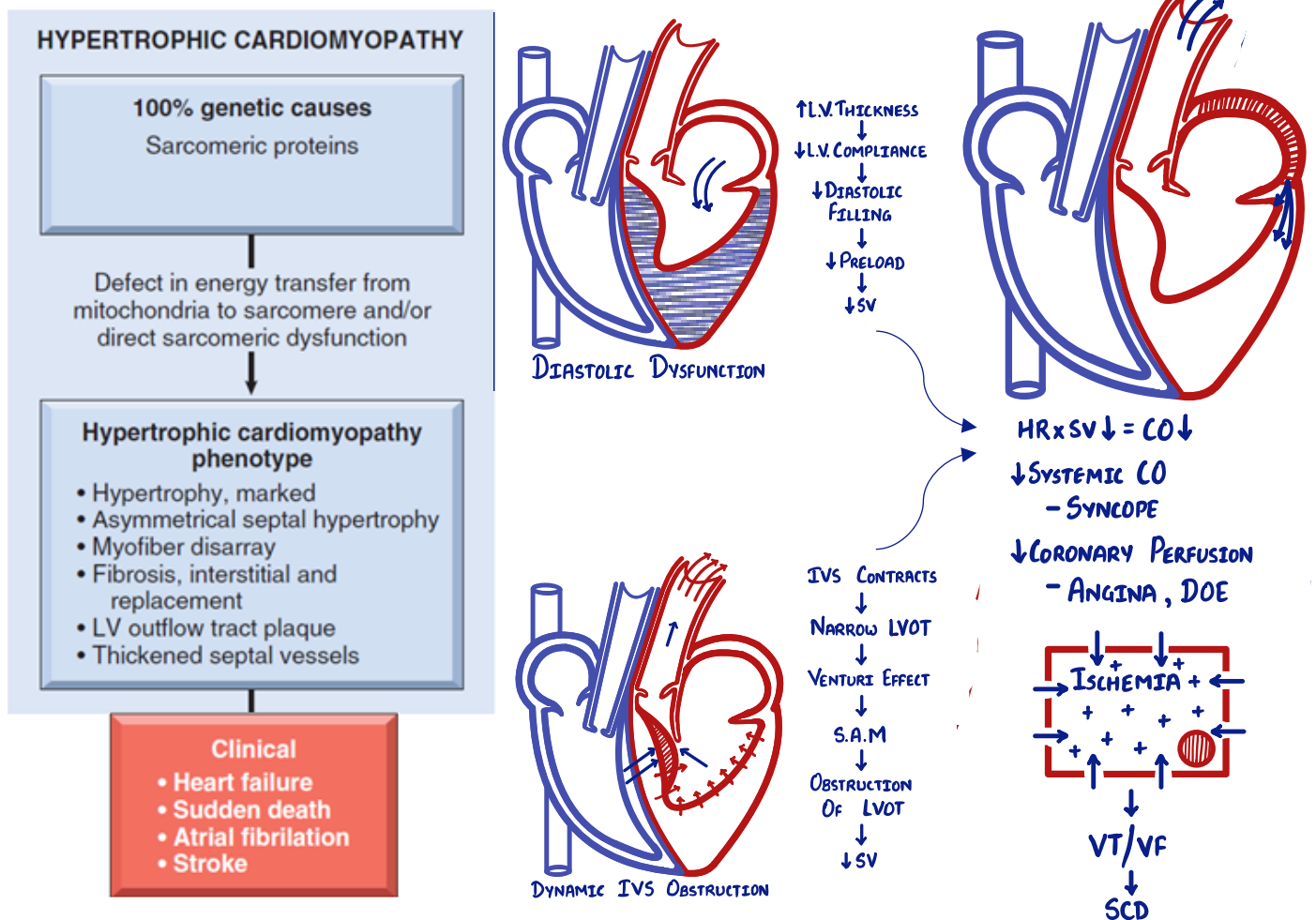


Figure 4. Pathogenesis of HCM

[Robbins Pg. 570; Fig 12.30]



(A) DIASTOLIC DYSFUNCTION

(1) ↑ Left Ventricular thickness

→ Left ventricular thickness is increased by **concentric, asymmetrical septal hypertrophy**
→ This causes:

(i) Decreased compliance

- Unable to stretch as much

(ii) Decreased left ventricular cavity size

- Narrow lumen

(2) Diastolic filling dysfunction

(i) Decreased Preload

(ii) Decreased Stroke Volume

(3) Decreased cardiac output

(B) DYNAMIC INTERVENTRICULAR SEPTUM OBSTRUCTION

(1) Venturi effect

→ During ventricular systole, the thickened ventricle contracts
→ Blood is pushed into the very **narrowed Left Ventricular Outflow Tract (LVOT)**
→ The high velocity of blood through the LVOT creates a **low-pressure vacuum suction**
→ This pulls the anterior leaflet of the mitral valve towards the septum
▪ This is called **Systolic Anterior Motion**

(2) Systolic Anterior Motion

→ Causes **obstruction of LVOT**
→ SAM causes the **anterior leaflet of the mitral valve** to block the already narrowed LVOT
→ Therefore, not much blood can be pumped out of the ventricle
→ **Decreased stroke volume**

(3) Decreased Cardiac Output

→ Decreases systemic output
○ Decreased perfusion to:

(i) Brain

- Causes **Syncope**

(ii) Coronary arteries

- Causes:

(a) Angina (myocardial ischemia)

(b) Dyspnoea on Exertion

(c) VTach/ VFib

→ Ischemia causes the myocardial cells to become **more permeable**

→ Cations leak in (Na^{2+} , Ca^{2+})

→ Myocardium thus becomes **hyperexcitable** due to excessive depolarization

→ This causes a fatal arrhythmia
▪ Causes **Sudden Cardiac Death**

SUDDEN CARDIAC DEATH (SCD)

- It is defined as unexpected death from cardiac causes, either without symptoms or within 1 to 24 hours of symptom onset.
- The mechanism of SCD is most often a lethal arrhythmia (ex: asystole/ ventricular fibrillation)
- Causes of SCD:

→ **CORONARY ARTERY DISEASE**

→ **CARDIAC CONDUCTION ABNORMALITIES**

→ **DILATED/ HYPERTROPHIC CARDIOMYOPATHY**

→ **CONGENITAL CORONARY ARTERIAL ABNORMALITIES**

→ **MYOCARDITIS**

→ **MITRAL VALVE PROLAPSE**

→ **PULMONARY HYPERTENSION**

→ **PERICARDIAL TAMPONADE**

→ **PULMONARY EMBOLISM**

→ **DRUGS OF ABUSE (COCAINE, METHAMPHETAMINE)**

(C) SYSTOLIC EJECTION MURMUR

→ Features:

(1) Harsh crescendo- decrescendo murmur

(2) Occurs during systole

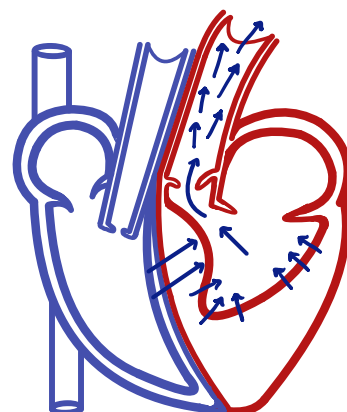
(i) As blood blows out of the ventricle, it hits the obstruction

- The sound gets **more intense**
- "**CRESCENDO**"

(ii) Due to systolic anterior motion, LVOT gets dynamically obstructed

- No blood is able to get out through the LVOT
- The sound gets **less intense**
- "**DECRESCENDO**"

MURMUR



DYNAMIC LVOT OBSTRUCTION

-SYSTOLIC EJECTION MURMUR



Figure 5. Systolic Ejection Murmur



(D) S4 HEART SOUND

→ Features:

(1) Indicative of diastolic dysfunction

(2) Due to Atrial hypertrophy

(i) Left ventricle is less compliant and has very low volume

- The left atrium therefore has to pump blood against the very high-pressure system in left ventricle ($P \propto \frac{1}{V}$)
- In order to do that, there is **compensatory left atrial enlargement (hypertrophy)**

(ii) Hypertrophied Left Atrium pushes blood into the small lumen of left ventricle

- Causes **S4** heart sound

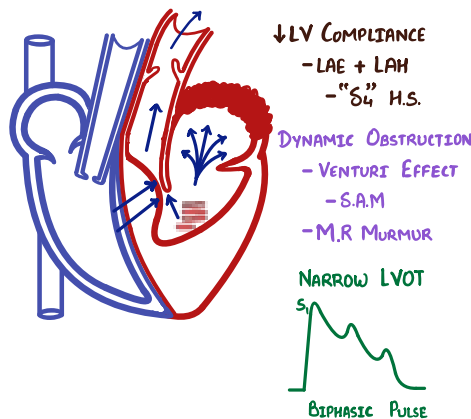


Figure 6

(E) MITRAL REGURGITATION

→ Features:

(1) Occurs due to **SAM** of anterior leaflet of mitral valve

→ During systole, left ventricle contracts

- As the mitral valve leaflet has shifted to block the LVOT, **blood flows back into the atrium**
- This is called **mitral regurgitation**

(2) **Holosystolic murmur**

→ Backflow of blood into the atrium produces a murmur

- This is a **holosystolic murmur**

(F) BIPHASIC PULSE

(1) **Pulsus Bisferiens**

→ It is another name for the **biphasic pulse**

(i) Initial peak

- Seen when blood is **pumped out**

(ii) 2nd peak

- Dynamic obstruction occurs, where there is a delay in blood being pumped out through LVOT into aorta
- The left ventricle eventually **overcomes the obstruction and pumps harder**
→ Causes the 2nd peak in the arterial pulse waveform

(2) **Spike and dome waveform**

→ **Spike and dome waveform** is also obtained while recording arterial pulse

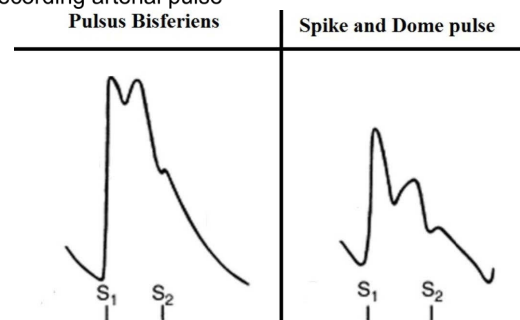
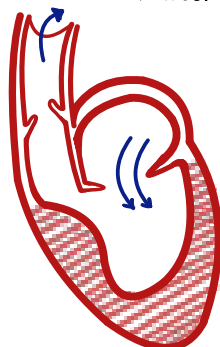


Figure 7 [wikidoc]

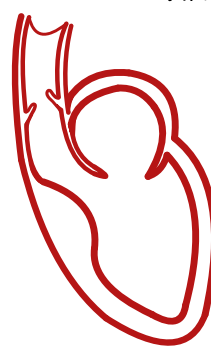
(V) MANEUVERS

PRELOAD



- ↑ PRELOAD → ↓ OBSTRUCTION
→ ↓ INTENSITY OF MURMUR
→ SQUATTING / PLR
- ↓ PRELOAD → ↑ OBSTRUCTION
→ ↓ INTENSITY OF MURMUR
→ STANDING / VALSALVA

AFTERLOAD



- ↑ AFTERLOAD → ↓ SV → ↑ ESV
→ ↓ OBSTRUCTION
→ ↓ INTENSITY OF MURMUR
→ HANDGRIPS → ⊕ SVRT
- ↓ AFTERLOAD → ↑ SV → ↓ ESV
→ ↓ OBSTRUCTION
→ ↑ INTENSITY OF MURMUR
→ AMYL NITRATE
→ HYDRALAZINE → ↓ SVR



(A) PRELOAD

- **PRELOAD** is the volume of blood entering the right atrium of the heart, through the superior & inferior vena cava, from all parts of the body
- It is the **VENOUS RETURN**

$$(\text{Preload} \propto \frac{1}{\text{Obstruction}} \propto \frac{1}{\text{Intensity of Murmur}})$$

(1) Increased preload

↑ **Preload** ⇒ ↓ **Obstruction** ⇒ ↓ **Intensity of Murmur**

(i) Mechanism

- More blood enters atria, to be pumped into ventricles
- This **increases size of left ventricle**
- This **decreases the obstruction** a little, opening up the LVOT
- Due to lesser obstruction, the **intensity of the murmur is decreased**

(ii) Ways to increase preload

- **Increase venous return**
- **Squatting**
 - Venoconstriction of veins in the legs, allows more blood to enter the heart
- **Passive leg-raise**
 - More blood flows into the heart due to gravity

(2) Decreased preload

↓ **Preload** ⇒ ↑ **Obstruction** ⇒ ↑ **Intensity of Murmur**

(i) Mechanism

- **Less blood enters atria**, less blood pumped into ventricles
- **Ventricles don't stretch as much** as there is less volume to accommodate
- **Obstruction is hence not relieved**, and is worsened
- Due to worse obstruction, the **intensity of the murmur is increased**

(ii) Ways to decrease preload

- **Decrease venous return**
- **Standing**
 - Blood pools in the veins in the leg, decreasing venous return
- **Valsalva maneuver**
 - ↑ **intra-thoracic pressure**
 - Occurs during **defecation** ("bearing down")- closing of glottis to stop air from going out
 - Blood flow from inferior vena cava into heart is decreased due to high pressure system created in the thorax

Remember

the obstruction is dynamic/functional, & therefore can be manipulated by maneuvers

(B) AFTERLOAD

- **AFTERLOAD** is the total peripheral resistance (resistance in the systemic vasculature) that the left ventricle has to overcome to pump out blood to all the organs
- It is the **SYSTEMIC VASCULAR RESISTANCE (SVR)**

$$(\text{Afterload} \propto \frac{1}{\text{Obstruction}} \propto \frac{1}{\text{Intensity of Murmur}})$$

(1) Increased afterload

↑ **Afterload** ⇒ ↓ **Obstruction** ⇒ ↓ **Intensity of Murmur**

(i) Mechanism

- Increased afterload implies that the left ventricle has to pump against a higher resistance
- This **decreases volume of blood** being pumped out of the left ventricle
 - Which means a **decreased stroke volume**
- Since stroke volume is decreased, more blood is left in the left ventricle, after contraction, which wasn't pumped out
 - this means an **increased End Systolic Volume (ESV)**

Remember

ESV is the volume of blood that remains in left ventricle after it has contracted

- This **increases size of left ventricle**, due to more blood
- This **decreases the obstruction** a little, opening up the LVOT
- Due to lesser obstruction, **the intensity of the murmur is decreased**

(ii) Ways to increase afterload

- **Increase systemic vascular resistance (SVR)**
- **Hand grips**
 - This increases the systemic vascular resistance

(2) Decreased afterload

↓ **Preload** ⇒ ↑ **Obstruction** ⇒ ↑ **Intensity of Murmur**

(i) Mechanism

- Less afterload implies that blood can easily be pumped out of the left ventricle
 - High pressure (left ventricle) to low pressure (systemic vasculature)
- This increases the volume of blood being pumped out of the left ventricle
 - **Increased stroke volume**
- Increased stroke volume **decreases the end systolic volume**
- **Obstruction is hence not relieved**, and is worsened
- Due to worse obstruction, the **intensity of the murmur is increased**

(ii) Ways to decrease afterload

- **Decrease systemic vascular resistance**
- **Vasodilators**
 - **Amyl Nitrate, hydralazine, isosorbide dinitrate**
 - Decreases SVR



VI) DIAGNOSIS

(A) HISTORY

≤ 35 y/o

SYNCOPE EVENTS & EXERTION
ANGINA & EXERTION

→ ATHLETES

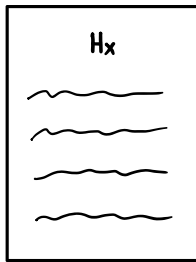


Figure 8. History taking

- (1) Age ≤ 35 years
 - (2) Syncopal events with exertion
 - (3) Angina
 - (4) Dyspnea on exertion
 - (5) Family history
- Genetic causes

Especially in athletes!

CLINICAL VIGNETTE

A previously healthy 26-year-old man is brought to the emergency department 20 minutes after collapsing while playing basketball. He has no previous history of illness. On examination, there is no pulse or respiratory effort. He is declared dead. Autopsy shows marked thickening of left ventricle. What was the cause of death?

Answer

SUDDEN CARDIAC DEATH DUE TO HYPERTROPHIC CARDIOMYOPATHY

- Hypertrophic cardiomyopathy is often identified because of **syncope, exertional dyspnea or angina**, following some **strenuous activity** (like athletes) in **younger individuals**
- Individuals who have the genetic mutations for hypertrophic cardiomyopathy frequently remain **asymptomatic**. It is when they put their heart under stress (physically!) they exhibit symptoms
- Tremendous exertion can lead to **complete dynamic obstruction with the already thickened interventricular septum**, which can lead to **Sudden Cardiac Death** due to a fatal arrhythmia

(B) INVESTIGATIONS

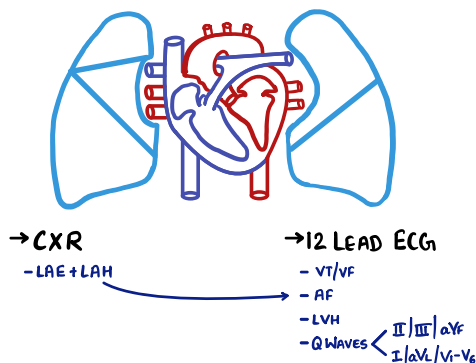


Figure 9. CXR & ECG

(1) Chest X Ray

- (i) Left atrial enlargement

(2) 12 lead ECG

- (i) VTach/VFib
- (ii) AFib
 - Due to LVH
- (iii) Left Ventricular Hypertrophy
 - Large R waves in V4, V5, V6
 - Deeper S waves in V1, V2, V3
- (iv) Deep Q waves
 - In inferior leads: II, III, aVF
 - In lateral leads: I, aVL, V5-V6
- (v) Giant inverted T waves

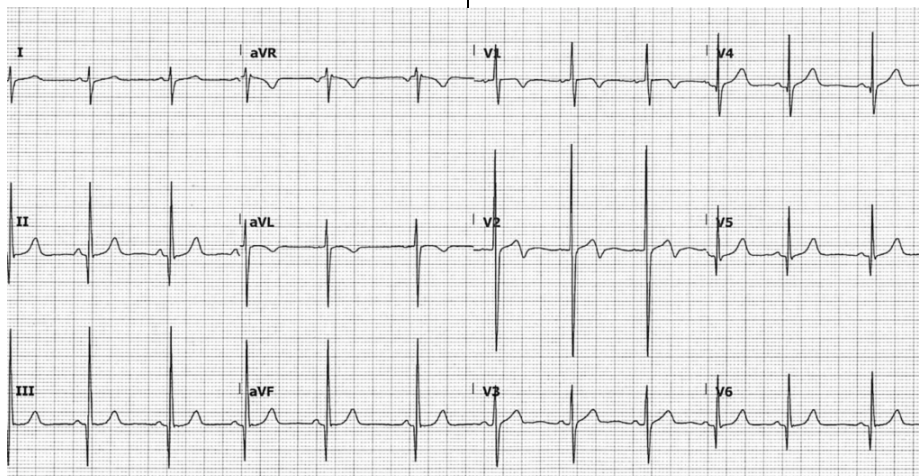


Figure 10. ECG changes in HCM

[11f]



(3) ECHO

- (i) Diameter of Ventricular Lumen ↓↓↓
- (ii) Wall thickness ↑↑↑
 - More in the **interventricular septum**
 - **Asymmetric hypertrophy**
- (iii) Ejection Fraction- usually normal
 - Due to hypertrophied myocardial cells, they are hypercontractile
 - Diastolic filling is reduced, but **stroke volume is maintained** up to an extent
- (iv) Doppler
 - **Systolic Ejection Murmur**
 - **Mitral regurgitation**

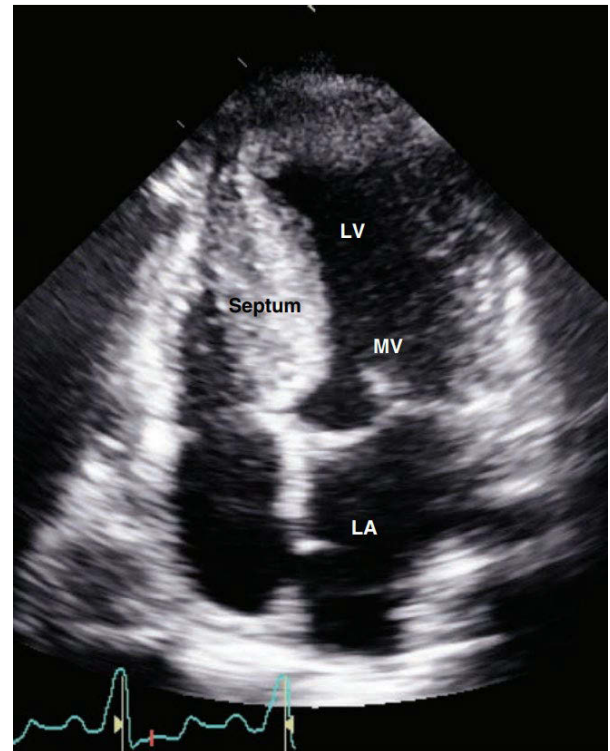
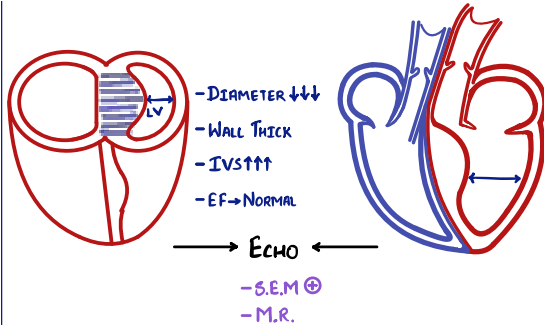


Figure 11. ECHO in HCM
[Harrisons Pg. 1794 Fig. 254-16]

VII) TREATMENT

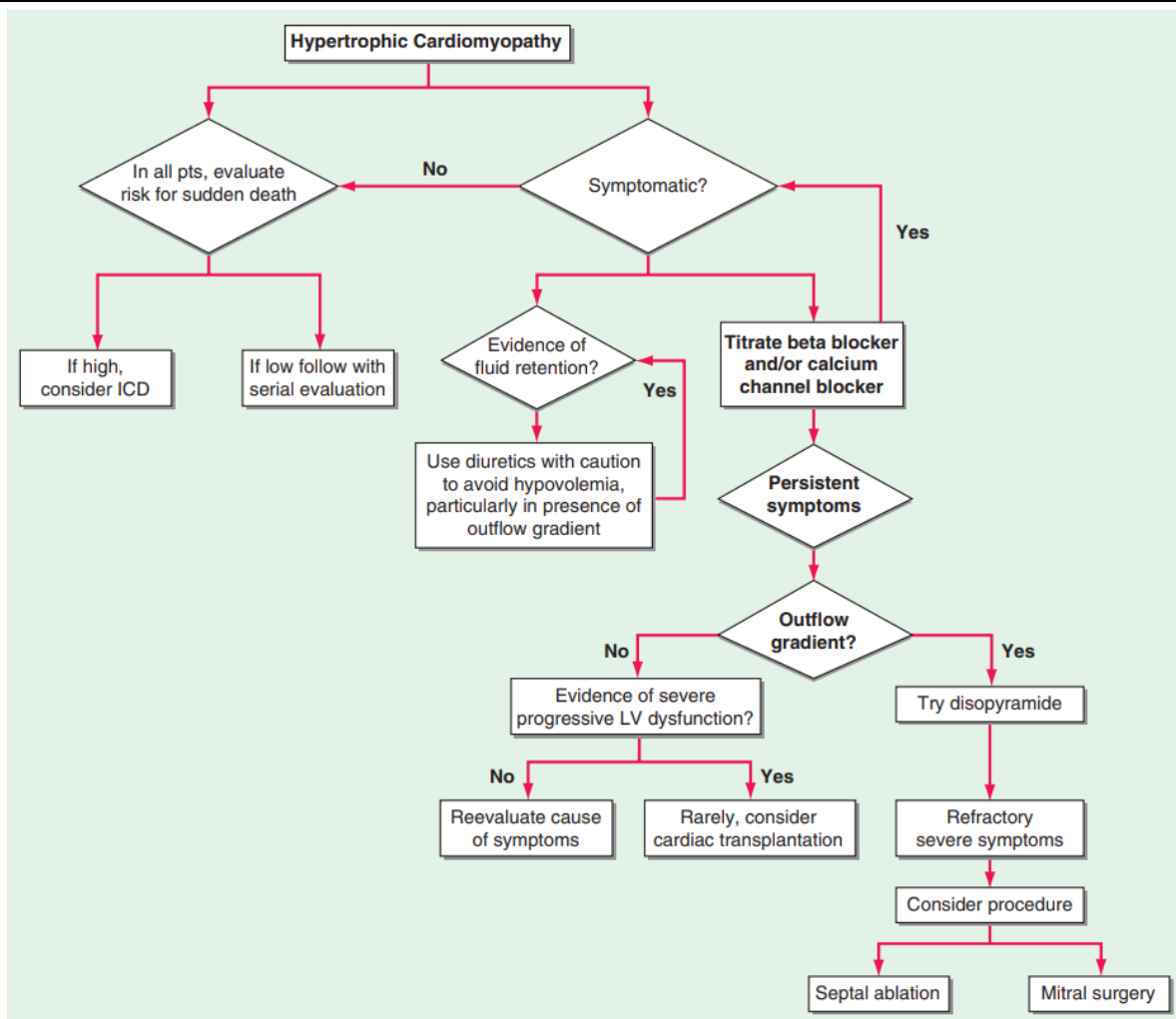


Figure 12. Treatment Algorithm for Hypertrophic Cardiomyopathy

[Harrisons Pg. 1795 Fig. 254-18]

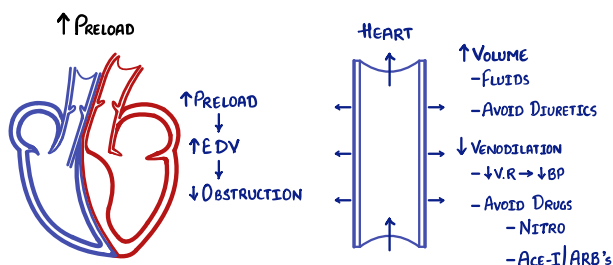


GOALS OF TREATMENT

Treat to decrease intensity of murmur
Reduce the dynamic obstruction
Increase the preload

(A) INCREASE PRELOAD

(1) Mechanism



(2) Methods

(i) Increase volume of blood

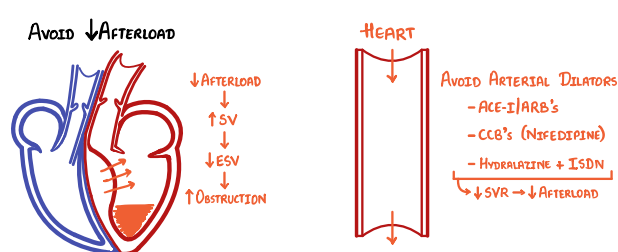
- **Fluids**
- Avoid drugs that decrease fluid volume
→ **Diuretics**

(ii) Reduce venodilation

- This decreases venous return, decreasing BP
- Avoid drugs that cause vasodilation
→ **Nitrates, ACE-I, ARBs**

(B) AVOID REDUCTION IN AFTERLOAD

(1) Mechanism

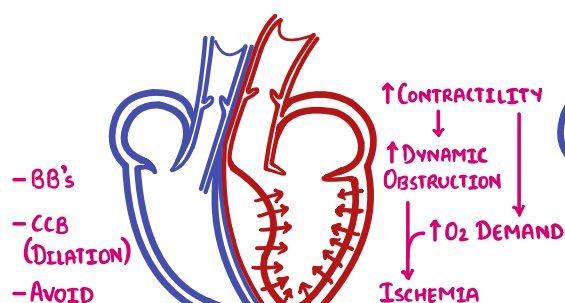


(2) Methods

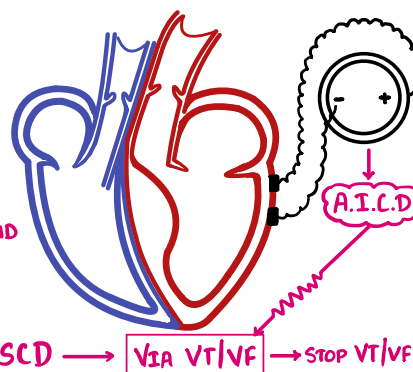
(i) Avoid arterial dilation

- Avoid drugs that cause arterial dilation
- They decrease SVR, thus decrease afterload
→ **ACE-I, ARBs**
→ **Calcium channel blockers:**
Dihydropyridines-like Nifedipine
→ **Hydralazine, isosorbide dinitrate**

AVOID ↑ CONTRACTILITY



↓ ARRHYTHMIAS



(C) AVOID INCREASE IN CONTRACTILITY

(1) Mechanism

→ Decreases oxygen demand, relieving the ischemia

(2) Methods

(i) Drugs that decrease contractility

- Reduce obstruction and oxygen demand
→ **β blockers**
→ **Calcium Channel Blockers: Non-dihydropyridines like Diltiazem, Verapamil**

(ii) Avoid drugs that increase contractility

- Positive inotropy increases obstruction and worsens ischemia
- Can cause Sudden Cardiac Death
→ **Digoxin, Dobutamine**

(D) DECREASE ARRHYTHMIAS

(1) Mechanism

→ Prevent VTach/ VFib, and ultimately SCD

(2) Methods

(i) Automated Implantable Cardioverter Defibrillator (AICD)

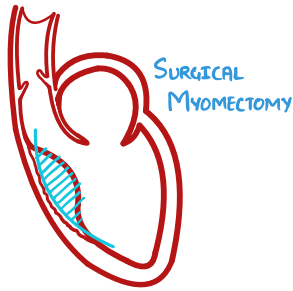
- Automatically delivers shocks to stop fatal arrhythmias
→ Consider AICD in **highly susceptible and symptomatic individuals**



(E) INVASIVE PROCEDURES

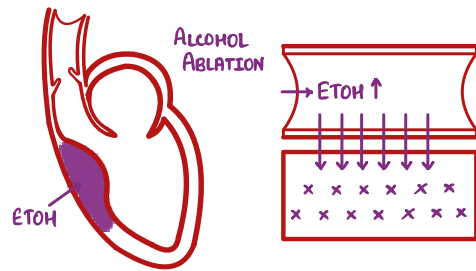
(1) Methods

(i) Surgical Septal Myomectomy



- Surgically remove the hypertrophied part of interventricular septum
- Relieves the obstruction

(ii) Alcohol Septal Ablation



- **Trans-coronary ablation of septal hypertrophy**
 - Catheter is directed into blood vessels
 - Alcohol is released through it into the hypertrophied wall
- Alcohol is **cardiotoxic**
 - Causes directed destruction of myocardial cells
 - Relieves the obstruction

VIII) SUMMARY

Causes	Morphology	Pathophysiology
Genetic: ● Mutation in β myosin heavy chain ○ Autosomal Dominant	Gross features: ● Asymmetric septal hypertrophy ● L/S: banana- like configuration of left ventricle ● Thickening of anterior mitral leaflet	Left Ventricular Hypertrophy Impaired left ventricle relaxion & filling Decreased compliance Diastolic dysfunction Decreased stroke volume, cardiac output Decreased peripheral & myocardial perfusion Blood pushed through narrow LVOT Venturi effect Systolic Anterior Motion Dynamic obstruction of LVOT
Secondary causes: ● Friedrich's ataxia ○ Autosomal Recessive ● Chronic HTN ● Aortic Stenosis	Microscopic features: ● Myocyte disarray ● Myocyte hypertrophy ● Concentric hypertrophy ○ Added in parallel ● Interstitial & replacement fibrosis ● Exaggerated myocyte branching	Complications ● Syncope ● Mitral regurgitation ● Systolic ejection murmur ● S4 ● Pulsus bisferiens ● Sudden Cardiac Death

Table 3. Effect of Preload & Afterload on Systolic Ejection Murmur

	Preload		Afterload	
	↑	↓	↑	↓
Method	Squatting Leg raise	Standing Valsalva	Hand Grip	Vasodilators
Obstruction	↓	↑	↓	↑
Intensity of Murmur	↓	↑	↓	↑



Clinical Features	Diagnosis	Treatment
● Frequently asymptomatic ● Heart failure ● Angina ● Exertional dyspnea ● Palpitations ● Arrhythmias ● Syncope ● Mitral regurgitation ● Focal MI	● History ● Investigations: ○ Chest X-Ray ▪ Left atrial enlargement ○ ECG ▪ Deep Q waves ▪ Giant inverted T waves ○ ECHO ▪ ↑ wall thickness ▪ ↓ LV lumen size ▪ EF: usually normal ▪ Mitral regurgitation seen in Doppler	● Increase Preload ○ Fluids ○ Avoid: ▪ Diuretics, Nitrates, ACE-I, ARBs ● Avoid reduction in afterload ○ Avoid: ▪ ACE-I, ARBs ▪ Calcium channel blockers: Dihydropyridines like nifedipine ▪ Hydralazine, isosorbide dinitrate ● Avoid increase in contractility ○ β blockers ○ Calcium Channel Blockers: ▪ Non- dihydropyridines like Diltiazem, Verapamil ○ Avoid: ▪ Digoxin, dobutamine ● Decrease Arrhythmias ○ AICD ● Invasive Procedures ○ Surgical Septal Myomectomy ○ Alcohol Septal Ablation

IX) APPENDIX

MAJOR RISK FACTOR		SCREENING TECHNIQUE
History of cardiac arrest or spontaneous sustained ventricular tachycardia ^a		History
Syncope	Nonvagal, often with or after exertion	History
Family history of sudden cardiac death		Family history
Spontaneous nonsustained ventricular tachycardia ^b	>3 beats at rate >120	Exercise or 24- to 48-h ambulatory recording
LV thickness >30 mm	Present in <10% of patients	Echocardiography
Abnormal blood pressure response to exercise ^b	Systolic blood pressure fall or failure to increase at peak exercise	Maximal upright exercise testing

^aImplantable cardioverter-defibrillator advised for patients with prior arrest or sustained ventricular tachycardia regardless of other risk factors. ^b Prognostic value most applicable to patients <40 years old.

Figure 13. Risk Factors for Sudden Cardiac Death in HCM

[Harrisons Pg. 1796: Table 256-6]



X) REVIEW QUESTIONS

- 1) Which is the most common type of cardiomyopathy?
 - a) Dilated
 - b) Hypertrophic
 - c) Restrictive
 - d) Arrhythmogenic
- 2) What is the most common pattern of transmission of hypertrophic cardiomyopathy?
 - a) Autosomal recessive
 - b) Autosomal dominant
 - c) X-linked recessive
 - d) X-linked dominant
- 3) Mutations in genes that encode sarcomeric proteins cause hypertrophic cardiomyopathy. Which of these genes is NOT implicated in the same?
 - a) β myosin heavy chain
 - b) Myosin binding protein C
 - c) Cardiac troponins
 - d) Titin
- 4) Systolic Anterior Motion is due to:
 - a) Movement of leaflet of tricuspid valve
 - b) Movement of leaflet of bicuspid valve
 - c) Movement of leaflet of semilunar valve
 - d) All of the above
- 5) A 67-year-old man comes to the ER with complains of chest pain and difficulty in breathing for 15 minutes, which started suddenly during his workout at the gym. He says he occasionally has difficulty in breathing, associated with sweating and pedal edema for 15 years. ECHO shows thickened left ventricular walls. What is the most probable cause for the patient's condition?
 - a) Mutation in certain genes
 - b) Friedreich's ataxia
 - c) Chronic hypertension
 - d) Noonan syndrome

- 6) Which abnormal heart sound is heard in hypertrophic cardiomyopathy?

- a) Absence of heart sounds
- b) S3
- c) S4
- d) S3 & S4

- 7) A 20-year-old woman is brought to the ER after she suddenly collapsed during her soccer practice. Her mother says that she was previously healthy and had no complaints. She is fearful as her husband had passed away in a similar situation, and the doctors had told her it was Sudden Cardiac Death. What changes can be seen in the patient's heart?

- a) Enlarged left atrium
- b) Enlarged left ventricle
- c) Fibrous endocardial plaque
- d) All of the above

- 8) A 58-year-old man comes to the hospital with complains of palpitations, chest pain and difficulty in breathing. He is a known hypertensive since 20 years. He has been taking Captopril for the same. A thorough cardiac workup is done to rule out any cardiac emergencies, and he is incidentally diagnosed with hypertrophic cardiomyopathy. After initial treatment to provide symptomatic relief, how will you manage the patient?

- a) Continue Captopril only
- b) Captopril + Spironolactone
- c) Metoprolol + Nifedipine
- d) Metoprolol + Verapamil

XI) REFERENCES

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RESTRICTIVE CARDIOMYOPATHY

Restrictive Cardiomyopathy

Medical Editor: Jan Camille Santico & Jude Loyola

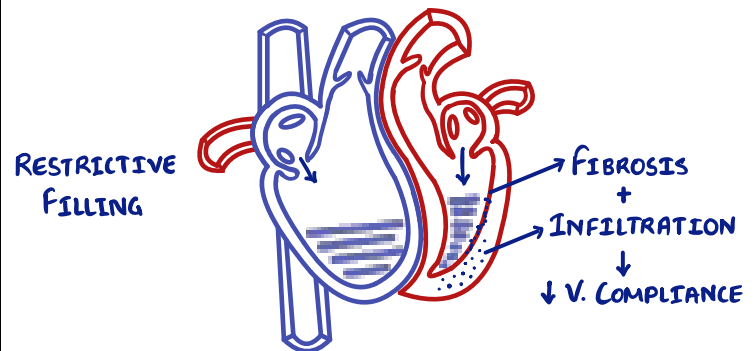
OUTLINE

- I) INTRODUCTION
- II) CAUSES
- III) PATHOPHYSIOLOGY
- IV) COMPLICATIONS
- V) DIAGNOSIS

- VI) TREATMENT
- VII) APPENDIX
- VIII) REVIEW QUESTIONS
- IX) REFERENCES

I) INTRODUCTION

- Cardiomyopathy is a disease process affecting the heart where there is **dysfunction of myocardium**.
- In **restrictive cardiomyopathy**, there is **fibrosis** or an **infiltrative process** involving the myocardium or endocardium
 - This results in decreased ventricular compliance, wherein the cardiac tissues lose their distensibility or stretch
 - The decreased ventricular compliance restricts the amount of blood which enters the ventricle during diastole, leading to a restrictive filling process
- In summary, restrictive cardiomyopathy is characterized by dysfunctional myocardium due to fibrosis or infiltration of the myocardium and/or endocardium, causing decreased ventricular compliance and diastolic filling.



II) CAUSES

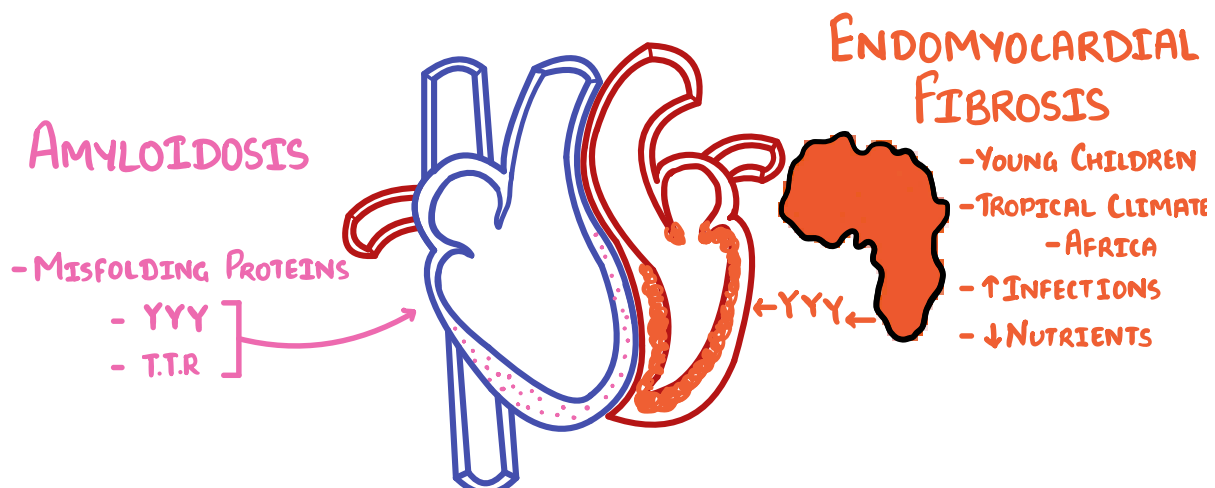
- Restrictive cardiomyopathy may be idiopathic or associated with distinct disorders that affect the myocardium [Robbins]

(A) AMYLOIDOSIS

- In amyloidosis, there is **misfolding of proteins** such as:
 - Antibodies (light chains)
 - Transthyretin
 - Transports retinol and thyroid hormone
- The dysfunctional proteins deposit along the myocardium of the heart, causing decreased ventricular compliance

(B) ENDOMYOCARDIAL FIBROSIS

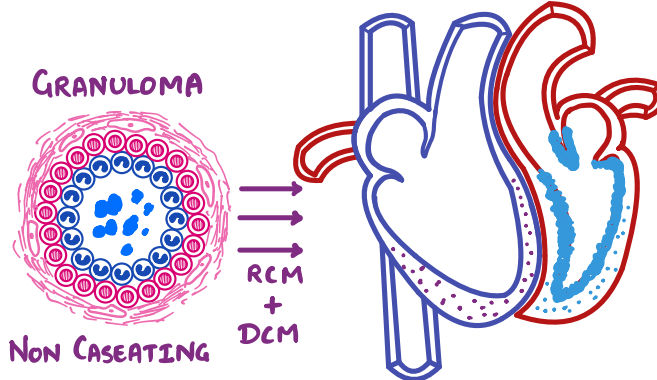
- Endomyocardial fibrosis is commonly found in young children living in tropical climates (e.g. Africa), where there are:
 - ↑ risk of infections
 - ↑ nutrient deficiencies
 - In this disease, there are **autoantibodies** which cause inflammation of the endocardium and myocardium, which subsequently lead to fibrosis
- The subsequent fibrosis leads to decreased ventricular compliance



(C) SARCOIDOSIS

- In sarcoidosis, the immune system creates **non-caseating granulomas**, which deposit on various tissues
 - Non-caseating granulomas have no necrotic tissue at its centre
 - It contains epithelioid cells and asteroid bodies surrounded by a ring of macrophages, lymphocytes, and fibrous tissue
- The granulomas deposit on the following organs:
 - Skin | Eyes | Joints | Heart
- Sarcoidosis can lead to both **restrictive cardiomyopathy** and **dilated cardiomyopathy**.

SARCOIDOSIS



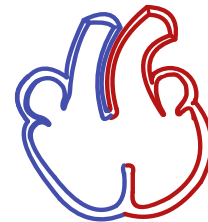
(D) ENDOCARDIAL FIBROELASTOSIS

- Endocardial fibroelastosis is commonly found in young children (≤ 2 years old) with congenital heart disorder
- In this disease, fibrosis develops in the endocardium, specifically the **subendocardium**
 - Fibrous and elastic tissue** deposits on these layers, decreasing ventricular compliance

ENDOCARDIAL FIBROELASTOSIS

- CHILDREN ≤ 2 Y/O

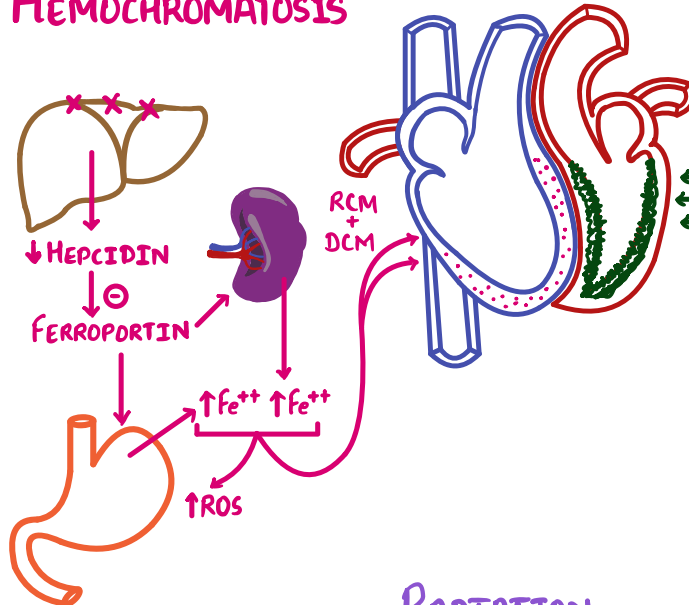
- CONGENITAL HEART D/O



(E) HEMOCHROMATOSIS

- Recall: The liver produces **hepcidin**, which regulates the activity of **ferroportin**.
 - Ferroportin modulates the
 - absorption of iron along the gastrointestinal tract
 - the release of iron from the spleen.
- In liver dysfunction, hepcidin production is impaired, affecting the regulation of ferroportin.
- With impaired ferroportin regulation, there is:
 - $\uparrow$ iron absorption from the GI tract
 - $\uparrow$ release of iron from the spleen
- The excess iron deposits on the myocardium of the heart
 - This increases the activity of **reactive oxygen species**, causing destruction and fibrosis of myocardial tissue
- Hemochromatosis can lead to both **restrictive cardiomyopathy** and **dilated cardiomyopathy**.

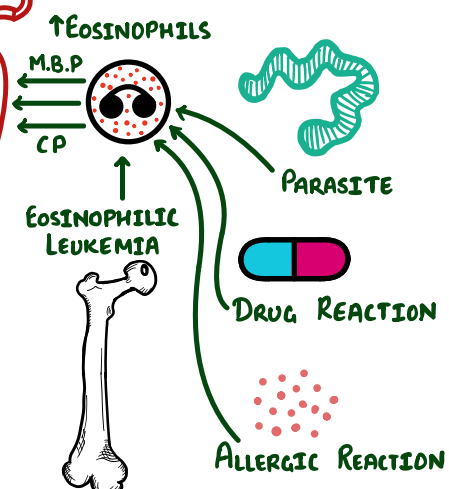
HEMOCHROMATOSIS



(F) LOEFFLER ENDOCARDITIS

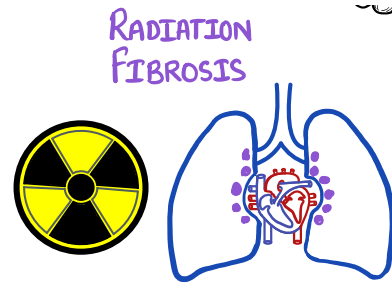
- In **Loeffler endocarditis**, there is a high level of **eosinophils**, which deposit on the myocardium.
- The increased eosinophil may be caused by:
 - Parasitic infection
 - Drug reaction
 - Allergic reaction
 - Eosinophilic leukemia
- Eosinophils release **major basic protein (M.B.P.)** and **cationic protein**, which cause inflammation and subsequent fibrosis of the endocardium and myocardium

LOEFFLER ENDOCARDITIS



(G) RADIATION FIBROSIS

- **Radiation fibrosis** may occur in patients who receive radiation therapy for tumor/s in the mediastinal area
 - Recall: The heart is within the middle mediastinum
- The radiation causes necrosis and subsequent fibrosis of myocardial tissue, reducing ventricular compliance

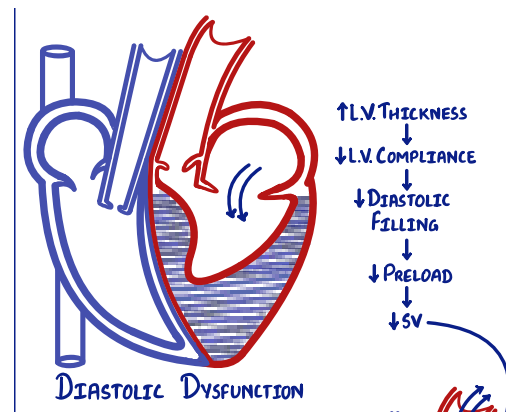


III) PATHOPHYSIOLOGY

(A) PATHOPHYSIOLOGY

- Restrictive cardiomyopathy is primarily characterized by dysfunctional myocardium due to fibrotic or infiltrative tissue
 - This affects both the right and left ventricle
- With the fibrotic/infiltrative tissue, there is:
 - ↓ ventricular compliance
 - ↓ ventricular cavity size
- During the diastolic filling process,
 - Early phase: normal expansion of ventricles
 - Middle and Late phases: limited expansion of ventricles
- Limited expansion of ventricles leads to:
 - ↓ diastolic filling
 - ↓ pre-load (amount of blood in the ventricles prior to contraction)
 - ↓ stroke volume
 - ↓ cardiac output

- This pathophysiology leads to a **diastolic dysfunction**



(B) HEART FAILURE

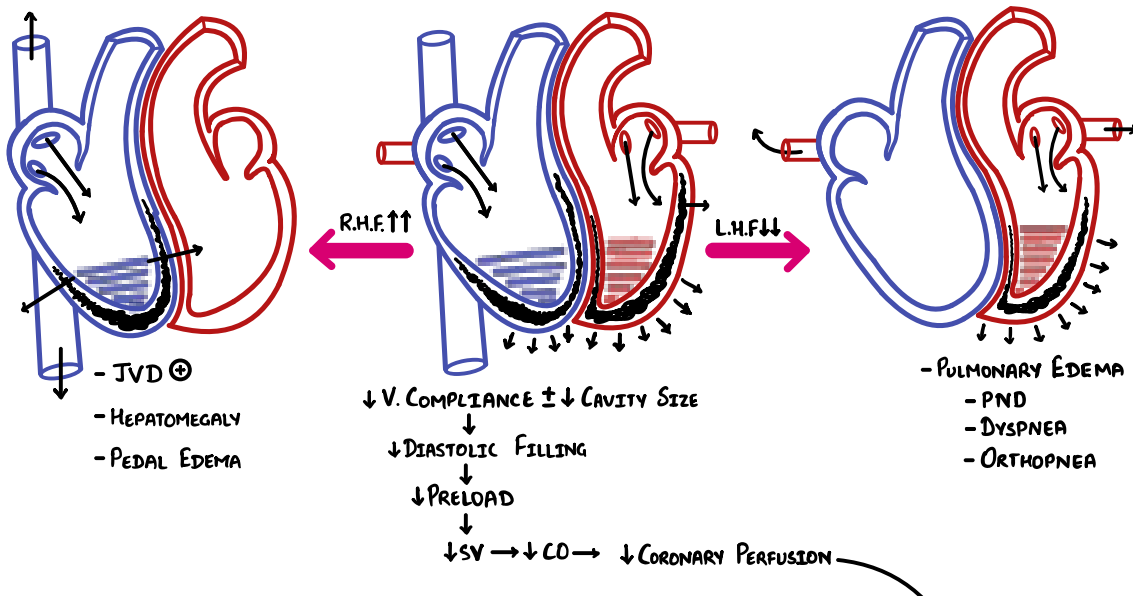
- A common complication of diastolic dysfunction is **heart failure**
- Right-sided heart failure is more common than left-sided heart failure in patients with restrictive cardiomyopathy

(1) Right-sided Heart Failure

- There is decreased compliance of the right ventricle (RV), which restricts the entry of blood
- This causes the following symptoms:
 - Jugular Venous Distension (JVD)
 - Hepatomegaly
 - Pedal Edema

(2) Left-sided Heart Failure

- There is decreased compliance of the left ventricle (LV), which restricts the entry of blood
- Blood is pushed back into the left atrium and the pulmonary circulation
- This causes symptoms of pulmonary edema, such as:
 - Dyspnea (shortness of breath)
 - Orthopnea (shortness of breath while laying down flat)
 - Paroxysmal nocturnal dyspnea (shortness of breath when lying prone during sleep)



IV) COMPLICATIONS

(1) Kussmaul's Sign

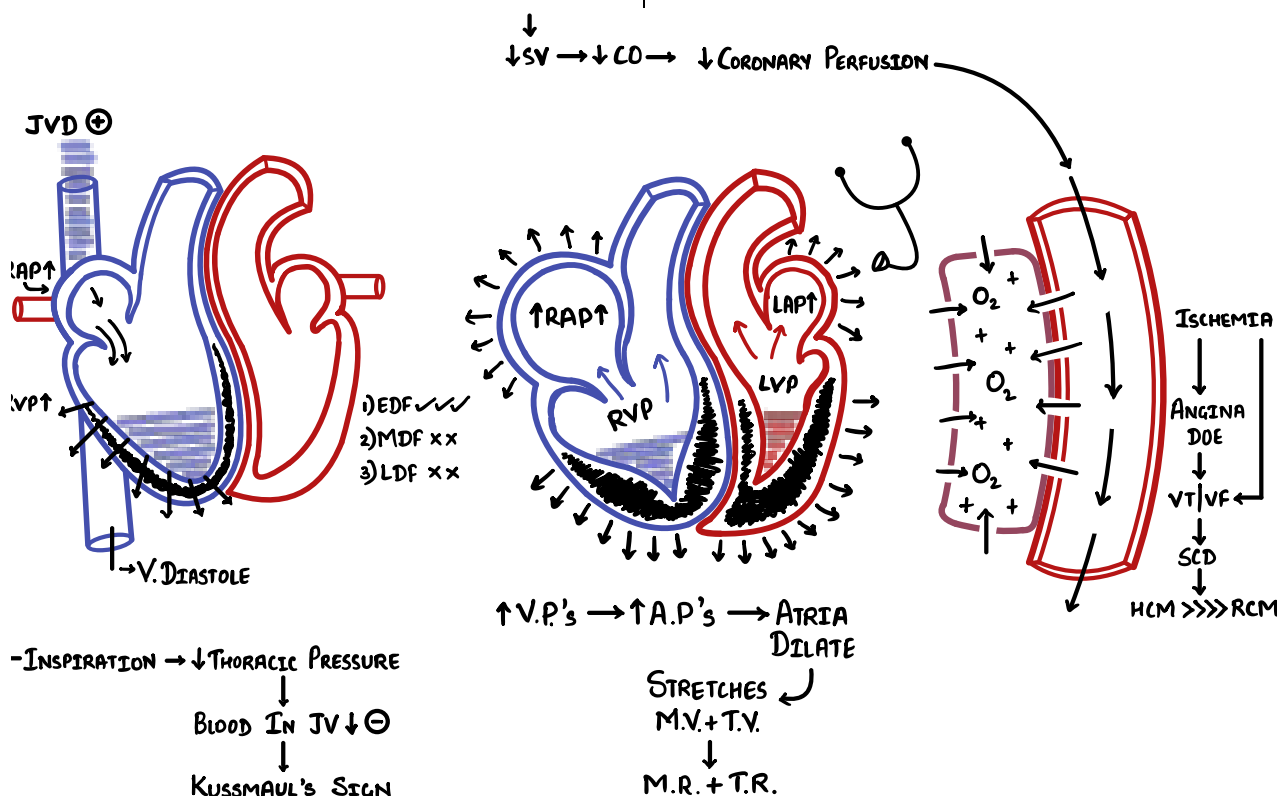
- **Kussmaul's sign** is the paradoxical increase in jugular venous pressure during inspiration
 - Jugular vein stays distended even during inspiration
- Recall: **Phases of Ventricular Diastole**
 - Early Diastolic Filling – valves open and blood rushes from the atrium to the ventricle
 - Mid-Diastolic Filling – blood from the vena cava pass through the atrium then to the ventricle
 - End Diastolic Filling – atrium contracts ("atrial kick") to push remaining blood to the ventricle
- With decreased ventricular compliance, blood only enters during the early diastolic filling phase
- During the mid and end diastolic filling phases, blood does not enter the ventricle, remaining in the vena cava and atrium
- During deep inspiration, the intrathoracic volume increases, and the intrathoracic pressure decreases
 - Under normal conditions, the decreased intrathoracic pressure allows blood in the vena cava to drop into the atrium
- In restrictive cardiomyopathy, the right atrial pressure and right ventricular pressure are elevated
 - This prevents blood from dropping into the atrium even during deep inspiration (Kussmaul's sign)

(2) Regurgitation

- The decreased ventricular compliance causes an increase in ventricular pressure
- To compensate, atrial pressure will also increase to continue pushing blood
 - Atrial pressure is also increased due to the increased volume of blood within that chamber
- Increased atrial pressure leads to **atrial dilation**
- Atrial dilation stretches the annulus of mitral and tricuspid valves, increasing the risk of mitral and tricuspid regurgitation
- These regurgitations are clinically detected via auscultation as **heart murmurs**

(3) Ischemia

- Recall: The pathophysiology of restrictive cardiomyopathy leads to **decreased cardiac output**
- Decreased cardiac output leads to
 - ↓ coronary perfusion
 - ↓ oxygen supply to the myocardium
 - Myocardial ischemia
- Ischemia can lead to:
 - Angina (chest pain)
 - Dyspnea
 - Ventricular fibrillation
 - Sudden cardiac death
- Ventricular fibrillation occurs more commonly in hypertrophic cardiomyopathy than restrictive cardiomyopathy



(4) Thromboembolic Events

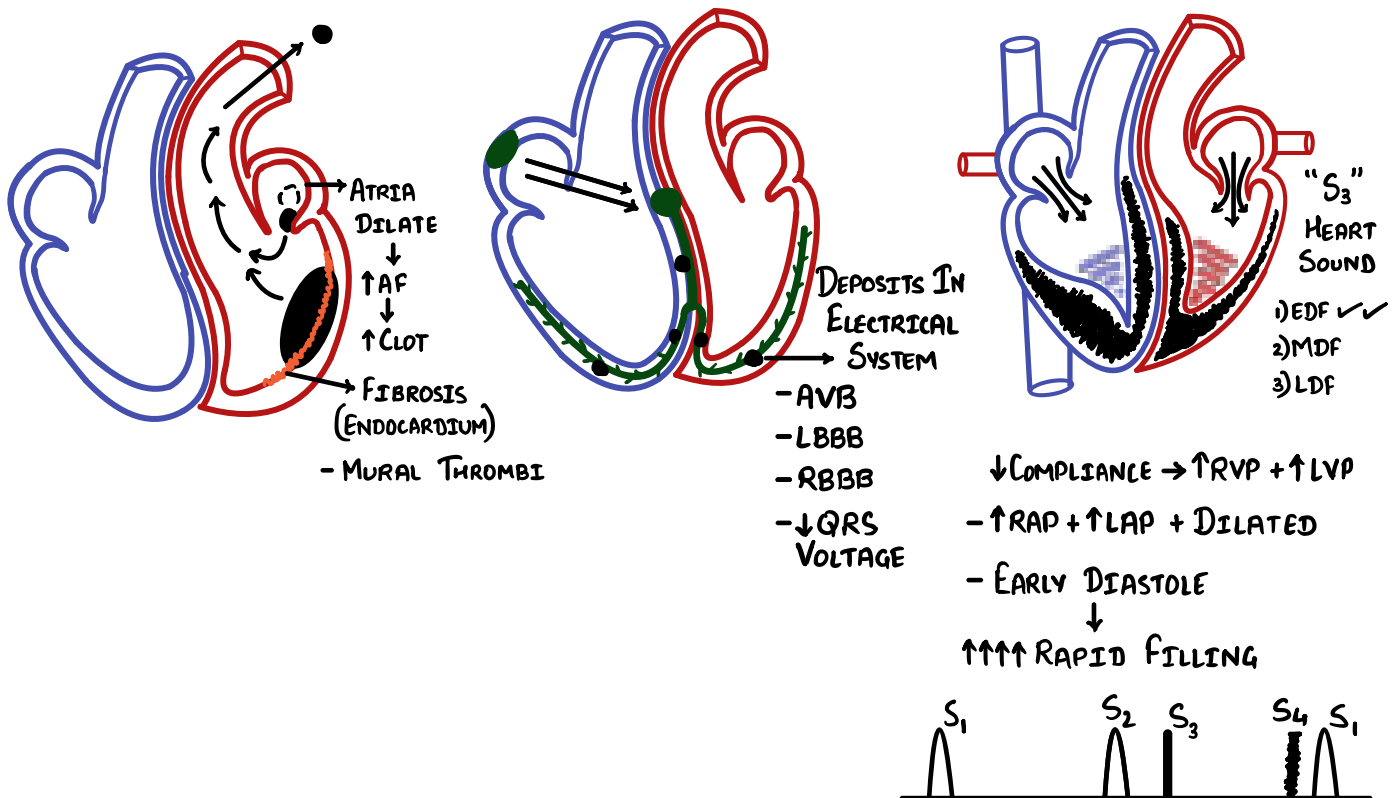
- Recall: The increased pressure and volume in the atria cause **atrial dilation**
- In atrial dilation, the myocardial tissue is stretched, altering their electrical activity
- Thus, atrial dilation increases the risk for arrhythmias such as **atrial fibrillation**
- In atrial fibrillation, there is a re-entrant circuit causing abnormal atrial contractions
- The loss of the "atrial kick" (atrial contraction during the end-diastolic filling phase) causes blood stasis within the atrium, increasing the risk of **thrombus/clot formation**
 - There is an increased risk for an **embolus** to break off from the clot and cause a stroke
- In conditions involving the endocardium (e.g. endomyocardial fibrosis, endocardial fibroelastosis, Loeffler endocarditis), there is endocardial inflammation/injury
 - Recall: Endothelial injury is one of the components of Virchow's Triad
 - There is increased risk of **mural thrombi formation**

(5) ECG Changes

- Deposits along the electrical conduction pathway of the heart can alter the electrical activity of nodes, increasing the risk for **atrio-ventricular blockades**
 - Example: Deposits along the left bundle branch diminish electrical activity reaching the ventricular tissue, causing **left bundle branch block**
- Deposits along the myocardium can lead to fibrous tissue formation
 - Recall: Fibrous tissue is non-contractile, and it cannot generate electrical activity
 - On ECG, this appears as **decreased QRS voltage**, particularly the R wave

(6) S3 and S4 Heart Sounds

- Recall: Decreased ventricular compliance leads to increased ventricular pressure, and subsequently increased atrial pressure and dilation
- In the early diastolic filling phase, ventricular pressure is at its lowest so there is rapid, turbulent filling of blood from the atrium, producing an **S₃ heart sound**
- When the atria hypertrophy due to longstanding increased pressure, these may produce a stronger kick/contraction, producing an **S₄ heart sound**
- The S₃ heart sound is more common than S₄ in patients with restrictive cardiomyopathy



V) DIAGNOSIS

- Patients with restrictive cardiomyopathy may be **asymptomatic** but they may present with symptoms
 - Sometimes, they present with some types of **dyspnea** because of the left-sided effects causing **pulmonary edema**
 - They may present with **ischemic chest pain** (angina, dyspnea on exertion) because of small reduction in cardiac output to the point of reducing cardiac perfusion
 - They can also present with right-sided heart symptoms
 - jugular venous heart distention, pedal edema

- Two common tests for patients with concerns of heart failure or ACS: **CXR** and **EKG**
 - May present with insignificant results for restrictive cardiomyopathy

(A) CHEST X-RAY

- If left-sided heart symptoms (CHF) are present, particular findings include:
 - Pulmonary edema
 - Pleural effusions
 - Atrial enlargement

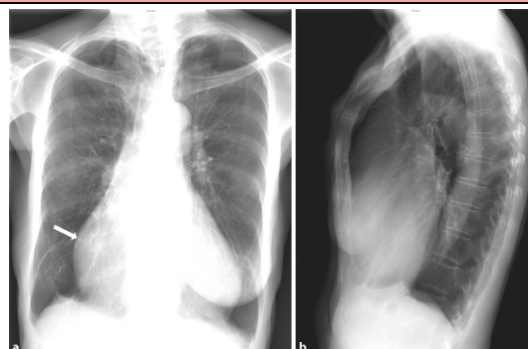
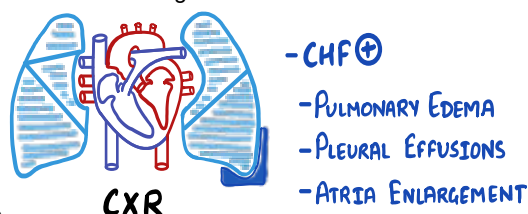
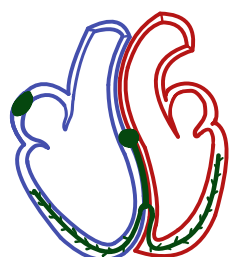


Figure 1. Right atrial enlargement (arrow) in patient with restrictive myocardiopathy [Bellman et al, 2017].

- Remember that these are **non-specific**

(B) 12 LEAD ECG



12 LEAD ECG

- AF ±
- AVB ±
- RBBB ± LBBB
- ↓ QRS VOLTAGE

- Atrial enlargement irritates the atria causing alterations of the electrical activity → increases the risk of **atrial fibrillation**
- Deposition of fibrotic tissue into the conduction system → conduction blocks
 - Deposits in the AV node = **AV block**
 - Deposits in the bundle branch = **right bundle branch block (RBBB)** and/or **left bundle branch block (LBBB)**
- Deposition of fibrotic tissue in the myocardium → alteration (reduction) in the electrical activity especially during the QRS complex where it is moving down to the ventricles and producing a nice QRS vector → **reduced QRS vector** because you don't have much myocardial tissue = **low QRS voltages**

Figure 2. Non-specific findings in EKG.

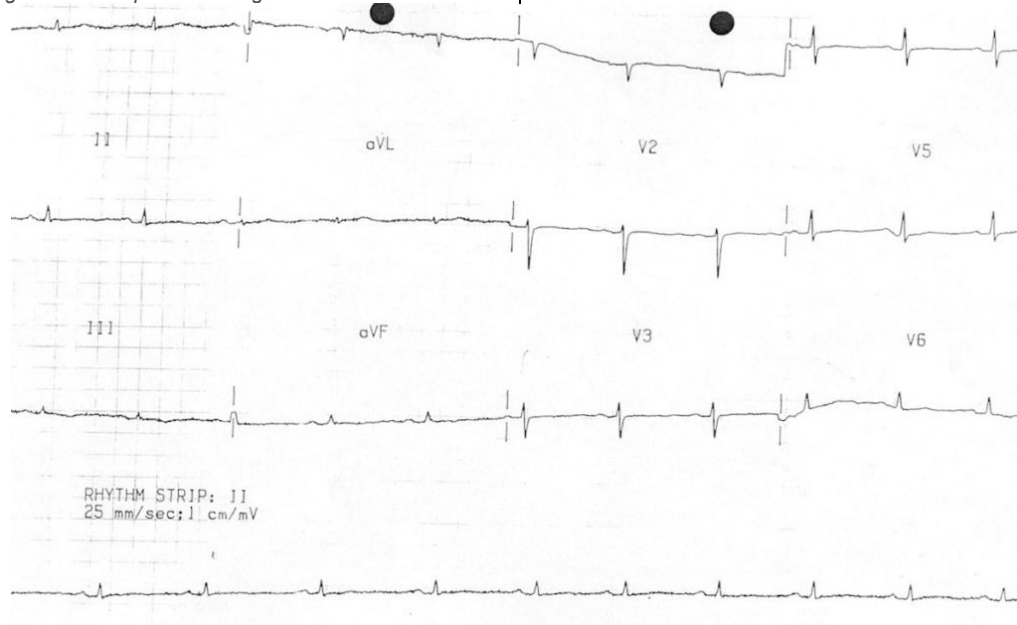


Figure 3. ECG of a patient with restrictive cardiomyopathy demonstrating low voltage QRS complex and widespread flattening of T waves [Burns & Buttner, 2021]



(C) ECHOCARDIOGRAPHY

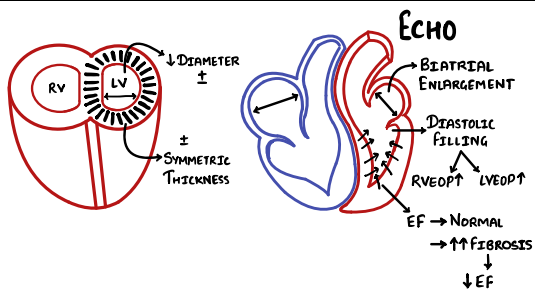


Figure 4. Echocardiography findings in coronal (A) and sagittal (B) sections.

- Best test to determine restrictive cardiomyopathy
- Particular findings:
 - **Symmetric thickening with slightly narrower diameter** of the ventricles (Figure 4A)
 - If the fibrotic mechanisms of the ventricle occur to the point where it makes it very rigid reducing the diameter
 - As compared to hypertrophic cardiomyopathy and dilated cardiomyopathy (very thin ventricular walls)
 - **Bi-atrial enlargement**
 - Significant reduction in **diastolic filling**
 - Observed with Doppler flow
 - High left and right ventricular end-diastolic pressures (LVEDP, RVEDP)
 - **Normal ejection fraction (EF)**
 - In cases where fibrosis is extensive, there is a possibility of reduction of EF

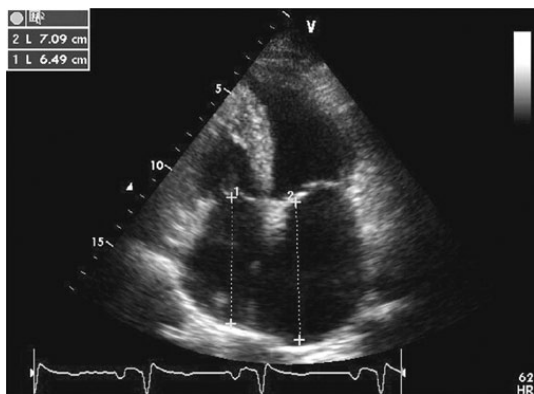


Figure 5. Echo of a patient with restrictive cardiomyopathy showing a disproportionately enlarged atria and a normal ventricular chamber size [Zwas et al, 2012].

(D) CARDIAC MRI

- Becoming more commonly utilized
- Gives a good look of the heart
- May highlight areas signs of infiltration or fibrosis in the myocardium

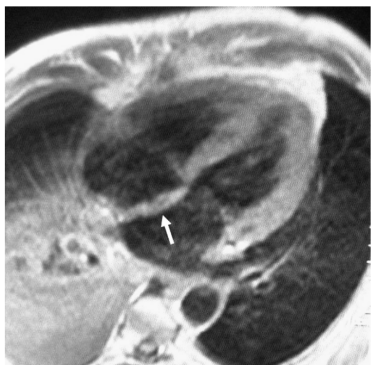


Figure 6. Amyloidosis. Fast spin-echo, T1-weighted image in four-chamber view reveals thickening of myocardium of both ventricles and bi-atrial dilatation. Characteristic of this condition is inter-septal thickening (arrow) [Gupta et al, 2011].

(E) CARDIAC CATHETERIZATION

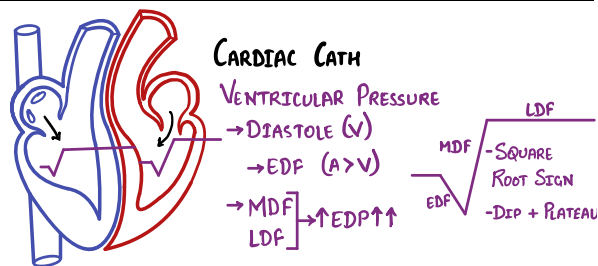


Figure 7. Cardiac catheterization.

- The ventricular activity can be observed with cardiac catheterization
- **Ventricular pressure curve**
 - Diastole: ventricles should be relaxed → pressure drops → makes it easier for the blood in the atria to flow down to the ventricles easily
 - **Early diastolic filling (EDF)**
 - Atrial pressure should be greater than the ventricular pressure so blood will naturally flow down to the ventricles
 - Will show as a drop in the ventricular pressure curve
 - **Mid- and late diastolic filling (MDF, LDF)**
 - Ventricles do not like blood coming into them resulting to a rapid rise in the end-diastolic pressure → rise in curve and then plateau
 - **Square root sign**: common finding in constrictive pericarditis
 - Also called **purple and plateau sign**

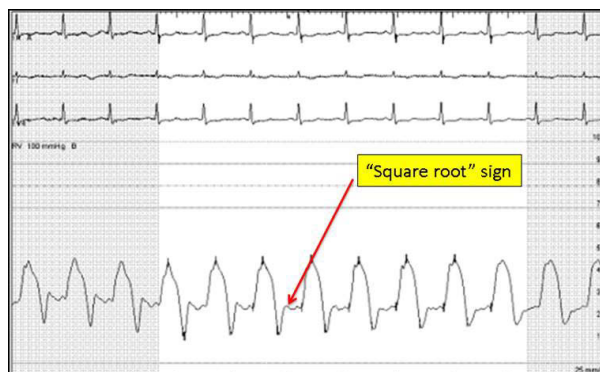


Figure 8. Right ventricular waveform showing a square root sign indicating constrictive pericarditis [ACC, 2016].

(F) ENDOMYOCARDIAL BIOPSY

- To determine the tissue in the endocardium and myocardium
 - Examples: Amyloid deposits, iron deposits, non-caseating granuloma, fibrous and elastic tissue, eosinophilic tissue
- In endomyocardial Bx, a sample is taken and is used to **identify the etiology**

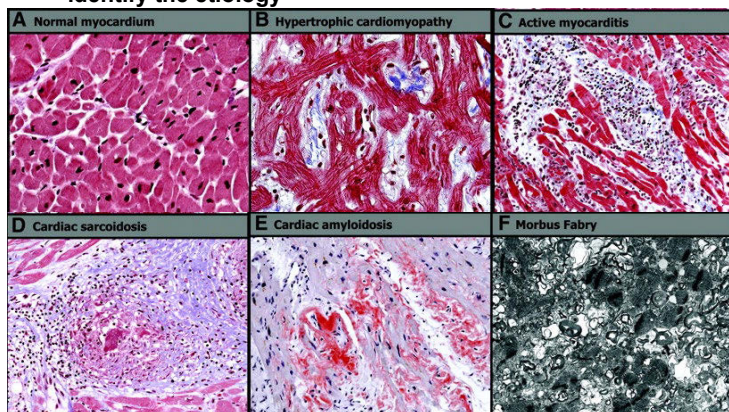


Figure 9. Examples of findings in endomyocardial biopsy [Yilmaz et al, 2010].

VI) TREATMENT

- Treatment is relatively similar to dilated cardiomyopathy and heart failure treatments

(A) ↓ PRELOAD

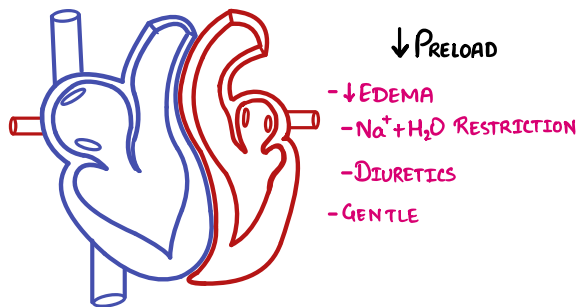


Figure 10. Ways to reduce preload gently: restriction of sodium and water, and diuretics.

- Remember that patients with RCM have reduction in diastolic filling
 - High diastolic filling processes can worsen the condition → blood goes back up in the lungs, to the lower extremities, etc. instead of going to the systemic circulation

(1) Reduce preload slowly and gently

- Therefore, the excessive amounts of preload should be returned **slowly and gently**
 - Too much reduction may lead to dehydration and hypotension

(2) Reduce the incidence of edema

- Restrict water and sodium intake
- Diuretics
 - In cases where there is still fluid overload leading to lower extremity edema and pulmonary edema
 - Help pull the water and sodium out of the circulation

(B) ↓ AFTERLOAD

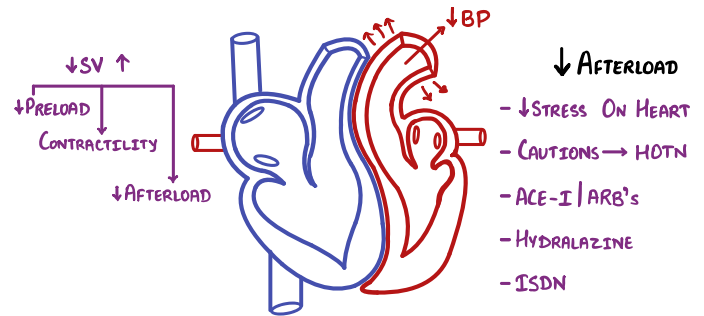


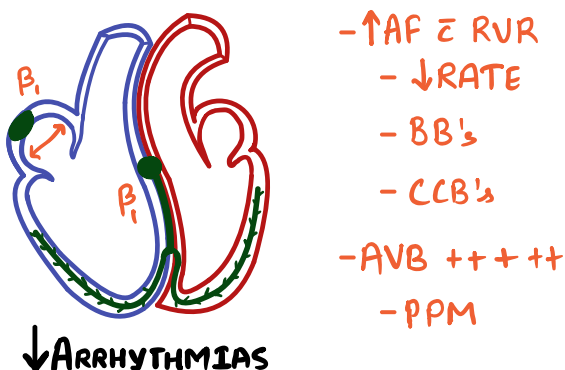
Figure 11. Management of RCM by reducing preload.

- Stroke volume (SV) is dependent on preload, contractility, and afterload
 - Contractility is normal in patients with RCM
 - Preload is reduced
 - Fixing the afterload reduces the stress in the ventricular myocardium
 - Therefore, **mildly reduce the afterload**

Effects of Reducing the Afterload

- Reduces stress in the heart → good SV and CO
- Cautions: **Hypotension**
 - May dilate the vessels → significant drop in the afterload accompanied by reduced preload → **significant drop in the SV** → hypotension
 - Reduce risk through medications that gently **dilate the arterioles** such as:
 - ACE-inhibitors and ARBs
 - Hydralazine
 - Isosorbide dinitrate (ISDN)

(C) ↓ ARRHYTHMIAS



(1) Atrial fibrillation ± rapid ventricular rate (RVR)

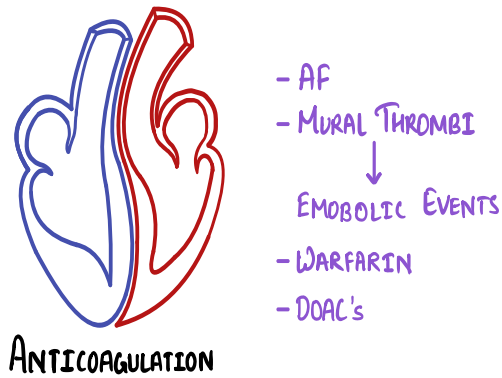
- RVR also called tachyarrhythmias
- Due to bi-atrial enlargement
- Can be addressed with medications that decrease rate and risk of arrhythmias
 - **Beta-blockers**
 - Block the β_1 receptors on the conduction system
 - Examples: metoprolol, esmolol
 - **Calcium channel blockers**
 - Block the Ca^{2+} channels in the conducting and myocardial cells → reduce Ca^{2+} entry → reduce action potentials → reduce contractility
 - Examples: diltiazem, verapamil

(2) AV block

- Significant AV blockade may need a **carbonate pacemaker**
- **Stay away from BB and CCB** → can significantly reduce heart rate

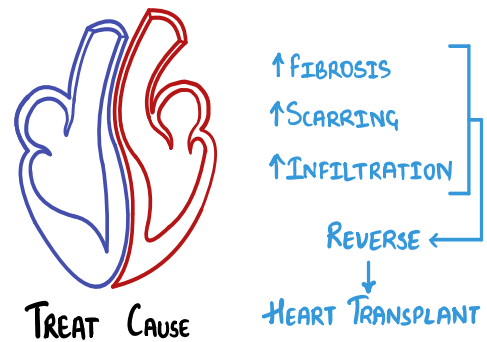


(D) ANTICOAGULATION



- ↑ risk of **AF** = ↑ risk for thromboembolic events
- ↑ risk of **mural thrombi**
 - Due to the fibrosis in the endocardium: fibroelastosis, endomyocardiofibrosis, Loeffler endocarditis
 - There is endothelial injury and reduction in the thromboembolic activities forming clots
- **Medications:**
 - Warfarin
 - DOAC's (e.g. rivaroxaban, apixaban, dabigatran)

(E) TREAT THE UNDERLYING CAUSE

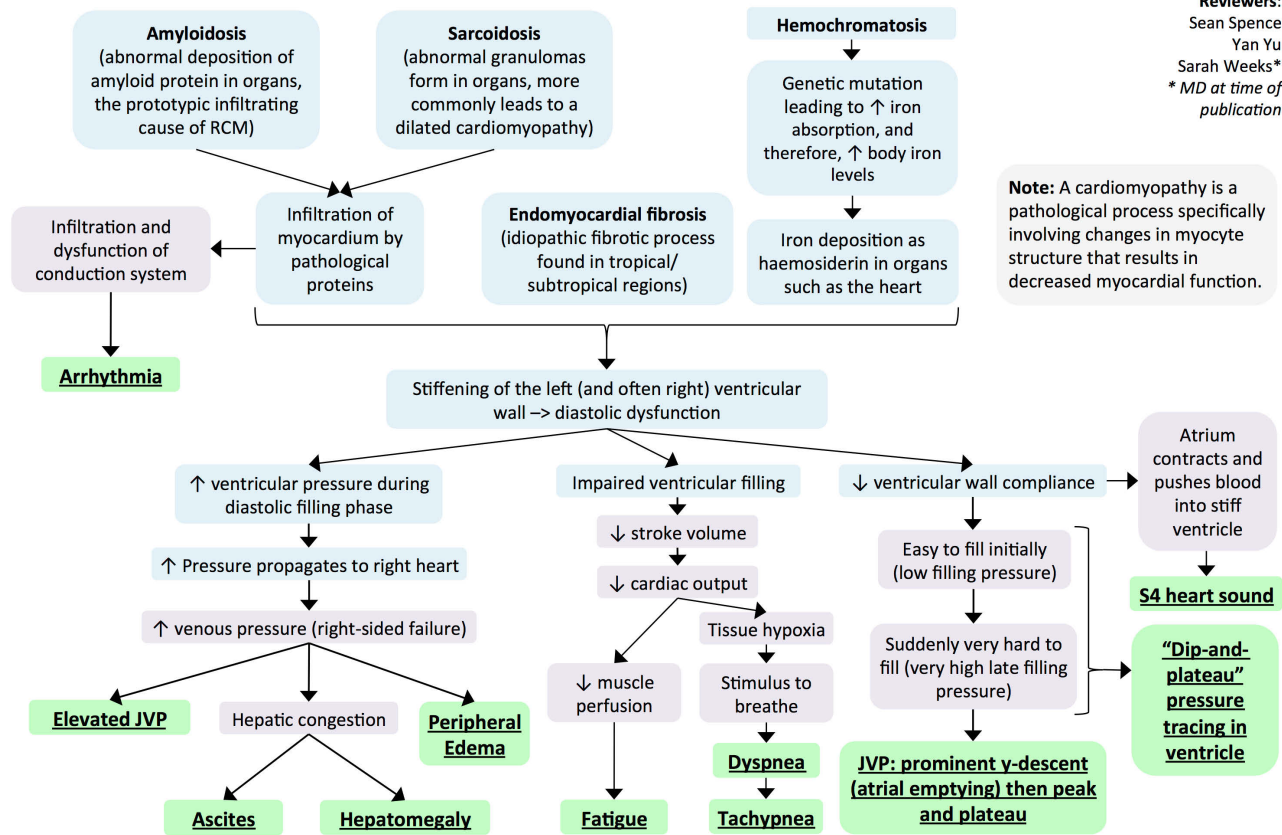


- Usual underlying causes to prevent progression:
 - **Amyloidosis**
 - May need chemotherapy, monoclonal Abs
 - **Sarcoidosis**
 - May need steroids, DMARDs
 - **Hemochromatosis**
 - May need iron chelating agent, phlebotomy
 - **Loeffler's**
 - May need steroids
- Sometimes these causes results to **irreversible damage** to the myocardium leading to extensive scarring, fibrosis and infiltration
 - Only way to reverse is through **heart transplant**



Restrictive Cardiomyopathy (RCM): Pathogenesis and clinical findings

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* MD at time of publication



Legend: Pathophysiology Mechanism Sign/Symptom/Lab Finding Complications Published February 21, 2014 on www.thecalgaryguide.com

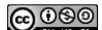


Figure 12. Pathophysiology of Restrictive Cardiomyopathy

[The Calgary Guide to Understanding Disease]

TABLE 254-5 Causes of Restrictive Cardiomyopathies
Infiltrative (Between Myocytes)
Amyloidosis
Primary (light chain amyloid)
Familial (abnormal transthyretin) ^a
Senile (normal transthyretin or atrial peptides)
Inherited metabolic defects ^a
Storage (Within Myocytes)
Hemochromatosis (iron) ^a
Inherited metabolic defects ^a
Fabry's disease
Glycogen storage disease (II, III)
Fibrotic
Radiation
Scleroderma
Endomyocardial
Possibly related fibrotic diseases
Tropical endomyocardial fibrosis
Hypereosinophilic syndrome (Löffler's endocarditis)
Carcinoid syndrome
Radiation
Drugs: e.g., serotonin, ergotamine
Overlap with Other Cardiomyopathies
Hypertrophic cardiomyopathy/ "pseudohypertrophic" ^a
"Minimally dilated" cardiomyopathy
Early-stage dilated cardiomyopathy
Partial recovery from dilated cardiomyopathy
Sarcoidosis
Idiopathic^a

^aCan be familial.

Figure 13. Causes of Restrictive Cardiomyopathies

[Harrison's Pg. 1792: Table 254-5]



VIII) REVIEW QUESTIONS

- 1) Which of the following is NOT characteristic of restrictive cardiomyopathy?
 - a) Decreased ventricular compliance
 - b) Decreased atrial pressure
 - c) Increased ventricular pressure
 - d) Decreased stroke volume
- 2) Which of the following is a symptom of right-sided heart failure?
 - a) Orthopnea
 - b) Paroxysmal nocturnal dyspnea
 - c) Pedal edema
 - d) Systolic murmur
- 3) Which of the following correctly describes endocardial fibroelastosis?
 - a) It is commonly found in young children with a congenital heart disorder
 - b) There is an increased level of eosinophils in the blood
 - c) Non-caseating granulomas are deposited along the cardiac tissue, subsequently causing fibrosis
 - d) The fibrous and elastic tissue are formed after administration of radiation therapy
- 4) Which of the following statements is FALSE?
 - a) When the jugular veins distend even during inspiration, this is Kussmaul's sign
 - b) In the mid-diastolic filling phase, the atrium contracts to push blood into the ventricle
 - c) Restrictive cardiomyopathy can manifest as decreased QRS voltage on ECG
 - d) Atrial dilation due to restrictive cardiomyopathy can increase the risk for arrhythmias
- 5) Which of the following is NOT a possible complication of restrictive cardiomyopathy?
 - a) Left bundle branch block
 - b) Myocardial ischemia
 - c) Mural thrombi formation
 - d) Aortic dissection
- 6) The following are findings of restrictive cardiomyopathy in CXR except:
 - a) Atrial enlargement
 - b) Ventricular enlargement
 - c) Pleural effusion
 - d) Pulmonary edema
- 7) The following are non-specific findings of restrictive cardiomyopathy in EKG:
 - a) Atrial flutter
 - b) Atrial fibrillation
 - c) Low QRS voltage
 - d) B and C
 - e) All of the above
- 8) Which is an echocardiographic finding in patients with restrictive cardiomyopathy?
 - a) Biventricular enlargement
 - b) Reduced ejection fraction
 - c) Asymmetric thickening with narrower diameter
 - d) All of the above

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PERICARDITIS AND PERICARDIAL EFFUSION

OUTLINE

I) ANATOMY
II) DISEASE STATES
III) CAUSES
IV) CLINICAL MANIFESTATIONS
V) PHYSICAL EXAMINATION

VI) DIAGNOSIS
VII) TREATMENT OF PERICARDITIS
VIII) QUESTIONS
IX) REFERENCES

I) ANATOMY

(A) PERICARDIUM

(1) Dissect the word

- “Peri-” means around
- “-Cardia” means heart

(2) Structure

- Surrounds or Covers the outside of the heart and the great vessels (e.g. aorta)

(i) Outer Fibrous Layer

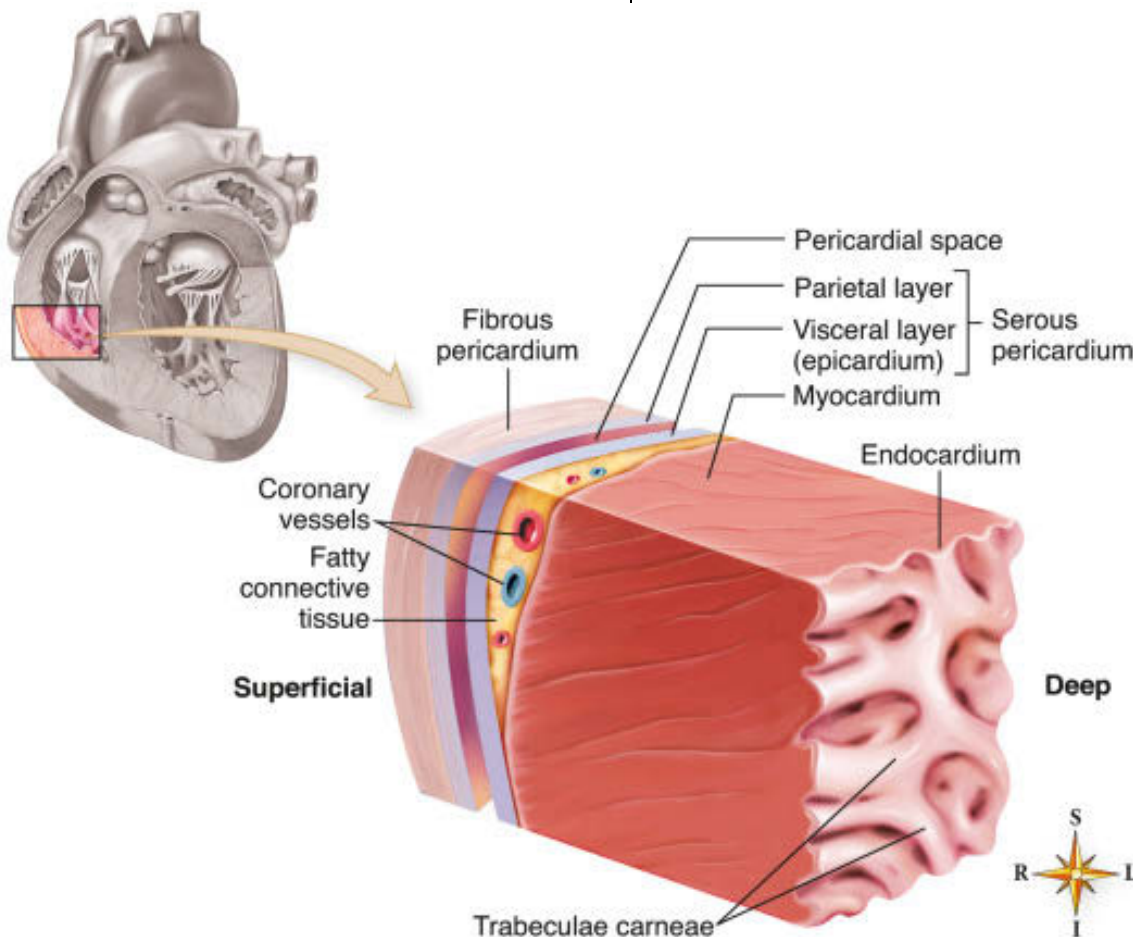
(ii) Inner Serous Layer is further divided into the ff:

- **VISCERAL LAYER OF SEROUS PERICARDIUM**
→ attaches to the **myocardium** (muscular layer of the heart)
- **PARIETAL LAYER OF SEROUS PERICARDIUM**
→ attaches to the outer fibrous layer
- In-between the two layers of the Inner Serous Layer is the **PERICARDIAL CAVITY** which contains the **PERICARDIAL FLUID**

(3) Functions

- Protects the heart by providing an extra cushion for the heart
- Pericardial fluid prevents a lot of friction during contraction-relaxation that promotes inflammation
- Protects the great vessels from kinking
- Anchors the heart
- Prevents overstretching of the heart due to overfilling of blood

*From **INTERIOR TO EXTERIOR**, the order of the layers of the heart is endocardium → myocardium → visceral layer of the serous pericardium (epicardium) → pericardial cavity → parietal layer of serous pericardium → fibrous pericardium [Snell]*



II) DISEASE STATES

(A) PERICARDITIS

(1) Definition

- Inflammation of the visceral layer of the serous pericardium, the parietal layer of the serous pericardium, and sometimes fluid accumulation in the pericardial cavity

(2) Types

(i) Acute

- Pericarditis of **less than 3 months**

(ii) Chronic

- Pericarditis of **more than 3 months**

(B) PERICARDIAL EFFUSION

(1) Step-by-Step Mechanism

- Inflammation of the visceral or the parietal layer of the serous pericardium causes cytokines to be released
- Cytokines** adjacent to the serous pericardium becomes more permeable.
- The endothelial cells of the blood vessels will loosen and more fluid leaks from the blood vessels to the pericardial cavity.
- More **fluid accumulates in the pericardial cavity**
→ **PERICARDIAL EFFUSION**

*One can have pericarditis **without** pericardial effusion. But most of the time pericarditis **leads to** pericardial effusion.*

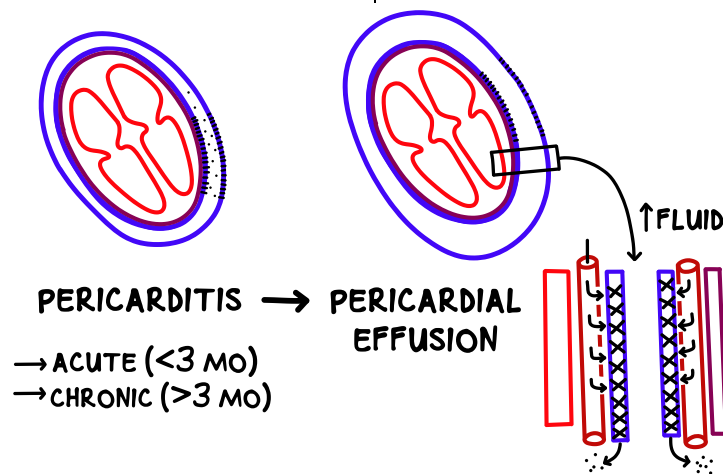


Figure 1. Pericarditis and Pericardial Effusion.

(C) CARDIAC TAMPONADE

(1) Step-by-Step Mechanism

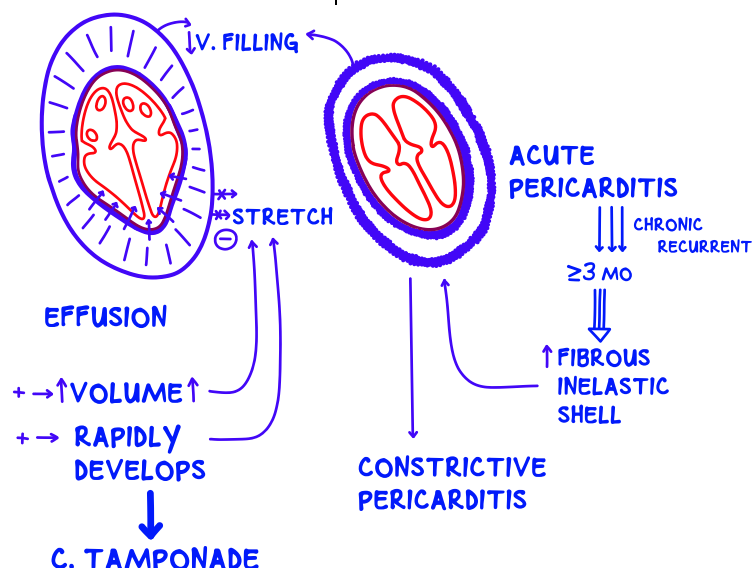
- In the presence of a **rapidly developing pericardial effusion**, there will be a significant increase in volume in the pericardial cavity
- Because the fluid accumulation occurred rapidly, the heart has no enough time to stretch. Failure to stretch can also be because the heart has reached its maximum stretch point.
- Failure to stretch causes the excess fluid to start squeezing on the heart → **CARDIAC TAMPONADE**

*Overall, cardiac tamponade will **reduce ventricular filling** reducing the cardiac output and so the blood pressure as well.*

(D) CONSTRICTIVE PERICARDITIS

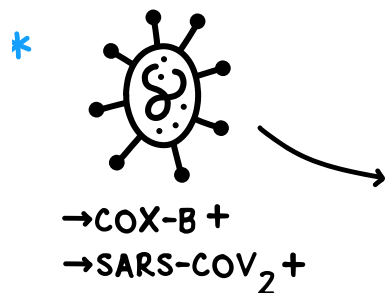
(1) Step-by-Step Mechanism

- If an acute pericarditis persists 3 months or greater (as chronic or recurrent), the fibrous/inelastic tissue around the pericardium increases.
- The increase in the **fibrous/inelastic tissue** don't allow blood to come in anymore (↓ ventricular filling)
→ **CONSTRICTIVE PERICARDITIS**

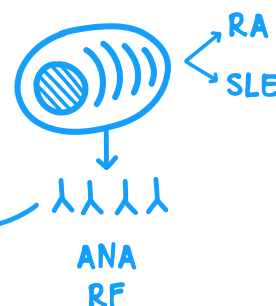


III) CAUSES	
(A) INFECTIOUS	(B) AUTOIMMUNE
(1) Mechanism - Invades the pericardium making it to release inflammatory mediators and cytokines → Blood vessels become more porous → Fluids leaks out to the pericardium → Pericarditis with/without pericardial effusion. (2) Viruses More common infectious etiology - Transmission is by respiratory droplets (i) <u>Coxsackie-B</u> (ii) <u>SARS-COV2</u> - Causes COVID - Transmission is by respiratory droplets - Gold Standard Test: RT-PCR (3) Bacteria Less common infectious etiology - Usually becomes a problem after a recent cardiothoracic surgery wherein the patient is being opened up allowing the bacteria to seed in (i) <u>Staphylococcus aureus</u> (ii) <u>Streptococcus pneumoniae</u> (iii) <u>Mycobacterium tuberculosis</u> <i>Most of the time pericarditis is idiopathic. But most of the time it is likely infectious.</i>	(1) Mechanism - Antibody-mediated process such as - Anti-nuclear antibodies - Rheumatoid factor - Antibodies cause inflammation or agitation to the pericardium (Figure 2). (2) Common Autoimmune Diseases (i) <u>Rheumatoid Arthritis</u> (ii) <u>Systemic Lupus Erythematosus (SLE)</u>
(C) UREMIA	
(1) Mechanism - Present in patients with: (i) <u>Chronic Kidney Disease (CKD)</u> - Usually end-stage renal disease on hemodialysis (ii) <u>Acute Kidney Injury</u> - Intensive kidney injury - Waste products such as UREA AND CREATININE fail to be secreted by the kidneys. Urea can deposit to the pericardium leading to inflammation and to fibrosis	

INFECTIOUS



AUTOIMMUNE



UREMIA

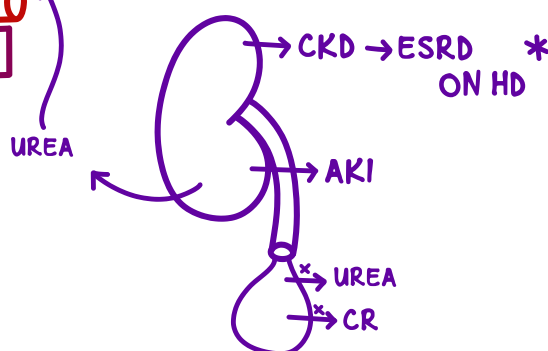


Figure 2. Infectious and Autoimmune Causa



(D) NEOPLASIA

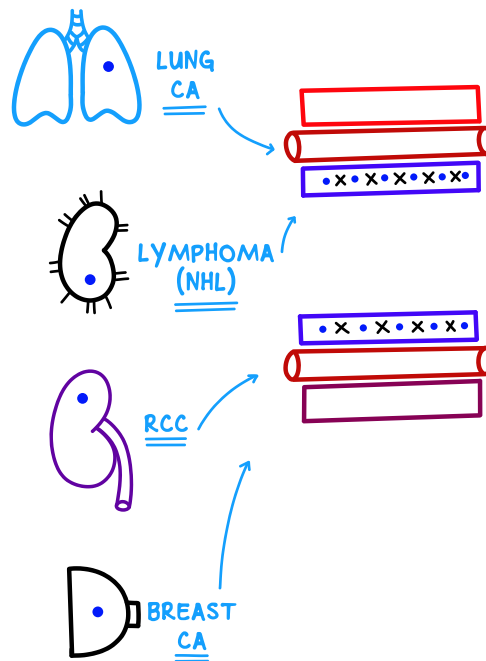
(1) Mechanism

- Primary cancers metastasize to the pericardium and manifest as pericarditis.
- Other causes should be ruled out.

(2) Neoplasia that are Most Likely to Metastasize

- Lung Cancer
- Lymphoma (Non-Hodgkin) and Leukemia
- Renal Cell Carcinoma (RCC)
- Breast Cancer

NEOPLASIA



(E) RADIATION

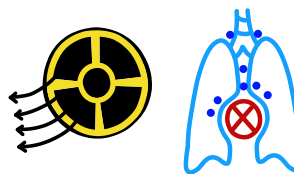
(1) Mechanism

- Radiation destroys the pericardial tissue causing the inflammatory cells to clear the debris.
- Fibrous tissue gets deposited to replace the destroyed pericardial tissue

(2) Use

- Chemotherapy in neoplasia

RADIATION



(F) POST-MYOCARDIAL INFARCTION

(1) Mechanism

- No blood getting into the heart
→ No oxygen is getting into the infarcted area of myocardium
- Myocardial cells start dying.
→ Immune cells clear up the destroyed tissue.
→ They release cytokines causing subsequent inflammation of the blood vessels near the pericardium.
- Blood vessels become more porous
→ Fluids leak out to the pericardium
→ Pericarditis with/without pericardial effusion.

(2) Implications

(i) 1-3 Days Post-MI

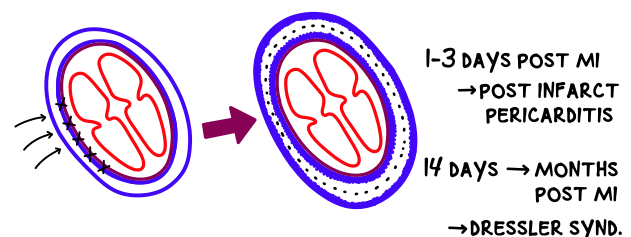
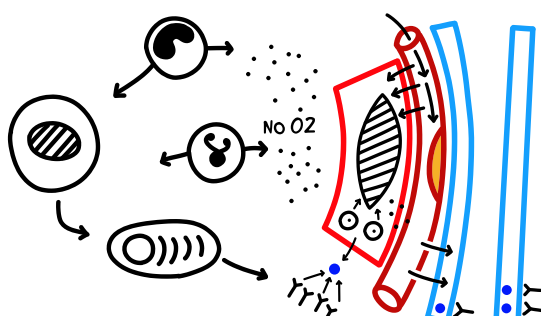
- Likely related to the infarct itself and the localized inflammation

(ii) 14 Days –Months Post-MI

▪ DRESSLER SYNDROME

- A condition in which there is inflammation and subsequent fibrosis of the infarcted area
→ During that process, they collect myocardial proteins and present them to lymphocytes
→ Lymphocytes make antibodies for the myocardial proteins
→ These antibodies can also attack other pericardial proteins that resemble the myocardial proteins.

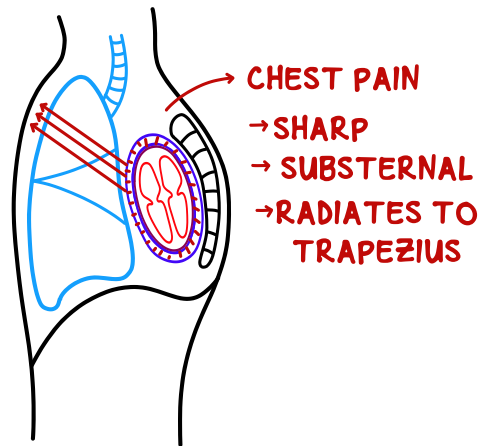
POST-MI



IV) CLINICAL MANIFESTATIONS

(1) CHARACTERISTIC chest pain

History	Pericarditis
Quality	Sharp (In comparison to angina which is a squeezing, tight, heavy pain.)
Location	Substernal
Radiation	Trapezius



(2) The pain is POSITIONAL

- Positional pain: ↑ and ↓ based on one's position.

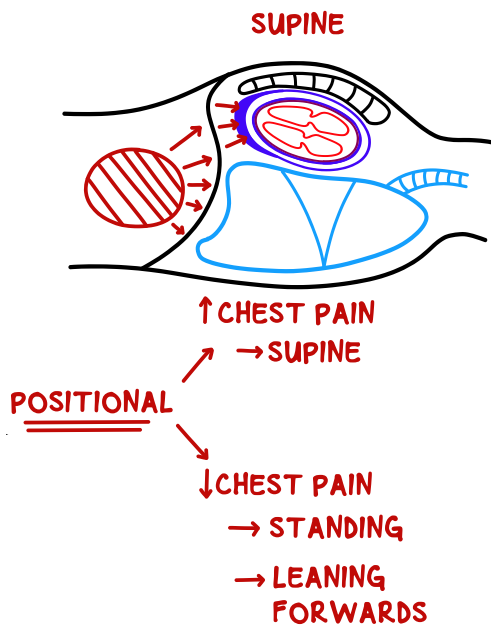


Figure 3: Positional pain

	Increasing pain	Decreasing pain
Position	Lying supine	Standing upright or leaning forward
Why?	Abdominal contents push on the diaphragm → diaphragm pushes on the pericardium (which has an effusion) causing pain	Diaphragm drops down (↓ compression) and heart moves anteriorly (↓ pressure)

(3) The pain is PLEURITIC

- Pleuritic pain: changes during respiratory cycles.
 - During inspiration → Inflation of the lung
 - Lungs expand towards the chest wall and also towards the heart
 - ↑ Pressure on the heart
 - ↑ Pain

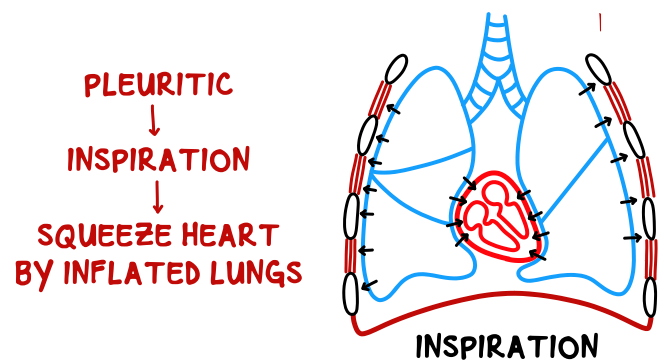


Figure 4: Pleuritic pain

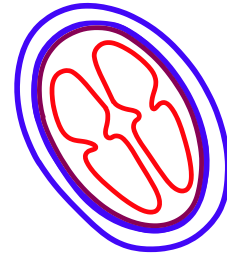


(1) Pericardial friction rub

- During:
 - Atrial systole
 - Ventricular diastole
 - Ventricular systole
- There is rubbing of the pericardium
 - Produces a sound that is called
 - **Scratchy triphasic heart sound**

**FRICITION
RUB**

→ **A. SYSTOLE**
→ **V. DIASTOLE**
→ **V. SYSTOLE**



(2) Pericardial effusion

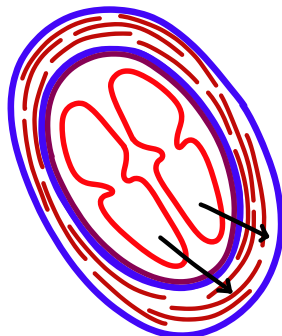
(i) Heart sound

- Normally: cardiac cycle produces S1 and S2 sounds

Sounds	Cause → closing of valves:
S1	Mitral and Tricuspid valves
S2	Aortic and Pulmonary valves

- When there is an effusion, those sounds travel through the fluid
 - **the sound is muffled, distant, and generally decreased**

± P. EFFUSION

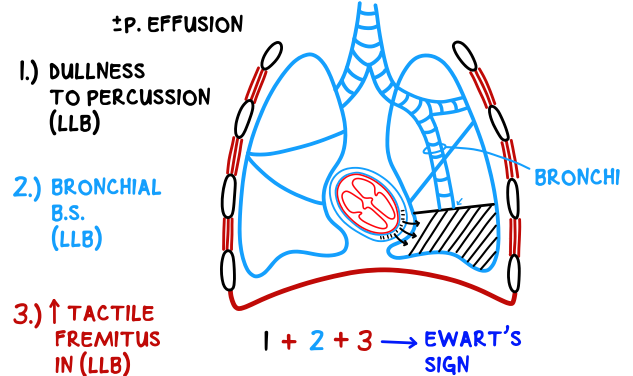


→ **S1**
→ **S2**

**MUFFLED
OR
DISTANT**

Figure 5: Due to pericardial effusion, S1 and S2 sounds are muffled or distant

(ii) Lung sounds



- In case of effusion (usually located at the apex of the heart where it is pooled), the lung is compressed (LLB; left lung base) and no air gets in that portion of the lung

(a) This portion (LLB) will show **dullness to percussion**

- Normally, air flow through the respiratory tract produces different breath sounds:
 - Tracheal sounds
 - Bronchial sounds
 - Bronchovesicular sounds
 - Vesicular sounds

(b) In case of a consolidation (or a similar state), air will not get into the alveoli of that certain portion (LLB), using the stethoscope the sound will be '**bronchial breath sounds**' instead of what would normally be '**vesicular breath sounds**'

- By placing the hand (hypothener eminence) on the back of the posterior portion of the left lung, then asking the patient to speak the words "ninety-nine"

(c) There would be an increased conduction of the air sounds and make the felt vibration on the hypothener eminence more intense, and that is called:
Tactile (vocal) fremitus

(a, b, and c) collectively are called: **EWART'S SIGN**

→ They are indicative of a large pericardial effusion that causes compression and atelectasis of the LLB



VI) DIAGNOSIS

(1) 12-lead ECG

ECG	Findings
	Normal
	ST↑ (Diffuse + concave)
	PR↓ (inferior leads)
	↓QRS VOLTAGE
	ST↑ (convex) Myocardia infarction

(2) Cardiac Imaging

Imaging technique	Benefits
Chest X-ray	Enlargement of the cardiac silhouette
ECHO	It is the best test. Shows effusion Also shows thickening of the pericardium
CT/ MRI of the chest	To rule out Pulmonary embolism (especially with pleuritic chest pain) Can also show pericarditis, and effusions

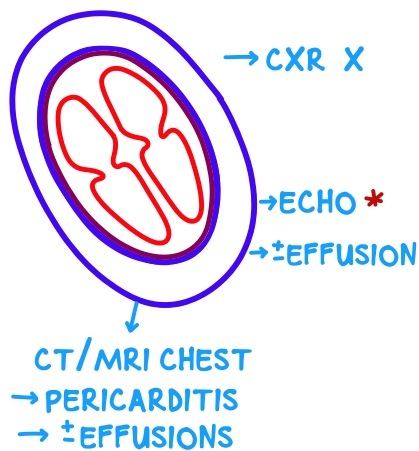


Figure 6: Cardiac imaging

(3) Criteria for diagnosis

- I. CP SPECIFIC FOR PERICARDITIS
- II. FRICTION RUB ⊕
- III. ECG Δ'S (ST↑ + PR↓)
- IV. NEW EFFUSION/ WORSE EFFUSION

(4) Pericardial Fluid Analysis

Indications	Tests
○ Purulent infection suspected (history of recent thoracic surgery) ○ High fevers (that don't respond to pericarditis therapy) ○ Septic appearance	○ Cultures ○ Gram stain ○ Acid fast stain
○ Malignancy	○ Cytology

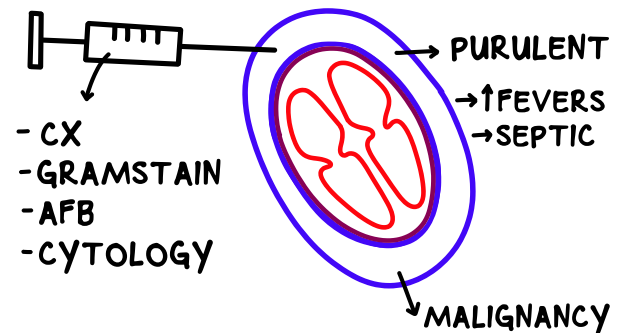


Figure 7: Pericardial fluid analysis

VII) TREATMENT OF PERICARDITIS

- Pericarditis is inflammation of the pericardium, so the primary goal of treatment is pain relief.

(A) NSAIDS

- High dose
 - Ibuprofen, Indomethacin, Aspirin (most common)
 - For 7-10 days

MECHANISM OF ACTION

- When the epithelial cells of the pericardium undergo inflammation, different membranes breakdown.

RECALL:

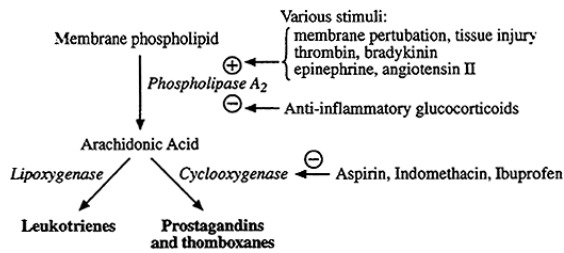


Figure 8. MoA of NSAIDs

- NSAIDs inhibit **cyclooxygenase** enzyme to reduce PG and LTs, these substances increase vascular permeability and cause WBC to flood into the area, which can exacerbate the inflammation.

(B) COLCHICINE

- The use of colchicine is controversial in cardiology however some studies have shown it **reduces recurrence of pericarditis**.

It can be used in combination with NSAIDs either:

- From the start of pericarditis
- If NSAIDs fail to reduce inflammation, colchicine can be added.

MECHANISM OF ACTION

- During inflammation, neutrophils use **microtubules** to help with diapedesis, phagocytosis. Colchicine inhibits the microtubules, therefore decreases migration and function of neutrophils.

(C) STEROIDS:

- Prednisone, Methylprednisolone
- Although it can have benefits, use of steroids should be avoided in pericarditis because they increase the recurrence rate.
 - EXCEPTION: patients with tuberculosis.

Cases when steroids are useful:

- For patients with contraindications to NSAIDs use, e.g. patients with uremia, peptic ulcer disease, chronic kidney disease
- Autoimmune diseases e.g. SLE, RA

I. ↑DOSE NSAIDS

→ IBUPROFEN
→ INDOMETHACIN
→ ASA (M/C)

+

II. COLCHICINE

→ ○MICROTUBULES
→ ↓RECURRENCE OF PERICARDITIS

III. STEROIDS XXX

→ UREMIA → ↑RECURRENCE PERICARDITIS
→ SLA + RA
→ CI TO NSAIDS

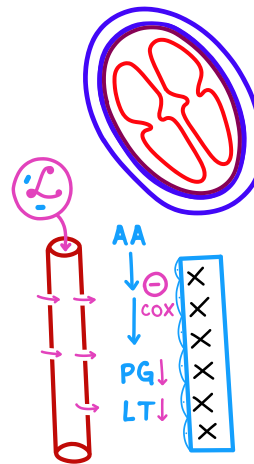


Figure 9. Drugs for Inflammation

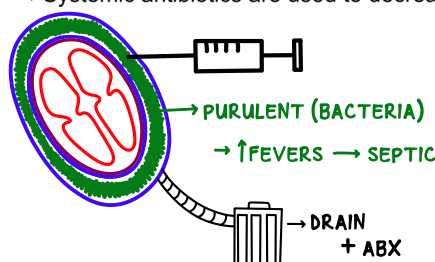
(D) INVASIVE TREATMENTS

INVASIVE TREATMENT OF PERICARDITIS

- Invasive treatments are performed in severe cases of pericarditis, like when there is **Purulent Bacterial Infection**
 - Signs: high fever, septic appearance

Treatment:

- Pericardiocentesis for lab testing and drainage
- Inserting a drain in the pericardial cavity to get rid of the purulent fluid
 - Systemic antibiotics are used to decrease risk of sepsis

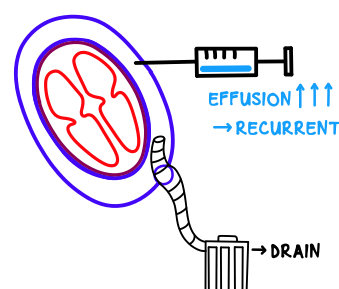


INVASIVE TREATMENT OF EFFUSION

- Treating the underlying pericarditis can't reduce the effusion or prevent progression, this is the main approach.
 - HOWEVER, if the effusion is increasing and the patient has a chronic disease (**malignancy**), invasive treatments are used.
 - Because these patients, the effusion can worsen and become recurrent.

Treatment:

- Pericardiocentesis or insert a drain to get rid of all the pericardial fluid.



VIII) QUESTIONS

1) Where is the location and radiation, respectively of chest pain in pericarditis?

Location Radiation

- a) Substernal —> Subscapular
- b) Trapezius —> Substernal
- c) Subscapular —> Substernal
- d) Substernal —> Trapezius

2) When is pericardial friction rub NOT experienced?

- a) A. Systole
- b) V. Systole
- c) A. Diastole
- d) V. Diastole

3) Dullness to percussion in the left lower lung area from atelectasis due to a large pericardial effusion is called?

- a) Müller's sign
- b) Mayne' sign
- c) Ewart's sign
- d) Kussmaul's sign

4) What are the ECG findings in pericarditis?

- a) ST-segment depression and PR segment elevation
- b) ST-segment elevation and PR segment depression
- c) Elevated and convex ST segment
- d) Increased QRS voltage

5) Which of the following is NOT amongst the criteria for diagnosis of pericarditis?

- a) Squeezing, tight chest pain
- b) Sharp chest pain
- c) Friction rub
- d) Changes in ECG

6) In which disease do steroids not increase the recurrence of pericarditis?

- a) SLE
- b) CKD
- c) TB
- d) RA

7) Which drug decreases the risk of recurrence?

- a) Colchicine
- b) Ibuprofen
- c) Prednisone
- d) Indomethacin

IX) REFERENCES

- Snell, R. (2012). *Clinical Anatomy by Regions* (9th Ed.). China" Lippincott Williams & Wilkins.





CARDIAC TAMPONADE

[Cardiac Tamponade](#)

Medical Editors: Camille, Maxine & Aldrich

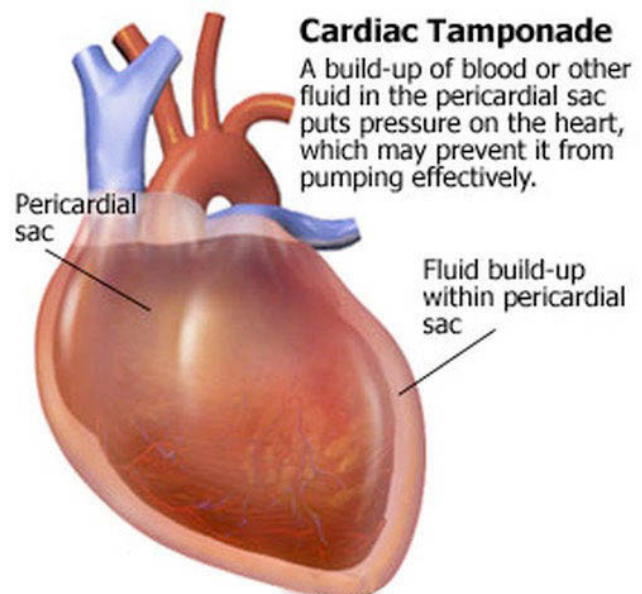
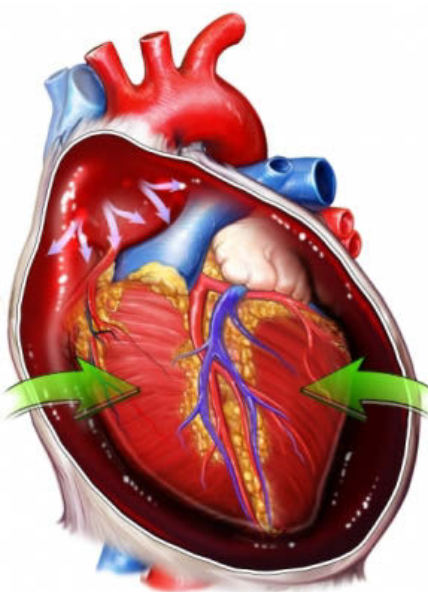
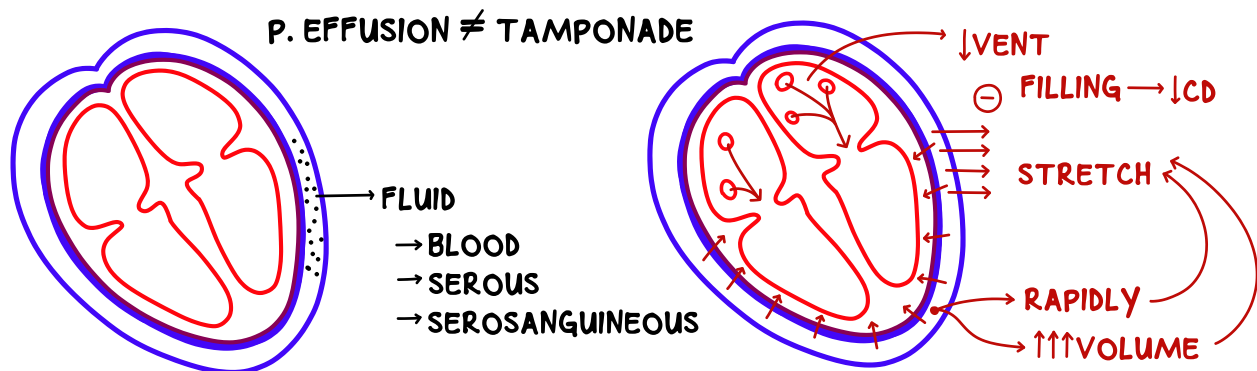
OUTLINE

- I) INTRODUCTION
- II) CAUSES
- III) PATHOPHYSIOLOGY
- I) CLINICAL FEATURES & PHYSICAL EXAM
- II) DIAGNOSIS
- III) TREATMENT – DEFEND THE MAP AT ALL COST!

- IV) TREATMENT – PERICARDIOCENTESIS & PERICARDIAL WINDOW
- TREATMENT SUMMARY
- V) APPENDIX
- VI) REVIEW QUESTIONS
- VII) REFERENCES

I) INTRODUCTION

- Recall: A fibrous sac called the **pericardium** surrounds the heart. The space in between is the **pericardial cavity**, which normally contains minimal fluid.
- **Cardiac tamponade** occurs when there is a rapid accumulation of fluid (e.g., blood, serous fluid) in the pericardial cavity
 - The pericardium cannot stretch
 - The fluid puts pressure on the heart and prevents it from pumping, reducing ventricular filling
- Cardiac tamponade is not the same as pericardial effusion
 - Both involve fluid accumulation in the pericardial cavity
 - However, they differ in terms of pathophysiologic mechanism



II) CAUSES

(A) HEMOPERICARDIUM

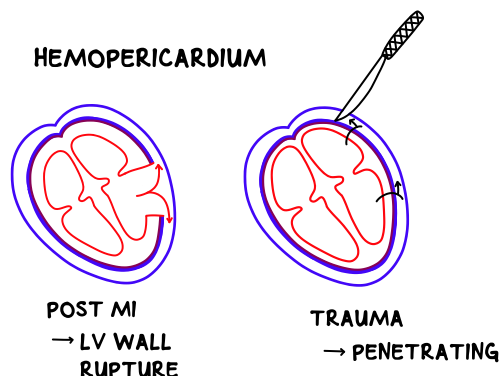
- Hemopericardium occurs when **blood** accumulates in the pericardial cavity.
- Fluid accumulation typically happens rapidly.

(1) Post-Myocardial Infarction

- Infarcted tissue is replaced with granulated tissue
- Granulated tissue is very weak, making that area thin and prone to rupturing
- **Left ventricular wall rupture** leads to rapid accumulation of blood in the pericardial cavity, causing cardiac tamponade

(2) Penetrating Trauma

- Penetrating trauma refers to an injury caused by a foreign object piercing the skin, damaging the underlying tissues
- Penetrating trauma which involves the heart may damage the atrial/ventricular walls, creating a hole through which blood leaks into the pericardial cavity

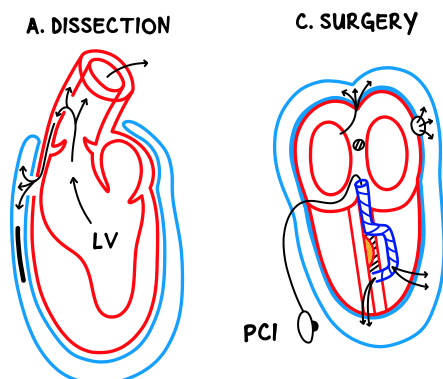


(3) Aortic Dissection

- The intimal lining of the aorta may weaken due to:
 - Smoking
 - Hypertension
 - Atherosclerosis
- When there is a tear in the intimal lining, blood enters through the tear and channels in between the intimal and medial layers
- It flows retrogradely, emptying into the pericardial cavity and causing hemopericardium

(4) Cardiac Surgery

- During cardiac surgery, the surgeon may damage structures in or near the heart and cause blood to leak into the pericardial cavity
 - Valve Repair
 - PCI
 - CABG
 - Ablation



(B) SEROUS / SEROSANGUINOUS

- Serous/Serosanguinous fluid accumulates in the pericardial cavity due to the causes of pericarditis.
- As opposed to hemopericardium, fluid accumulation happens gradually.

(1) Infectious

- Infectious pathogens which enter the body via hematogenous spread or direct inoculation (e.g., surgery) damage the pericardium

(i) Viral

- More common cause of pericarditis than bacterial infections
- Clinical presentation: low-grade fever, respiratory symptoms
- Examples: Coxsackie B virus, SARS-CoV-2 virus

(ii) Bacterial

- Clinical presentation: high-grade fever, septic appearance
- Examples: *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Mycobacterium tuberculosis*

(2) Neoplastic

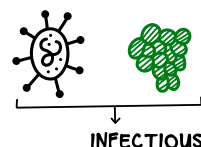
- Primary cancers can metastasize to the other sites such as the pericardium and cause inflammation
- Examples of primary cancers:
 - Lung cancer
 - Lymphoma
 - Renal cell carcinoma
 - Breast cancer

- Excessive urea in the blood deposit on the pericardium, causing inflammation
- Conditions which cause excessive serum urea levels include:
 - Chronic Kidney Disease / End Stage Renal Disease
 - Acute Kidney Injury

(4) Autoimmune

- Autoantibodies are generated and destroy the pericardial tissue
- Examples:
 - Systemic Lupus Erythematosus
 - Rheumatoid Arthritis

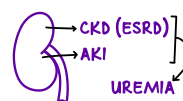
SEROUS/SEROSANGUINOUS EFFUSION



INFECTIOUS



NEOPLASIAS



UREMIA



III) PATHOPHYSIOLOGY

(A) INFLAMMATION

- Serous/Serosanguinous fluid accumulation in the pericardial cavity is mediated by inflammation
- As a response to inflammation, cytokines and histamine are released
- These travel to the local capillaries and increase their permeability
- Fluid leaks through the capillaries and accumulate in the pericardial cavity

Summary

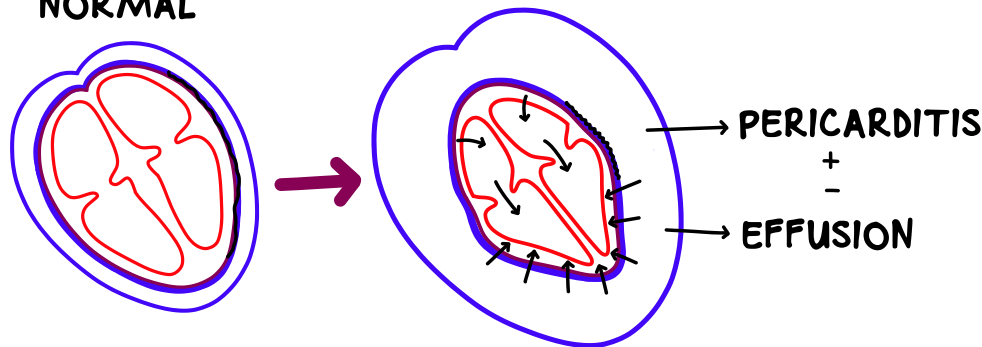
Pericarditis

- Inflammation
- Increased capillary permeability
- Fluid extravasation into the pericardial cavity
- Pericardial effusion

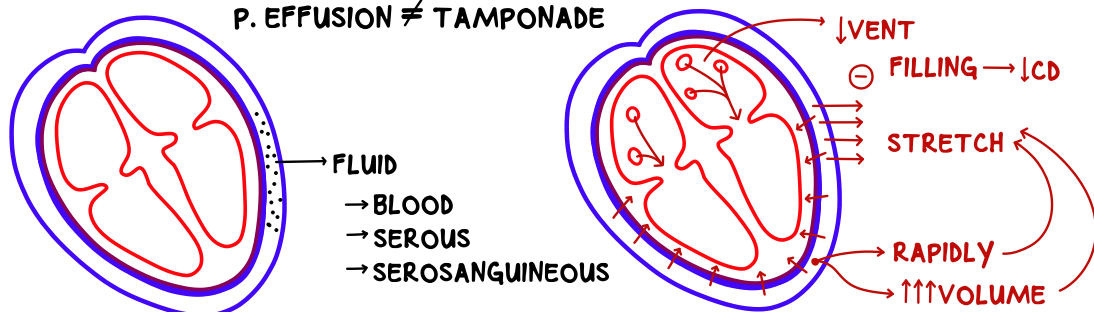
(B) PERICARDIAL EFFUSION VS CARDIAC TAMPONADE

- Pericardial effusion refers to the buildup of fluid in the pericardial cavity
- Cardiac tamponade occurs when the fluid in the pericardial cavity starts compressing the heart
 - The increased pressure on the heart reduces the inflow of blood into the atria and ventricles
 - This reduces preload/ventricular filling, stroke volume, and cardiac output
- When fluid is accumulating in the cavity, you want the pericardium to naturally stretch
 - The stretch accommodates the added volume of fluid
- Rapid or excessive accumulation of fluid increases the likelihood of cardiac tamponade
 - When there is rapid accumulation,
 - Fluid inhibits the “stretch” process
 - There is not enough time to stretch and accommodate the inflow of blood
 - Instead, the fluid will squeeze the heart, reducing the ventricular filling process and cardiac output, leading to **cardiogenic shock**
 - When there is excessive accumulation (increased volume)
 - The pericardium cannot stretch anymore, so the fluid starts exerting pressure on the heart

NORMAL



P. EFFUSION ≠ TAMPONADE



I) CLINICAL FEATURES & PHYSICAL EXAM

- Overarching theme: patients have ↑ intrapericardial pressure:

Mechanism 1:

- Due to rapid accumulation of the fluid and there is not enough time for the pericardium to stretch and accommodate the fluid
- The intrapericardial pressure increases exertion onto the actual heart

Mechanism 2:

- volume accumulation exceeds the allowable pericardial volume hence the pressure starts to be exerted on the heart

- Most common cause of pericardial effusion:

o Pericarditis

- ↑ Inflamed pericardium → muffled heart sounds
- If there's not much fluid → friction rub

(A) CARDIOGENIC SHOCK

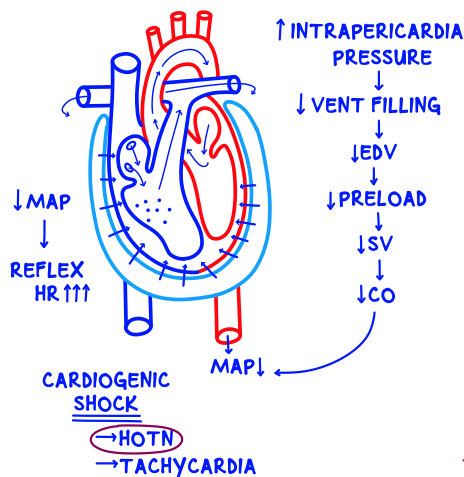


Figure 1. Cardiogenic shock pathophysiology.

- Pericardial tamponade is one example which causes cardiogenic shock:

Mechanism 1	Mechanism 2	Clinical manifestation
↑ intrapericardial pressure ↓ ↑ pressure within ventricles ↓ ↓ ventricular capacity or size ↓ ↓ fluid or blood passing through the ventricles ↓ significant ↓ in ventricular filling (EDV)	↓ blood from coming from the SVC & IVC into the right side of the heart ↓ ↓ blood pumped into the pulmonary circulation & back into the pulmonary veins ↓ ↓ blood coming into the LA and LV → arterial circulation	Cold, Clammy lower and upper extremities
↓ preload → ↓ SV → ↓ CO → ↓ MAP ↓ Cardiogenic shock		Significant hypotension

Sequelae:

↓ preload → ↓ SV → ↓ CO → ↓ MAP → Significant hypotension ↓	
Cardiogenic shock	Activates carotid and aortic arch baroreceptors ↓ Signals to medulla ↓ ↑ Sympathetic outflow to the heart = ↑ HR (Reflex tachycardia), ↑ contractility, ↑ vasoconstriction

(B) DYSPNEA

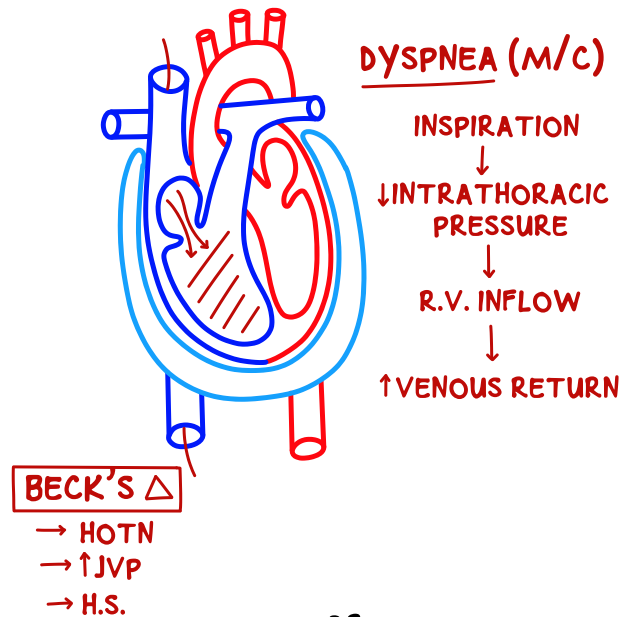


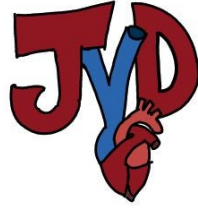
Figure 2. Dyspnea and Beck's triad pathophysiology.

Table 1. Dyspnea.

Mechanism	Clinical manifestation
↑ Inspiration ↓ ↓ Intrathoracic pressure = ↑ negative pressure ↓ ↑ sucks blood from SVC and IVC → RA ↓ ↑ Venous return ↓ ↑ RV inflow, ↑ RV volume → ↑ EDV → ↑ Preload → ↑ SV → ↑ CO	Dyspnea to augment the ↑ VR (compensatory mechanism) ↓ ↑ BP



JUGULAR VENOUS DISTENSION



HYPOTENSION



BECK'S TRIAD

SIGNS OF CARDIAC TAMPONADE



MUFFLED HEART SOUNDS

(1) Fluid accumulation

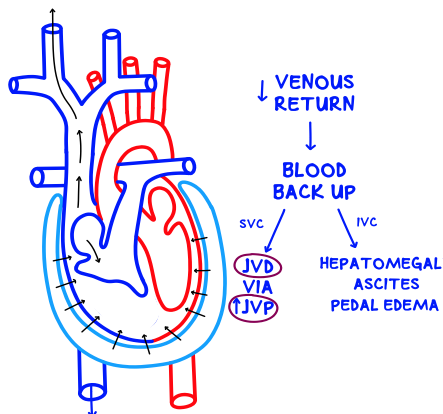


Figure 3. Fluid accumulation pathophysiology.

- Increased intrapericardial pressure:
 - Left side of the heart has a thicker myocardium and can offset the pressure exerted on it
 - Right side of the heart is more impaired because it has a thinner myocardium → easier to collapse
 - Once smaller, harder for blood to flow from RA → RV

Mechanism	Clinical manifestation
↓ VR into the right side of the heart ↓ ↑ Blood backs up into SVC → brachiocephalic vein → jugular vein ↓ ↑ Blood backs up down into IVC → blood pools into the area of liver/ abdomen/ lower extremities	↑ Jugular vein distention via ↑ JVP Hepatomegaly Swollen abdomen Ascites Pedal Edema

(2) Decreased heart sounds

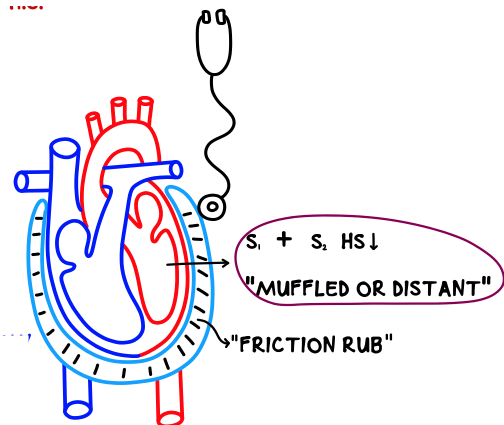


Figure 4. Decreased heart sounds pathophysiology.

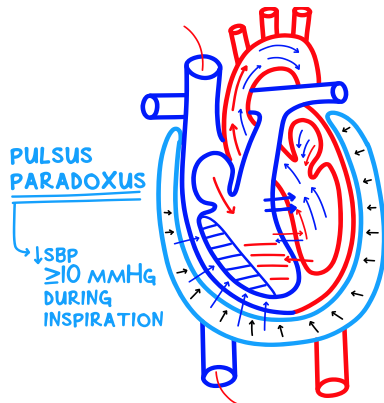
- ↑ Blood / fluid surrounding the heart affects the transmission of heart sounds
 - S1, S2
 - Heart sounds travel from: ventricular chambers > myocardium > big pericardial cavity
 - ↓ intensity of S1, S2

Mechanism	Clinical manifestation
↑ Pericardial fluid ↓ ↓ Transmission and intensity of heart sounds	Muffled / distant heart sound



(D) PULSUS PARADOXUS

- Other conditions wherein this is present:
 - Severe COPD
 - Right ventricular dysfunction
 - Pulmonary hypertension
 - Massive pulmonary embolism
- However, if other symptoms mentioned above are also available → high degree suspicion of cardiac tamponade
- Definition:
 - Pulsus paradoxus is an exaggerated drop in systemic blood pressure of greater than or equal to 10 mmHg during inspiration [Borlaug]
 - Moderate to severe cardiac tamponade, and occasionally constrictive pericarditis, induce hemodynamic changes that enhance the inspiratory fall in systolic blood pressure [Borlaug]



- During a normal cycle of inspiration and expiration → cardiac output changes

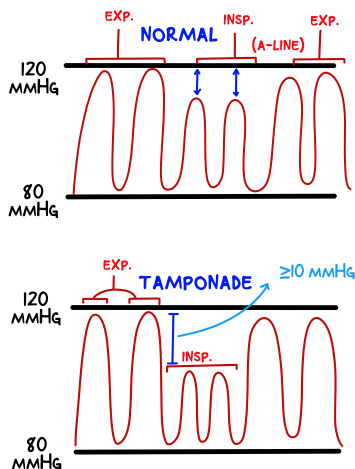


Figure 5. (Upper) Respirophasic waveform from a normal person. (Lower) Respirophasic waveform from someone with pulsus paradoxus.

- Looking at someone's pulse → best thing to do is look at the arterial line waveform

Table 2. Respirophasic waveform differentiation between a normal person and if with cardiac tamponade.

	Normal	Cardiac Tamponade
Inspiration	↓ Intrathoracic pressure = ↑ negative pressure ↓ suck blood from SVC & IVC into the heart ↓ ↑ blood return to the heart = ↑ VR ↓ ↑ Blood volume in the RV ↓ Minimal shift of interventricular septum into the LV ↓ Minimal ↓ LV inflow ↓ LV and aortic outflow	↑ Intrapericardial pressure squeezes the heart, but worse on the right side because RA and RV are thinner ↓ VR due to ↓ Minimal space despite of the RA, RV despite ↓ Intrathoracic pressure ↓ Significant shift of interventricular septum into the LV ↓ Significant ↓ LV inflow ↓ LV and aortic outflow Intrapericardial pressure > pressure of VR into the right side of the heart
Expiration	Goes back up to 120 mmHg or stays the same because of ↑ intrathoracic pressure ↓ Squeezes blood into the left side of the heart ↓ ↑ VR to the left side of the heart ↓ Minimal shift of interventricular septum into the RV ↓ Small ↑ in amount of blood going into the LV and out into the aorta More Venous inflow, more blood outflow	

SUMMARY

Table 3. Clinical manifestations.

Clinical manifestation	Pathophysiology
Cold, clammy lower and upper extremities	↓ perfusion into peripheral arteries
Significant hypotension	↓ preload → ↓ SV, ↓ CO → ↓ MAP
Reflex tachycardia	Compensation from ↓ MAP → activates Sympathetic outflow to the heart
Dyspnea (most common)	↓ Intrathoracic pressure = ↑ negative pressure ↑ VR, EDV, Preload ↑ SV, CO

↑ Jugular vein distention via ↑ JVP	↑ pressure onto Right side of heart → ↓ VR → blood accumulation in SVC
↑ Hepatomegaly Swollen abdomen Ascites Pedal Edema	↑ pressure onto Right side of heart → ↓ VR → blood accumulation in IVC
Pulsus paradoxus	Intrapericardial pressure > pressure of VR into the right side of the heart



II) DIAGNOSIS

OVERVIEW

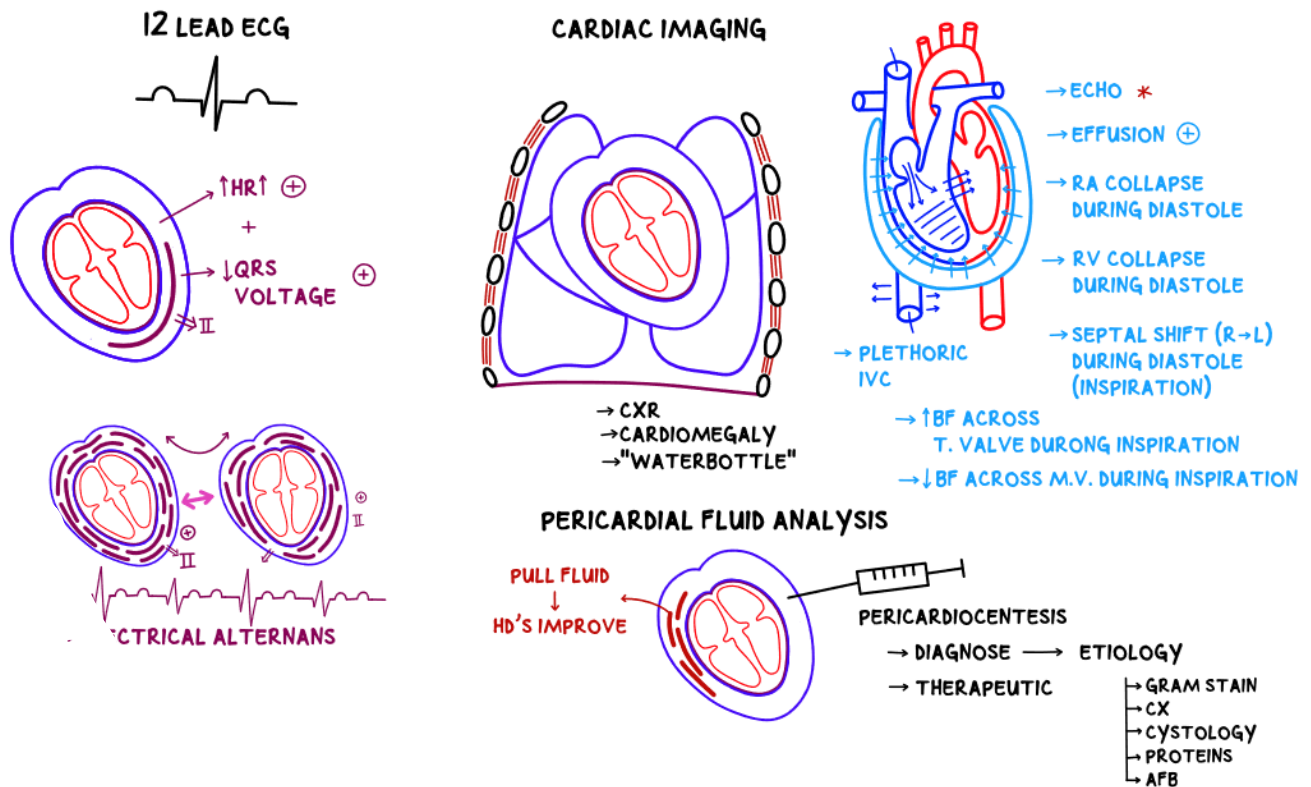


Figure 6. Overview of cardiac tamponade diagnosis

Risk factors

- Hemopericardium
- Serosanguinous effusion

Vitals shows

- Hypotension
- Tachycardia
- Jugular venous distension
- When listening to the heart
 - Decreased or muffled heart sound
- Complaining of dyspneic
 - Short of breathing and breathing a little bit faster
 - Because they're trying to augment their venous return
- Arterial line waveform
 - There's **pulsus paradoxus**
 - ≥ 10mm drop in systolic blood pressure during inspiration

"Okay, what kind of things do I need to look for right away to rule out cardiac tamponade?"

Diagnostic tools

- 12-lead EKG
- Chest X-Ray
- Echocardiogram
- Pericardiocentesis



(A) 12-LEAD EKG

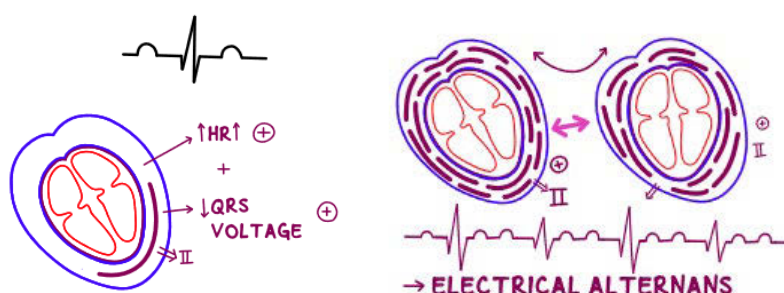
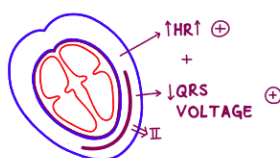


Figure 7. 12-lead EKG in diagnosing cardiac tamponade

Clinical vignette

- Patient with cardiac tamponade may also present with chest pain
 - **More commonly present with dyspnea**
 - We better get an EKG as well for someone represent with dyspnea



Reflexive tachycardia

- Sinus tachycardia
- Atrial fibrillation
 - Cardiac tamponade can definitely **worsen** someone's already present atrial fibrillation

Electrical alternans

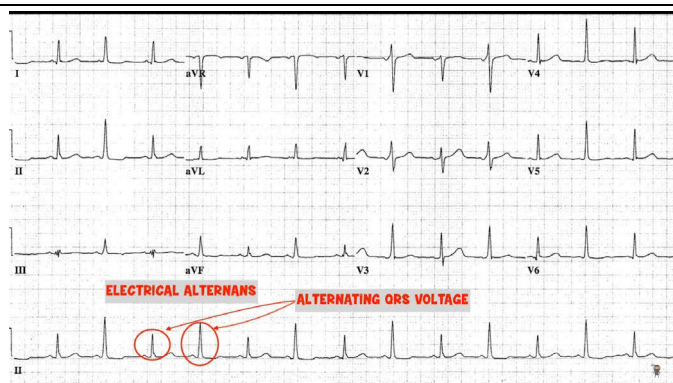
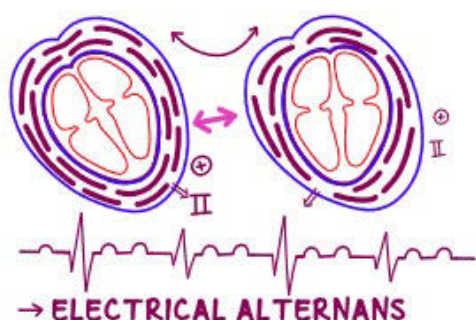


Figure 8. (Left) Cardiac motion in cardiac tamponade (Right) EKG showing electrical alternans with alternating QRS voltage

- Apex of the heart **swinging from the left to right** whenever it's going through actual cardiac cycle

(i) Normal situation

- Take lead II as example
 - It's designed to pick up the **mean QRS vector** that's directed toward it
- In this normal position → mean QRS vector is kind of tilted a little bit to the left
 - Vector shown in the [Figure 8 \(Left\)](#)

(ii) In pericardial effusion

- Heart is swinging to another direction
 - **Mean QRS vector** is **pointing toward different direction**
 - Maybe a little bit away from positive electrode of lead II
- Causes alteration in QRS complex → **alternate between larger and smaller QRS complexes**

Low QRS complex

Normal condition

- When someone has ventricular depolarization
 - Mean QRS vector that points toward positive electrode of lead II
 - Electrical vector as it moving to the positive electrode → **produce upward deflection**

Patient who has lots of fluid inside pericardial cavity

- **Electrical activity has to move through**
 - Ventricle → large pericardial fluid in the pericardial cavity → chest wall
- Anytime there are air, fluid, blood, etc. that's **occluding or restricting the electrical activity** getting to the electrodes on the chest
 - This **lowers the QRS voltage**

Additional Information [Bharat K Kantharia, M. D, 2021]

- According to Medscape, electrical alternans is a broad term that describes alternate-beat variation in the **direction, amplitude, and duration** of **any component** of the electrocardiograph (ECG) waveform (ie, P, PR, QRS, R-R, ST, T, U)
- **Pathophysiology**
 - **Alternans due to cardiac motion**
 - Found in pericardial effusion and cardiac tamponade
 - Total electrical alternans
 - Conduction alternans (P, PR, QRS)
 - Repolarization alternans (ST, T, U)

Side Note

- So, we can actually appreciate total electrical alternans in EKG of patient with cardiac tamponade.



- However, it's easier to notice the large and small QRS complexes than the other components of the EKG waveform at a glance

- Remember patient may present with dyspnea
 - Dyspnea is indication for EKG and chest X-Ray
- **EKG can't diagnose cardiac tamponade**
 - Not an absolute necessary test
 - EKG helps rule out some other things and potentially key in some adjunctive tests
 - "Oh, this could be cardiac tamponade"

EKG won't be a true diagnostic test

(B) CHEST X-RAY

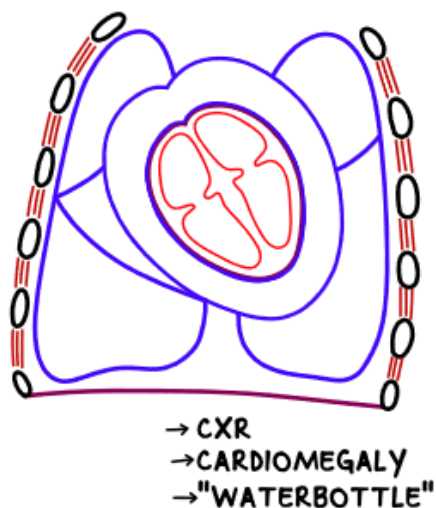


Figure 9. Chest X-Ray

- Enlargement of the heart → cardiomegaly or **enlargement of the cardiac silhouette**
 - **Water bottle sign**
- Because we have **fluid within the pericardial cavity** makes the weird configuration
 - **But this is not diagnostic for someone with cardiac tamponade**

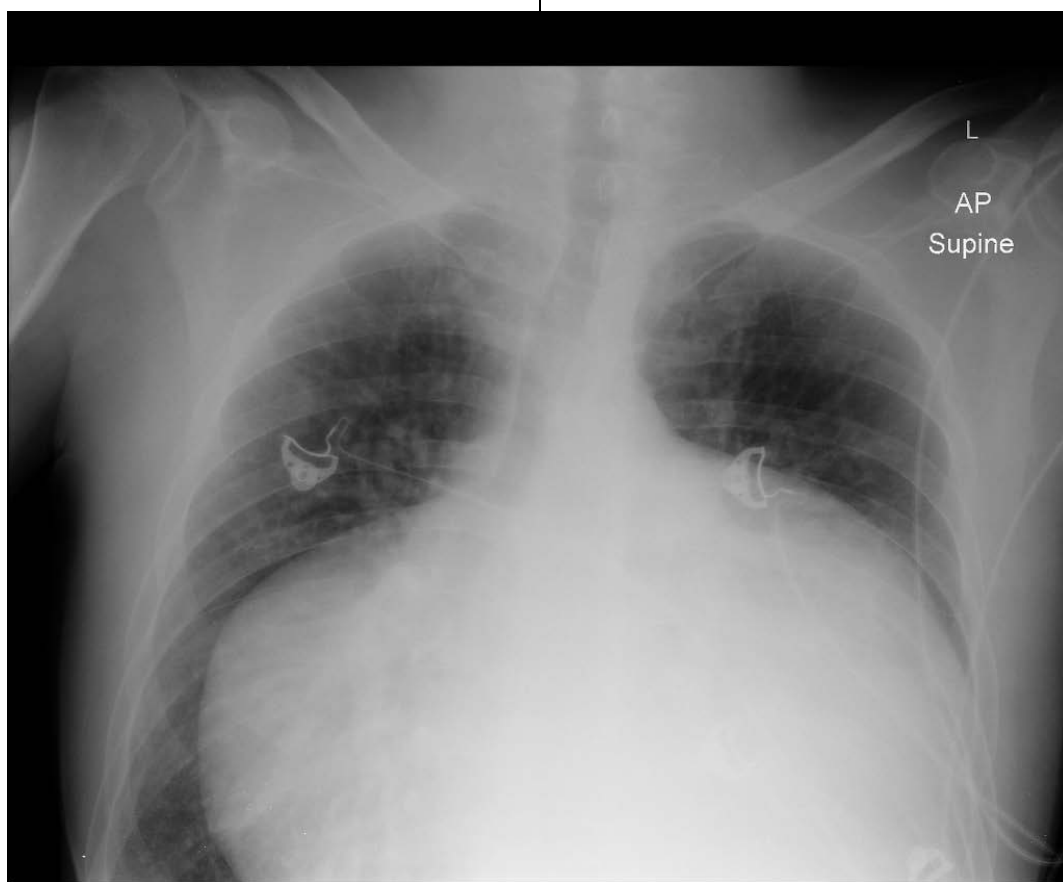


Figure 10. Water bottle sign [Jarvis, M., 2016]



● Gold standard test for diagnosing cardiac tamponade

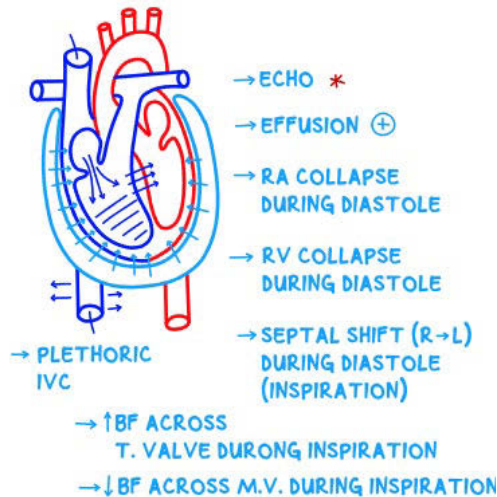


Figure 11. Echocardiogram

Is there any effusion?

- Doesn't matter about volume
 - Sometimes we can have large volume of fluid within pericardial cavity
 - And still isn't enough to start actually compressing the heart and reducing cardiac output
- What matter is either **volume is rapidly accumulated** or the **volume truly at the largest point**
 - Where the **pericardium can't stretch** and accommodate the volume anymore → **Reduces cardiac output**
- If the **intrapericardial pressure is high** → it's going to **start squeezing**
 - Remember more likely hit **the right side of the heart**
 - Because it is **thinner**

Right ventricle

- Whenever blood is coming into the ventricles during **diastolic period**
 - If the **pericardial pressure is high**
 - Squeeze on the ventricle
 - Reduce the blood coming into the ventricle during diastole
 - **Right ventricular collapse**

Right atrium

- Whenever blood is coming from the superior vena cava (SVC) or inferior vena cava (IVC) into the **right atrium during diastole**
 - Remember pericardial pressure squeezes the right atrium harder
 - Especially whenever it's trying to accept blood during diastole
 - Causes right atrium to collapse

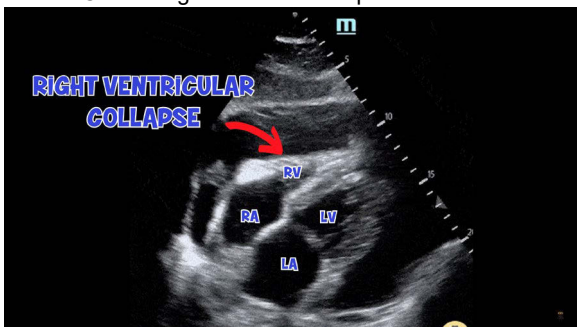


Figure 12. Right ventricular collapse in cardiac tamponade

- Refer to minute **48:16** of the lecture video for better visualization

Superior vena cava (SVC) & inferior vena cava (IVC)

- Right side pressure so high**
 - Venous return is being reduced
 - Causes blood to **backflow into SVC and IVC**
- Ultrasound on inferior vena cava
 - See if it was big or small
 - Dilated inferior vena cava is indicative of high right atria pressure → **Plethoric IVC**

Septal shift

- We have the patient breath in
 - Blood will come from SVC and IVC into the right side of the heart
 - Try to accumulate and wants to stretch to accommodate the blood
 - But can't stretch against the pericardium
- Blood in right ventricle pushes on the septum
 - And shifts the septum into left ventricle during **diastolic filling process** → **septal bounce / septal shift during diastole**
- Shifting during diastole** particularly **during inspiratory phase** → right to the left
 - Bowing of the interventricular septum from the right side to the left side during diastole when they take a breath in

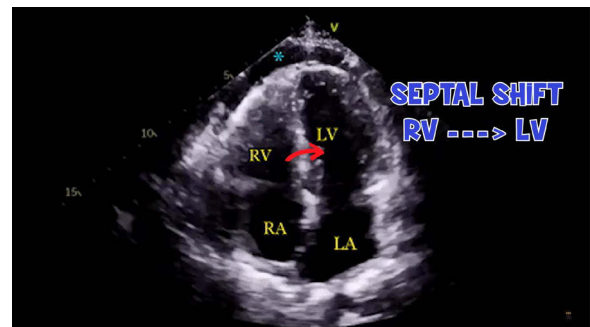


Figure 13. Septal shift in cardiac tamponade

- Refer to minute **49:49** of the lecture video for better visualization

Respirophasic changes in transvalvular velocities

- When they take a breath in → increases venous return on the right side of the heart
 - Deep breath in
 - Decrease in intrathoracic cavity pressure
 - Suck air into our lungs and suck blood into the heart
 - Sucks blood into the right side of the heart

(i) Tricuspid valve

- Blood start blasting across the tricuspid valve more during inspiration → **respirophasic changes in transvalvular velocities**
 - Increase in blood flow across the tricuspid valve during inspiration**

(ii) Bicuspid valve

- Subsequently, because we're causing the **septal shift** (shift the right ventricle toward the left ventricle)
 - Reduce the inflow of blood from the left atrium to the left ventricle**
 - Blood flow across the mitral valve during inspiration decrease**
 - Because the **decreased cavity size**

● During inspiration

Blood Flow Across	
Tricuspid valve	Mitral valve
Increased	Decreased



PERICARDIAL FLUID ANALYSIS

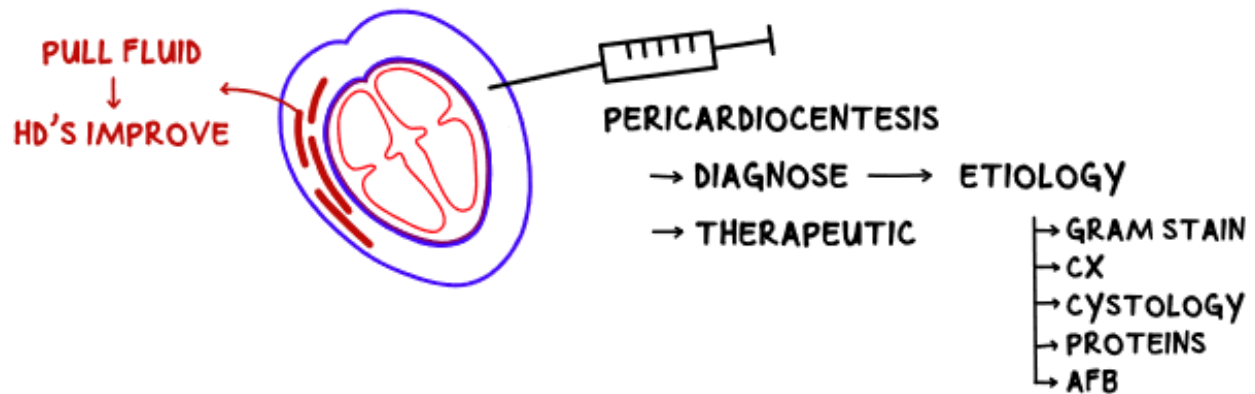


Figure 14. Pericardial fluid analysis

- Sometimes cardiologists will not say tamponade yet
 - We may have all these findings
- The true way to see is this cardiac tamponade nor not
 - **They're hemodynamically unstable**
 - **Pull some of the actual blood or fluid from the pericardial activity**
- If their **hemodynamics improve** after pulling fluid off via pericardiocentesis
 - **Diagnose cardiac tamponade**
- If someone has a lot of fluid within the pericardial cavity
 - We definitely want to do a pericardiocentesis to be able to pull off and **therapeutically treat them**

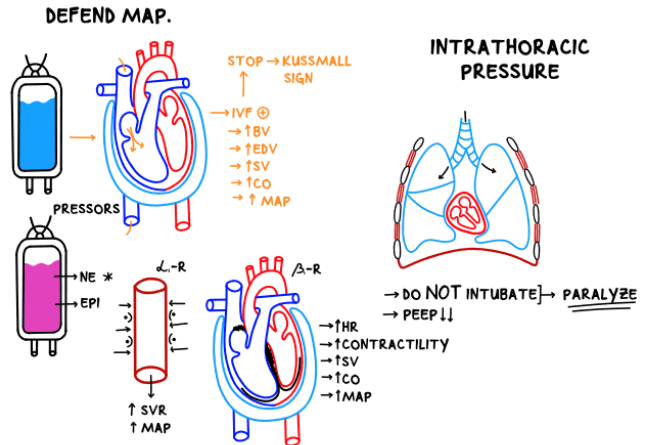
Benefit

- **Diagnostic**
 - Diagnose someone with cardiac tamponade
- **Determine the etiology**
 - Utilize the fluid and send off all the different tests
 - Gram stain
 - Cultures
 - Cytology
 - Different proteins
 - Acid-fast bacillus stain
- **Therapeutic treatment**
 - If we pull off fluid, **hemodynamic improve**
 - Which actually gets them out of the cardiogenic shock



III) TREATMENT – DEFEND THE MAP AT ALL COST!

- **Definitive treatment is pericardiocentesis**
 - Eventually maybe they need a drain
- Cardiology team coming and they're like
 - "All right buddy we're going on our way, we'll get ready to go ahead and tap that pericardial cavity, pull some of the fluid off and we're going to be heroes"
- **Until then we're got to keep our patient alive**
 - They're in **cardiogenic shock**, so they're
 - Hypotensive
 - Tachycardic
 - **Risk of going into cardiac arrest**
- **Stabilize them** in the interim until we can get that ultimate treatment



"Mean arterial pressure is my goal"

(A) CONSIDER INTRAVENOUS FLUID (IVF)

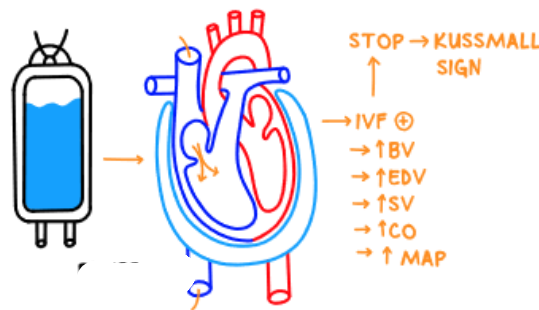


Figure 15. IV Fluid treatment

Fluids we can give

- Lactated ringers
- Normal saline

Whole idea behind giving intravenous fluid

- Trying to **augment their blood volume** → **augment their blood pressure**
- Give fluid → **increase blood volume**
 - Increase the **venous return** into the right side of the heart
 - Increase **diastolic volume**
 - Increase **stroke volume (SV)**
 - Increase **cardiac output (CO)** and **blood pressure (BP)**

Remember that

$$CO = HR \times SV$$

$$BP = CO \times TPR$$

Cautions

- There are certain points where fluids are **no longer beneficial** and sometimes problematic
 - **Fluid should be stopped** when we see evidence of **Kussmaul's sign**
- **Kussmaul's sign** is a kind of way to tell
 - "Hey, my right atrium and right ventricle are not going to accept any more fluid."
- So, giving them more fluid isn't going to help them
 - It might even potentially hurt them

Kussmaul's sign



Figure 16. Kussmaul's sign

- Refer to minute [57:54](#) of the lecture video for better visualization

- **Kussmaul's sign** is when the **jugular venous pressure (JVP)** stays the **same or rises** even during **inspiration**
- What's supposed to happen to jugular venous pressure whenever we take inspiration
 - Deep breath in
 - Intrathoracic cavity pressure drops
 - Suck blood into the heart
 - Naturally JVP should drop
- But if **JV stays the same height or even rises** a little bit
 - It tells us that **the blood is not going into the right atrium and right ventricle**
 - Not very much venous return if we give them more blood



(B) PRESSORS

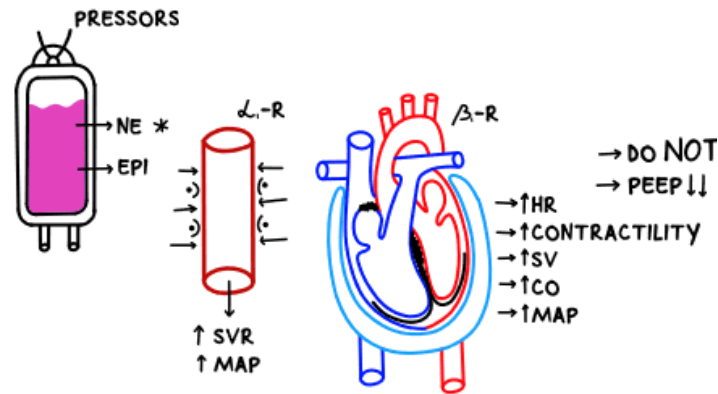


Figure 17. Pressors

- Support their blood pressure in the interim
- **Titrate the pressure toward a particular MAP goal**
 - **MAP ≥ 65mmHg** is enough to perfuse the organs

Drugs

- | | |
|--|--|
| <ul style="list-style-type: none"> • Norepinephrine <ul style="list-style-type: none"> ◦ More preferred here | <ul style="list-style-type: none"> • Epinephrine |
|--|--|

Mechanism of action

Epinephrine and norepinephrine acts on

- **α₁-receptors on our vessels**
 - Cause the vessels to undergo **vasoconstriction**
 - Increase **systemic vascular resistance (SVR)**
 - Increase **MAP**

Remember that

$$BP = CO \times SVR$$

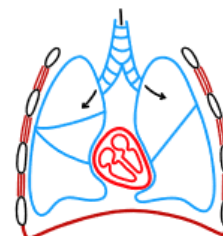
$$MAP = \frac{SBP + [2 \times DBP]}{3}$$

β₁-receptor on the heart

- Particularly on the **nodal system**
- Increase **heart rate**
 - Increase **contractility**
 - Increase in both will eventually increase **stroke volume**
 - Increase **cardiac output**
 - Increase **MAP**

(C) INTRATHORACIC PRESSURE

- **Reduce the intrathoracic pressure**
 - This **helps suck blood into the heart**
 - Increase **venous return**
- If we increase the intrathoracic pressure
 - **Reduce the venous return**
 - **DO NOT DO THIS**



→ **DO NOT INTUBATE** → **PARALYZE**
→ **PEEP ↓↓**

DO NOT INTUBATE DYSPNEIC PATIENT

- They may be staying alive right now
 - Because their **inspiratory efforts** are what's actually **keeping their blood pressure up**
- Because every time they suck air in
 - Increase **venous return**
 - **Keep the blood pressure high enough to survive**
- If we intubate them
 - We **take away the actual ability for them to suck air in**
 - Because we have to **paralyze them**
 - **Reduce muscle effort** to be able to inspire air

If we did intubate the patient and survive

- Don't want to keep the pressure in the airways higher especially during expiration → **PEEP (positive end-expiratory pressure)**
- Right side of the heart hates PEEP
 - Because whenever **PEEP is high** → **intrathoracic pressure is high**
- **Keep PEEP on the lower end of normal**
 - **Reduce the intrathoracic pressure**

Reminder

- **DON'T INTUBATE**
 - Generally, we have to kind of **paralyze these patients**
 - There's a momentary them where **they aren't actually having any inspiratory effort**
 - There's **no reduction in intrathoracic pressure**
 - **Less blood** getting return to heart
 - **Stroke volume drops**
 - **Cardiac output drops** → **cardiac arrest**



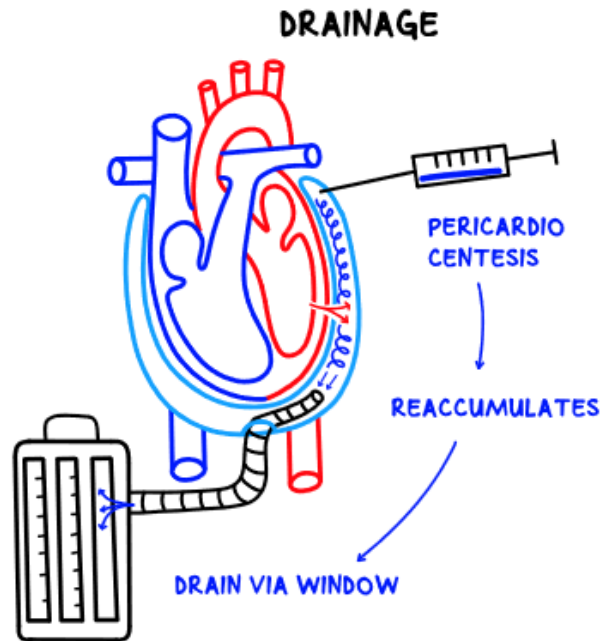


Figure 18. Pericardiocentesis & pericardial window

(A) PERICARDIOCENTESIS

- **Ultimate treatment → Pericardiocentesis**
 - We drain the fluid from the pericardium cavity
- Cardiology will come
 - “Okay baby, give me that actual central line kit”
 - They’re going to pop in via
 - Parasternal long axis view or
 - Subxiphoid view
 - And they’re going to pop a needle into the pericardial cavity
- When they pop the needle into the pericardial cavity
 - They’re going to **suck any fluid from the pericardial cavity as much fluid as they can**
 - **Until their hemodynamics improve**
 - Maybe they had a 50mm effusion but rapidly accumulate
 - We pull up 50mm and oh they’re better
 - We pull off until they’re hemodynamically improve

Patients with conditions below

- **Left ventricle just exploded**
 - And they’re just blasting blood into the pericardial cavity
- **Aortic dissection or**
- **Some type of traumatic event**
- We can do pericardiocentesis to these patients **but it’s going to reaccumulate**
 - It may temporize them

(B) PERICARDIAL WINDOW

- But after we’ve done pericardiocentesis
 - **If it’s reaccumulate → it won’t help**
- We’re putting drain via **pericardial window**

Procedure

- Going from the **parasternal axis** or **subxiphoid view** → poke our needle in
 - Go ahead and thread our guide wire into there like some type of pigtail catheter → plug that drain
- Sometimes we can do this under **ultrasound guidance** or **CT guidance**
 - The best thing to do is do it under surgery where they actually open the patient up and do it
- But in certain pinches, maybe we have to do this ultrasound-guided or CT-guided
- Plug a drain up into the pericardial cavity
 - It’s going to continue to keep sucking some of this actual fluid into the pericardial into the actual drain

Whole goal

- Figure out whatever was causing it
 - **Aortic dissection** → repair
 - **Left ventricular wall rupture**
 - Resecting the infarcted area and closing the rupture zone with
 - Teflon or Dacron patches or by using of biologic glues [Jamshid Shirani, 2021]
 - **Coronary** → Bypass
- Fix the issues and use the drain as kind of interim thing for the **next 24-48 hours**

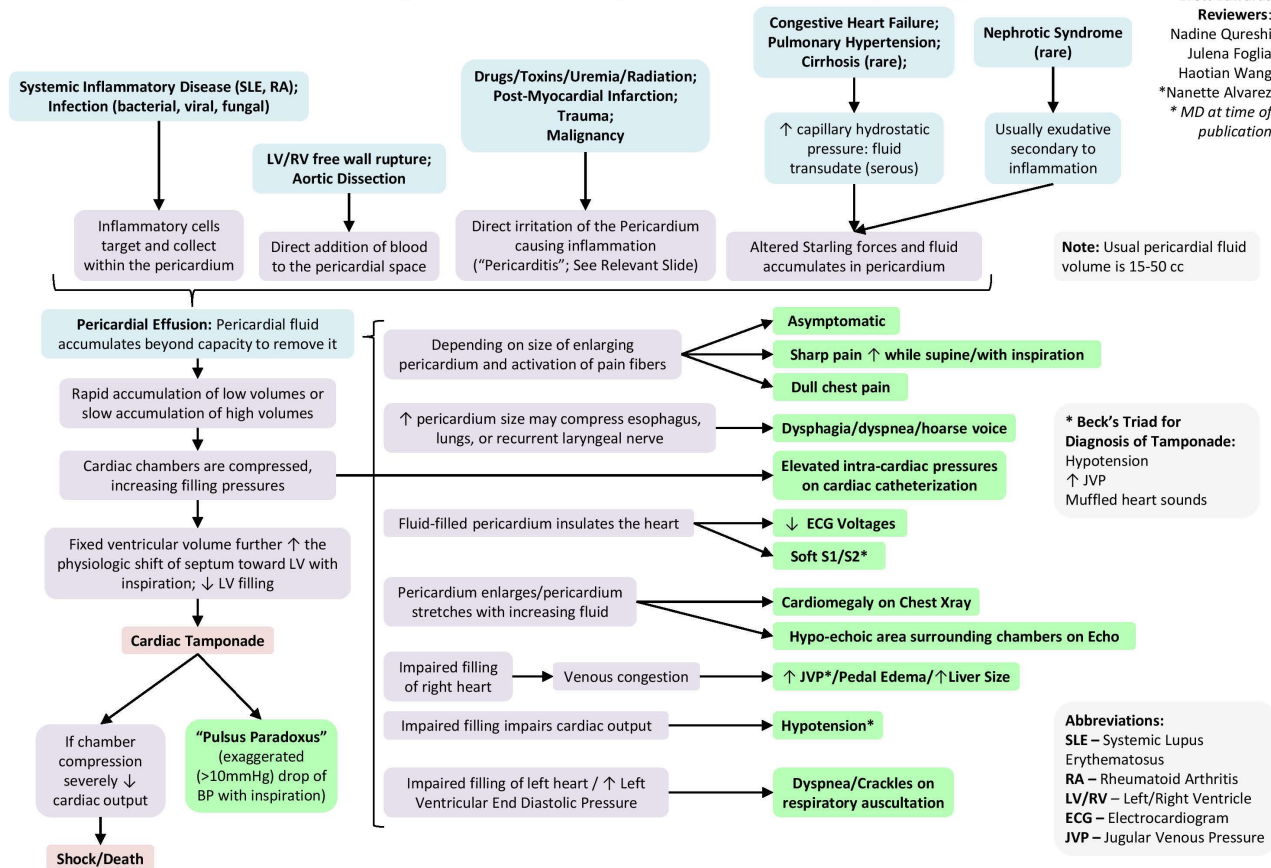
TREATMENT SUMMARY

- **Defend the MAP**
 - Fluid
 - Pressor
 - **Stay away from intubating if possible**
 - If you have to, lower the PEEP
- **Drain the fluid via pericardiocentesis**
 - If they have some issues where it’s rapidly reaccumulating → Continuously drain fluid or blood via pericardial window
 - A way of temporizing them until we fix the underlying cause for their actual cardiac tamponade



Pericardial Effusion & Tamponade: Pathogenesis and clinical findings

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Legend: Pathophysiology Mechanism Sign/Symptom/Lab Finding Complications Published January 10, 2015 on www.thecalgaryguide.com



Figure 1. Pathophysiology of Cardiac Tamponade and Pericardial Effusion

[The Calgary Guide to Understanding Disease]

Table 4. Abbreviations.

BP	Blood pressure	JVD	Jugular venous distention	RA & RV	Right atrium and right ventricle
CO	Cardiac output	JVP	Jugular venous pressure	SV	Stroke volume
EDV	End-diastolic volume	LA & LV	Left atrium and left ventricle	SVC	Superior vena cava
IVC	Inferior vena cava	MAP	Mean arterial pressure	VR	Venous return

FORMULAS

Cardiac output

$$CO = HR \times SV$$

Symbol	Explanation
CO	Cardiac output ● Amount of blood that's being pumped out from the heart per minute
HR	Heart rate ● Beats per minute
SV	Stroke volume ● Amount of blood that's being pumped out from the heart per beat ● Equals venous return/preload ○ Amount of blood that comes back to the heart per beat

Blood pressure

$$BP = CO \times TPR$$

Symbol	Explanation
BP	Blood pressure ● Pressure exerted by blood to artery wall
CO	Cardiac output ● Amount of blood that's being pumped out from the heart per minute
TPR	Total peripheral resistance ● Affects afterload ● Can also be written as SVR (systemic vascular resistance)

Mean arterial pressure

$$MAP = \frac{SBP + [2 \times DBP]}{3}$$

Symbol	Explanation
MAP	Mean arterial pressure ● This pressure is related with the perfusion to organs Perfusion pressure = $MAP - CVP$ ● CVP represents central venous pressure
SBP	Systolic blood pressure ● Blood pressure observed during the systolic phase of the heart
DBP	Diastolic blood pressure ● Blood pressure observed during the diastolic phase of the heart



VI) REVIEW QUESTIONS

1) Hemopericardium can be caused by the following EXCEPT:

- a) Penetrating trauma
- b) Myocardial infarction
- c) Systemic lupus erythematosus
- d) Aortic dissection

2) Which of the following is NOT a cause of serous/serosanguinous effusion?

- a) Renal cell carcinoma metastasis
- b) Coxsackie B virus
- c) Elevated serum urea
- d) Myocardial Infarction

3) These are the components of the Beck's triad in cardiac tamponade, EXCEPT?

- a) Absent heart sounds
- b) Hypotension
- c) Jugular venous distension
- d) Wide pulse pressure

4) Which of the following is true for pulsus paradoxus?

- a) an exaggerated drop in systemic blood pressure of greater than or equal to 10 mmHg during inspiration
- b) may be caused by diseases such as pulmonary hypertension and massive pulmonary embolism
- c) during expiration, there is a decrease of 10 mmHg as well
- d) a & b

5) What is the most common symptom of someone having cardiac tamponade?

- a) Chest pain
- b) Dyspnea
- c) Nausea
- d) Vomiting

6) What is the more probable cause of the lower QRS voltage finding in EKG of someone with cardiac tamponade? (May choose more than 1)

- a) Amyloidosis
- b) Cardiac motion
- c) Fluid accumulation in pericardium
- d) Improper placement of the leads
- e) Sarcoidosis
- f) Using very old leads

7) Whenever we found electrical alternans in EKG, we can be certain that this is cardiac tamponade without any further investigation

- a) True
- b) False

8) What finding that we can found from chest X-Ray of people with cardiac tamponade?

- a) B-lines
- b) Boot-shaped heart
- c) Ground-glass opacity
- d) Water bottle sign

9) Both right and left side of the heart are affected equally in cardiac tamponade

- a) True
- b) False

10) Findings below can be seen with echocardiography in patients with cardiac tamponade (May choose more than 1)

- a) Localized akinesis of the right ventricular wall
- b) Larger black area around the myocardium → indicative of effusion
- c) Left ventricular collapse
- d) Right ventricular collapse
- e) Septal shift (right ventricle → left ventricle)
- f) Plethoric inferior vena cava
- g) Considerable thickening of the left ventricle
- h) Smaller left ventricle lumen during inspiratory phase
- i) Increased transvalvular velocity via tricuspid valve
- j) Increased transvalvular velocity via mitral valve

11) Options below are the benefits of pericardiocentesis in patient with cardiac tamponade, EXCEPT?

- a) Diagnose someone with cardiac tamponade
- b) Determine the etiology of the cardiac tamponade
- c) Improve the hemodynamic of the patient
- d) Treat the underlying cause

12) When should we stop giving the fluid to patient with cardiac tamponade?

- a) When there's cold acral
- b) When Kussmaul's sign can be seen
- c) When the heart rate is becoming extremely low
- d) When the patient has dyspnea

13) How epinephrine and norepinephrine help the patient with cardiac tamponade before getting pericardiocentesis?

- a) Vasoconstriction + increase heart rate & contractility → increase MAP
- b) Vasoconstriction + decrease heart rate & contractility → decrease MAP
- c) Vasodilation + increase heart rate & contractility → increase MAP
- d) Vasodilation + decrease heart rate + contractility → decrease MAP

14) What is the reason not to intubate patient with cardiac tamponade?

- a) Paralyze the patient → reduce muscle effort to inspire air → more blood entering the heart → more MAP
- b) Paralyze the patient → reduce muscle effort to inspire air → less venous return → less MAP
- c) High PEEP → high intrathoracic pressure → less venous return → less MAP
- d) Low PEEP → low intrathoracic pressure → more venous return → more MAP

15) What is the next procedure if someone is known to have fluid reaccumulate inside pericardial cavity after pericardiocentesis?

- a) Activate cath lab
- b) Pericardial window
- c) Give furosemide
- d) Restrict fluid intake

VII) REFERENCES

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OUTLINE

- I) OVERVIEW
- II) CAUSES
- III) CLINICAL MANIFESTATION AND PE FINDINGS
- IV) DIAGNOSIS

- V) RESTRICTIVE CARDIOMYOPATHY VS CONSTRUCTIVE PERICARDITIS
- VI) TREATMENT
- VII) QUESTIONS
- VIII) REFERENCES

I) OVERVIEW

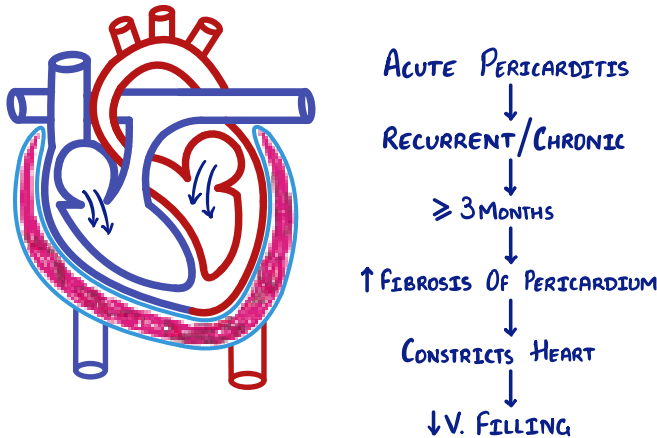


Figure 1. Pathophysiology of constrictive pericarditis.

Constrictive Pericarditis

- Recall that the serous pericardium has parietal and visceral layers
- An insult to the pericardium leads to inflammation
- Acute pericarditis → recurrent or chronic insult (≥ 3 months) → progress to increasing fibrosis of the pericardium → produces an inelastic pericardium → constriction of the heart → reduces the amount of blood coming to the heart during ventricular filling (↓ **ventricular filling**)
- Ventricular filling is unimpeded during early diastole but is reduced abruptly when the elastic limit of the pericardium is reached [Harrison's Principles of Internal Medicine]
 - As compared to cardiac tamponade, ventricular filling is impeded throughout diastole

II) CAUSES

(A) INFECTIONS

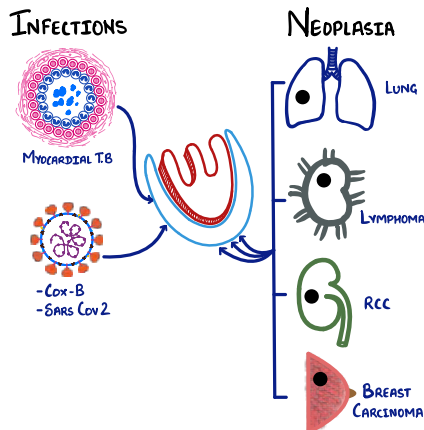


Figure 2. Infectious and neoplastic causes of constrictive pericarditis.

(1) *Mycobacterium tuberculosis*

● Must-know

- Constrictive pericarditis can be seen in tuberculosis (TB) infections
- Produce non-caseating granulomas that deposit in the pericardium leading to extensive fibrosis

(2) Viral Infections

- **Coxsackie B virus** and the **SARS-CoV-2**
- Idiopathic causes of constrictive pericarditis are most likely suspicious for a viral cause
- Leads to constrictive pericarditis if there are recurrent attacks

(B) NEOPLASIA

- Second most common cause
- Primary cancers from the lungs, lymph nodes (lymphomas or even leukemias), kidneys (renal cell CA) and breast can **metastasize** to the pericardium → constrictive pericarditis since neoplasms are usually chronic conditions

(C) RADIATION

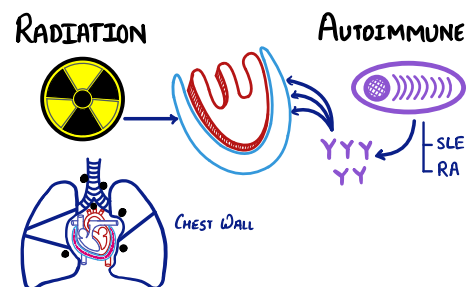


Figure 3. Radiation and autoimmune causes of constrictive pericarditis.

- Usually caused by radiation therapy for cancers within the chest wall area
- While radiation therapy attacks the cancer cells, it also simultaneously attacks the pericardium causing chronic inflammation → chronic pericarditis

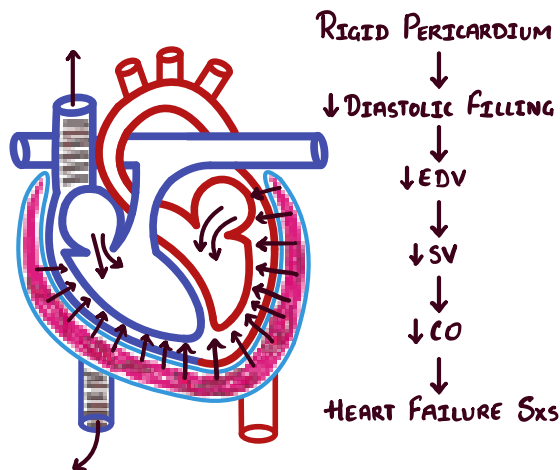
(D) AUTOIMMUNE

- **SLE or Rheumatoid arthritis**
 - Consistent flare-ups from these conditions result to frequent attacks of autoantibodies to the pericardium



III) CLINICAL MANIFESTATION AND PE FINDINGS

(A) HEART FAILURE-LIKE SYMPTOMS



- RHF Sxs >>>> LHF Sxs**
- **JVD ⊕**
 - **HOTN**
 - **HEPATOMEGALY**
 - **PULMONARY EDEMA**
 - **ASCITES**
 - **PEDAL EDEMA**

Figure 4. Heart failure-like symptoms in constrictive pericarditis.

(1) Pathophysiology

- Rigid pericardium → inability of the ventricles to expand during diastole → ↓ **diastolic filling** → ↓ end-diastolic volume (EDV) → ↓ stroke volume (SV) → ↓ **cardiac output (CO)**
 - Filling is the best in early phases of diastole and then significantly reduces in the middle and late phases
- Reduced CO can manifest as heart failure-like symptoms

(2) Right-Sided Heart Failure-Like Symptoms

- Right-sided HF symptoms are more severe than left-sided HF symptoms
 - Constricting pericardium has a greater push on the right side of the heart producing a higher pressure
- **Jugular venous distension**
 - Reduction in blood returning in the right ventricle (RV) → blood goes back up into the channels where they are coming from (IVC and SVC)
- **Hepatomegaly**
 - Pooling of blood to the IVC
- **Ascites**
- **Pedal edema**

(3) Left-sided heart failure symptoms

- **Hypotension**
 - Reduced left-side ventricular filling → ↓ SV → hypotension
- **Paroxysmal nocturnal dyspnea** from pulmonary edema
 - Presents as shortness of breath while laying down or while exertion

(B) KUSSMAUL'S SIGN

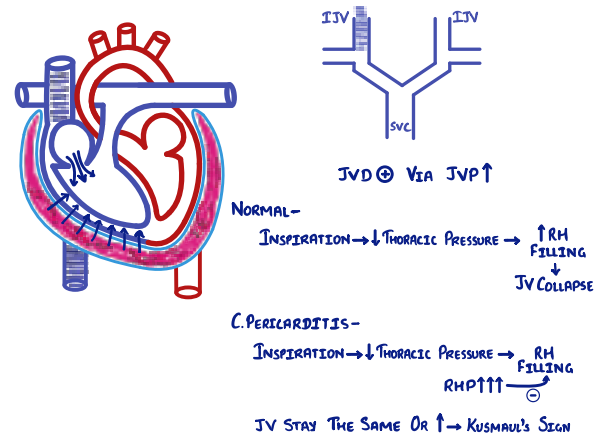


Figure 5. Kussmaul's sign in constrictive pericarditis.

- Defined as the paradoxical increase in the JVP during inspiration

(1) Review of Anatomy

- SVC branches into the brachiocephalic veins and then internal jugular (IJV) and the subclavian vein
- IJV is found in the neck

(2) JVP in a Normal Patient

- Inspiration → ↓ intrathoracic pressure → creates a "sucking effect" that yanks blood from SVC and IVC to the right side of the heart → ↑ venous return or right heart filling → **jugular vein should collapse**

(3) JVP in Patients with Constrictive Pericarditis

- Since the right-sided pressure is still high (from constricting pericardium), inspiration DOES NOT cause blood to flow back to the heart from the IJV → **jugular vein stays the same or even increased**
- This is **Kussmaul's sign**

(C) PERICARDIAL KNOCK

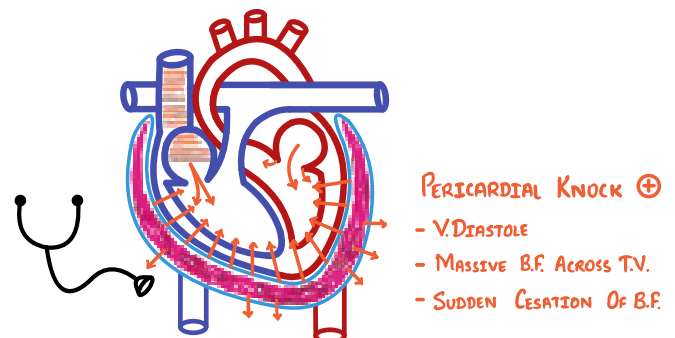


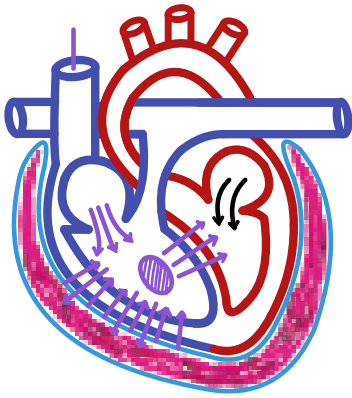
Figure 6. Pericardial knock in constrictive pericarditis.

- Defined as the sound heard from the rapid ventricular filling against a rigid pericardium
 - Due to a massive blood flow across the tricuspid blood on early diastole
 - Sudden cessation of blood flow
- Heard through auscultation during ventricular diastole
- Very specific for patients with constrictive pericarditis

- Since both atria have huge amounts of blood from pooling, these amounts of blood rush down to the non-expandable ventricles once mitral and tricuspid valves open
- The ventricles cannot expand due to the rigid pericardium → **sudden cessation of blood flow** → producing the characteristic pericardial knock



(D) PULSUS PARADOXUS



PULSUS PARADOXUS (20-30%)

→ SBP ↓ ≥ 10 mmHg DURING INSPIRATION

C. TAMPONADE

Figure 7. Pulsus paradoxus in constrictive pericarditis.

- Found in 20-30% of patients with constrictive pericarditis
- Not specific for constrictive pericarditis
 - Found more specifically in **cardiac tamponade** (must-know)
- Defined as the decrease in systolic blood pressure by ≥ 10 mmHg during inspiration

(1) BP Wave in Normal Patients

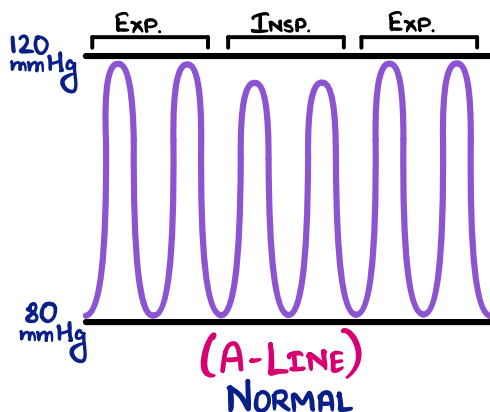


Figure 8. A-line in normal patients.

- Normal pressure waves are observed during expiration
 - Increase in flow to left ventricle (LV) and mildly bow the septum into the right ventricle (RV) → more venous inflow and more blood outflow in the LV
- During inspiration, blood flow increases into the RV and mildly bow the septum into the LV → mild reduction of venous inflow and blood outflow in the LV → a subtle change in SBP as seen in Figure 7

(2) BP Wave in Patients with Constrictive Pericarditis

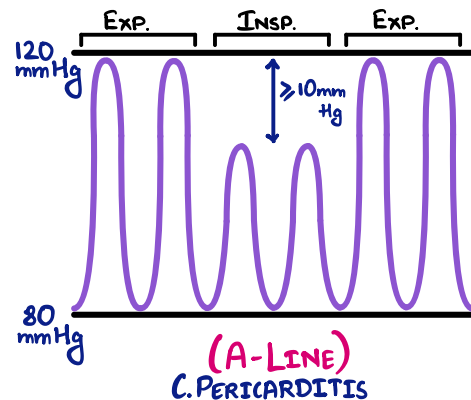


Figure 9. A-line in patients with constrictive pericarditis.

- Normal pressure waves during expiration
- During inspiration, rigid pericardium does not allow outward expansion of the ventricle → pushes the septum more significantly into the LV → significant reduction of volume inflow and outflow in the LV → produces a significant change in SBP
- If difference between expiratory and inspiratory cycle is **≥ 10 mmHg**, it is indicative of **pulsus paradoxus**

- For constrictive pericarditis, focus on the following clinical manifestations and physical exam findings:
 - **Heart failure-like symptoms** (R >>> L)
 - **Jugular venous distension** with **Kussmaul's sign**
 - **Pericardial knock**



IV) DIAGNOSIS

(A) CT/MRI

- Shows thickening of the pericardium

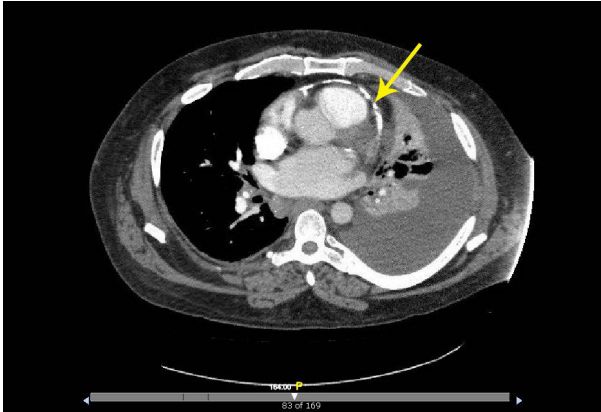


Figure 10. Pericardial calcification (yellow) as seen in cardiac CT with contrast [Tariq et al, 2016].

(B) 12-LEAD ECG

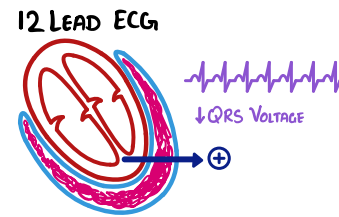


Figure 11. Low QRS voltage in constrictive pericarditis.

(1) Low QRS Voltage

- Due to fibrous tissue, it impedes the electrical flow from the heart to the electrodes → electrodes can sense a decrease in amplitude = **low QRS voltages** or “baby” QRS complexes
 - Normal ventricular polarization: QRS vector points downwards and into the left
- Not specific** for constrictive pericarditis
 - May only indicate that there is impediment of the electrical flow
- Low diagnostic significance

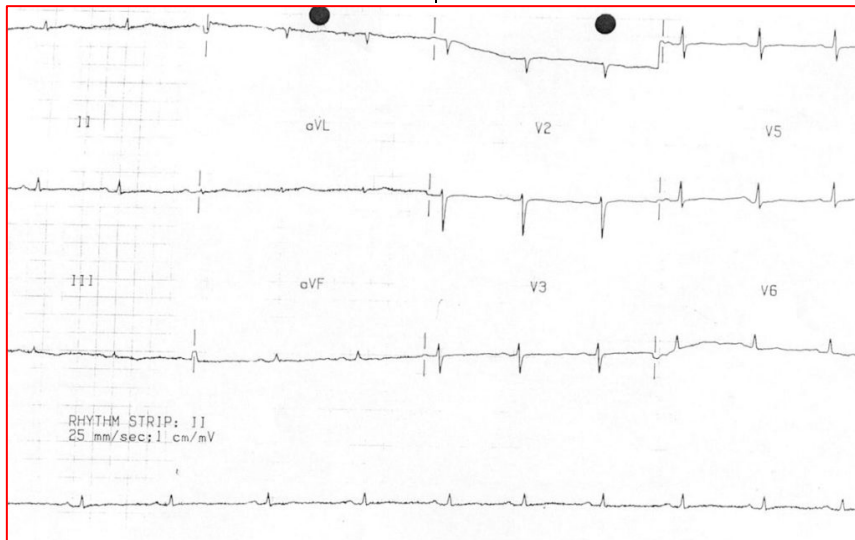


Figure 12. Low QRS voltage.

(C) CHEST X-RAY

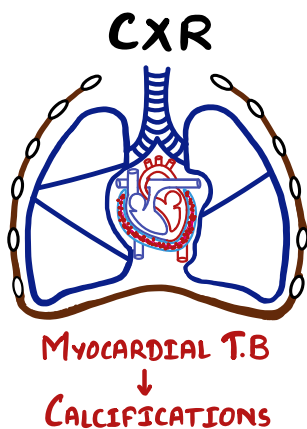


Figure 13. CXR findings in constrictive pericarditis.

- Lateral view of the chest may show **calcifications** of the pericardium
 - Especially in *M. tuberculosis*
- Not specific** for constrictive pericarditis
- Low diagnostic significance

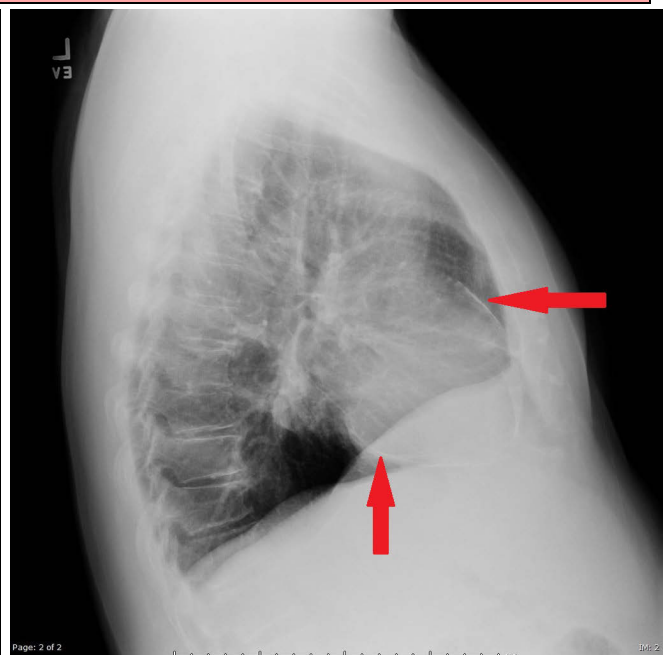


Figure 14. Radiographic image showing calcifications (arrow) in a patient with tuberculous pericarditis (Gibson, 2019).



(D) ECHOCARDIOGRAPHY

- True diagnostic test

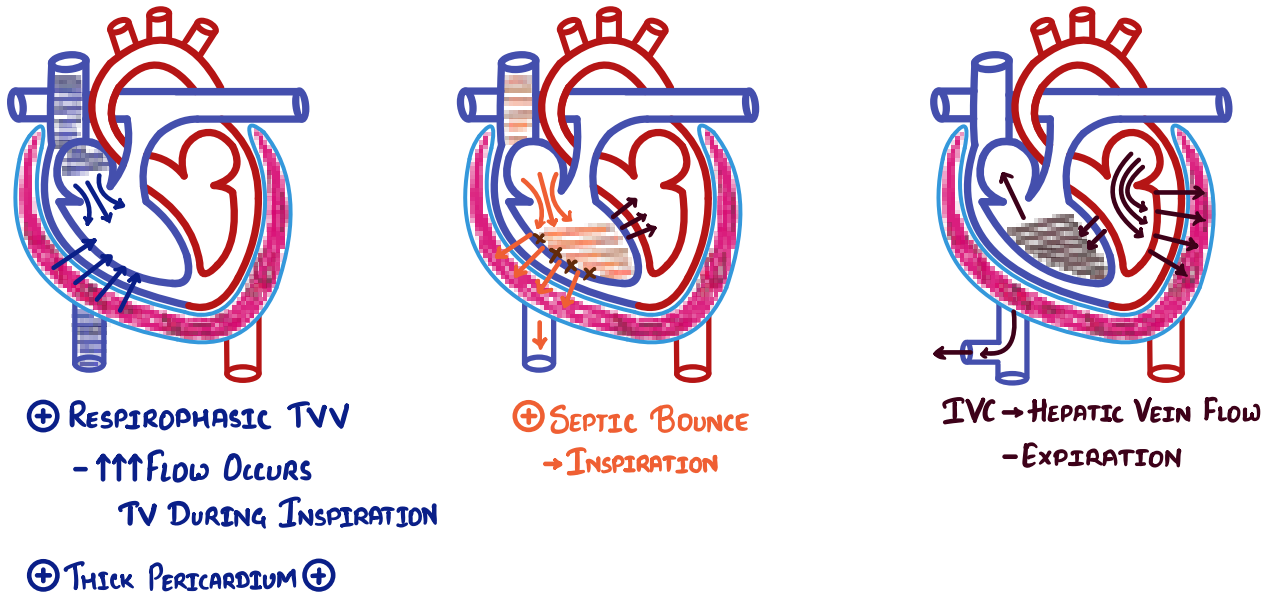


Figure 15. Echo findings in constrictive pericarditis.

(1) Pericardial Thickening

- Obvious finding in echocardiography

(2) Significant Changes in Respirophasic Transvalvular Velocity (TVV)

- ↑↑↑ flow and velocity across the tricuspid valve during inspiration
 - During inspiration, blood cannot flow from the IJV to the heart because of high pressures in the right side of the heart (recall the mechanism of [Kussmaul's Sign](#))
 - Once the valves open, huge amounts of blood flood down the ventricles and suddenly cease due to the rigid pericardium

(3) Septal Bounce During Inspiration

- Inspiration: blood flow is higher on the right side of the heart due to ↓ intrathoracic pressure
- Because of rigid pericardium, there is a high right-sided pressure → ventricles cannot expand → blood bounces to the septum

Check [31:00-31:10](#) of the video for a sample echocardiogram

(4) IVC-to-Hepatic Vein Flow During Expiration

- Expiration: blood flow is higher on the left side due to ↑ intrathoracic pressure
- Because of rigid pericardium, blood inflow to the left ventricle pushes the septum inwards → blood sitting on the RV is pushed into different channels via IVC and SVC → blood pushed in the IVC then diverts to the hepatic vein

(E) CARDIAC CATH

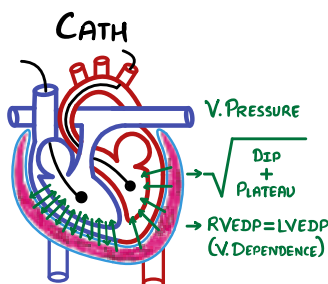


Figure 16. Cath findings in constrictive pericarditis.

- Cath can measure the different pressures in the LV and RV

(1) Dip and Plateau Sign

- Also called the **square root sign**
- Early phase of diastole is the most important for the ventricles because that's the only time they have a rapid inflow of blood → shows a drop in pressure
- As the blood flow stops, rigid pericardium does not allow ventricles to expand leading to higher pressures → rise in pressure then plateau

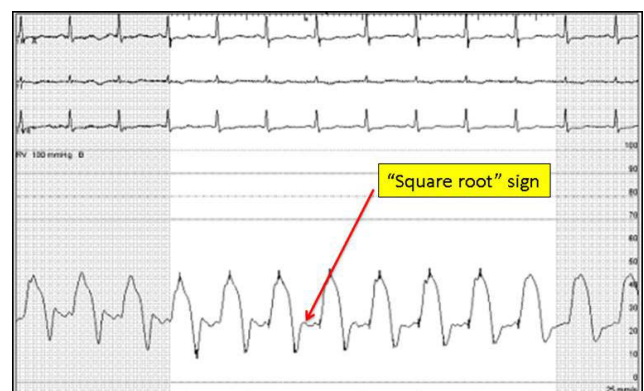


Figure 17. Square root sign.

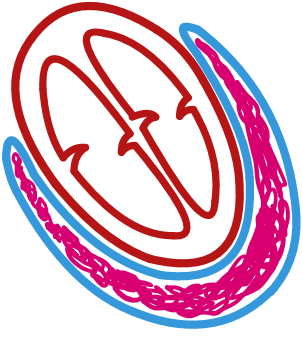
(2) Ventricular Dependence

- Because pericardium is constricting the entire part of the heart, ventricles become dependent of one another → ventricular pressures are equal during diastole
 - **RVDP = LVDP**



V) RESTRICTIVE CARDIOMYOPATHY VS CONSTRICTIVE PERICARDITIS

Table 1. Comparison between constrictive pericarditis and restrictive cardiomyopathy.

	CONSTRICTIVE PERICARDITIS	RESTRICTIVE CARDIOMYOPATHY
	Involves the pericardium 	Involves the myocardium 
PE FINDINGS		
Pericardial knock	(+)	(-)
Extra heart sounds	(-)	S3 ± S4 (in later stages)
Valvular disease	(-)	Mitral regurgitation ± tricuspid regurgitation (due to bi-atrial enlargement)
Kussmaul's sign	(+)	(+)
Pulsus paradoxus	20-30% of patients	Rare
EKG		
Low QRS voltage	(+)	(+)
Conduction blocks	(-)	(+)
ECHO		
Appearance	Thick pericardium	(-)
Respirophasic changes	Significant with TVV and septal bounce	Very minimal without septal bounce
CATH		
Square root sign	(+)	(+)
Ventricular dependence	(+) LVEDP = RVEDP	(-) LVEDP >>> RVEDP (at least 5 mmHg)



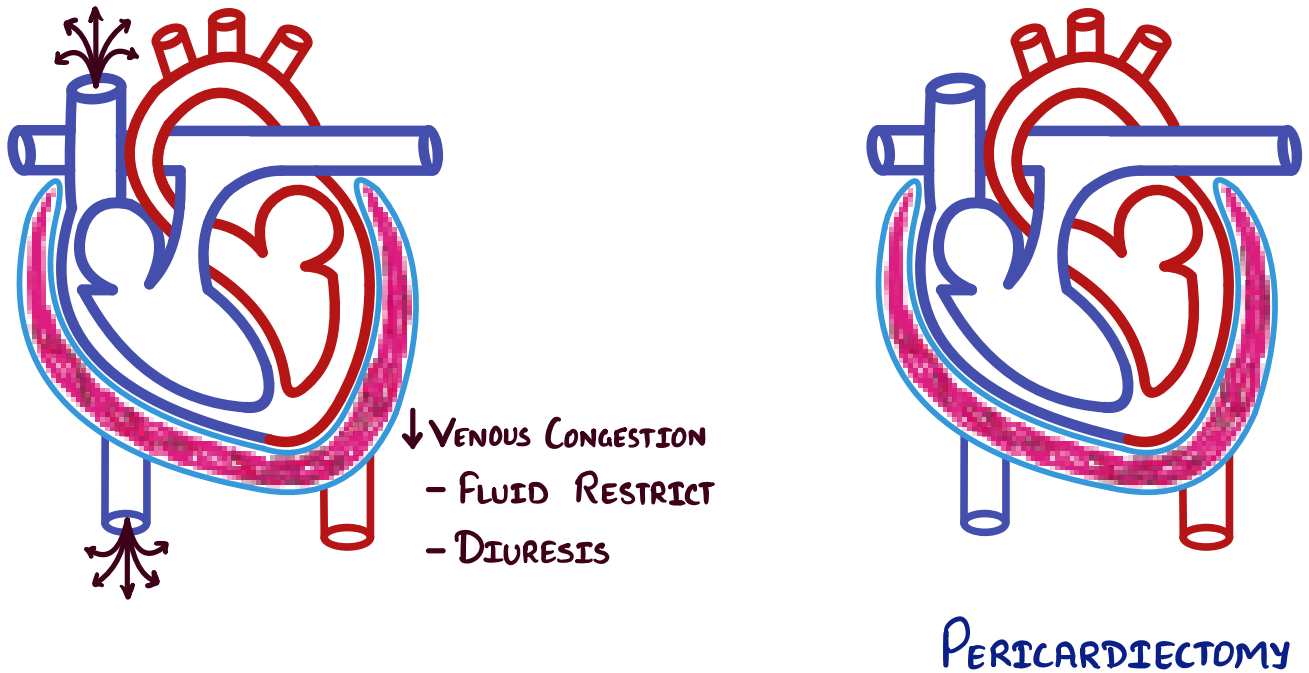


Figure 18. Treatment of constrictive pericarditis.

(A) REDUCE VENOUS CONGESTION

- Fluid restriction (to some degree)
- Diuretics
 - If fluid restriction failed to work

(B) PERICARDIECTOMY

- Surgical process that removes the pericardium
- **Definitive treatment**

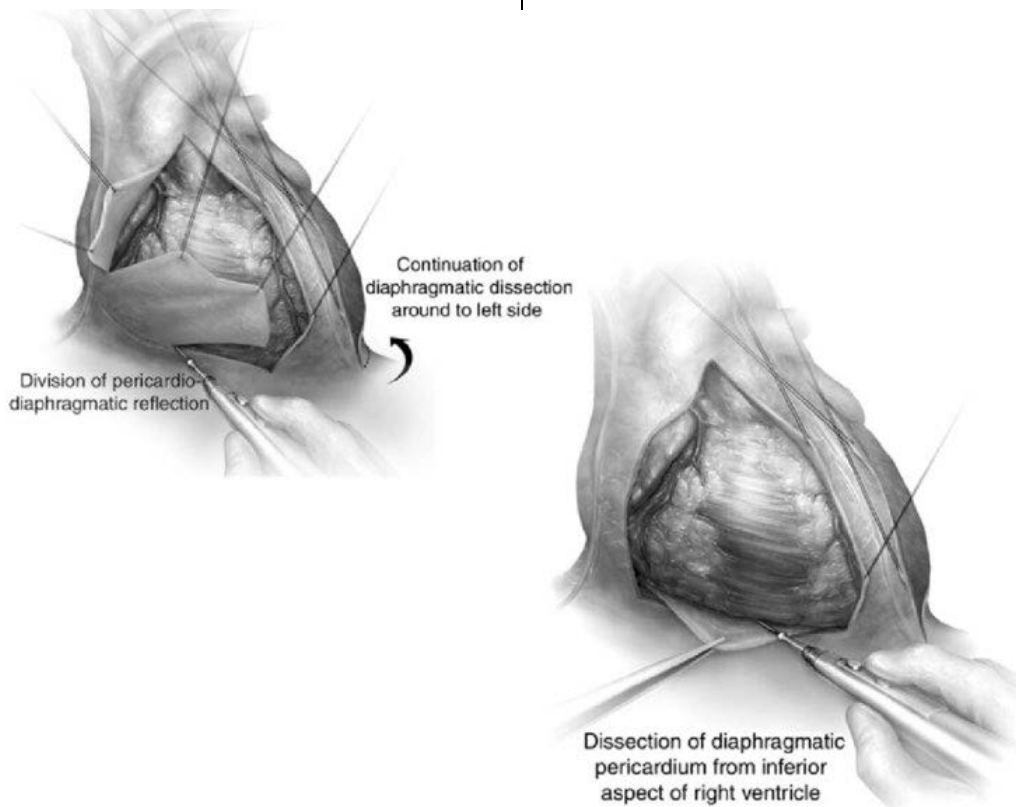


Figure 19. Radical pericardiectomy [Cho, 2012].

VII) QUESTIONS

- 1) What causes pericardial calcifications as seen in chest X-rays?
 - a) Coxsackie B virus
 - b) *M. tuberculosis*
 - c) SARS-CoV-2
 - d) *M. leprae*
- 2) All of the following primary cancers can metastasize to the pericardium EXCEPT:
 - a) Hepatocellular cancer
 - b) Invasive ductal carcinoma
 - c) Lymphoma
 - d) Renal cell carcinoma
- 3) Which of the following symptoms are more commonly seen in patients with constrictive pericarditis?
 - a) Hypotension
 - b) Shortness of breath during exertion
 - c) Jugular venous distension
 - d) All of the above
- 4) Which of the following is FALSE about the PE findings in constrictive pericarditis?
 - a) Kussmaul's sign describe the paradoxical increase in the JVP during inspiration
 - b) Pericardial knock is very specific for patients with constrictive pericarditis
 - c) Hypotension is a left heart failure symptom that can be observed in patients with constrictive pericarditis
 - d) Pulsus paradoxus is a specific PE finding in constrictive pericarditis wherein an SBP decrease of ≥ 10 mmHg is observed during inspiration
- 5) The following are specific diagnostic echo findings for constrictive pericarditis EXCEPT:
 - a) Pericardial thickening
 - b) Increase in flow and velocity across the tricuspid valve during expiration
 - c) Septal bounce during inspiration
 - d) IVC to hepatic vein flow during expiration
- 6) Which of the following is seen in restrictive cardiomyopathy but NOT in constrictive pericarditis?
 - a) Pericardial knock
 - b) Kussmaul's sign
 - c) Low QRS voltage
 - d) Mitral regurgitation

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TRICUSPID VALVE STENOSIS & REGURGITATION

[Tricuspid Valve Stenosis & Regurgitation](#)

Medical Editor: Jude Loyola

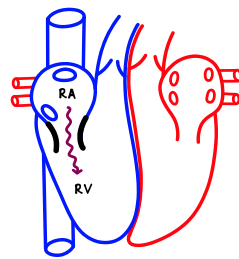
OUTLINE

- I) CAUSES AND PATHOPHYSIOLOGY
- II) CLINICAL FEATURES AND EXAM FINDINGS
- III) DIAGNOSIS
- IV) TREATMENT

- V) APPENDIX
- VI) QUESTIONS
- VII) REFERENCES

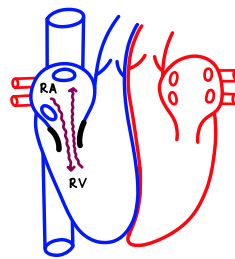
I) CAUSES AND PATHOPHYSIOLOGY

TRICUSPID STENOSIS



DIASTOLE

TRICUSPID REGURGITATION



SYSTOLE

Figure 1. Tricuspid valve stenosis and regurgitation.

(A) PATHOPHYSIOLOGY

(1) Tricuspid Valve Stenosis

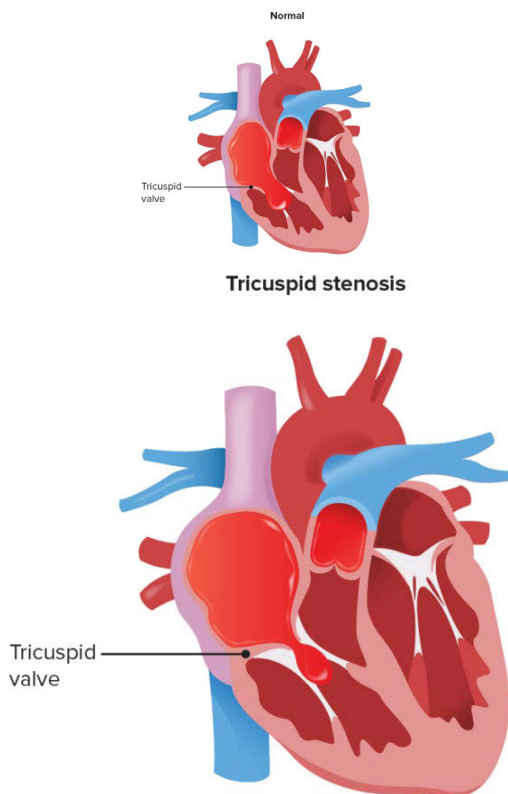


Figure 2. Tricuspid stenosis [Lecturio].

- Tricuspid valve (TV) is **fibrotic** and **stiff** → valves cannot open well
- During ventricular diastole, blood should be flowing down *naturally* from the right atrium (RA) to the right ventricle (RV)
 - When the tricuspid valve is fibrotic, there is **↓blood flow** from the RA to RV

(2) Tricuspid Valve Regurgitation

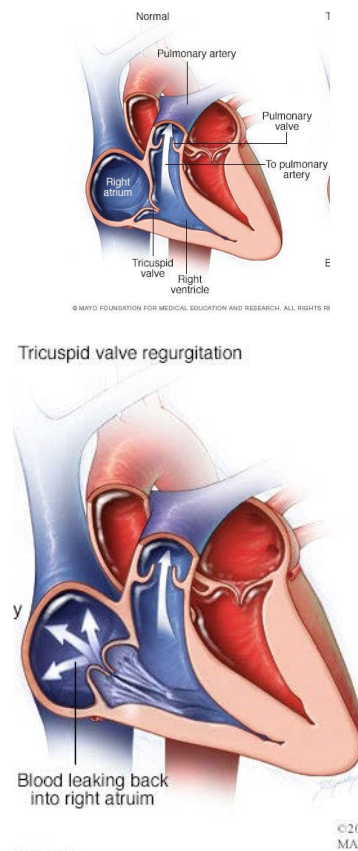


Figure 3. Tricuspid regurgitation [Mayo Clinic].

- Tricuspid valve is **floppy** that fails to form a good seal
- During ventricular systole, blood is pushed to the pulmonary trunk
 - In tricuspid regurgitation, blood goes back into the right atrium



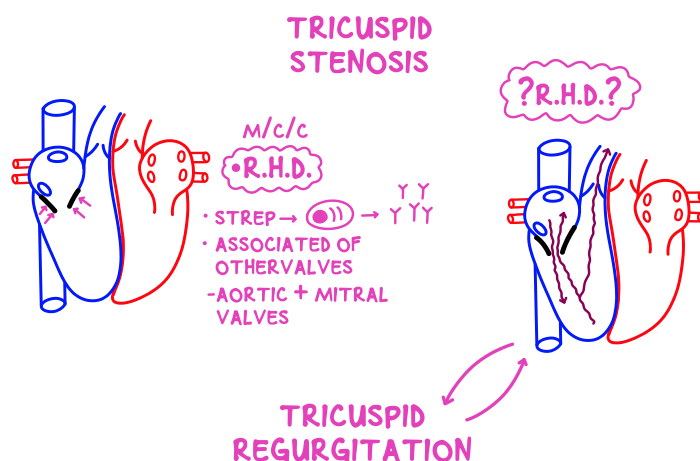


Figure 4. Rheumatic heart disease causing both tricuspid valve stenosis and regurgitation.

(1) Tricuspid Valve Stenosis

(i) Rheumatic Heart Disease

- Most common cause
- Secondary to patients with rheumatic fever
 - *Strep* infections trigger the immune system to produce antibodies → autoantibodies attack the valve producing inflammation → valves replaced by fibrous tissues
- Post-*Strep* infection complication
- Associated involvement of **mitral** and **aortic valves**
 - More commonly targeted than TV

(2) Tricuspid Valve Regurgitation

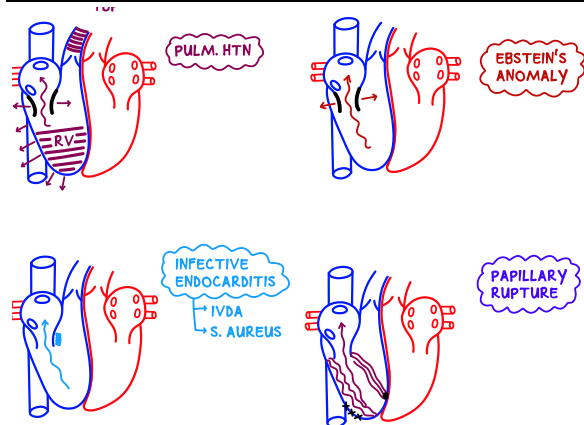


Figure 5. Causes of TV regurgitation.

(i) Rheumatic Heart Disease

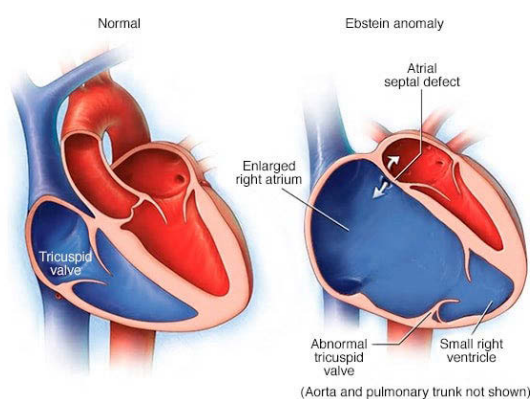
- RHD can also cause tricuspid valve regurgitation (very paradoxical)

(ii) Pulmonary Hypertension

- ↑pressure in the pulmonary arteries
- As a result, the RV works really hard to pump blood out of the ventricle → less blood leaves the ventricle because of the high pressure → blood stays within the ventricles → **dilation of the ventricles**
- If the ventricles are dilated, the annulus of the tricuspid valve becomes stretched farther away → ↑blood backflow to the RA

(iii) Infective Endocarditis

- Seen in IV drug abusers
 - Susceptible to *S. aureus*
- *S. aureus* can bind to the valves forming **vegetations** → releases enzymes that erode the valve → TV does not form a good seal → backflow of blood



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Figure 6. Ebstein's anomaly [Mayo Clinic].

- Congenital anomaly
- TV leaflets hang down really low into the ventricles and are displaced farther away → no good seal → backflow of blood

(v) Papillary Rupture

- Secondary to myocardial infarction
- Recall: Papillary muscles connect the tricuspid valve through the chordae tendinae
 - When the papillary muscles contract, they pull down the TV leaflets which keep them tight
- If there is an infarction, papillary muscles may be damaged → chordae tendinae become loose and cannot produce a tight tricuspid valve



II) CLINICAL FEATURES AND EXAM FINDINGS

(A) TRICUSPID STENOSIS

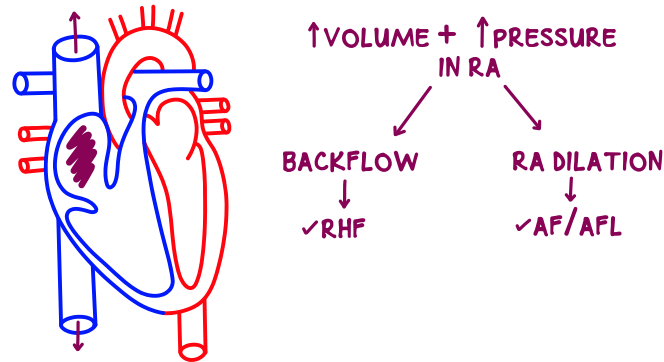


Figure 7. Clinical features of tricuspid stenosis.

- ↑blood in the RA → ↑atrial pressure so it can push against the stenotic TV
- This causes backflow of blood in the SVC and IVC producing features of **right heart failure (RHF)**
- As pressure accumulates inside the RA, it has to accommodate the increased volume → **RA dilation** → can cause arrhythmias (AF and AFL)
- As the right atrium increase its size, it compresses other structures

(1) Right Heart Failure Symptoms

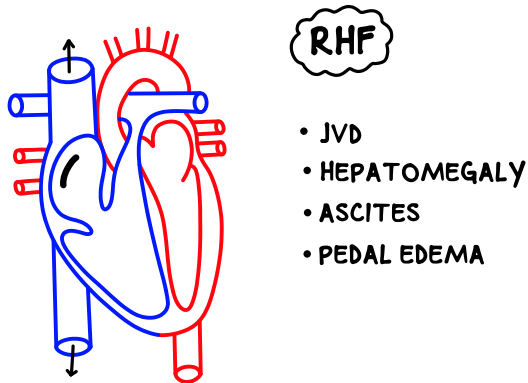


Figure 8. Right heart failure symptoms of tricuspid valve diseases.

- **Jugular venous distension**
 - Backflow in the SVC → blood goes up to the cephalic vein and then IJV
- **Hepatomegaly, ascites and/or pedal edema**
 - Backflow in the IVC → swelling of abdominal and lower extremity structures

(2) Right Atrial Dilation

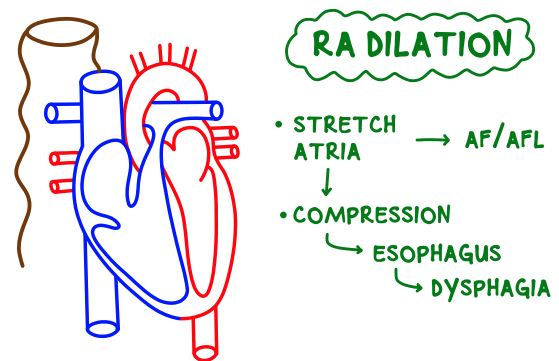


Figure 9. Effects of right atrial dilation.

(i) Stretching of the atrial tissue

- Electrical circuits in the RA is sensitive to stretch → increased risk of arrhythmias such as **atrial fibrillation** and **atrial flutter**
- Present with tachycardia
- Can also increase the risk of blood flow stasis → **clot formation** → can embolize to the lungs (pulmonary embolism)
- Can lead to **dysphagia** (difficulty with swallowing)

(3) Murmur

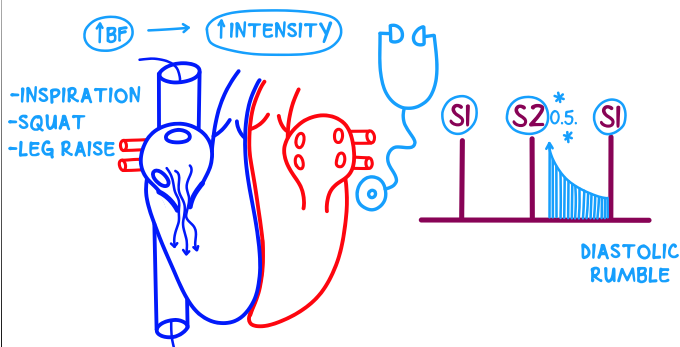


Figure 10. Opening snap with diastolic rumble which is a characteristic murmur in tricuspid stenosis.

- Sometimes, symptoms are very mild or relatively asymptomatic
- Produces an **opening snap + diastolic rumble**
 - Recall that TV stenosis happens during diastole (between S2 and the 2nd S1)
 - Characterized by high pitched sound (opening snap) then a rumbling sound until the end of ventricular diastole

Recall:

- S1: closure of tricuspid valve and mitral valve
- S2: closure of aortic and pulmonary valve

- Accentuated by increasing venous return
 - More blood in the RA → more blood flowing across the valve
 - Through **inspiration, squats or leg raises**



(B) TRICUSPID REGURGITATION

(1) Right Heart Failure Symptoms

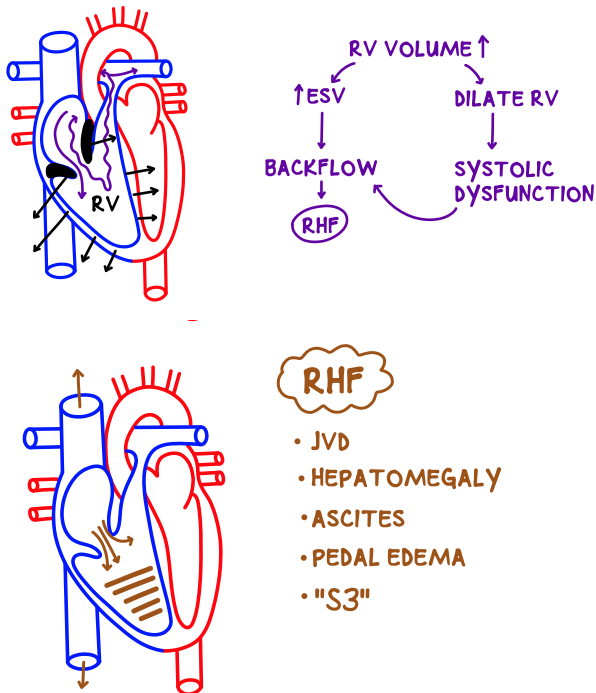


Figure 11. Right heart failure symptoms in tricuspid regurgitation.

(i) ↑RV volume

- ↑blood after systole to be pushed out so there are high volume of blood remaining in the RV = **↑end-systolic volume** → backflow in the IVC and SVC = RHF symptoms
- RA dilates as a compensatory mechanism → eccentric hypertrophy → systolic dysfunction → backflow of blood → RHF symptoms
 - **Eccentric hypertrophy:** dilation and increased muscle size in eccentric fashion
- RV dilation stretches out TV → worsening of regurgitation

(ii) RHF symptoms:

- JVD, hepatomegaly, ascites, pedal edema
- S3 heart sound
 - Blood flows down rapidly to the ventricle during the early phase diastole → producing S3 heart sound

(2) Murmur

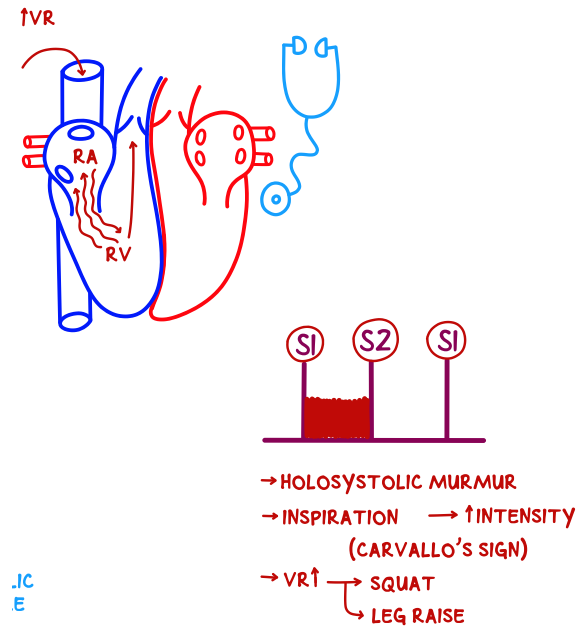


Figure 12. Holosystolic murmur characteristic of tricuspid regurgitation.

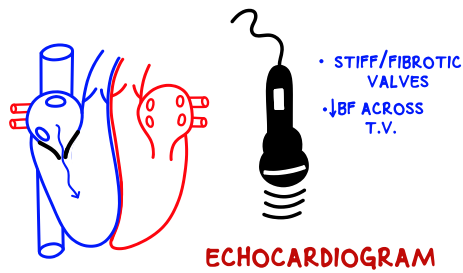
- Produces a **holosystolic murmur** heard during the first S1 and S2 in the left midsternal border
 - Flushing sound all throughout the systolic period
- Intensified by increasing venous return (inspiration, squat and/or leg raises)
 - **Carvallo's sign**
 - Increased intensity of tricuspid valve regurgitation murmur during inspiration
 - Inspiration → ↓intrathoracic pressure → pulls more blood into the right atrium
- Anything that decrease venous return can decrease the intensity of the murmur
 - Standing, Valsalva maneuver



III) DIAGNOSIS

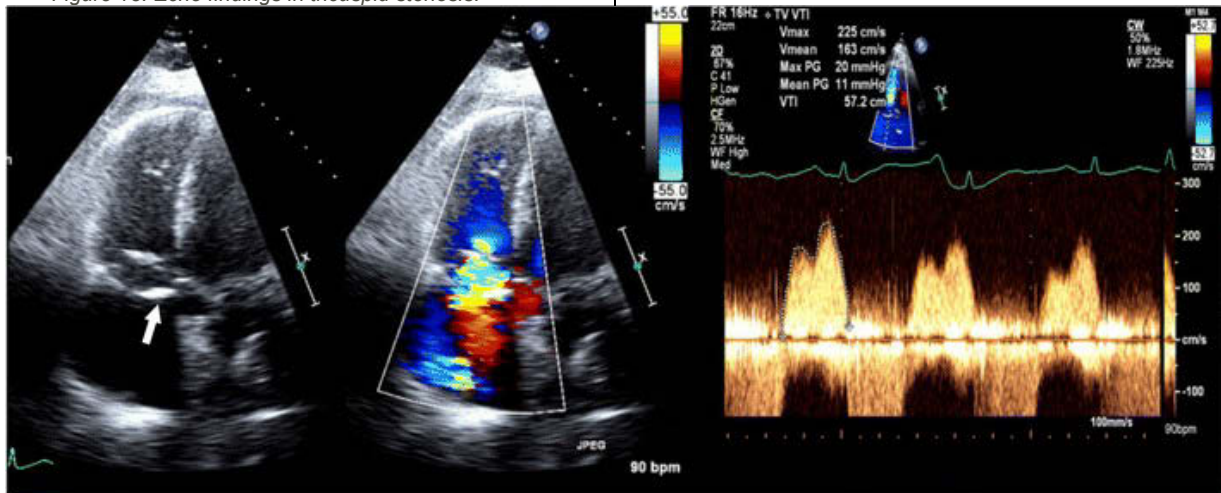
(A) ECHOCARDIOGRAM

(1) Tricuspid Stenosis

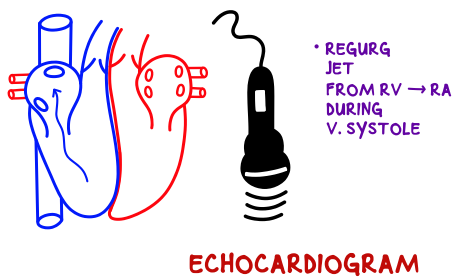


- Thick and fibrotic valves
- Reduction in blood flow across TV
 - Using Color Doppler to check the blood flow from RA to RV

Figure 13. Echo findings in tricuspid stenosis.



(2) Tricuspid Regurgitation



- Some etiological factors may be seen
 - Infective endocarditis: eroded valves
 - Ebstein's anomaly: low hanging TV
 - Papillary muscle rupture: fallen off papillary muscle
- Regurgitation jet from the RV to the RA during ventricular systole

Figure 15. Echo findings in tricuspid regurgitation.

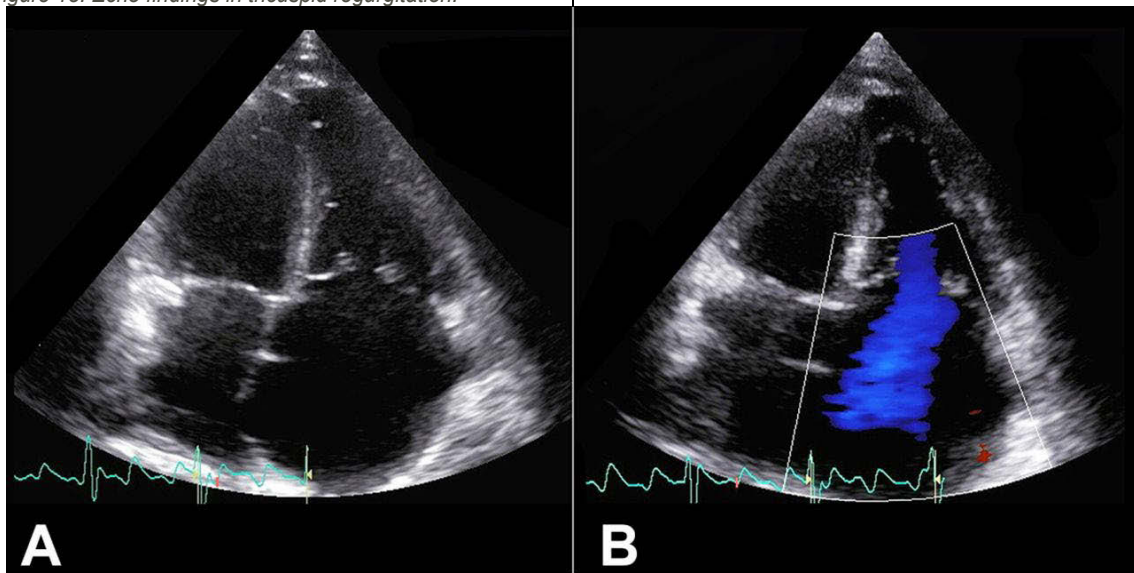
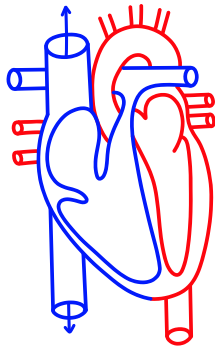


Figure 16. (A) Right ventricular and atrial enlargement with subsequent leaflet malcoaptation. (B) Broad-based regurgitant jet across the tricuspid valve by colour-flow Doppler [Fender et al, 2016].



IV) TREATMENT

(A) MANAGEMENT OF RIGHT HEART FAILURE SX



- FLUID RESTRICT
- NA RESTRICT
- DIURESIS
- STOCKINGS

HEART FAILURE

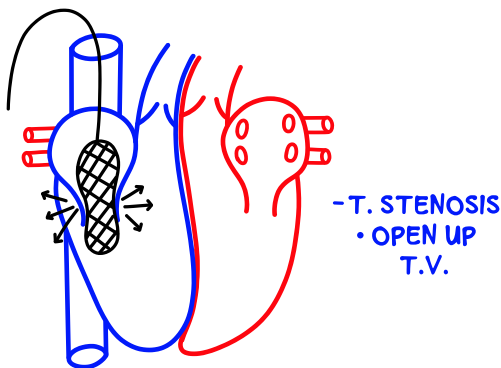
Figure 17. Management of RHF symptoms.

- Depends on the severity
 - Mild: mild symptoms or asymptomatic
 - Moderate to severe: can cause congestive heart Sx

(1) Management

- Fluid restriction
- Na⁺ restriction
- Diuretics
 - e.g. Furosemide
 - For patients with volume overload causing ascites and edema
- Compression stockings
 - For pedal edema

(B) BALLOON VALVULOPLASTY



- T. STENOSIS
• OPEN UP
T.V.

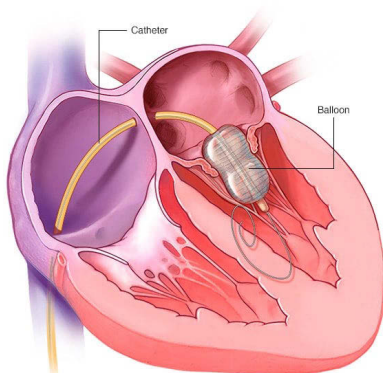


Figure 18. Balloon valvuloplasty. Second image from Mayo Clinic (2021).

- First-line modality for patients with mild to moderate TV stenosis
- Catheter to the RA across the TV, inflate a balloon that pushes the TV outwards to open the valve more

(C) VALVE REPLACEMENT

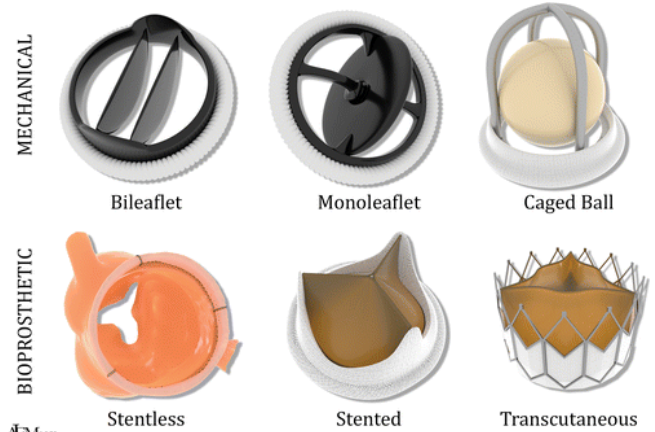


Figure 19. Different types of mechanical and bioprosthetic valve replacements [Rajiah et al. 2019].

(1) Indications

- Severe TVS that is refractory to valvuloplasty
- Tricuspid valve regurgitation

(2) Types of Replacement Valves

(i) Mechanical Valve

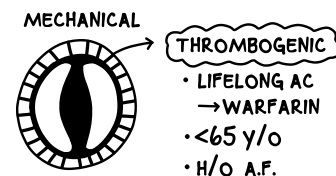


Figure 20. Mechanical valves.

- Made from metals or metalloids
- **Highly thrombogenic** → increased risk of pulmonary clot
- Requires **lifelong anticoagulation**
 - Warfarin
 - Aspirin (if Warfarin cannot be tolerated)
- Indicated for patients who are:
 - <65 years old
 - With a prior history of atrial fibrillation
- Not indicated for older patients (>65 years) who have high risk of bleeding
- Low risk of endocarditis

(ii) Bioprosthetic Valve

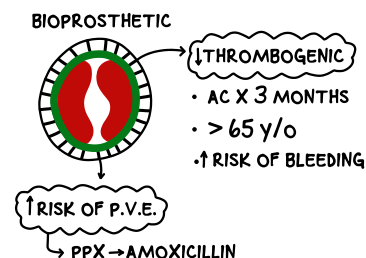
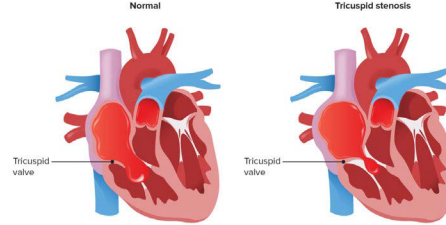
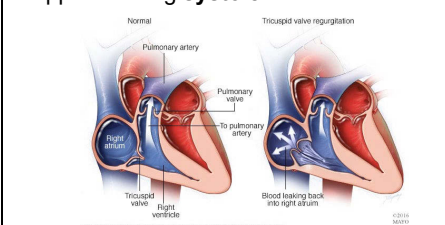


Figure 21. Bioprosthetic valves.

- Bovine valves
- **Lower thrombogenic nature**
- Does not require lifelong anticoagulation
 - Anticoagulation for at most 3 months
- Indicated for patients >65 years of age and those with high risk of bleeding
- **High risk of prosthetic valve endocarditis**
 - May require prophylaxis (amoxicillin or ampicillin)



	TRICUSPID STENOSIS	TRICUSPID REGURGITATION
Pathophysiology	Fibrotic and stiff tricuspid valve → reduced blood flow to the right ventricle Happens during diastole 	Floppy tricuspid valve → failure to seal during systole → backflow of blood to the right atrium Happens during systole 
Causes	Rheumatic heart disease - Most common cause - Post-<i>Strep</i> condition where autoantibodies attack the valves causing inflammation and fibrosis - With associated involvement of the mitral and aortic valves	Rheumatic heart disease Pulmonary hypertension - High pressure in the pulmonary arteries → less blood leaves the ventricle → blood stasis in the ventricles → RV dilation Infective endocarditis <i>S. aureus</i> forming vegetations and releasing enzymes causing valve erosion Ebstein's anomaly - Congenital condition where tricuspid valve leaflets hang down low into the ventricles Papillary rupture - Damage to the papillary muscles causing a loose chorda tendinae that connect to the TV
Clinical Features	Right heart failure symptoms - JVD, ascites, hepatomegaly, pedal edema Atrial stretching - Causing arrhythmias (AF and A Flutter) - Increased risk of clot formation and pulmonary embolism Compression of esophagus causing dysphagia	Right heart failure symptoms - JVD, ascites, hepatomegaly, pedal edema - S3 heart sound
Murmur Characteristic	Opening snap + diastolic rumble during diastole Heard at the left parasternal border, 4th ICS	Holosystolic murmur Heard at the left midsternal border
	Accentuated by increasing venous return (inspiration, squats or leg raises)	
Echo Findings	Thickened valves Reduction in blood flow across TV	Eroded valves (infective endocarditis), low hanging TV (Ebstein's anomaly) or fallen off papillary muscle (PM rupture) Regurgitation jet
Treatment	Management of RHF symptoms through: - Fluid restriction - Na⁺ restriction - Diuretics - Compression stockings	
	Balloon valvuloplasty	
	Valve replacement - For severe TV stenosis that is refractory to valvuloplasty - Tricuspid regurgitation - Mechanical or bioprosthetic valves can be used depending on the age of the patient and/or the risk of bleeding	



VI) QUESTIONS

- 1) Which of the following is TRUE regarding TV stenosis?
 - a) Most common cause of TV stenosis is rheumatic heart disease caused by *S. aureus*
 - b) TV stenosis happens during systole
 - c) TV stenosis secondary to RHD usually involves other valves
 - d) None of the above
- 2) Which of the following is NOT a cause of tricuspid regurgitation?
 - a) Rheumatic heart disease
 - b) Infective endocarditis caused by *S. viridans*
 - c) Ebstein's anomaly
 - d) Myocardial infarction
- 3) Which of the following does NOT describe the clinical finding in tricuspid regurgitation?
 - a) Upon auscultation, a holosystolic murmur can be heard
 - b) Upon auscultation, an opening snap can be heard
 - c) Both TV regurgitation and TV stenosis can present with JVD, ascites, pedal edema and hepatomegaly
 - d) None of the above
- 4) Which of the following describes the clinical finding in tricuspid stenosis?
 - a) It's more common to find ascites in TV stenosis than regurgitation
 - b) Patients with tricuspid stenosis can present with tachycardia and dyspnea
 - c) Murmur from TV stenosis is described as a flushing sound all throughout the systolic period
 - d) Standing can intensify the murmur in TV stenosis
- 5) Which is NOT a characteristic of mechanical valves?
 - a) Indicated for younger (<65) patients and Px with high risk of bleeding
 - b) Mechanical valves require a prophylaxis of ampicillin or amoxicillin
 - c) Mechanical valves require a lifelong anticoagulation with aspirin or warfarin
 - d) None of the above

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PULMONARY VALVE STENOSIS & REGURGITATION

Pulmonary Valve Stenosis & Regurgitation

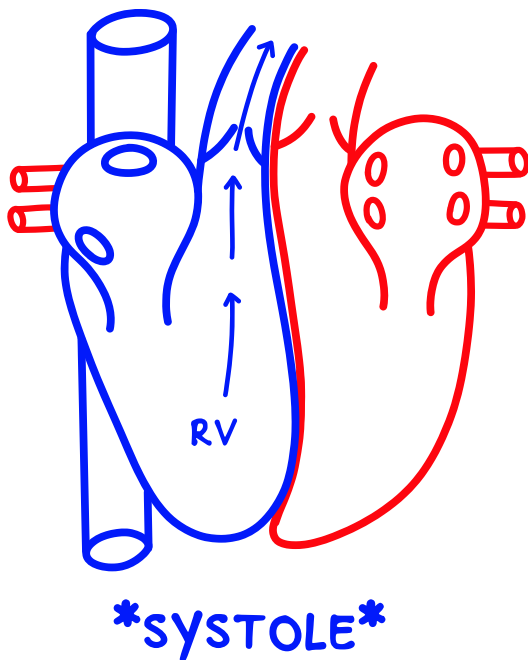
Medical Editor: Dr. Ana Guerra

OUTLINE

- | | |
|---|-----------------------|
| I) DEFINITIONS | V) DIAGNOSIS |
| II) CAUSES AND PATHOPHYSIOLOGY | VI) TREATMENT |
| III) CLINICAL FEATURES AND PHYSICAL EXAM: PULMONIC STENOSIS | VII) REVIEW QUESTIONS |
| IV) CLINICAL FEATURES AND PHYSICAL EXAM: PULMONIC REGURGITATION | VIII) REFERENCES |

I) DEFINITIONS

(A) STENOSIS



- In physiological situations the pulmonary valve **prevents a backflow from the pulmonary artery into the right ventricle.**

Patients with pulmonic stenosis:

- Valve becomes **fibrotic and sclerotic**
 - **Doesn't allow blood to exit** out of the right ventricle into the pulmonary artery
 - **Systole is affected.**

CLINICAL FEATURES Overview

(will be discussed in more detail later)

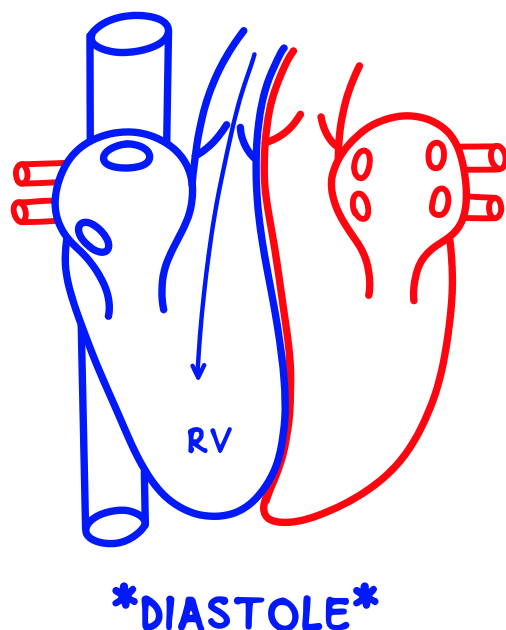
- (1) Right Ventricular Hypertrophy
- (2) Right Heart Failure
- (3) Cyanosis
- (4) Microangiopathic Hemolytic Anemia (MAHA)

PHYSICAL EXAM Overview

(will be discussed in more detail later)

- S4 heart sound

(B) REGURGITATION



Patients with pulmonic regurgitation

- **Valves aren't able to create a good seal** that will prevent blood to backflow from the pulmonary artery into the ventricle
 - There is a **space left** when valves try to close
 - **Diastole is affected.**

CLINICAL FEATURES Overview

(will be discussed in more detail later)

- (1) Right Ventricle Dilation
- (2) Right Heart Failure

PHYSICAL EXAM Overview

(will be discussed in more detail later)

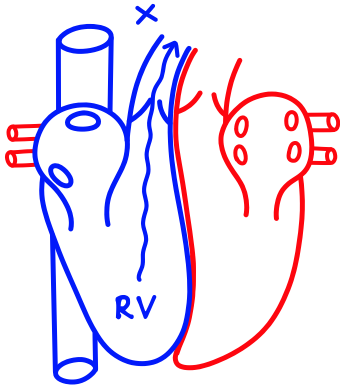
- Diastolic Heart Murmur
- S3 heart sound



II) CAUSES AND PATHOPHYSIOLOGY

(A) PULMONIC STENOSIS

Congenital → Most common cause



(1) Tetralogy of Fallot

→ Four congenital defects that involve the heart:

- (i) Right Ventricular hypertrophy
- (ii) Overarching aorta
- (iii) Ventricular septal defect
- (iv) Pulmonic stenosis

→ The stenosis can involve the valves or it can be located in the infundibulum (right below the valves).

→ Narrowing of the right ventricular outflow tract.

(2) Noonan Syndrome

→ Genetic condition

- (i) Short stature
- (ii) Intellectual disability
- (iii) Hypertelorism
 - Large distance between both eyes.
- (iv) Webbed neck
- (v) Pulmonic stenosis

(3) Congenital Rubella Syndrome

→ Due to the rubella infection during the birthing process

→ Clinical features "Three C's"

- (i) Cataracts
- (ii) Cochlear defects
- (iii) Cardiac abnormalities

→ Ductus arteriosus

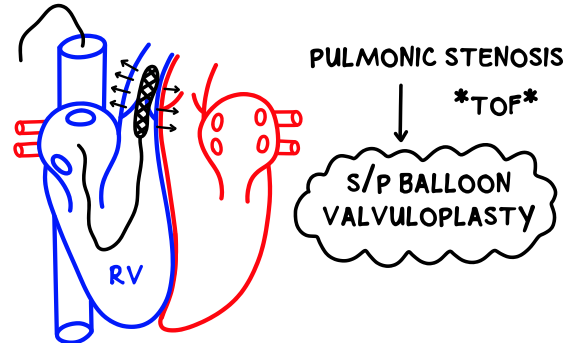
→ Pulmonic stenosis

(B) PULMONIC REGURGITATION

(1) Balloon Valvuloplasty

→ Patients with pulmonic stenosis that are treated with balloon valvuloplasty are in high risk of developing pulmonic regurgitation.

→ Usually associated with tetralogy of Fallot.



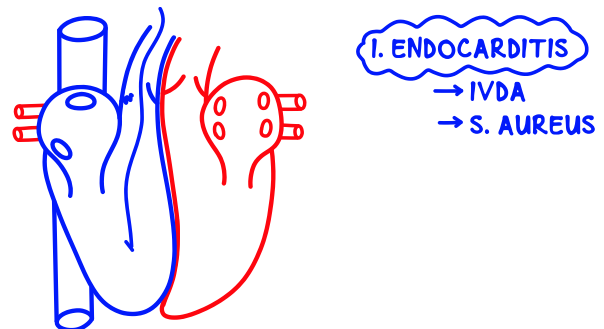
(2) Infective Endocarditis

→ High risk in **IV drugs abusers**

→ Usually caused by **S. aureus**

→ Formation of vegetations that erode away the valves.

→ Second most common cause.



(3) Carcinoid Syndrome

→ Usually in neoplasia that involve the lungs or the IG tract.

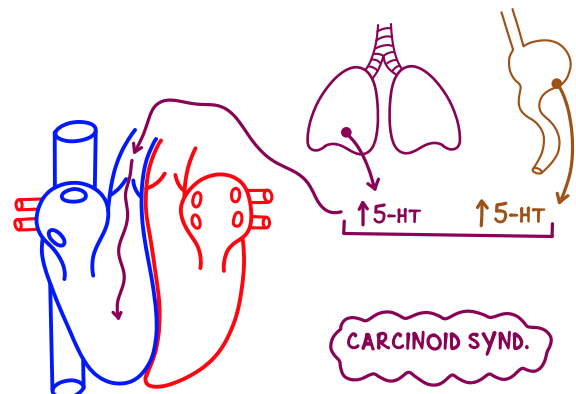
→ Some tumors have the ability to produce 5-HT (serotonin)

→ It triggers fibrosis → **Fibrous depositions around the valves**

→ Can cause stenosis but because of the fibrosis valves are unable to close off properly during diastole

→ **Regurgitation.**

→ Third most common cause.



III) CLINICAL FEATURES AND PHYSICAL EXAM: PULMONIC STENOSIS

(A) CLINICAL FEATURES

→ Blood can't leave the ventricle because of the stenosis

(1) Right Ventricular Hypertrophy

- As an attempt to compensate the stenosis of the valve, the **cardiac muscle starts to grow** in order to overcome the pressure of the valves.

→ Ventricle walls get thicker → **Concentric hypertrophy**

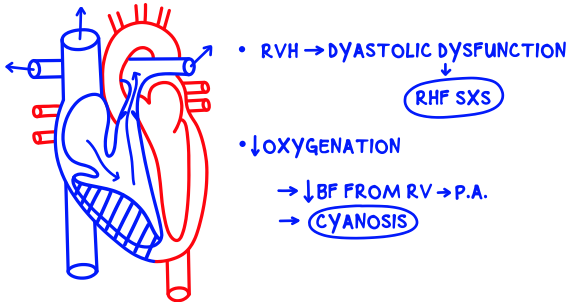
→ **Difficulty to fill the ventricles**

→ **Diastolic dysfunction:**

(i) Right heart failure symptoms

(ii) Hypoxemia and cyanosis

- Due to the decrease of blood going to the lungs.
- Bluish discoloration of mucus membranes.



(2) Right Heart Failure

(i) Blood backs up superior vena cava

- It backs up the jugular vein → **Jugular vein distension.**

(ii) Blood backs up inferior vena cava

- It backs up into the liver and spleen circulation → **Hepatosplenomegaly**
- If it causes fluid to accumulate in the peritoneal cavity → **Ascites.**
- If it accumulates within the lower extremities circulation → **Pedal edema.**

(iii) S4 heart sound

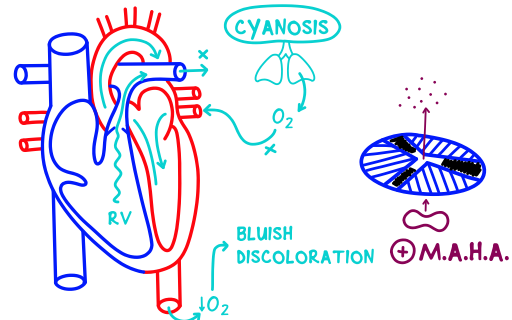
- As the ventricle muscle starts to grow, the atrium needs to send blood more strongly → **Atrium hypertrophy and production of the S4 heart sound.**

(3) Cyanosis

- Less blood is flowing into the lungs due to the stenosis
- Less oxygen will be bound to the hemoglobin of the red cells
- **Bluish discoloration.**

(4) Microangiopathic Hemolytic Anemia (MAHA)

- When red cells try to cross through the narrow space between the valves they can break causing anemia.



(B) PHYSICAL EXAM

When listening on the **upper sternal border along the second intercostal space** in a patient with stenotic pulmonic valves you will find:

(i) Systolic Heart Murmur: Ejection click

→ **Between S1 and S2**

- S1: Whenever tricuspid and mitral valves close.
- S2: Whenever pulmonary and aortic valves close.

→ Ejection click:

- Occurs when valves slightly open, letting blood squirt through that area.

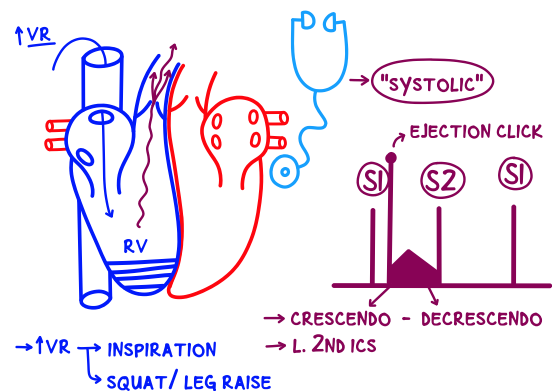
→ The sound will be louder during early phases of systole but it'll start to decrease as ventricle starts to empty.

→ **"Crescendo"** as the blood flows across the pulmonic valves.

→ **"Decrescendo"** as the blood leaves the ventricle.

So you will hear...

Ejection click → Crescendo → Decrescendo



You can ask the patient to **inspire, squat or raise their legs** to augment the intensity of the murmur → Pours more blood into the right side of the heart.



IV) CLINICAL FEATURES AND PHYSICAL EXAM: PULMONIC REGURGITATION

(A) CLINICAL FEATURES

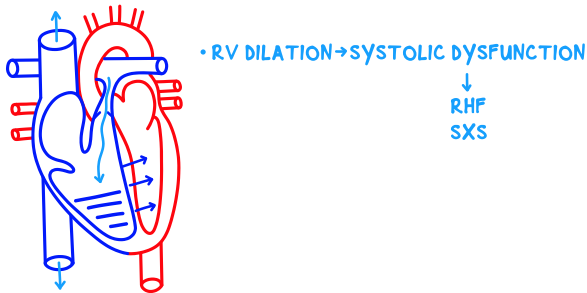
→ Valves can't create a good seal → **Blood will flow back into the right ventricle**

(1) Right Ventricle Dilation

- As an attempt to accommodate the large volume of blood that is coming back, the ventricle dilates, increasing its storage capacity.

→ Ventricle walls get thinner → **Eccentric hypertrophy**
 → **Difficulty to contract the ventricles and pump blood out**
 → **Systolic dysfunction:**

(i) Right Heart Failure Symptoms



(2) Right Heart Failure

(i) Blood backs up superior vena cava

- It backs up the jugular vein → **Jugular vein distension.**

(ii) Blood backs up inferior vena cava

- It backs up into the liver and spleen circulation → **Hepatosplenomegaly**
- If it causes fluid to accumulate in the peritoneal cavity → **Ascites.**
- If it accumulates within the lower extremities circulation → **Pedal edema.**

(iii) S3 heart sound

- As the blood flow back into the ventricle during early diastole it creates a **turbulent flow**
 → **Classic S3 type of heart sound**

(B) PHYSICAL EXAM

When listening on the **left second intercostal space** in a patient with pulmonic regurgitation valves you will find:

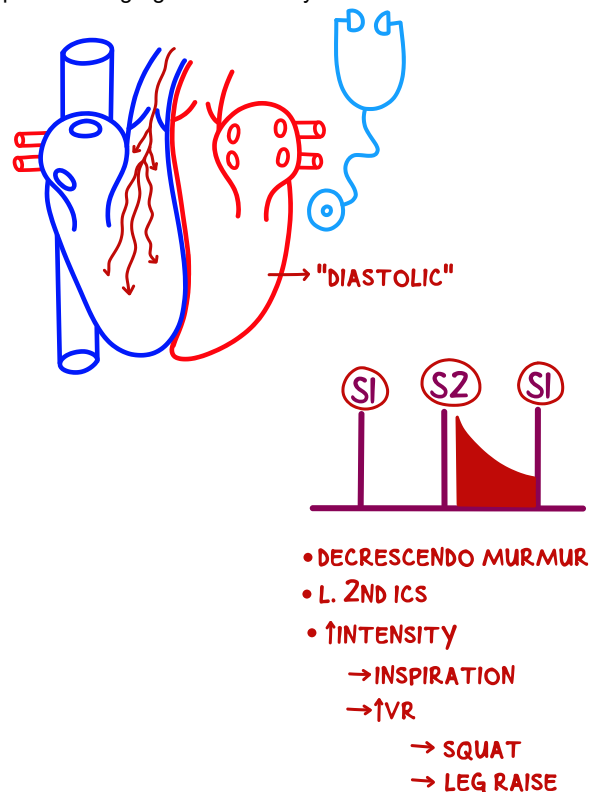
(i) Diastolic Heart Murmur

→ **Between S2 and S1**

- It will be louder right after S2, as the blood flows back rapidly through the valves in early stages of ventricular diastole.
- It will decrease as blood starts to flow back more slowly in late stages of diastole.

→ **Diastolic decrescendo murmur** → **Graham Steell murmur**

You can ask the patient to **inspire, squat or raise their legs** to augment the intensity of the murmur → Pours more blood into the right side of the heart.



V) DIAGNOSIS

(A) PULMONIC STENOSIS

(1) Clinical Features

- RHF symptoms
- Cyanosis
- MAHA
- S4 heart sound

(2) Physical Exam

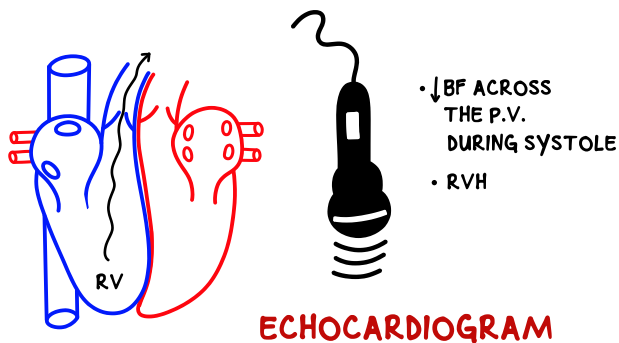
- Ejection click → Crescendo → Decrescendo murmur

(3) Echocardiogram

1) Color Doppler:

- Decreased amount of blood flow during ventricular systole.

2) Right ventricular hypertrophy .



(B) PULMONIC REGURGIATION

(1) Clinical Features

- RHF symptoms.
- S3 heart sound.

(2) Physical Exam

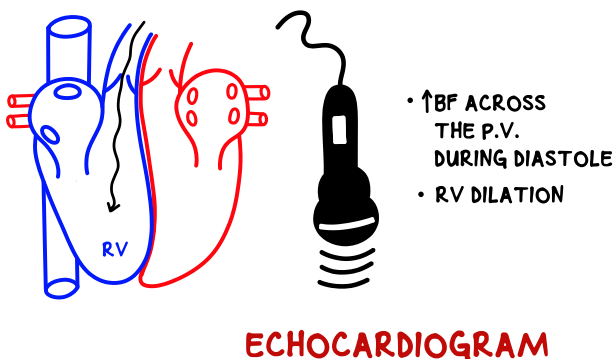
- Diastolic decrescendo murmur → Graham Steell murmur.

(3) Echocardiogram

1) Color Doppler

- Increased amount of blood across the pulmonic valve during diastole.

2) Right ventricular dilation.



VI) TREATMENT

(A) HEART FAILURE TREATMENT

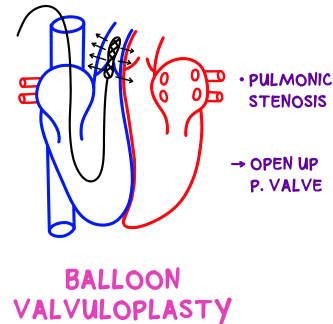
- 1) Fluid restrict
- 2) Restrict sodium
- 3) Diuretics (e.g. furosemide)
- 4) Compression stockings

(B) VALVULAR INTERVENTION

(1) Balloon Valvuloplasty

→ Indicated for patients with severe pulmonic stenosis

→ A balloon is fitted between the pulmonic valves and pushes open to create an open space that will allow blood to flow in.



(2) Valve Replacement

→ Indicated for patients who:

- a. Received a balloon valvuloplasty and didn't show any significant improvement.
- b. Have pulmonic valve regurgitation with severe symptoms.

(i) Mechanical valve

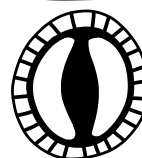
→ Long lifespan

→ They require lifetime anticoagulation treatment for its high thrombogenic risk.

→ Warfarin

→ More commonly used in younger persons or patients who are already taking anticoagulant treatment.

MECHANICAL VALVE



- LONG LIFE SPAN
- ↑ THROMBOGENIC
- LIFELONG AC
- WARFARIN
- <65 y/o
- AF OR ON A.C.

(ii) Bioprosthetic valve

→ Short lifespan (10 years).

→ Low thrombogenic risk

→ Anticoagulant treatment for three months.

→ Used in older persons or with high bleeding risk.

→ High risk of prosthetic valves endocarditis.

→ PPX with Amoxicillin

BIOPROSTHETIC



- SHORT LIFE SPAN
- ↓ THROMBOGENIC
- AC X 3 MONTHS
- >65 y/o
- ↑ BLEEDING RISK
- ↑ RISK OF P.V.E.
- PPX - AMOXICILLIN





MITRAL VALVE STENOSIS & REGURGITATION

Mitral Valve Stenosis & Regurgitation

Medical Editor: Jona, Aldrich, Jude & Uta

OUTLINE

I) INTRODUCTION
II) CAUSES
I) CLINICAL FEATURES AND PHYSICAL EXAMS
II) IAGNOSIS

III) TREATMENT
IV) APPENDIX
V) REVIEW QUESTIONS
VI) REFERENCES

I) INTRODUCTION

(1) Mitral Valve

- Valve that separates left atrium and left ventricle

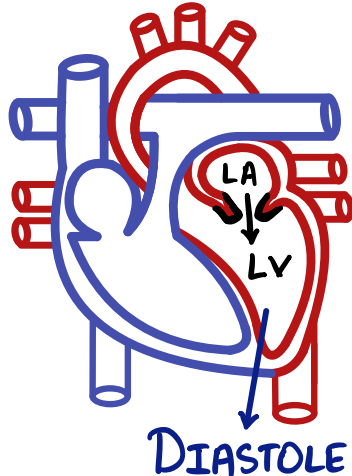
(i) Anatomy of the Mitral Valve Apparatus

- **Annulus ring** – fibrous ring of the mitral valve which holds the leaflets and serves as orifice to the left ventricle
- **Leaflets** – off of the annulus ring
- **Chordae tendineae** – off of the leaflets and connected to the papillary muscles
- **Papillary muscles** – extensions of the myocardium that pull the chordae tendineae to keep the valve leaflets close to on another

- Any disease process affecting any of the components of the mitral valve apparatus will lead to **mitral regurgitation**.

(2) Mitral Valve Stenosis

- A condition in which the mitral valve is very **FIBROTIC AND CALCIFIED** (stenotic)
- In effect, it slows the blood flow from the left atrium to left ventricle
- A **DIASTOLIC** problem (Figure 1)



MITRAL STENOSIS

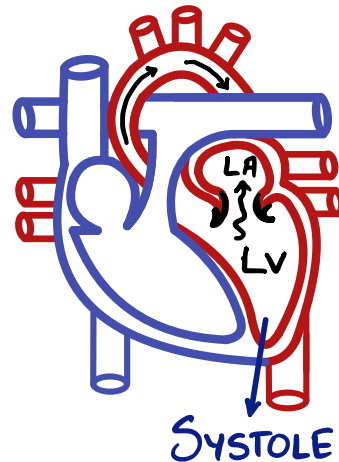
- FIBROTIC / CALCIFIED VALVE
- LA $\xrightarrow{x}$ LV

Figure 1. Mitral Valve Stenosis.

(3) Mitral Regurgitation

- A condition in which the mitral valves have **POOR SEAL**
- In effect, whenever the ventricles contract, the blood is being pushed back to the left atrium = **backflow**
 - Normally in systole, blood is being pushed from the left atrium to the aorta

Figure 2)



MITRAL REGURGITATION

- POOR SEAL
- BACKFLOW FROM LV $\rightarrow$ LA

Figure 2. Mitral Valve Regurgitation.



II) CAUSES

(A) MITRAL STENOSIS

(1) Rheumatic Heart Disease

- Immunologic hypersensitivity reaction to **Group A Streptococcus** (Beta-hemolytic bacteria) antigens [Sattar]
- Caused by molecular mimicry
 - Bacterial M protein resembles proteins in human tissue [Sattar]
- **AUTO-ANTIBODIES** attack the mitral valves → inflammation of mitral valves → stenosis of the valves (Figure 3)
 - Auto- means from self
- Can also be seen in the following:
 - Mitral regurgitation
 - Aortic stenosis
 - Aortic regurgitation
 -

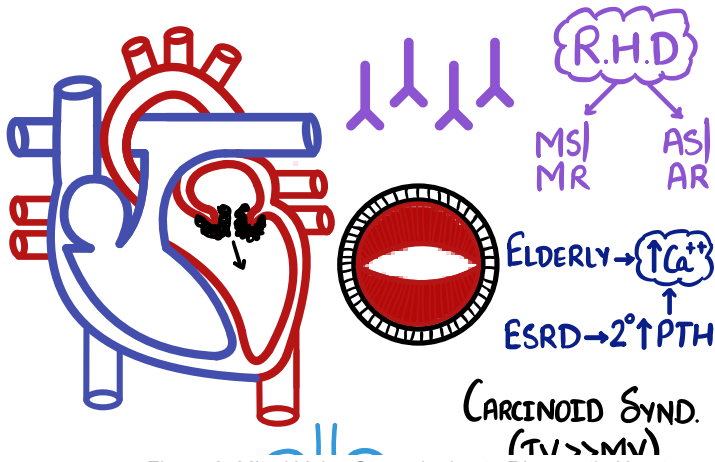


Figure 3. Mitral Valve Stenosis due to Rheumatic Heart Disease and Calcifications.

(2) Increase Calcium Deposition (Calcifications)

- Increase in **CALCIUM DEPOSITS** in the mitral valves make them stiff and less pliable → blood will not be able to move easily (Figure 3)

(i) Elderly

- Lots of Ca^{2+} depositions in the cardiac valves particularly in mitral valves

(ii) End-stage Renal Disease (ESRD)

- Patients with ESRD develop **secondary hyperparathyroidism**
 - Parathyroid hormone (PTH) – increases the Ca^{2+} levels in the blood → increase in deposition of Ca^{2+}

- Seen more in tricuspid valves than in mitral valves
- Occurs when a tumor in the gastrointestinal tract starts secreting chemicals such as **AS SEROTONIN OR 5-HYDROXYTRYPTAMINE (5-HT)** (Figure 4)
 - **Serotonin** causes a fibrotic reaction in the mitral valves pliable → blood will not be able to move easily
- Tumor may spread into the liver → to the right heart → to the lungs

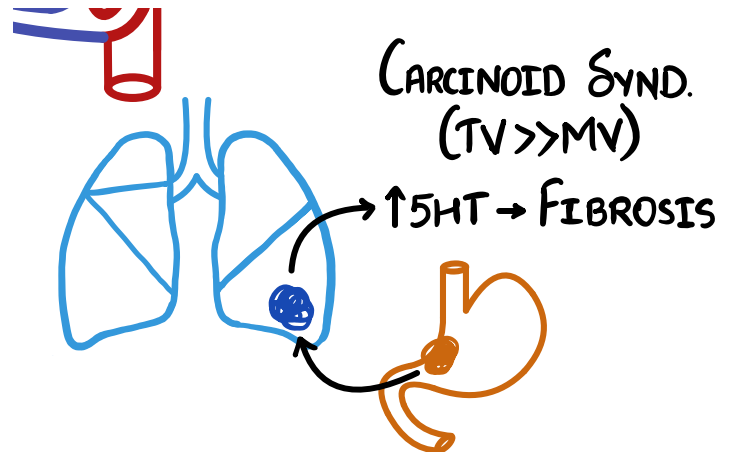


Figure 4. Mitral Valve Stenosis due to Carcinoid Syndrome.



(B) MITRAL REGURGITATION

(1) Primary Mitral Regurgitation

- Results from the actual disease of the mitral valve apparatus

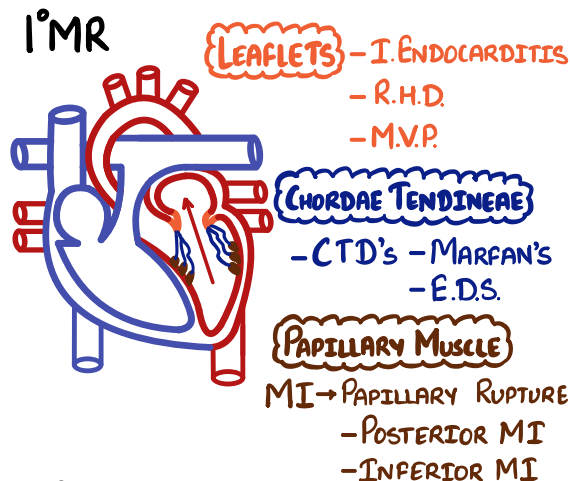


Figure 5. Causes of Primary Mitral Regurgitation.

(i) Infective Endocarditis (IE)

- Inflammation of endocardium that lines the surface of the cardiac valves → **direct damage to valves** → MR (Figure 5)
- Usually due to bacterial infection
- Streptococcus viridans** is the most common cause [Sattar]
- Forms a bulky vegetation in the valves [Sattar]

(ii) Rheumatic Heart Disease

- Anterior and posterior leaflets of the mitral valve should come together and block blood flow from going into the LA during systole.
- Inflammation of the valves → **thickening of the leaflets due to fibrosis** → valve leaflets can't snap shut → MR (Figure 5)

Infective endocarditis results in marked bulky vegetation.

Meanwhile, rheumatic heart disease results in small vegetation [Sattar].

(iii) Mitral Valve Prolapse

- Ballooning of mitral valve into the left atrium during systole
- Due to **MYXOMATOUS PROLIFERATION OF THE ZONA SPONGIOSA** of the valve making it floppy or easily bent → MR (Figure 5)
 - Myxomatous proliferation**- accumulation of ground substance

(iv) Connective Tissue Diseases

- Causes weakening of the chordae tendineae → unable to generate a good tautness of the leaflets → MR (Figure 5)
- Examples include
 - Marfan Syndrome
 - Osteogenesis Imperfecta

(v) Myocardial Infarction

- May cause **PAPILLARY RUPTURE**
- Tend to affect the posterior leaflets more
- Posterior MI or Inferior MI can destroy the papillary muscles that anchor the posterior leaflets → unable to pull chordae tendineae and keep them taut → leaflets can't close properly → MR (Figure 5)

Infective endocarditis and myocardial infarction can cause acute mitral regurgitation which is a hemodynamic emergency

(2) Secondary Mitral Regurgitation

- Due to primary left ventricular dysfunction with normal mitral valve leaflets and chord
- Unlikely to produce acute mitral regurgitation

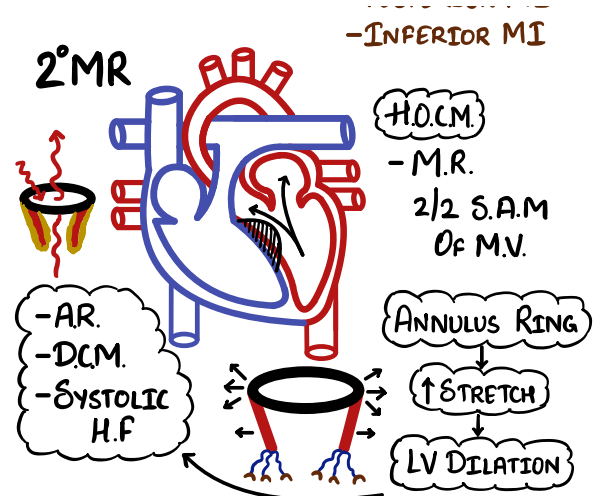


Figure 6. Causes of Mitral Regurgitation.

(i) Conditions that cause Left Ventricular Dilation

- Disease process that stretches the annulus ring → leaflets are pulled far away from each other → poor seal → MR (Figure 6)
- Examples include:
 - AORTIC REGURGITATION** – Backflow of blood from the aorta into the left ventricle during diastole
 - DILATED CARDIOMYOPATHY** – Dilation of all four chambers of the heart; Results in systolic dysfunction
 - SYSTOLIC HEART FAILURE**

(ii) Hypertrophic Obstructive Cardiomyopathy

- Greater **thickening of ventricular septum** than the left ventricular free wall
- Blood can't squeeze out from the left ventricle because of the thickened ventricular septum
- But this also creates more space in the orifice of the mitral valves leading to MR (Figure 6)
 - SYSTEMIC ANTERIOR MOTION OF THE MITRAL VALVE** - Displacement of the distal portion of the anterior leaflet of the mitral valve toward the left ventricular outflow tract obstruction [Lasala et al.]

MUST KNOW

Table 1. Different Causes of Mitral Regurgitation and the Affected Components of Mitral Valve Apparatus

Leaflets	Chordae Tendineae
- Infective Endocarditis - Rheumatic Heart Disease - Mitral Valve Prolapse	Connective Tissue Diseases
Papillary Muscles	Annulus Ring
Myocardial Infarction	Left Ventricular Dilation



MITRAL STENOSIS

MITRAL STENOSIS

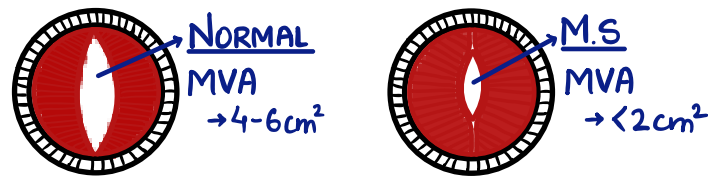


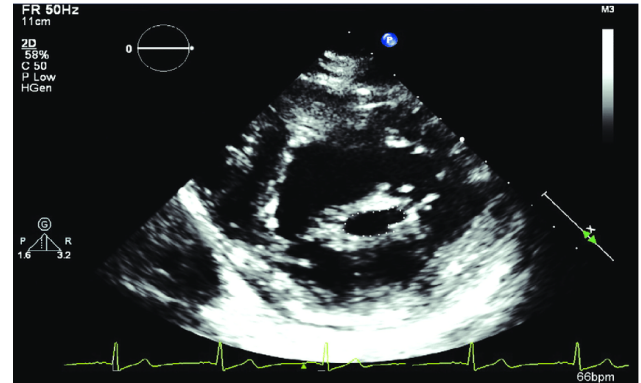
Figure 7. Normal mitral valve vs stenotic mitral valve

(1) Normal mitral valve

- **Structure**
 - Anterior and posterior leaflet
 - Has opening or orifice → blood coming and out
- **Mitral valve surface area**
 - Normally the large of orifice is 4-6 cm²

(2) Patient with mitral stenosis

- Blood is trying to squeeze through the tiny area → **very small orifice**
- **Surface area dropping below the normal point (< 2 cm²)**
 - Very narrow area
 - Reducing the blood flow from the left atrium into the left ventricle
- Mitral valve becomes so **fibrotic, calcified, sclerotic** in a way that it reduces a lot of flow
 - Because there is narrowing of the mitral valve orifice

Figure 8. Mitral valve seen with echocardiography in the parasternal short-axis view. Mitral valve area (MVA) measurement by planimetry in a patient with severe rheumatic mitral valve stenosis with MVA of 0.9 cm². [Prokself, Katja, 2014]

(B) FORWARD HEART FAILURE

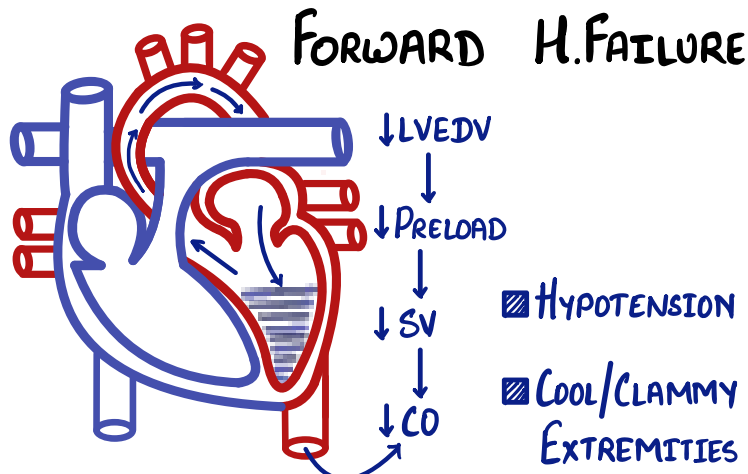


Figure 9. Forward heart failure

(1) Pathophysiology

- Imagine where a patient has **less blood that's able to get from left atrium into the left ventricle**
 - Not filling the left ventricle appropriately with the volume that we want during diastole
 - **Low left ventricular end-diastolic volume (EDV)**
- Remember blood volume in the heart that can affect stroke volume → **preload**
 - **Drop preload**
 - **Drop stroke volume**
 - **Drop cardiac output**
- Causes **forward heart failure problems**
 - **Less blood filling into left ventricle**
 - Drop the amount of blood that go into systemic circulation

(2) Patient may present with

- **Hypotension**
 - Unable to perfuse particular organs
- **Cool/clammy types of extremity**
 - Due to reduction in diastolic volume
- May have similar presentation with **heart failure**
 - There's no problem getting blood out of the heart
 - We just **don't have enough volume that's coming into the left ventricle**
 - Because of the stenotic valve
 - So, we're not pumping enough volume out



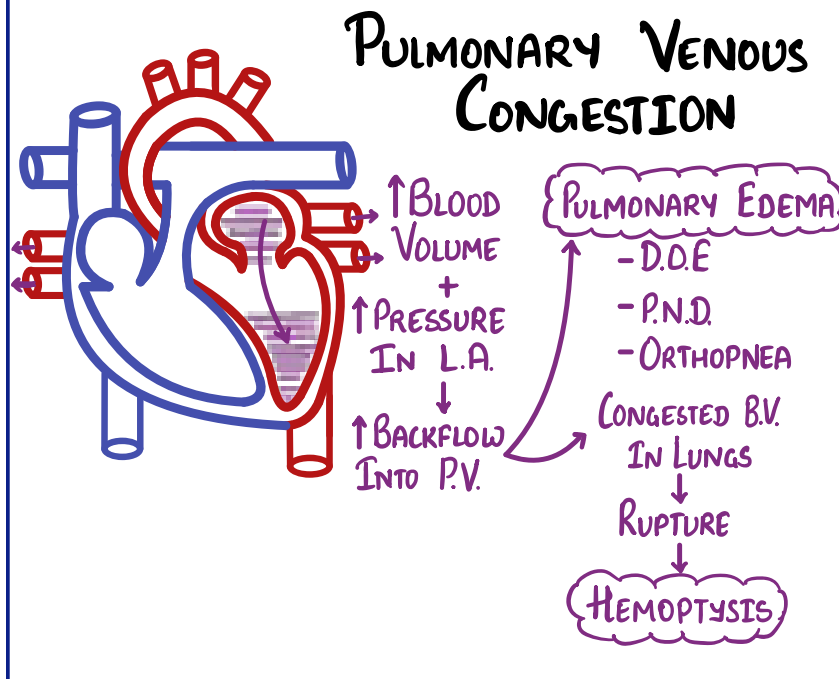


Figure 10. Pulmonary venous congestion

(1) Patient may present with pulmonary edema

- **Dyspnea on exertion**
 - Shortness of breath when walking
 - Because they're not getting enough oxygenation across the lungs
- **Paroxysmal nocturnal dyspnea**
 - Laying down flat because their actual hypoxia can worsen
- **Orthopnea**
 - Difficulty breathing occurs when they're lying flat
- **Hemoptysis**

(2) Mechanism

- Blood starts accumulating in left atrium
 - **Increased pressure in left atrium**
- If the left ventricle is not getting a lot of blood
 - **Blood starts accumulating in the left atrium**
 - High blood volume in left atrium
- When **left atrium** has a lot of volume and **can't actually expand/distend** to accommodate the volume
 - **The pressure in the left atrium starts to go up**
- Start causing **backflow** into the nearest vessels → **into pulmonary veins → pulmonary capillaries**
 - Starts third-spacing into the tissue layers between the actual alveoli and pulmonary capillaries → **pulmonary edema**

(3) Hemoptysis

- Because the volume and pressure so high
 - It causes lots of **backflow that it can congest some blood vessels in the lungs**
 - To the point where the **pressure in those blood vessels increase**
 - And actually cause them to **rupture** because holding onto too much volume
 - Cause blood to actually enter into airway and cough those → **hemoptysis**

(4) Review

- **Problem with getting blood into the left ventricle**
 - Dropped preload
 - Dropped stroke volume
 - Hypotension
 - Cool clammy poor perfused extremities
- Not getting blood from the left atrium to the left ventricle
 - **Blood is accumulating in left atrium**
 - Pressure increase
 - Backflow into pulmonary venous circulation
 - Cause pulmonary edema
 - **Cause some congestion of the blood vessel in the lungs to the point they may rupture**
 - Cause hemoptysis



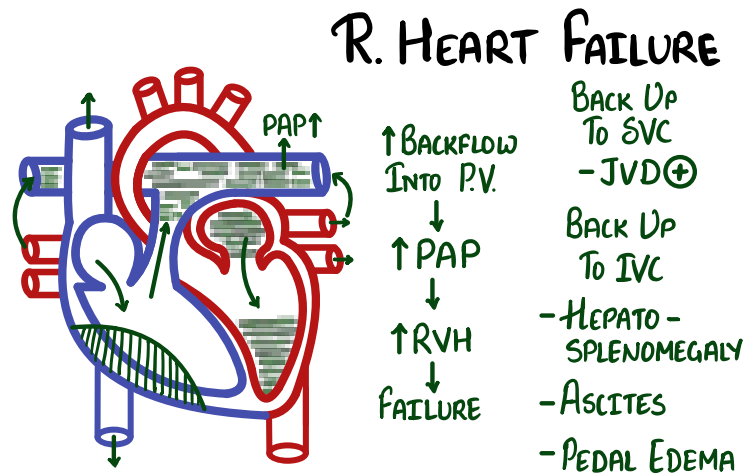


Figure 11. Right heart failure

(1) Issues

- Heart isn't able to get blood from the left atrium into left ventricle
 - Because the valve isn't letting blood get through
- Blood accumulates inside of the atrium
 - Increased pressure
 - Backflow into pulmonary vein
- When it backflow to pulmonary vein from pulmonary capillaries → pulmonary arteries
 - Blood pressure in the pulmonary arteries goes up
- Pulmonary artery pressures higher
 - Right ventricle has to work harder to pump blood into pulmonary arteries against the high pressure

(2) Process in a nutshell

- Backflow into pulmonary vein
 - Increase pulmonary artery pressure
 - Increase right ventricular strain

(3) Right ventricle hypertrophy → RV failure

- Right ventricle undergoes **right ventricular hypertrophy**
 - Thicken up to push blood **against the high pressure**
- Over time this can lead to failure
- If we're causing this ventricle to work harder → **narrowing the lumen**
 - Not able to fill the right ventricle properly
 - Blood start **backing up into superior vena cava (SVC) and inferior vena cava (IVC)**
 - Failure symptom

(4) Blood backs up into

- Superior vena cava (SVC)**
 - Jugular venous distension
- Inferior vena cava (IVC)**
 - Hepatosplenomegaly**
 - Swelling or accumulation around the liver and spleen
 - Ascites**
 - Accumulation in peritoneal cavity
 - Pedal edema**
 - Third space into the tissue of lower extremities → pedal edema

(5) Whole point

- Remember left-sided heart failure is caused by the stenotic mitral valve



(E) LEFT ATRIAL DILATION

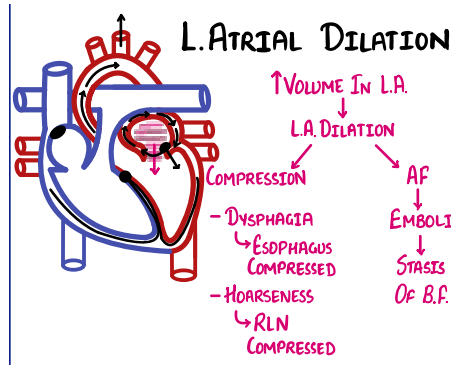


Figure 12. Left atrial dilation

- Blood flow from left atrium to left ventricle is reduced because of the stenotic valve
 - **Blood volume and pressure inside left atrium increases**
- Generally, whenever there's **high volume state**
 - Left atrium undergo dilation to accommodate the volume

(1) Compression symptoms

- Left atrium compress things nearby
- **Dysphagia**
 - Esophagus behind the left atrium
 - May have dysphagia due to esophageal compression
- **Hoarseness**
 - Nerve underneath the aorta → **recurrent laryngeal nerve compressed**
 - Sometimes it's big enough to compress that → hoarseness of the patient's voice

(2) Electrical circuit stretch

- Stretches the electrical circuit

- We have SA node, AV node, bundle branches
- When we stretch left atrium
 - Creates an opportunity for **electrical circuit to develop** and **generate increasing types of atrial arrhythmia**
 - Significant atrial arrhythmia → **atrial fibrillation**
- Electrical alteration and lead to increase the risk of atrial fibrillation
 - Risk of atrial fibrillation → **Increase the risk of emboli**

(3) Emboli

- Not getting effective atrial contraction
 - **Blood stays within atrium**
 - Cause **clots** to form in left atrium
 - Clot pops off and goes into **systemic circulation**
- **Clot goes to these organs**
 - **Brain** → embolic stroke
 - **Spleen** → Splenic infarcts
 - **Kidney** → Renal infarcts
 - **Mesenteries** → Mesenteric ischemia
- **Stasis of blood flow due to stenotic valve not letting blood go from left atrium to left ventricle**

MITRAL REGURGITATION

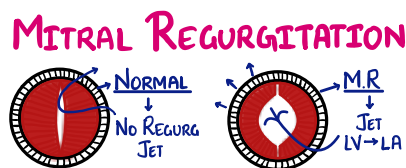


Figure 13. Mitral regurgitation

- In mitral regurgitation, blood going back from the left ventricle into left atrium → not forming a good seal

(4) Normal mitral valve

- Whenever the actual ventricles go into systole
 - Leaflets will come and close together → doesn't allow for blood to go back into left atrium
 - No regurgitation jet of blood back into the left atrium

(5) Patient with mitral regurgitation

- Due to the valve leaflets **not actually having a good connection or seal between one another**
- Left ventricle contract → pushes blood as supposed to go into the aorta
 - It will just move through mitral valve and **jet back into the left atrium during systole**



(F) ACUTE MITRAL REGURGITATION

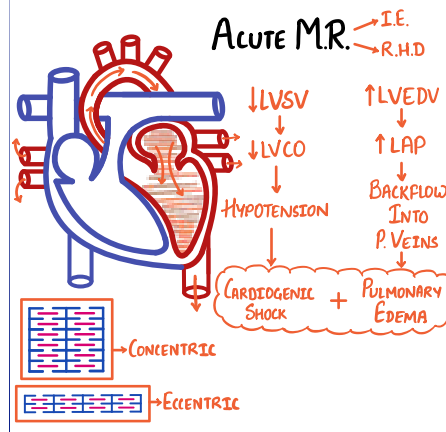


Figure 14. Acute mitral regurgitation

- Remember they can develop acutely due to
 - Infective endocarditis**
 - Myocardial infarction**
 - They might have **papillary muscle rupture**
 - Acute rheumatic heart disease** like **rheumatic fever**

(1) Pathophysiology - Systole

- Imagine left ventricle contract and push blood into aorta to systemic circulation
 - Due to valve issue, blood will go back into left atrium during systole**
- Two directions of blood flow during systole**
 - Let's say **75% of blood went to aorta** and **25% blood went back into left area**
- Amount of **blood getting out of the heart is reduced** → **reduction in left ventricular stroke volume**

- Because some of blood regurgitate back into the left atria
 - Reduction in left ventricular stroke volume
 - Reduction in left ventricular cardiac output
 - **Hypotension**
 - To the point where it can lead to shock state → **cardiogenic shock**
 - Scary situation where the patients can be **extremely hypotensive**

(2) Pathophysiology - Diastole

- During systole, the left ventricle pump the blood back into left atrium during systole
- During **diastole, the blood is going to flood back** from the left atrium to left ventricle during diastole
 - Plus, it's also **going to get the blood that's supposed to be coming from the pulmonary vein**
- Next issue → **left ventricular end diastolic volume (volume overload)**
 - Left ventricle is full
 - Because **blood is continuing to keep going back and forth between left ventricle and left atrium**
 - The valve flaps aren't being very helpful
- Blood's start pushing back into left atrium because left ventricle is getting overfilled**
 - If continue getting overfill
 - Eventually start pushing blood to pulmonary situation

- Normally, ventricles will dilate when there are so much volume
 - But in **acute situation, they don't have time to be able to dilate**
- Pressure starts increasing** because not dilating to accommodate volume
 - High left ventricular end diastolic volume
 - Causes high left atrial pressure
 - Causes pulmonic congestion
 - Particularly severe pulmonary edema
 - To the point where they can be extremely hypoxic

(3) Clinical findings

- Dyspnea on exertion
- Dyspnea at rest
- Paroxysmal nocturnal dyspnea
- Orthopnea

Remember these findings can be found in acute mitral regurgitation in patient secondary to infective endocarditis or an acute MI



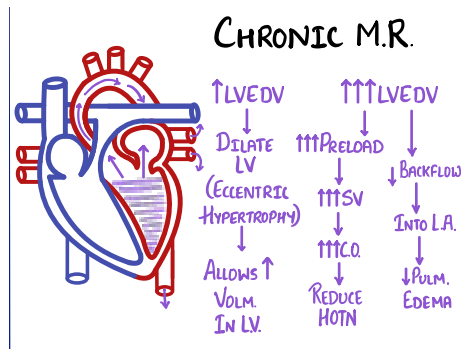


Figure 15. Chronic mitral regurgitation

- Left ventricular stroke volume reduced → they're not getting as much volume out of the heart
 - Lot of blood is getting pushed back into the left atrium
 - What are the ways our heart tries to accommodate?

(1) Hypertrophy

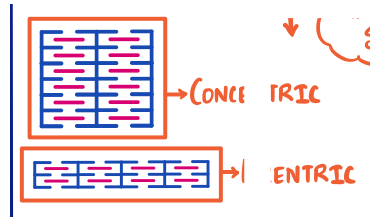


Figure 16. Eccentric vs concentric hypertrophy

- Left ventricular diastolic volume is very high → Volume overload state
 - Dilate the left ventricle
- 2 types of hypertrophy
 - **Eccentric hypertrophy**
 - Have muscle cells and sarcomeres
 - Add sarcomeres in linear fashion like in series
 - Muscle cells get longer
 - Causes actual ventricular walls thin but the ventricles to be dilated
 - **Concentric hypertrophy**
 - We have muscle cell and take sarcomeres
 - Add sarcomeres in parallel to one another
 - Become bigger and thicker
- In these patients, they actually develop **eccentric hypertrophy**
 - Their actual muscle cells get longer and cause their ventricles to get thinner
 - But their actual **lumen of the ventricle is larger** to accommodate all that volume
 - Less back flow into the left atrium → less back flow into pulmonary circulation
- If the contractility is good
 - Higher left ventricular end-diastolic volume → Higher preload → Produce higher stroke volume → Higher cardiac output → hyperdynamic state
- Frank Starling's law
 - Increase preload, increase stretch
 - Increase stroke volume, increase cardiac output
- **This helps to reduce the hypotension in these chronic stage**
 - Also **reduce the back flow** because of the dilation process → less pulmonary edema
 - **Lessen the symptoms**

(2) Clinical presentation

- They're often asymptomatic
 - They may have worsening symptoms particularly they may get more hypotensive during exertion
 - Shortness of breath
 - Fatigue
- They're relatively asymptomatic, but **when they have issues where their contractility drops**
 - Aren't able to maintain good cardiac output
 - **Decompensated state**
- **Ejection fraction or contractility starts dropping**
 - Decreased or might still have good preload
 - Drop stroke volume
 - Drop cardiac output
 - Potentially worsen their hypotension
 - Potentially go into cardiogenic shock
- **Causes non-specific symptoms but not as severe**
 - Fatigue
 - Dyspnea on exertion
 - Cool/clammy extremities

DECOMPENSATED CHRONIC M.R.

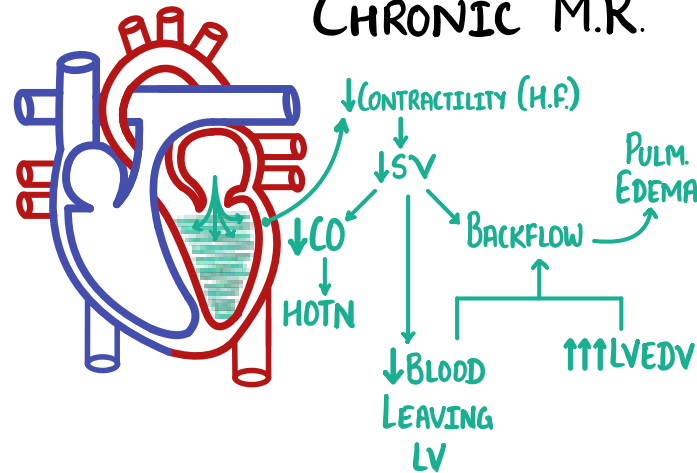


Figure 17. Decompensated chronic mitral regurgitation

● Progressing toward heart-failure

- Dilate the ventricles too much → they get thin and weak
- If this disease continue to progress
 - Start developing heart failure
 - Contractility drop
 - Cardiac output drop
 - Hypotensive

(1) Primary problem

- **High left-ventricular end-diastolic volume**
 - They already have so much blood within their left side of the heart
 - Now accumulating even more blood
- In this situation
 - **There's backflow again**
 - Lead to pulmonary edema
- Someone who has decompensated chronic mitral regurgitation
 - Developing heart failure → **might presenting like an acute mitral regurgitation patient**
- **Acute → Chronic → convert into decompensated state that kind of go back to acute mitral regurgitation**

(I) LEFT VENTRICLE DILATION

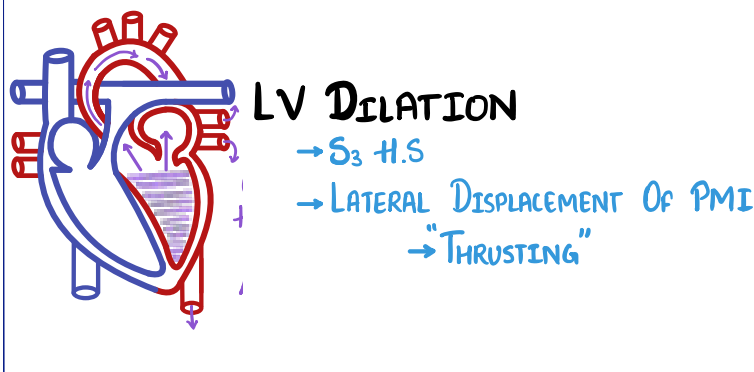


Figure 18. Left ventricle dilation

- Left ventricle dilate → good allowing for blood to enter the ventricle
 - Whenever the ventricles go into diastole process
 - Blood rapidly flows
 - **Produces turbulent flow and bounces off the ventricular wall → produce S₃ heart sound**
- Left ventricle is huge → **displacing left ventricle more laterally**
 - PMI (point of maximal density) usually near apex
 - **PMI is going to be displaced more laterally**
- **Every time the ventricle contracts**
 - Remember preload is really high
 - Stroke volume is really high
 - **Intense thrusting quality when we're palpating near the PMI**
 - **Very strong thrusting quality due to hyperdynamic**
 - Blood's keep on pounding and producing that thrusting quality against the chest wall



II) IAGNOSIS

(A) MITRAL STENOSIS

(1) Heart Murmurs

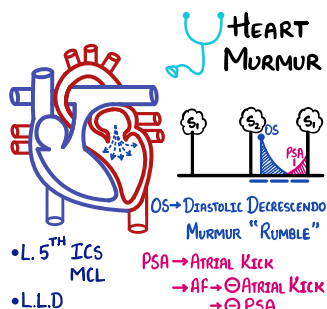


Figure 19. Opening snap with a decrescendo murmur characteristic of mitral stenosis.

- Problem: **Fibrotic/sclerotic valve** that does not allow blood flow from the LA to LV during ventricular **diastole**
 - Whenever the blood moves across the valve, it may cause the valve to bow a little bit producing a **snapping sound (opening snap)**
 - After the opening snap, the blood rushes out quickly during the early phase so the sound is initially loud and eventually softens (**diastolic decrescendo or a rumble**)
 - When the atria contracts, there may be **pre-systolic accentuation**
 - Due to atrial kick
 - In patients with **atrial fibrillation**:
 - (-) atrial kick → (-) presystolic accentuation
- Best to listen at the **left 5th intercostal space (ICS), midclavicular line (MCL)**
 - Can be isolated in a **left lateral decubitus position**

Recall:

- Ventricular diastole occurs during **S2** to the **second S1**
 - Early phase: rapid filling of the ventricle
 - Mid-phase: ventricles are slightly filled
 - Late phase: atria contract to fill the remaining 10-20% of blood to the ventricles

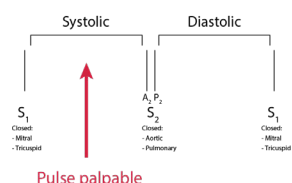


Figure 20. Normal heart sounds [Al-Hadithi, 2021].

Listen to the heart murmurs [here](#).

(2) ECG

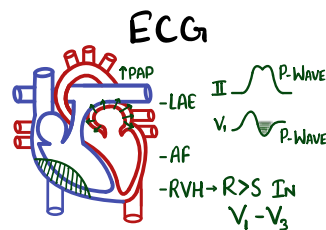


Figure 21. Mitral stenosis on ECG.

- Non-specific findings on ECG

(i) Findings:

- **Left atrium enlargement**
 - Due to dilation of the left atrium from increased pressure and volume
 - Characterized by (1) **large M wave** in lead II and (2) **biphasic p-wave with a deeper terminal component** in lead V1
- **Atrial fibrillation**
 - Left atrial dilatation increases the risk for atrial fibrillation
- **Right ventricular hypertrophy**
 - Due to ↑↑↑ pressure in the pulmonary arteries
 - Causes **R > S** from V1 to V3

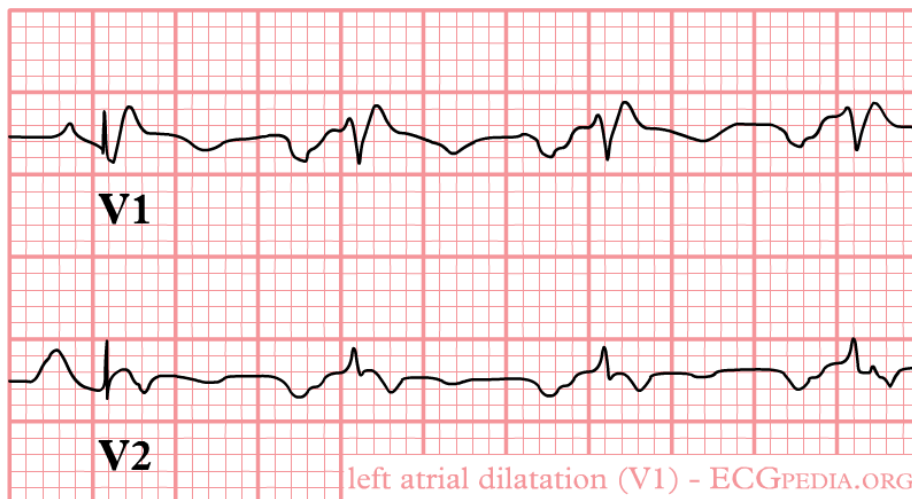


Figure 22. ECG image of left atrial dilatation secondary to mitral stenosis showing biphasic P wave with terminal dilatation > 40 ms duration and > 1 mm deep [Gibson, 2020].



(3) Chest X-Ray

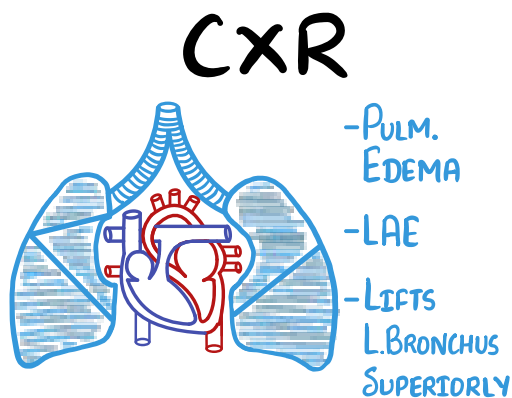


Figure 23. Chest X-ray findings of mitral stenosis.

• Non-specific findings

(i) Findings:

- Pulmonary edema
- Left atrial enlargement
- Lifts the left bronchus superiorly
 - !! May be asked in exams !!

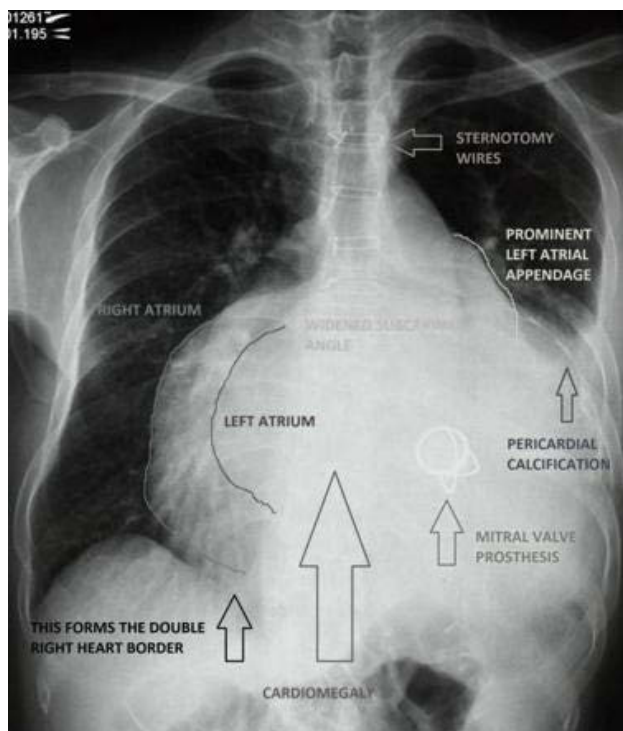


Figure 24. Labeled chest X-ray findings showing mitral stenosis [Rasuli, 2020].

(4) Echocardiography

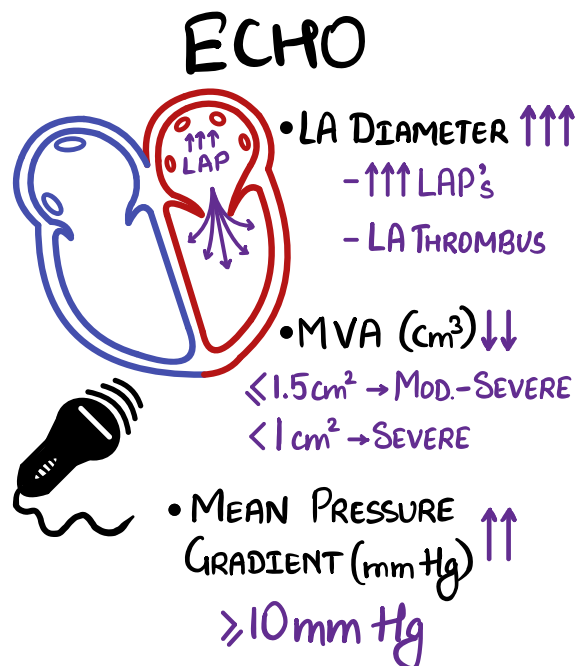


Figure 25. Echocardiographic findings on mitral stenosis.

- Can definitely diagnose mitral stenosis and classify its severity
- Helps with deciding between non-invasive and invasive management

(i) Left Atrium Diameter

- Thick and sclerotic mitral valves
- ↑↑↑ LA diameter due to LA dilation
 - Secondary to high amounts of volume and pressure present in the LA = ↑↑↑ LA pressure
- Larger LA diameter, worse degree of stenosis
- LA thrombus may be present

(ii) Mitral Valve Area

- The smaller the orifice, the smaller the area, more severe degree of stenosis
 - Higher pressure for the atrium to push blood

Table 1. Severity of mitral valve stenosis according to mitral valve area.

Classification	MV area (cm ²)
Normal	4-6 cm ²
Moderate to severe	<1.5 cm ²
Severe	<1 cm ²

(iii) Mean Pressure Gradient

- Defined as the amount of pressure to exert across the valve
 - The higher the mean pressure gradient, the more severe the degree of stenosis
- ≥10 mmHg = severe type of mitral stenosis

Echocardiographic finding can be viewed from 1:09:04 to 1:09:17.



(1) Heart Murmurs

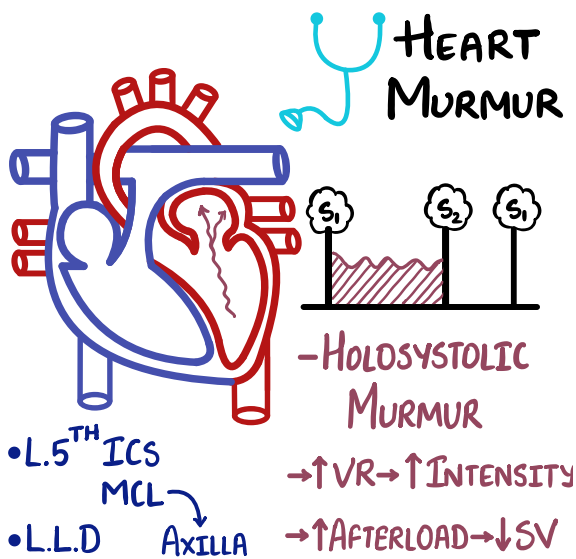


Figure 26. Holosystolic murmur heard in mitral regurgitation.

- Problem: Mitral valve leaflets do not form a good seal → **backflow of blood** during the ventricular systole
 - Recall that ventricular systole occurs between the 1st S1 and S2 (Figure 2)
- During the onset of systole, the murmur at the same intensity continues throughout the entire process of the systole (**holosystolic murmur**)
 - "Holosystolic" means throughout the entire systole
- Best heard at the **left 5th ICS, MCL**
 - Can radiate at the level of the **axilla**
 - Spraying of the blood back to the left atrium can hit the walls of LA
 - Better heard in **left lateral decubitus (LLD)**

(i) Factors that Increases the Intensity of the Murmur:

- Anything that **increases venous return (VR)** to the left side of the heart
 - Squats, leg raises, **expiration**
 - **Expiration:** Lungs get smaller → squeeze pulmonary blood back to the LA → ↑VR to the left side of the heart
 - **Inspiration:** Fills the right side of the heart
 - Can be observed in tricuspid valve diseases
- Anything that **increases afterload**
 - ↑blood in the LV → LV contraction pushes more blood across the mitral valve and into the LA → ↑afterload → ↑volume in the LV → ↑intensity of the murmur

Listen to the heart murmurs [here](#).

(2) ECG

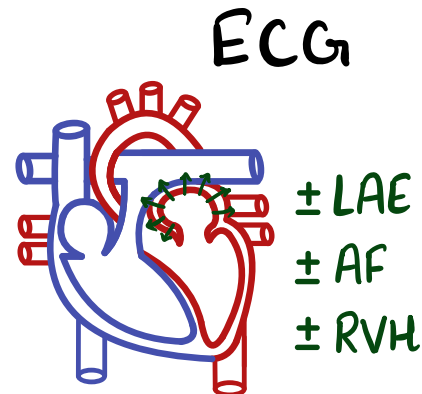


Figure 27. Non-specific ECG findings of mitral regurgitation.

- Non-specific findings
 - ± **left atrial enlargement (LAE)**
 - ± **atrial fibrillation**
 - Due to left atrial dilatation
 - ± **right ventricular hypertrophy**
 - Due to increased pulmonary artery pressure

(3) Chest X-Ray

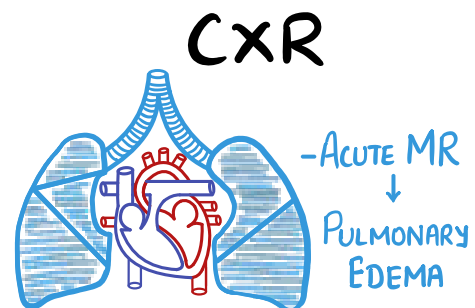


Figure 28. Chest X-ray findings in mitral regurgitation.

- Non-specific findings
- Main finding in acute mitral regurgitation: **pulmonary edema**

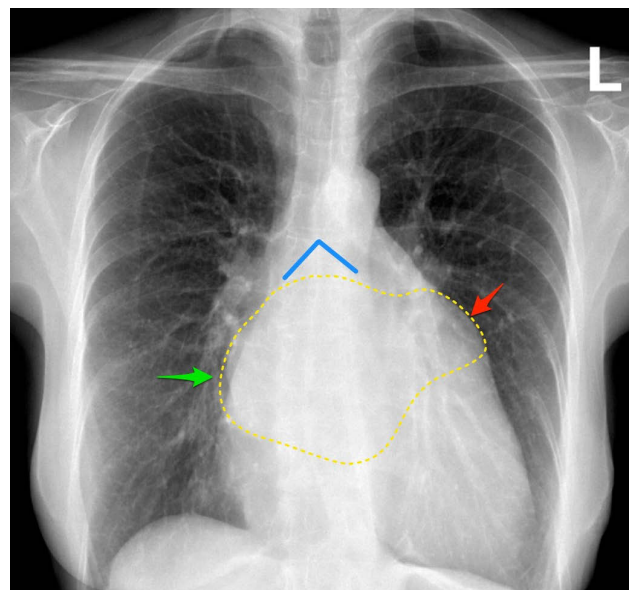


Figure 29. The rough outline of the left atrium (yellow) can be inferred by the presence of a double border on the right (green arrow), splaying of the carina (blue) and prominence of the left atrial appendage (red arrow) [Holland, n.d.].

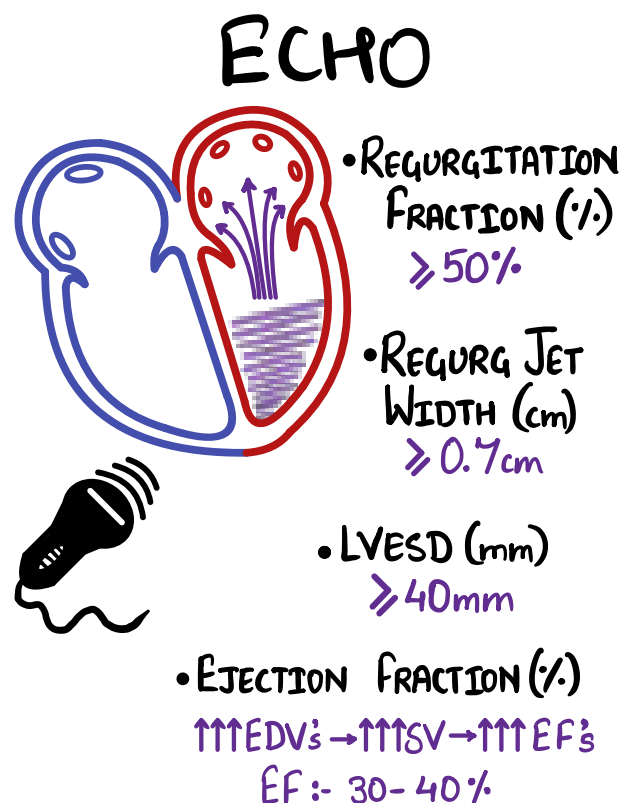


Figure 30. Echocardiographic findings in mitral regurgitation.

- Can be used to confirm MR and classify its severity

(i) Regurgitation Jet

- Characterized by (1) regurgitation fraction and (2) regurgitation jet
- **Regurgitation Fraction (%)**
 - $\geq 50\%$ = severe and needs aggressive management
- **Regurgitation Jet Width (cm)**
 - ≥ 0.7 cm = may need valve replacement

(ii) Left Ventricular End-Systolic Diameter (LVESD, mm)

- Patients with MR have $\uparrow\uparrow\uparrow$ **left ventricular end-diastolic volume** because blood pushed back to the LA is going back down the LV
- **The larger and dilated LV are, the worst case scenario**
 - Can progress to heart failure
 - ≥ 40 mm

(iii) Ejection Fraction

- Patients with MR have **hyperdynamic** hearts
- $\uparrow\uparrow\uparrow$ EDV $\rightarrow$ $\uparrow\uparrow\uparrow$ SV $\rightarrow$ $\uparrow\uparrow\uparrow$ EF ($\geq 60\%$)
- In decompensated stage of MR:
 - Heart contractility starts to drop $\rightarrow$ heart cannot maintain the cardiac output $\rightarrow$ blood accumulates in the ventricle resulting to:
 - Backflow of blood to the lungs $\rightarrow$ **pulmonary edema**
 - Blood cannot get out of the heart due to poor contractility $\rightarrow$ **hypotension**
- **EF 30-60%** is a significant type of mitral valve regurgitation regardless whether symptomatic or asymptomatic

Acronyms:

- EDV: end-diastolic volume
- SV: stroke volume
- EF: ejection fraction

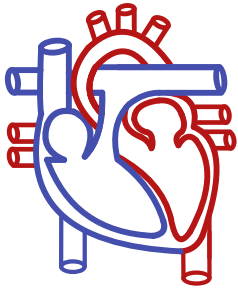
Echocardiographic finding can be viewed from [1:19:31 to 1:19:42](#).



III) TREATMENT

(1) Heart failure (right and left-sided)

- Fluid restriction
- Sodium restriction
- Diuretics
- ACE-Inhibitors*
- Beta blockers*
- Aldosterone antagonist* (aldactone, eplerenone)



HEART FAILURE

- FLUID + Na⁺ RESTRICT
- DIURETICS
- ACE-I's ±
- BB's ±

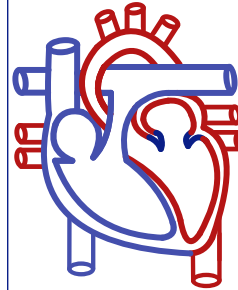
Figure 31: Treatment for heart failure symptoms

*if tolerated

(A) SYMPTOMATIC TREATMENT

(2) Atrial fibrillation

- Anti-coagulants
 - Warfarin
 - Why? Patients with mitral valve disease have a valvular type of atrial fibrillation with high risk of emboli, more often in mitral stenosis
- Rate + rhythm control



ATRIAL FIBRILLATION

- ↑ Risk Of EMBOLUS (MS >> MR)
→ AC. → WARFARIN
- RATE + RHYTHM CONTROL

Figure 32: Treatment for atrial fibrillation



(C) MITRAL STENOSIS

(1) Percutaneous mitral balloon commissurotomy (PMBC)

- What?
 - Introduce catheter into heart with attached deflated balloon
 - Inflate balloon when catheter arrived at stenotic valve to stretch, open the valve
- Indications:
 - Asymptomatic patient:
 - Mitral valve surface area **less than 1 cm²** (severe)
 - Symptomatic patient:
 - Mitral valve surface area **less than 1.5 cm²**
- Contraindication:
 - Heavy calcifications on valve

(2) Valve replacement

- Indication:
 - When PMBC is contraindicated (heavy calcification)
 - When PMBC failed
- 2 types of valves exist:
 - Mechanical heart valve
 - Bioprosthetic heart valve
- (i) Mechanical valve
 - Duration: lifetime, forever
 - Complication: risk of thrombi → need anti-coagulants forever
 - Indications:
 - Young patients
 - Patients already on anti-coagulation
 - Patients with low bleeding risk

(ii) Bioprosthetic valve

- Less thrombogenic → anti-coagulation needed only short-term (~3 months)
- Duration: 10 years
- Complication: infective endocarditis
- Indication:
 - Older patients
 - High bleeding risk

MITRAL STENOSIS

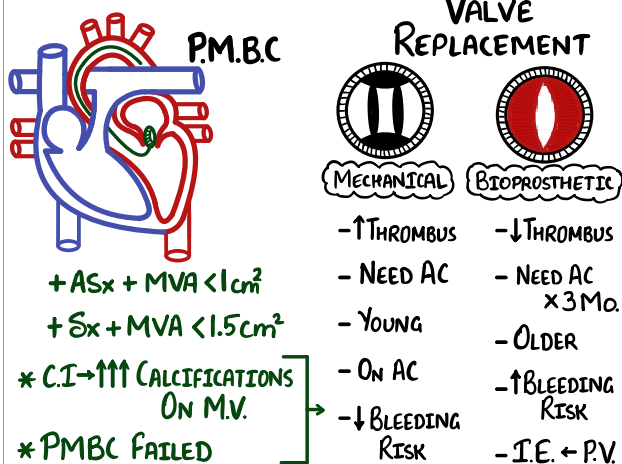


Figure 33: Surgical treatment of mitral stenosis

(D) MITRAL REGURGITATION

(1) Symptomatic treatment

- To stabilize patient before surgery (valve replacement)
 - (i) Acute mitral regurgitation
 - Remember: acute mitral regurgitation can appear after...
 - Infective endocarditis
 - MI
 - Stabilize patient by treating:
 - **Pulmonary edema**
 - Bi-level positive airway pressure (Bipap)
 - Why? Helps to push edema out of interstitial spaces
 - Diuretics (furosemide)
 - **Hypotensive shock**
 - Positive inotropes (dobutamine, milrinone)
 - Why? Increase stroke volume
 - Afterload reducers (nitroprusside, hydralazine, nifedipine, ACE-I)
 - Why? Decrease afterload by relaxing aortic vessels and thus increase cardiac output and blood pressure
 - IABP (intra-aortic balloon pump)
 - Inflates during diastole (to fill heart), relaxes during systole
 - Indication: when drugs fail (inotropes, afterload reducers)

After hemodynamically stabilizing the patient, immediately replace valve. Until valve is replaced patient is at risk to go into complete cardiogenic shock and die.

(ii) Chronic mitral regurgitation

- Often asymptomatic
- Indications for valve replacement (1 is enough):
 - Left ventricular end systolic diameter (LVESD)
 - Over 40mm
 - Any type of secondary mitral regurgitation and failed medical therapy (heart failure treatment)
 - Dilated cardiomyopathy
 - Aortic regurgitation
 - Systolic heart failure of other reasons
 - ...
 - Left ventricular ejection fraction
 - Below 60%

MITRAL REGURGITATION

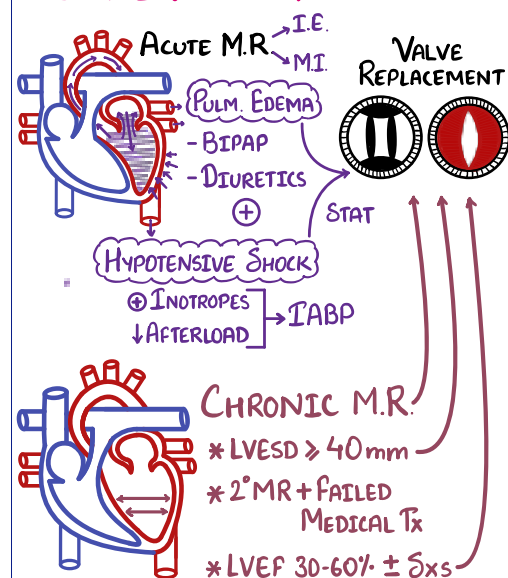


Figure 34: Surgical treatment of mitral regurgitation



IV) APPENDIX

Table 1-2 Summary

	Causes	Clinical Picture	Diagnosis	Treatment
Mitral Stenosis	● Rheumatic Heart Disease ● Calcifications ● Carcinoid Syndrome	● Forward heart failure ○ Hypotension ○ Cool/clammy extremities ● Pulmonary venous congestion ○ Dyspnea on exertion ○ Paroxysmal nocturnal dyspnea ○ Orthopnea ○ Hemoptysis ● Right heart failure ○ SVC ▪ Jugular venous distension ○ IVC ▪ Hepatosplenomegaly ▪ Ascites ▪ Pedal edema ● Left atrial dilation ○ Compression of recurrent laryngeal nerve ▪ Dysphagia ▪ Hoarseness ○ Atrial fibrillation ▪ Increased risk of emboli • Embolic stroke • Splenic infarct • Renal infarct ● Mesenteric ischemia	● Heart murmurs ○ Opening snap with a rumble/diastolic decrescendo ± presystolic accentuation ● ECG ○ LAE ○ Atrial fibrillation ○ Right ventricular hypertrophy ● CXR ○ Pulmonary edema ○ LAE ○ Superior deviation of the left bronchus ● Echocardiography ○ ↑↑↑ LA diameter ○ ↓↓ Mitral valve area ● ↑↑↑ Mean pressure gradient	● Drugs for HF and AFib ● Balloon valvuloplasty ● Valve replacement
Mitral Regurgitation	● Infective Endocarditis ● Rheumatic Heart Disease ● Mitral Valve Prolapse ● Connective Tissue Diseases ● Myocardial Infarction ● Left Ventricular Dilation ● Hypertrophic Obstructive Cardiomyopathy	● Acute mitral regurgitation ○ Hypotensive ○ Cardiogenic shock ○ Pulmonary edema ● Chronic mitral regurgitation ○ Hyperdynamic state ○ Reduced pulmonary edema ○ Left ventricle enlargement ● Decompensated mitral regurgitation ○ Similar with acute MR ● LV dilation ○ S₃ heart sound ○ Lateral displacement of PMI ● “Thrusting” quality	● Heart murmurs ○ Holosystolic murmur ● ECG ○ LAE ○ Atrial fibrillation ○ Right ventricular hypertrophy ● CXR ○ Pulmonary edema ● Echocardiography ○ Regurgitation fraction ≥ 50% ○ Regurgitation jet width ≥ 0.7 cm ○ LVESD ≥ 40 mm ● EF 30-60% (severe)	● Drugs for HF and AFib ● Valve replacement



V) REVIEW QUESTIONS

- 1) Which of the following are causes of acute mitral regurgitation?
 - a) Infective Endocarditis
 - b) Rheumatic Heart Disease
 - c) Myocardial Infarction
 - d) Both A and C
 - e) Both B and C
- 2) Which chemical causes fibrosis of the mitral valves in Carcinoid Syndrome
 - a) norepinephrine
 - b) serotonin
 - c) vasopressin
 - d) dopamine
 - e) prostaglandin
- 3) What is the normal mitral valve surface area that can be checked with echocardiography?
 - a) 4-6 cm²
 - b) 2-4 cm²
 - c) > 4 cm²
 - d) < 2 cm²
- 4) Patient with mitral stenosis might have present with similar symptoms as patient with heart failure
 - a) True
 - b) False
- 5) It is possible for a patient with mitral stenosis to present with hemoptysis
 - a) True
 - b) False
- 6) Mitral valve stenosis increases chance of having atrial fibrillation due to enlargement of the ventricle
 - a) True
 - b) False
- 7) Patient with chronic mitral regurgitation is unlikely to be asymptomatic because of the eccentric hypertrophy of the left ventricle
 - a) True
 - b) False
- 8) LV dilation in mitral regurgitation will give the findings of S₄ heart sound and "thrusting" quality against the chest wall
 - a) True
 - b) False
- 9) How is the murmur in mitral regurgitation different than that of mitral stenosis?
 - a) Murmur is best heard in the left 5th ICS, MCL
 - b) Murmur has an opening snap with a rumble
 - c) Intensity of the murmur increases with squatting and leg raises
 - d) Murmur is holosystolic
- 10) What is the definitive diagnostic modality for mitral valve diseases?
 - a) ECG
 - b) Chest X-ray
 - c) Physical examination
 - d) Echocardiography
- 11) What echocardiographic finding is NOT found in mitral stenosis?
 - a) Increased LA diameter
 - b) Decreased ejection fraction
 - c) Increased mean gradient pressure
 - d) None of the above
- 12) What echocardiographic finding is NOT found in mitral regurgitation?
 - a) Increased mitral valve area
 - b) Increased LVESD
 - c) Increased jet width
 - d) None of the above

- 13) Percutaneous mitral balloon commissurotomy is indicated in...

- a) Acute mitral regurgitation
- b) Chronic mitral regurgitation
- c) Mitral stenosis
- d) Mitral stenosis and regurgitation

- 14) Intra-aortic balloon pump is indicated in...

- a) Acute mitral regurgitation
- b) Chronic mitral regurgitation
- c) Mitral stenosis
- d) Mitral stenosis and regurgitation

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AORTIC VALVE STENOSIS & REGURGITATION

Aortic Valve Stenosis & Regurgitation

Medical Editor: Camille Santico

OUTLINE

I) CAUSES
I) CLINICAL FEATURES
II) DIAGNOSIS
III) TREATMENT

IV) APPENDIX
V) REVIEW QUESTION
VI) REFERENCES

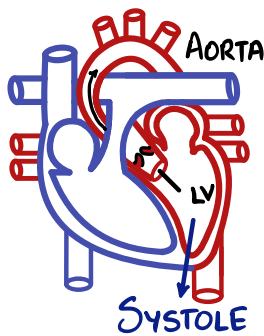
I) CAUSES

- The aortic semilunar valve functions to:
 - Facilitate the one-way flow of blood from the left ventricle (LV) to the aorta
 - Prevents backflow of blood from the aorta to the left ventricle (LV)

- There are two types of aortic valve disease:
 - Aortic stenosis**
 - Aortic regurgitation**

(A) AORTIC STENOSIS

- Stenosis is the failure of a valve to open completely [Robbins, 2020]
- The aortic valve is **fibrotic/sclerotic/calcified**, preventing it from opening well
 - The aortic valve is narrowed
 - This makes it difficult for blood to flow from the LV to the aorta during systole
 - It produces a **systolic murmur**



AORTIC STENOSIS

- FIBROTIC/CALCIFIED
- LV $\xrightarrow{x}$ AORTA

(1) Rheumatic Heart Disease

- Rheumatic fever is an acute, immunologically mediated disease which typically occurs after infection with **group A streptococcus bacteria** [Robbins and Coltran, 2020]
 - Infection $\rightarrow$ pharyngitis / Strep throat $\rightarrow$ immune system produces antibodies which attack the mitral and aortic valves $\rightarrow$ inflammation of the valves (carditis)
- Rheumatic heart disease is characterized by fibrotic valvular disease
 - results from the autoimmune destruction of heart valves
 - Chronic sequelae of acute rheumatic carditis [Robbins and Coltran, 2020]
- RHD can cause:
 - Aortic stenosis
 - Aortic regurgitation
 - Mitral stenosis
 - Mitral regurgitation

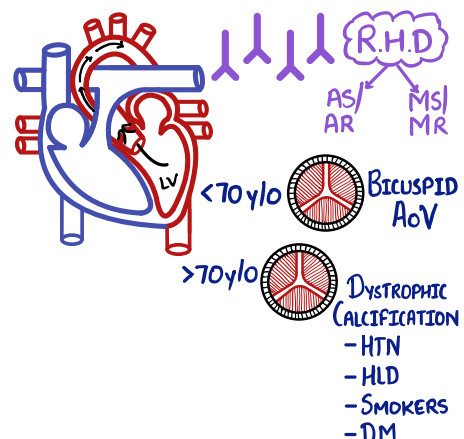
(2) Bicuspid Aortic Valve

- Bicuspid aortic valve** is a congenital abnormality wherein there are only **two functional cusps/leaflets** due to incomplete separation during development [Robbins and Coltran, 2020]
 - Recall: The aortic valve normally has three leaflets
 - This congenital problem only becomes apparent later in life
- Bicuspid aortic valves are more susceptible to calcification
 - This makes the valves less pliable, allowing less blood flow

(3) Dystrophic Calcification

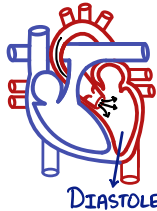
- Dystrophic calcification** of the aortic valves is usually the consequence of **age-associated "wear and tear"** [Robbins and Coltran, 2020]
 - Old age increases the susceptibility to calcification of aortic valves
- Typically occurs in persons > 70 years old
- The risk factors for dystrophic calcification are the same factors which increase the risk of atherosclerosis:
 - Hypertension
 - Hyperlipidemia
 - Smoking
 - Diabetes
- Atheromatous plaques which deposit on the aortic valves cause calcification and fibrosis of valves
 - This makes the valves less pliable, allowing less blood flow

AORTIC STENOSIS



(B) AORTIC REGURGITATION

- The aortic valve is **poorly sealed**, allowing blood to backflow into the left ventricle during diastole
 - It produces a **diastolic murmur**
- Recall:**
 - The aortic valve leaflets are anchored to the walls of the aorta by connective tissue
 - Anything that causes the walls to dilate will lead to aortic regurgitation (e.g., aortic aneurysm)
 - A dilated aortic root pulls apart the leaflets of the aortic valve, preventing it from closing properly



AORTIC REGURGITATION
- POOR SEAL OF A.V.
- AORTA → LV

- An **aortic aneurysm** is a balloon-like bulge in the aorta which typically results from weakening of the aortic walls.
 - It is a common cause of aortic dilatation

(1) Hypertension

- High blood pressure induces shear stress on the aortic walls
- The walls may weaken, increasing the risk for aortic aneurysm formation

(2) Connective Tissue Disease

- Connective tissue diseases weaken the elastic lamina and externa of the aorta, causing it to balloon/expand
- Examples:
 - Marfan's Syndrome
 - Ehlers-Danlos Syndrome

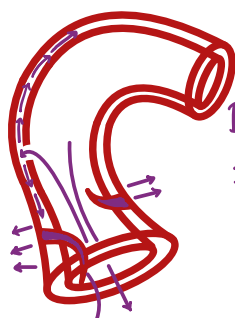
(3) Aortitis

- An inflammatory process causes:
 - Destruction of the vessel wall
 - Cystic medial necrosis of the vessel wall
- As a result, the walls of the aorta weaken and dilate/stretch, forming an aneurysm
- Examples:
 - Takayasu's Arteritis
 - Syphilis
 - HLA-B27 haplotypes
 - Reactive arthritis / Reiter's Syndrome
 - Ankylosing Spondylitis

(4) Aortic Dissection

- Aortic dissection occurs when blood separates the laminar planes of the media to form a blood-filled channel within the aortic wall [Robbins and Coltran, 2020]
- Blood dissects through the tunica intima and tunica medi of the aorta
 - The dissected blood can go retrograde (back towards the heart) or antegrade (away from the heart)
- When the dissected blood flows retrograde, it compresses the connective tissue which anchors the leaflets, preventing them from maintaining proper position
 - This prevents the leaflets from closing properly, subsequently causing aortic regurgitation
- Risk factors for aortic dissection include:
 - Hypertension
 - Dyslipidemia
 - Smoking

AORTIC REGURGITATION



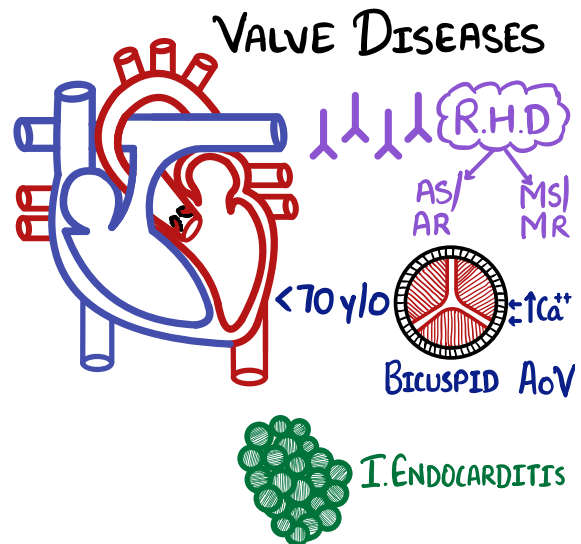
AORTIC ROOT DISEASES

DILATED AORTIC ROOT

I) AORTIC ANEURYSM'S

- HTN
- CTD's
- AORTITIS
- MARFAN'S
- EDS
- GCA / TAKAYASU'S
- SYPHILIS
- ANK. SPOND.
- REACTIVE ARTH.

II) AORTIC DISSECTION



VALVE DISEASES

R.H.D.
AS/AR
MS/MR

<70 y/o
Bicuspid AoV
↑Ca⁺⁺

I. ENDOCARDITIS

(5) Rheumatic Heart Disease

- The antibodies formed in response to group A Streptococcus infection causes destruction or inflammation of the leaflets
 - This causes the leaflets to become stiff, preventing them from closing properly

(6) Bicuspid Aortic Valve

- Bicuspid aortic valves are more susceptible to calcification
 - This causes the valves to become stiff, preventing them from closing properly

- Bicuspid aortic valves also have a higher risk for infective endocarditis

(7) Infective Endocarditis

- Infective endocarditis is a microbial infection of the heart valves or mural endocardial [Robbins and Coltran, 2020]
- The invading pathogens destroy the aortic valve
 - This causes the valves to stiffen, preventing them from closing properly



I) CLINICAL FEATURES

(A) AORTIC STENOSIS

Classic presentation: **SAD: Syncope + Angina + Dyspnea**

Why these symptoms? What is the mechanism?

(1) DYSPNEA

[Dyspnea: Shortness of breath]

- In aortic stenosis → the valve is **fibrotic**
 - Difficulty in pumping blood out against the valve
 - Requires higher pressure
 - (↑) LV end diastolic pressure (↑) **LVEDP**
 - **Thickening** of the Left ventricle
 - Left Ventricular Hypertrophy (**LVH**)
- (↑) **LVEDP** + **LVH** → (↓) Capacitor of ventricle
 - (↓) Ventricular filling
 - Blood cannot flow from L.A. to L.V.
 - **Backflow** to pulmonary circulation
 - **Pulmonary edema!**
 - **Dyspnea**
- On **exertion** (with **LVH**) → (↑↑) Heart Rate
 - (↓) Diastolic filling time
 - (↓) Ventricular filling
 - (↑) **Backflow** + **pulmonary edema**
 - Worsening **Dyspnea**

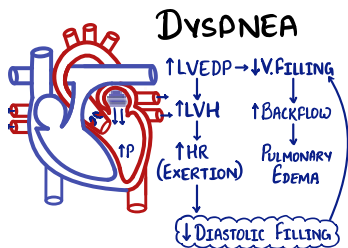


Figure 1: Dyspnea due to Aortic Stenosis

(2) ANGINA

[Angina: Chest pain]

- LVH** → (↑) **O₂ demand**
 - + Squeezes the coronary vessels
 - (↓) Coronary blood flow
 - (↓) **O₂ supply**
- On **exertion** → (↑) **O₂ demand**
 - + (↑↑) Heart Rate
 - (↓) Diastolic filling time
 - (Remember: Coronary flow occurs on ventricular diastole)
 - Therefore, (↓) Coronary flow
 - (↓) **O₂ supply**
- (↑) **O₂ demand** + (↓) **O₂ supply** = **Mismatch**
 - **Ischemia** of the muscle
 - **Angina**

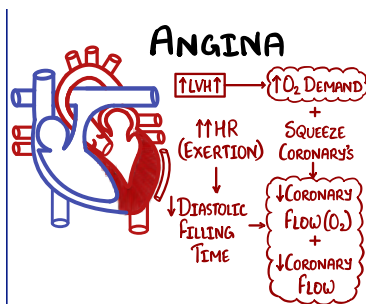


Figure 2: Angina due to Aortic Stenosis

(3) SYNCOPE

- (↑) **LVEDP** + **LVH** → **Fixed cardiac output**
 - (The LV is exerting maximal amount of pressure to pump as much blood out of the ventricle)
 - As long as **C.O.** and **MAP** (mean arterial pressure) are maintained and enough to perfuse the vessels that supply the brain, there will be no problem.
- On **exertion** (2 mechanisms)
 - Vasodilation** of the blood vessels
 - (↓) SVR (Systemic vascular resistance)
 - (↓) **MAP** (Even with a **fixed cardiac output**)
 - (↓) Brain perfusion
 - **Syncope**
 - severe **Dehydration** (& volume depletion)
 - (↓) Stroke volume → (↓) **Cardiac output**
 - (↓) MAP → (↓) Brain perfusion → **Syncope**

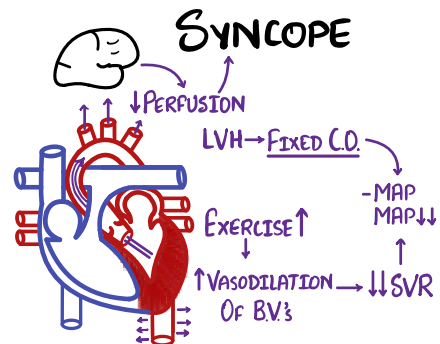


Figure 3: Syncope due to Aortic Stenosis

(4) LEFT VENTRICULAR HYPERTROPHY

(i) Left Ventricular Heave

- LVH** → (↑↑↑) force of contractions → **LV Heave**
 - (Patient can feel the contraction against the chest wall)

(ii) "S4" heart sound

- LVH** → (↑) **LVEDP** → (↑) LAP (Left Atrial Pressure)
 - **Atrial Hypertrophy**
 - **Atrial kick** (on contraction in the late phase of diastole)
 - **"S4" heart sound**

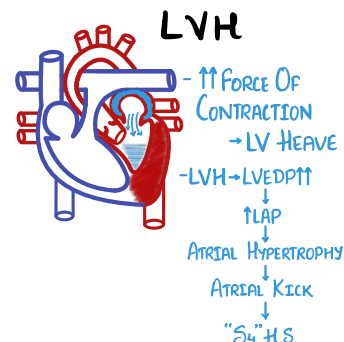


Figure 4: LVH effects in Aortic Stenosis



(B) AORTIC REGURGITATION

There are 2 types: Acute & Chronic

(1) Acute Aortic Regurgitation:

Caused by:

- Infective Endocarditis
- Acute Rheumatic Heart Disease
- Aortic Dissection

Cardiogenic Shock & Hypotension:

Acute AR is like **Cardiogenic Shock**.

- When the LV contracts → tries to push blood into the aorta → the aortic valve is not preventing the back flow
- Some of the blood will be pumped into the systemic circulation and the rest will return back to the LV, this causes several problems:
 - Stroke volume in LV **decreases**
 - (↓) **CO** → (↓) blood pressure
 - Leads to **HYPOTENSION** which can cause **CARDIOGENIC SHOCK**
- **Compensatory mechanism:** Increased heart rate → **TACHYCARDIA**

Pulmonary Edema:

- (↑) **LVEDV** as there is blood from the atrium and blood coming back from the aorta.
- This causes some of the blood to go back to the left atrium, since the heart has no time to remodel and dilate to accommodate that volume.
- Increases left atrial pressure → back flow of blood into the pulmonary circulation → **PULMONARY EDEMA**
 - o **Can be presented as:** Hypoxia, Dyspnea on exertion, Dyspnea at rest, Paroxysmal Nocturnal Dyspnea, Orthopnea

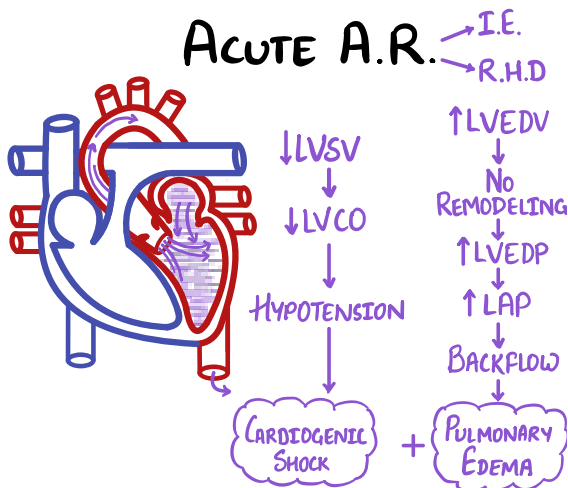


Figure 5. Causes and Pathophysiology of Acute AR

(2) Chronic Aortic Regurgitation:

This is when the ventricles have had time to remodel and dilate for the increased blood volume.

Eccentric Hypertrophy:

- (↑↑↑) **LVEDV** → trigger LV dilation due to volume overload → **eccentric hypertrophy** of the LV (muscle cells are added in series)

Reduced Pulmonary Edema and Hypotension:

- LV increases in size → allows more volume in the LV → lower the LVEDP → lower left atrial pressure → reduces the backflow → **reduces pulmonary edema** → Patients might not have a lot of symptoms, it can be present but only with high exertion
- (↑↑↑) **LVEDV** → (↑↑↑) preload → (↑↑↑) **SV** → (↑↑↑) **CO** → hyperdynamic hearts with ejection fraction of 60-65% → **reduced hypotension**
 - o Relatively asymptomatic

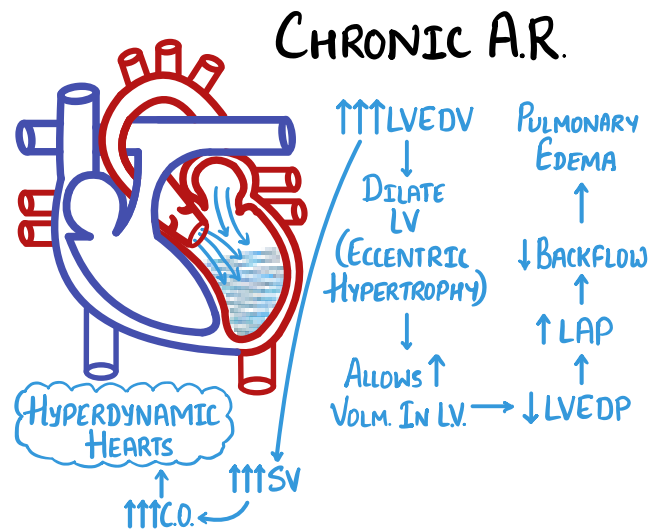


Figure 6. Chronic AR leading to Hyperdynamic Heart



(3) Decompensated Chronic AR:

- Heart failure progression → Dilated LV with his blood volume cannot be tolerated anymore → muscle starts getting weaker → (↓) contractility → (↓) SV → (↓) CO

Hypotension & Pulmonary Edema:

- Despite the (↑↑↑) LVEDV, the low contractility would not allow for the blood to be pushed out → can lead to symptoms of **HYPOTENSION**
- (↓) SV → (↑↑↑) LVEDV → can back flow into the left atrium → accumulates in the pulmonary circulation → **PULMONARY EDEMA**
- Similar to Acute Aortic Regurgitation

Wide Pulse Pressure:

- $PP = SBP - DBP$
- Patients with AR have (↑↑↑) LVEDV → (↑↑↑) SV → (↑↑↑) blood pumped in systole → (↑↑↑) SBP
- When blood is pushed from the ventricle to the aorta, the aorta is very elastic, it can stretch and distend to accommodate for all the blood volume then it recoils to push blood to all the systemic vessels
 - ▶ Since there is regurgitation, the valves are not preventing back flow of blood into the LV during diastole
 - o In diastole, the blood shoots back into the LV and (↓↓↓) diastolic blood pressure abruptly
 - o SBP/DBP can be 200/40, that is a huge difference

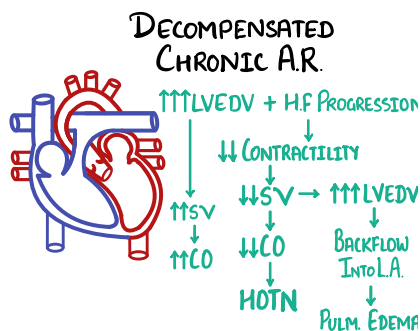


Figure 7. Decompensation of Chronic AR

Water Hammer Pulse (Corrigan's pulse):

- Bounding pulses due to (↑↑↑) SBP and when you raise the arm there is an **abrupt drop in blood pressure**.

Hill's Sign:

- Measuring the lower extremity blood pressure vs upper extremity blood pressure (e.g. brachial pressure vs popliteal pressure)
 - o (↑↑↑) Lower extremity blood pressure compared to upper extremity, the SBP can be >60 mmHg in difference.

Other Signs:

Tableau 1. There are many signs in AR

Sign	Description
deMusset's Sign	Head bobbing with each cardiac cycle.
Mueller's Sign	Systolic pulsations of uvula.
Duroziez's sign	Systolic and diastolic bruit heard when the femoral artery is partially compressed, to and fro murmur.
Traube's Sign	Pistol shot murmur on femoral arteries.
Rosenbach's Sign	Systolic pulsation of liver.
Gerhard's Sign	Systolic pulsations of spleen.

(i) LV Dilation:

- Allow for rapid ventricular filling → turbulent flow → produces **S3 heart sound**
- (↑↑↑) SV → intense contractions → **thrusting PMI** and lateral displacement of PMI

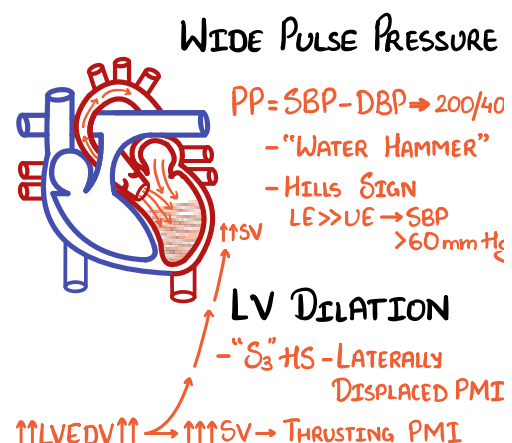


Figure 8. Wide Pulse Pressure and LV Dilation found in AR

ABBREVIATIONS:

- LVH: Left Ventricular Hypertrophy
- LVEDP: Left Ventricular End Diastolic Pressure
- LA: Left Atrium
- LV: Left Ventricle
- CO: Cardiac Output
- MAP: Mean Arterial Pressure
- SVR: Systemic Vascular Resistance
- LAP: Left Atrial Pressure
- SV: Stroke Volume
- SBP: Systolic Blood Pressure
- DBP: Diastolic Blood Pressure
- AR: Aortic Regurgitation
- PP: Pulse Pressure
- PMI: Point of Maximal Intensity



II) DIAGNOSIS

(A) AORTIC STENOSIS

(1) Ejection click → Crescendo-Decrescendo systolic murmur

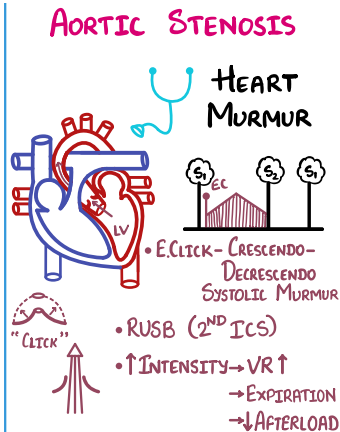


Figure 9. Physical examination (Auscultation) in Aortic Stenosis.

- Recall:
 - S1 to S2: systole**
 - S2 to S1: diastole**
- Location:
 - RIGHT UPPER STERNAL BORDER, 2nd ICS**
 - Radiation to the **CAROTIDS**

Table 1. Auscultatory findings in Aortic stenosis.

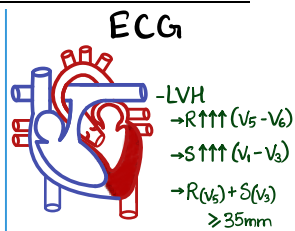
Problem	Pathophysiology	Physical Examination
Stenotic aortic valve	- blood flow resistance through the aorta during contraction (SYSTOLE) → Doming of the calcified, fibrotic, stenotic valves → ejection clicking sound	Murmur RIGHT AFTER S1 (EC) (ventricular systole)
	LV pushes out remaining ↑ blood out of the ventricle ↓	Murmur intensity after EC INCREASES at early phase
	Over time, ↓ blood going out	Murmur intensity after EC DECREASES at latter phase

(i) Factors that ↑ Intensity of murmur:

- ↑ **VR**:
 - ↑ blood flow volume going out into stenotic valve at a longer time
- ↑ **Expiration**:
 - Push blood from the actual lungs → ↑ LV blood volume
- ↓ **Afterload**:
 - pressure the ventricle must work against to eject a certain amount of blood → determines SV
 - Ex: Hand grip maneuvers

(2) ECG

- ↑ **LVH**
 - ↑↑↑ R waves at Leads V5-V6
 - ↑↑↑ S waves at Leads V1-V3
 - RV5 height (amplitude) + SV3 → if ≥ 35 mm, diagnostic of LVH



(3) Chest X-Ray

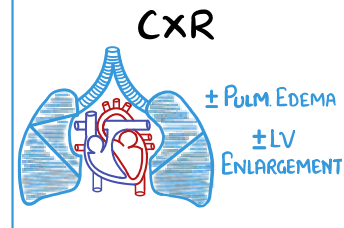


Figure 10. Chest X-Ray in Aortic Stenosis.

- ± show:
 - LVH
 - Pulmonary edema

(4) 2D ECHO

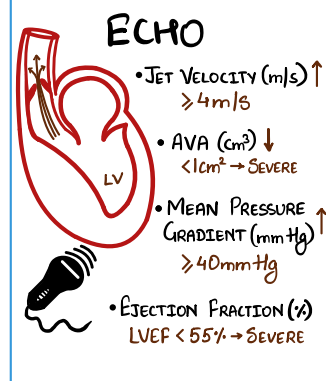


Figure 11. 2D Echo in Aortic Stenosis.

- The most important test for any valve disease**
- For aortic stenosis, assessment of aorta around the outflow tract is important:
 - Thick, fibrotic, stenotic valve
 - Determine how small the orifice is → area, velocity, pressure gradient
 - Can check the ejection fraction of the LV

Table 2. 2D Echo results in Aortic stenosis.

Component	Description	Pathologic
Aortic valve area (cm²)	Area of the orifice of the aortic valve	Severe: <1 cm²
Jet velocity (m/s)	Speed of blood flow that overcomes the small orifice for it to be able to pass through	Severe: ↑ ≥ 4 m/s
Mean pressure gradient (mmHg)	LV pressure exerted for blood flow to overcome the small orifice	Severe: ↑ ≥ 40 mmHg
Ejection fraction (%)	LV must be hyperdynamic	LV ejection fraction <55 %

- If LV has hypertrophy, weak, constant pressure that it needs to work, low ejection fraction → must be concerned already due to its severity



(B) AORTIC REGURGITATION

(1) Decrescendo diastolic murmur

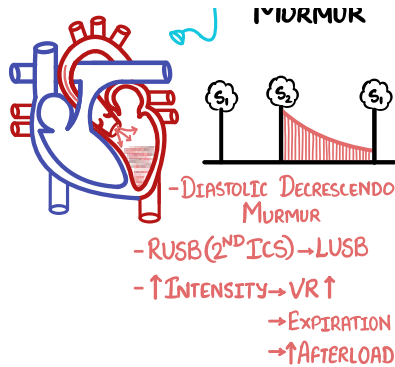


Figure 12. Physical examination (Auscultation) in Aortic Regurgitation.

- Recall:
 - S1 to S2: systole
 - S2 to S1: diastole**
- Smashing of blood back from the aorta into the LV while it's in diastole (filling of blood)
 - Quality: Blowing and loud
- Location:
 - RIGHT UPPER STERNAL BORDER, 2nd ICS**
 - Radiation to **LEFT UPPER STERNAL BORDER**

Table 3. Auscultatory findings in Aortic regurgitation.

Problem	Pathophysiology	Physical Examination
Regurgitant valve	Aortic semilunar valve has a pathology and becomes regurgitant ↓ At DIASTOLE , it DOES NOT snap shut ↓	Murmur RIGHT AFTER S2 (ventricular diastole)
	Blood flow goes back into LV while it is at the early parts of DIASTOLE ↓	Murmur intensity HIGHEST at early phase
	Over time, ↓ blood flow moving through aortic semilunar valves ↓ ↓ blood flow hitting into LV wall	Murmur intensity ↓ GRADUALLY at latter phase

(i) Factors that ↑ Intensity of murmur:

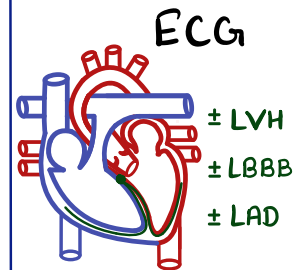
- ↑ **VR**
 - ↑ Preload
 - ↑ blood volume in the LV via squatting or passive leg raises
- ↑ **Expiration:**
 - ALWAYS increases the intensity of Left sided murmurs
- ↑ **Afterload:**
 - pressure the ventricle must work against to eject a certain amount of blood → ↑ blood flow flooding back in which increases the pressure

(ii) Factors that ↓ Intensity of murmur:

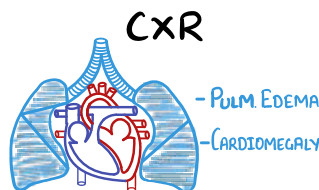
- ↓ **VR, ↑ Inspiration and ↓ afterload** → ↑ Stroke volume which means there's ↓ left ventricular end diastolic volume → ↓ blood being pushed out

(2) ECG

- Not really helpful since it may show random findings
- ↑ **LVH**
- LBBB:**
 - Stretch of bundle branches (especially with the left bundle branch) due to distention and dilation
 - May cause a **BLOCK**
- LAD:**
 - due to distention and dilation → ↓ Mean QRS vector
- ↑ **LVH**
 - ↑↑↑ R waves at Leads V5-V6
 - ↑↑↑ S waves at Leads V1-V3
 - RV5 height (amplitude) + SV3 → if ≥ 35 mm, diagnostic of LVH



(3) Chest X-Ray



- Not a really helpful diagnostic tool
- ± show:
 - Cardiomegaly due to large LV dilation
 - Pulmonary edema

(4) 2D ECHO

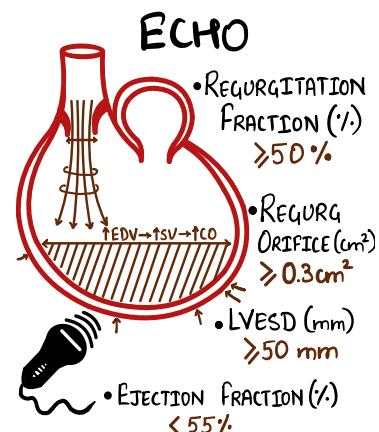


Figure 13. 2D Echo in Aortic regurgitation.

- The most important test for any valve disease
- Massive LV dilation to accommodate a large blood volume within the ventricle

Table 4. 2D Echo in Aortic regurgitation.

Component	Description	Pathologic
Regurgitation orifice (cm²)	Area of the orifice of the aortic valve	High risk: ≥ 0.3 cm ²
Regurgitation fraction (%)	Amount of blood regurgitated into LV in %	≥ 50 %
LV End Systolic Diameter (mm)	Amount of blood within the LV right before it contracts (Systole) Information tell us its dilation and accumulation of ↑ blood + ↓ contractility	≥ 50 mm
Ejection fraction (%)	LV must be hyperdynamic ↑ EDV → ↑ SV → ↑ CO	LV ejection fraction < 55 % warrants an intervention



III) TREATMENT

(A) AORTIC STENOSIS

(1) Medical Management (Mild – Moderate Aortic Stenosis)

(i) Indications

- For patients diagnosed with aortic stenosis but the categorization of the aortic valve surfaces areas, jet velocities, and mean pressure gradients are NOT too bad
 - Particularly for mild and moderate aortic stenosis which are not very symptomatic
 - May have little syncope, angina, and dyspnea on exertion
- For patients who do not need immediate intervention
- Should be **RECOMMENDED TO PATIENTS REGARDLESS OF SEVERITY** (Figure 1)

Managing patients diagnosed with aortic stenosis medically are not very helpful because there is more restriction than giving of medications.

(ii) Avoid Certain Medications (Figure 1)

(a) Venodilators

- If they venodilate, they ↓ preload into the right side of the heart → ↓ diastolic filling process → ↓ stroke volume → ↓ cardiac output → ↓ blood flow to the organs
- Example
 - Nitroglycerine

(b) Beta-Blockers (BB) and Calcium Channel Blockers (CCB)

- Can ↓ heart rate and contractility → ↓ stroke volume → ↓ cardiac output → ↓ blood flow to the organs

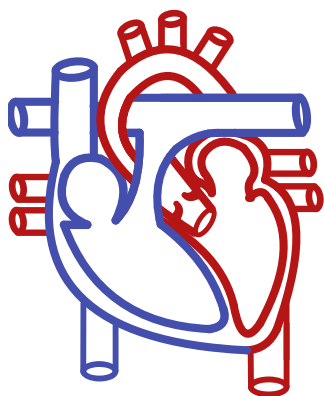
(c) Dehydration and Excessive Exertion

- Causes vasodilation of the blood vessels → ↓ systemic vascular resistance while cardiac output is fixed → ↓ disallowing perfusion to the brain → syncope

(iii) Be Cautious of Certain Medications (Figure 1)

(a) Arterial vasodilators

- Dilation of arteries → ↓ systemic vascular resistance → ↓ mean arterial pressure → ↓ blood flow to the organs
- Examples
 - Hydralazine
 - Isosorbide dinitrate
 - Nitroprusside
 - ACEs
 - ARBs
 - Nifedipine



MEDICAL MANAGEMENT (MILD-MOD. A.S.)

- AVOID VENODILATOR → ↓ PRELOAD → ↓ SV
- AVOID BB/CCBs → ↓ HR + ↓ CONTRACTILITY → ↓ SV
- AVOID EXCESSIVE EXERTION
- BE CAUTIOUS w/ VASODILATORS → ↓ SVR → ↓ MAP

Figure 14. Medical management of Mild to Moderate Aortic Stenosis.



(2) Valve Replacement

- Important therapeutic intervention

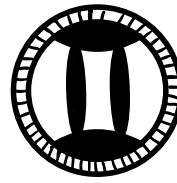
◦ **USED IN BOTH AS AND AR**

(i) Mechanical Valves (Figure 2)

- Have **HIGH RISK OF THROMBUS FORMATION**
- Patient will need lifelong anticoagulation (warfarin)
- For patients who are **younger (<60-65 years old)** because:
 - Valves last for a long time
 - Younger patients are healthier
 - Younger patients have low bleeding risk
 - Probably they are also in anticoagulation like atrial fibrillation (AF)

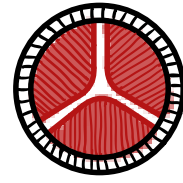
(ii) Bioprosthetic Valves (Figure 2)

- Have **LOW RISK OF THROMBUS FORMATION**
- Patient will need anticoagulation (warfarin) but only for about 3 months
- For patients who are **older and (>60-65 years old)** because:
 - Valves don't last very long (~10 years)
 - Older patients have lower life expectancy
 - Younger patients have high bleeding risk
- Patients are at high risk of infective endocarditis
 - Requires prophylaxis with amoxicillin



MECHANICAL VALVE

- ↑ THROMBUS
- LIFELONG AC
- YOUNG
- ↓ BLEEDING RISK



BIOPROSTHETIC VALVE

- ↓ THROMBUS
- AC x 3 Mo.
- OLDER
- ↑ BLEEDING RISK
- ↑ RISK OF I.E.

Figure 15. Types of Valve Replacements.

(3) Therapeutic Interventions

- Therapeutic interventions to prevent the progression of aortic stenosis to full-blown heart failure and other complications

(i) Percutaneous Balloon Valvuloplasty (PBV) (Figure 3)

(a) Procedure

- Procedure used to dilate the aortic valve
- Threading a catheter up through the femoral arteries and into the stenotic aortic valve
- Balloon at the tip of the catheter is inflated **stretching the stenotic aortic valve** → ↑ surface area of the aortic valve → ↑ blood flow through the aortic valve

(b) Indication

- AS patients without significant calcifications

(c) Contraindication

- ↑↑↑ **CALCIFICATIONS**

(ii) Valve Replacement

(a) Indications (Figure 3)

- Symptomatic **AND** Categorization of severe aortic stenosis
 - Symptoms
 - Syncope on exertion
 - Angina on exertion
 - Dyspnea on exertion
 - Severe Aortic Stenosis – determined by echo
 - Must have ↑ Jet velocity (≥ 4 m/s)
 - ↓ Aortic valve areas ($<1\text{cm}^2$)
 - ↑ Mean pressure gradients (≥ 40 mmHg)
 - ↓ Ejection Fraction ($<55\%$)
- Asymptomatic **AND** Ejection Fraction $<55\%$ AND may or may not in need of cardiac surgery for some other particular reason
- Failure of PBV
- PBV is contraindicated

(b) Procedure

(i) Surgical (Figure 3)

- Involves opening up the patient to replace the valve
- For **PATIENTS WITH LOWER SURGICAL RISK** and with have some other complications.
- Example: Patient who needs coronary artery bypass graft (CABG)

(ii) Trans-aortic valve replacement (TAVR) (Figure 3)

- Taking catheter run through the femoral artery to the aorta → valve replacement
- For **PATIENTS WITH HIGH SURGICAL RISK** hence not good candidates for surgery

(c) Either Mechanical or Bioprosthetic Valves (Figure 2)

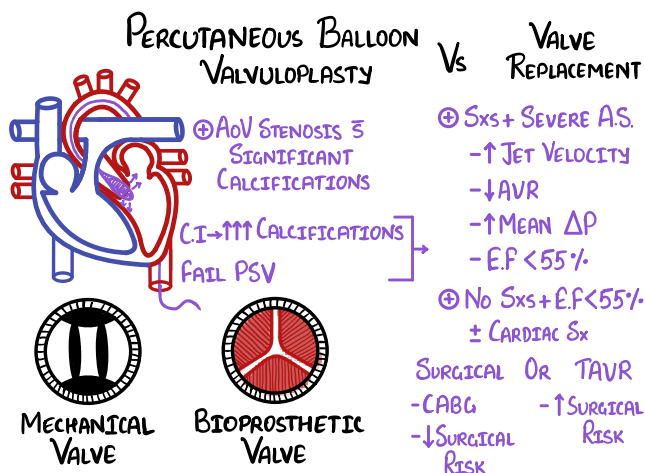


Figure 16. Percutaneous Balloon Valvuloplasty and Valve Replacement.



(1) Acute Aortic Regurgitation (Figure 4)**(i) Causes**

- **INFECTIVE ENDOCARDITIS**
 - Inflammation of endocardium lining the cardiac valves
 - Usually due to *Streptococcus viridans* infection [Sattar]
- **AORTIC DISSECTION**
 - Tear in the aortic wall [Sattar]
- **RHEUMATIC HEART DISEASE**
 - Immunologic hypersensitivity reaction to **Group A Streptococcus** antigens resulting in inflammation of the valves and eventually, stenosis [Sattar]

(ii) Complications**(a) Hypotension**

- Due to flooding tons of blood back into the left ventricle → ↓ stroke volume → ↓ cardiac output → hypotension

(i) Medications

- **INOTROPES** - Heart squeezes harder → ↑ CO → ↑ BP
- **AFTERLOAD REDUCERS** - Dilation of vessels = ↓ afterload → easier for the blood to go from the left ventricle to the aorta → ↑ BP
 - Hydralazine
 - Nitroprusside
 - ACE inhibitors
 - ARBs

(ii) Valve replacement STAT**(iii) Contraindication**

- **INTRA-AORTIC BALLOON PUMP** – can result in death

(b) Pulmonary edema

- ↓ Ejection fraction → ↑ left ventricular end-diastolic volume → ↑ left ventricular pressure → difficult for the blood to go to the left ventricle from the left atrium → ↑ left atrial pressure → backflow of blood from the left atrium back to the pulmonary circulation
- Can cause intense **hypoxia and shortness of breath**

(i) Treatments

- **BILEVEL POSITIVE AIRWAY PRESSURE (BIPAP)** – to push some of the fluid out the interstitial spaces
- **DIURETICS** – also pushes fluid out of the interstitial spaces
 - Example: Furosemide

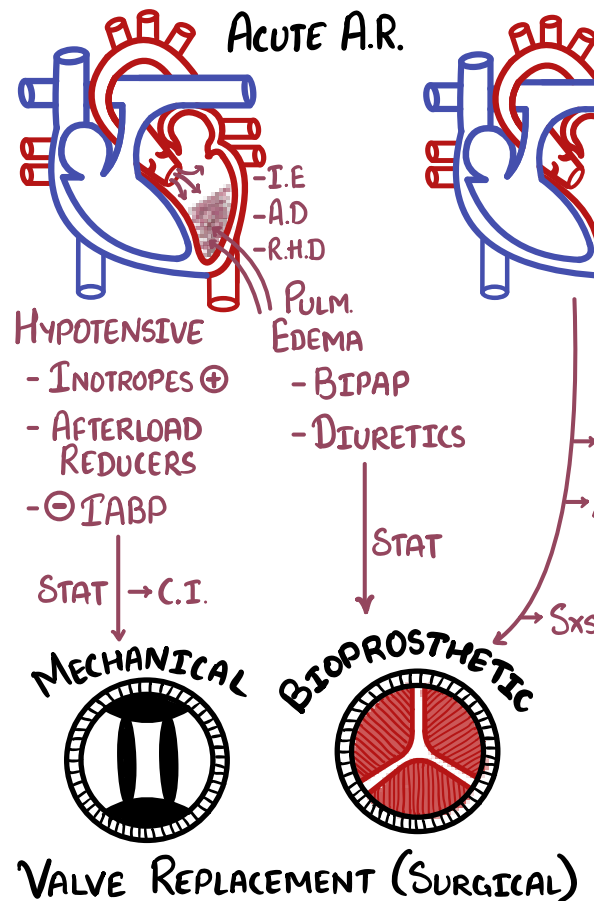
(ii) Valve replacement STAT

Figure 17. Treatment for Acute Aortic Regurgitation.



(2) Chronic Aortic Regurgitation (Figure 5)

(i) Treatment of Underlying Heart failure

- Fluid and sodium restriction
- Diuretics
 - Furosemide
- Reduce remodeling – ACE inhibitors
- ARBs
- Beta blockers
- Afterload reduces (hydralazine, nitroprusside, etc.)

(ii) Valve Replacement

(a) Indications

- Aortic regurgitation **AND** Ejection fraction is dropping (<55%) regardless if symptomatic or not
- Asymptomatic **AND** Ejection Fraction <55% **AND** may or may not in need of cardiac surgery for some other particular reason
- Symptomatic **AND** Categorization of severe aortic regurgitation
 - Left ventricular end systolic diameter (LVESD) ≥ 50 mm – means ventricles are overloaded
 - $\uparrow$ Regurgitation fraction ($\geq 50\%$)
 - $\uparrow$ End regurgitation orifice (≥ 0.3 cm²)

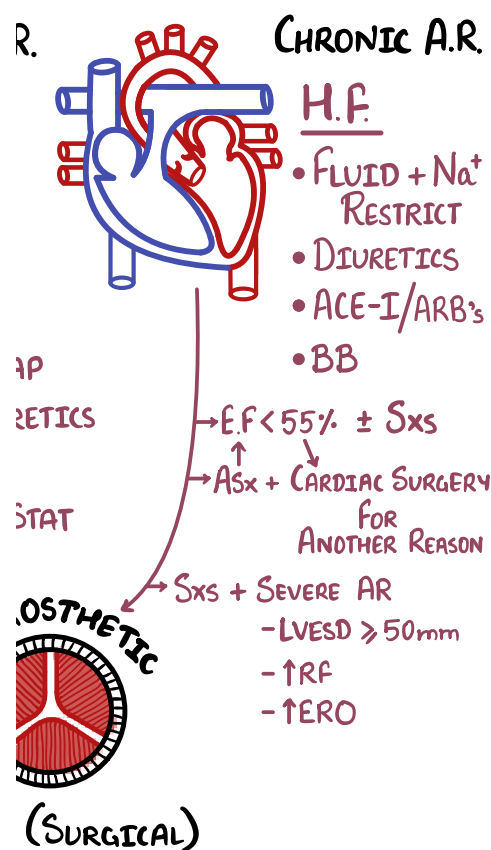


Figure 18. Treatment for Chronic Aortic Regurgitation.

(3) Trans-aortic Valve Replacement (TAVR)

- There's **not much literature to support TAVR** for acute regurgitation
- Patients go straight surgical
 - Either mechanical or bioprosthetic valves
- Explorations are still being done in the use of TAVR in AR

IN ACUTE AORTIC REGURGITATION, STABILIZE THE PATIENT USING MEDICATIONS THEN VALVE REPLACEMENT STAT.

IN CHRONIC AORTIC REGURGITATION, TREAT THE UNDERLYING HEART FAILURE THEN VALVE REPLACEMENT STAT (AS NEEDED)



Table 1-5 Summary

	Causes	Clinical Picture	Diagnosis	Treatment
Aortic Stenosis	- Aortic valve is <u>narrowed</u> due to fibrosis or calcification - Blood flow is decreased - A systolic murmur is produced Causes: - Rheumatic Heart Disease - Bicuspid Aortic Valve - Dystrophic Calcification	- SAD symptoms (Syncope, Angina, Dyspnea) (↑) on exertion - S4 heart sound - LV Heave	- Ejection click → Crescendo-Decrescendo systolic murmur ECG: RV5 height (amplitude) + SV3 → if ≥ 35 mm, diagnostic of LVH CXR: LVH, Pulmonary edema 2D ECHO: AVA < 1 cm²; Jet velocity ≥ 4 m/s; MPG ≥ 40 mmHg; LVEF $< 55\%$	- Avoid venodilators - Avoid BB / CCB - Avoid excessive exertion and dehydration - Be cautious of arterial vasodilators Therapeutic Interventions - PBV - Valve replacement
Aortic Regurgitation	- Aortic valve leaflets fail to close <u>properly</u> due to: - Dilated aortic wall; or - Damaged valves - This allows <u>backflow of blood</u> from the aorta to the left ventricle Causes: - Hypertension - Connective Tissue Disease - Aortitis - Aortic Dissection - Rheumatic Heart Disease - Bicuspid Aortic Valve - Infective Endocarditis	Acute AR: Cardiogenic Shock (Hypotension, Tachycardia); Pulmonary Edema (Hypoxia, Dyspnea on exertion or at rest, orthopnea) Chronic AR: Relatively Asymptomatic due to reduced hypotension and pulmonary edema, may have S3 heart sound and thrusting PMI due to LV Dilation Decompensated Chronic AR: Similar to Acute AR	- Decrescendo diastolic murmur ECG: LVH, LBBB, LAD CXR: Pulmonary edema, Cardiomegaly 2D ECHO: RO ≥ 0.3 cm²; RF $\geq 50\%$; LVESD ≥ 50 mm; LVEF $< 55\%$	Acute AR - Inotropes and Afterload reducers for hypotension - BIPAP and Diuretics for pulmonary edema - Therapeutic Intervention: Valve replacement Chronic AR - Fluid and Na restriction - HF drugs (diuretics, ACEi, ARBs, BB, afterload reducers) - Valve replacement



V) REVIEW QUESTION

1) Which of the following statements is FALSE?

- a) A stenotic aortic valve produces a systolic murmur.
- b) Rheumatic heart disease may cause aortic stenosis but not regurgitation.
- c) Atheromatous plaque formation increases the risk for dystrophic calcification of the aortic valve.
- d) In a patient less than 70 years old, one possible cause of aortic stenosis is bicuspid aortic valve.

2) Which of the following are causes of aortic regurgitation?

- a) Giant Cell Arteritis
- b) Marfan's Syndrome
- c) Aortic Dissection
- d) All of the Above

3) The following statements are true, EXCEPT?

- a) The aortic valve leaflets are anchored to the aortic walls.
- b) In aortic regurgitation, the valve is poorly sealed, decreasing the amount of blood that can pass from the left ventricle to the aorta
- c) Aortic regurgitation produces a diastolic murmur
- d) Aortic regurgitation may be due to inflammatory and infectious causes.

4) What differentiates aortic stenosis from aortic regurgitation?

- a) Nothing, both display a diminished ejection fraction.
- b) They differ in presentation in the cardiac cycle: aortic stenosis appears during S2 and aortic regurgitation appears during S1.
- c) They differ in presentation in the cardiac cycle: aortic stenosis appears during systole and aortic regurgitation appears during diastole.
- d) None of the above.

5) Which of the following is diagnostic of aortic regurgitation?

- a) Regurgitation fraction of $\geq 40\%$
- b) LVEF $<35\%$
- c) Pulmonary infiltrates in CXR
- d) Regurgitation orifice of $\geq 0.3 \text{ cm}^2$

6) All of the statements are true in managing aortic stenosis EXCEPT:

- a) It is recommended to patients regardless of severity
- b) There are many drugs use in AS and restricted medications are rare.
- c) Extensive calcification is a contraindication in Percutaneous Balloon Valvuloplasty
- d) Valve replacement is indicated in patients who are symptomatic and are categorized as having severe aortic stenosis.
- e) Trans-aortic valve replacement can be use in AS if there is high surgical risk.

7) All of the statements are true in managing aortic regurgitation EXCEPT:

- a) Intra-aortic balloon pump is a contraindication in patients with acute aortic regurgitation
- b) Furosemide is a pharmacological management for acute AR if there is pulmonary edema
- c) Management of chronic AR involves treating underlying heart failure
- d) Valve replacement is indicated in patients who are asymptomatic, have an EF $<55\%$, and who may need CABG.
- e) Trans-aortic valve replacement can be use in AR if there is high surgical risk.

VI) REFERENCES

- Kumar, V., Abbas, A. K., & Aster, J. C. (2021). Robbins and Cotran pathologic basis of disease (tenth edition.). Philadelphia, PA: Elsevier/Saunders.





OUTLINE

- I) MAIN HEADING IN
- II) CONTENT FORMATTING
- III) APPENDIX

- IV) REVIEW QUESTIONS
- V) REFERENCES

I) CAUSES

(A) DEFINITION

- **Endocarditis:** inflammation of the endocardium
 - Inflammation, damage or destruction of the endocardium → forms microbial vegetations
- Recall: The **endocardium** lines the ventricles and more importantly, the valves of the heart

(B) TYPES OF INFECTIVE ENDOCARDITIS (IE)

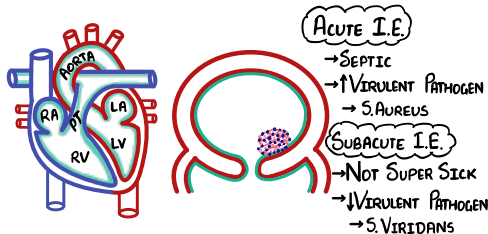


Figure 1. Types of infective endocarditis.

(1) Acute Infective Endocarditis

- Patients look really **septic** (really sick individuals)
 - Hypotensive, high fever, new heart failure symptoms and septic emboli
- Due to a highly virulent pathogen: *S. aureus*

(2) Subacute Infective Endocarditis

- Nonspecific symptoms: low-grade fever, dyspnea and fatigability
- More difficult to diagnose
- Usually due to a low virulent pathogen: *S. viridans*

Table 1. Acute vs subacute IE (Harrison's).

	Acute IE	Subacute IE
Usual Etiology	<i>S. aureus</i> B-hemolytic streptococci Pneumococci Aerobic gram-negative bacilli	<i>S. aureus</i> (sometimes) <i>S. viridans</i> Enterococci HACEK Coagulase-negative staph/strep (prosthetic valves)
Manifestations	High-grade fever (39.4-40°C) Acute/decompensated heart failure	Low-grade fever (rarely >39.4°C) Weight loss, abdominal symptoms, pleurisy
Course	Rapid Hematogenously seeded extracardiac sites Complications are common	Indolent, subtle, and non-specific symptom Rarely metastasizes
Prognosis	Poor (if untreated)	Better prognosis

(C) ABNORMAL VALVES

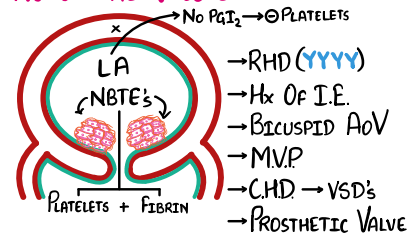


Figure 2. Causes of abnormal valves.

- Predisposes individuals to IE
- Endocardial cells release prostacyclins (PGI₂) and NO → inhibits platelet aggregation
 - Damage to endocardial cells results in inability to release PGI₂ and NO → cannot inhibit platelet aggregation → platelets attach to exposed collagen in damaged endocardium → **platelet plug** forms → fibrin mesh stabilizes the platelet plug

(1) Causes of Damaged Heart Valves

Table 2. Causes of abnormal heart valves.

Causes	Rationale
Rheumatic heart disease	Excessive amounts of antibodies that damage the endocardial lining
History of infective endocarditis	Pathogen damages the endocardium → fibrosis exposing the collagen, platelet plug forms, etc.
Bicuspid aortic valve	Patients with bicuspid aortic valve form calcifications and very susceptible to IE
Mitral valve prolapse	Damage to the valve leaflets causing MV degeneration
Congenital heart defects	VSD, truncus arteriosus, TOF, etc ● Underlying valvular damage increases the risk of IE
Prosthetic valves	Very high risk for binding of pathogens, platelets and thrombin

- **NBTEs:** non-bacterial thromboemboli
 - Composed of platelets and fibrin
 - Increases risk for bacterial infection



(D) BACTEREMIA

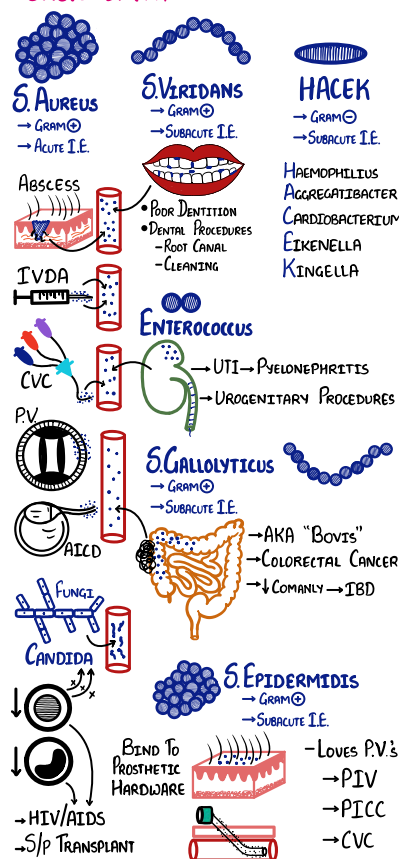


Figure 3. Bacterial and fungal organisms that can cause infective endocarditis.

- NBTEs increase the opportunity for bacterial infection, multiply and colonize → form microbial vegetations leading to damaged valves

(1) *S. aureus*

- Remember: most common cause of **acute IE**
- Gram-positive bacteria
- One of the few types of pathogens that can damage a healthy valve
 - Other bacteria commonly damage a compromised valve

Table 3. Common causes of *S. aureus* spread in the bloodstream.

Causes	Rationale
Skin abscesses	Remember that <i>S. aureus</i> is part of the <u>skin flora</u> ◦ Skin abscesses form a break in the skin → allowing spread of the bacteria in the bloodstream
IV drug abuse	Using dirty needles that increases risk of injecting bacteria in the bloodstream
Catheters and prosthetic hardware introduction	Example: Central venous catheters ◦ Catheter is pushed through the skin allowing the bacteria to reach the bloodstream
Prosthetic heart valves, pacemakers, AICD	AICD: automated implanted cardioverter defibrillator

(2) *S. viridans*

- Remember: most common cause of **subacute IE**
- Gram positive bacteria
- Part of the oral flora
 - So any break in the normal barriers introduces the bacteria in the bloodstream
- Examples:
 - Poor dentition
 - Dental procedures (cleaning and root canal)

• Subtypes of *S. viridans*

- *S. mitis*
- *S. mutans*
- *S. oralis*
- *S. sanguinis*
- *S. milleri*
- *S. sobranus*

(3) HACEK

- Stands for ***Haemophilus spp*, *Aggregatibacter spp*, *Cardiobacterium spp*, *Eikenella carodens* and *Kingella spp***
- Gram negative rods
- Causes subacute IE
- Part of the oral flora
 - Has similar mechanism of introduction to *S. viridans*

(4) *Enterococcus*

- Part of the urogenital tract
- Causes of spread:
 - **UTI, specially pyelonephritis**
 - Bacteria can enter the renal circulation
 - **Catheter, urinary stent** and other urogenital procedures
 - Provides opportunity for the bacteria to enter through a break in the integrity of the walls

(5) *Streptococcus gallolyticus*

- AKA *Strep bovis*
- Associated with the following:
 - **Colorectal cancer**
 - **Inflammatory bowel disease** (ulcerative colitis or Crohn's disease)

(6) *Staphylococcus epidermidis*

- Gram positive bacteria
- **Loves prosthetic valves** and other prosthetic hardware (AICD or pacemakers)
- Prominent in the skin
- Can travel the bloodstream through a break in the skin
 - PIV, PICC line, CVC

(7) *Candida*

- Fungi
- Not very common pathogen that can cause IE except for **immunocompromised** patients (e.g. HIV, s/p transplant)
 - In immunocompromised individuals, neutrophils and lymphocytes cannot clear *Candida* in the bloodstream



II) CLINICAL FEATURES AND PHYSICAL EXAMINATION

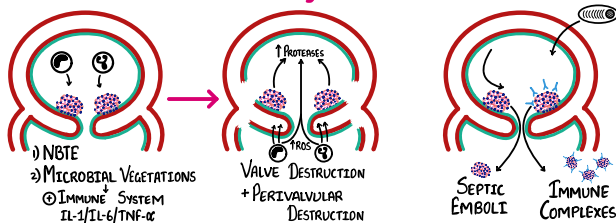


Figure 4. Pathophysiology of infective endocarditis.

Recap:

- Inflammation of the endocardium from abnormal valve and bacteremia
 - Exposure of the underlying collagen and formation of platelet plug
 - Platelet plug stabilized by fibrin → **NBTEs**
 - Bacteremia → pathogen sticks to NBTE in the surface → infiltrates the NBTE → **microbial vegetation**
 - Vegetations stimulate the immune system bringing neutrophils, macrophages, etc. → increases production of cytokines (IL-1, IL-6, TNF- α)

Summary:

- 1) NBTE formation
- 2) Microbial vegetations
- 3) Immune response

(A) IMMUNE RESPONSE

- Immune cells (macrophages and neutrophils) attack the pathogens releasing ROS and proteases
 - Microbes release proteases as well
- Proteases and ROS start eroding both the valvular and perivalvular tissue causing **valve and perivalvular destruction**
 - One of the worst case scenarios
 - Creates an opportunity for abscess formation and prosthetic valve dysfunction
- Vegetations may flick off becoming **septic emboli**
 - Similar to clots in atrial fibrillation
 - May be right-sided or left-sided (*more common*)
- Plasma cells produce antibodies (Ab) against the microbes attacking bacterial antigens (Ag) → circulating Ab-Ag complexes (also called **immune complexes**) which deposit throughout the body

(B) ↑CYTOKINES

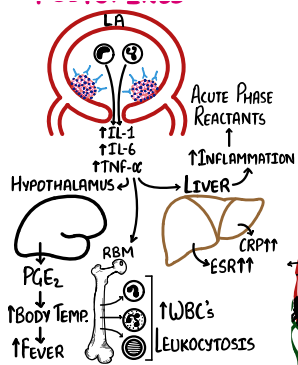


Figure 5. Clinical manifestations from increased cytokines. Take note that this can occur at any valve.

- **IL-1, IL-6 and TNF- α**
 - Stimulates the hypothalamus to release PGE₂ → increases the body temperature → **fever**
 - Stimulates the bone marrow to produce white blood cells → **leukocytosis** (CBC)
 - "We need more help"
 - Stimulates the liver to produce **acute phase reactants** (↑↑CRP and ↑↑ESR)
 - Alerting the body of increased inflammation
 - Very non-specific

(C) ↑VALVE DESTRUCTION

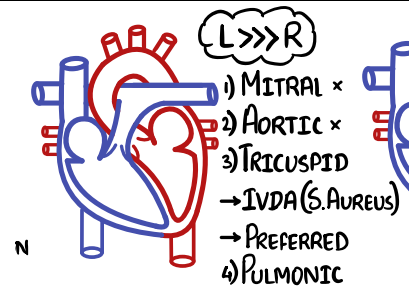


Figure 6. Preference of heart valves in infective endocarditis.

- **Left-side is more commonly affected than right-side**
 - Recall: left side – mitral and aortic; right side – tricuspid and pulmonic valves
 - Commonly affected valves arranged in order: **(R) mitral > aortic > (L) tricuspid > pulmonic**
 - EXCEPT for IV drug abusers with *S. aureus* in which the **tricuspid** valve is preferred
 - Mnemonic: **TRI** not doing drugs

(1) Mitral Valve Destruction

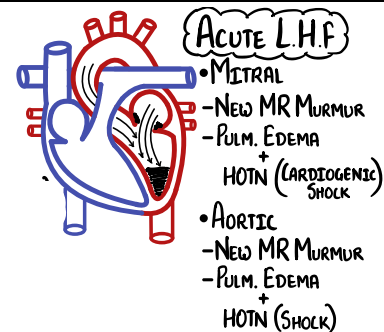


Figure 7. Acute left-sided heart failure symptoms from aortic and mitral valve destruction.

- MV is degenerated or chewed away → shortening of the MV → allows backflow of the blood → **new MV regurgitation murmur**
- Accumulated regurgitated blood flow back to the LV → overfilling of blood → blood accumulation in the left side of the heart → back up of blood in the lungs → **pulmonary edema**
- Every time the ventricle contracts, accumulated blood in the LV can be pushed to the left atrium → ↓**stroke volume** → ↓cardiac output → **hypotension** → **cardiogenic shock**
 - Example: normal SV is 70 mL; in mitral regurgitation, 50 mL is pushed to the aorta while 20 mL is pushed to the LA → decreased stroke volume

(2) Aortic Valve Destruction

- New aortic regurgitation
- Pulmonary edema
- Hypotension

(3) Acute Left-Sided Heart Failure

- Due to involvement of aortic and/or mitral valves
- Symptoms:
 - Shortness of breath due to pulmonary edema
 - Dyspnea on exertion
 - Paroxysmal nocturnal dyspnea
 - Hypoxemia
 - Hypotension
 - Cold extremities (ill-perfused extremities)
 - New aortic and/or mitral regurgitation



(D) PERIVALVULAR DESTRUCTION

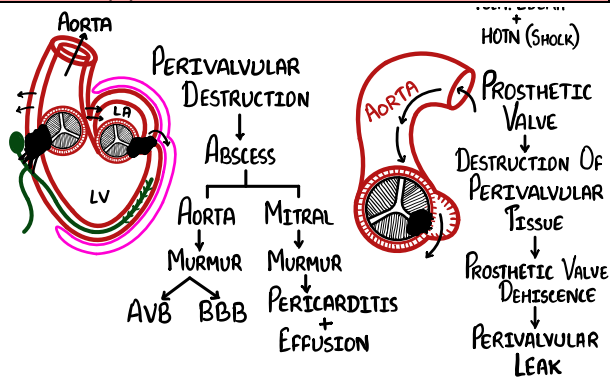


Figure 8. Perivalvular destruction in native and prosthetic valves.

- Vegetation on the valve eats away the perivalvular tissue leading to formation of annular abscess
 - Perivalvular destruction → abscess

(1) Aortic Valve

- Perivalvular destruction in the aortic valve produces **murmur** due to inflammation and dilatation of the aorta
 - Annular destruction may also involve the **AV node** and the **bundle system** leading to **AV blocks** and **bundle branch blocks**

(2) Mitral Valve

- Perivalvular vegetations in the mitral valve can infiltrate the pericardium → **pericarditis ± pericardial effusion**

(3) Prosthetic Valves

- Perivalvular tissues should anchor the prosthetic valve
 - Destruction of the perivalvular tissue separates it from the prosthetic valve leading to **prosthetic valve dehiscence**
- Prosthetic valve dehiscence produce a leak into the ventricle leading to **perivalvular leak**
 - Leads to **prosthetic valve dysfunction**

(E) SEPTIC EMBOLI

(1) Right-Sided Emboli

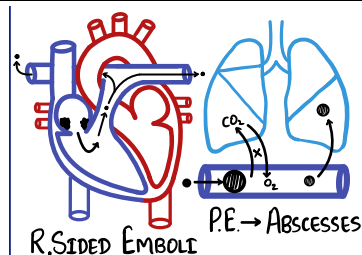


Figure 9. Right-sided emboli resulting to pulmonary embolism and lung abscesses.

- Flicking off pieces of the vegetations in the tricuspid valve → moves to the pulmonary circulation → occludes blood flow → **pulmonary embolism**
 - Symptoms:
 - Dyspnea
 - Increased sputum
- Smaller emboli can pass through the capillaries and infiltrate the lung tissue → **lung abscesses**
 - Small enough and can infiltrate to the lung tissue → **lung abscesses**

(2) Left-Sided Emboli

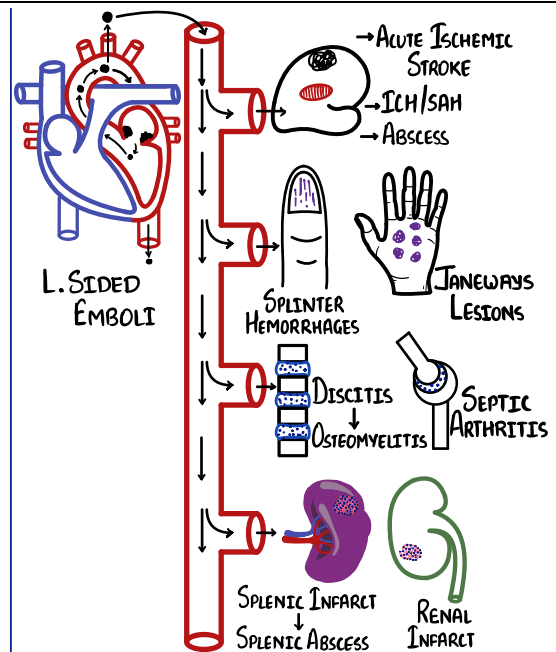


Figure 10. Left-sided emboli causing a variety of clinical manifestations.

- Flicking off pieces of the vegetations moving to the systemic circulation going to different organs of the body (Table 3)

Table 4. Effects of infiltration of vegetation to different organs and blood vessels.

Organ/Vessels	Complication	Symptoms or Clinical Signs
Carotid system	Acute ischemic stroke	Neural deficits, dysarthria, gait preferences, sensory deficits
Brain and its vessels	ICH, subarachnoid hemorrhage Brain abscesses	
Vessels of the nailbeds	Splinter hemorrhages (Figure 11)	
Vessels to the palms and soles	Janeway lesions (Figure 12) o Painless lesions	
Vertebrae	Discitis or spondylitis → osteomyelitis o Destruction of the discs and vertebrae	Back pain
Joint Tissue	Septic arthritis	Hot painful tender joints
Spleen and its vessels	Splenic infarct Splenic abscess	Significant amount of abdominal pain
Kidney vessels	Renal infarct	Flank pain ↓ urine output ↑ BUN or Cr





Figure 11. Splinter hemorrhages.



Figure 12. Janeway lesions on the hypothenar eminence [Arora et al, 2012].

(F) ↑IMMUNE COMPLEXES

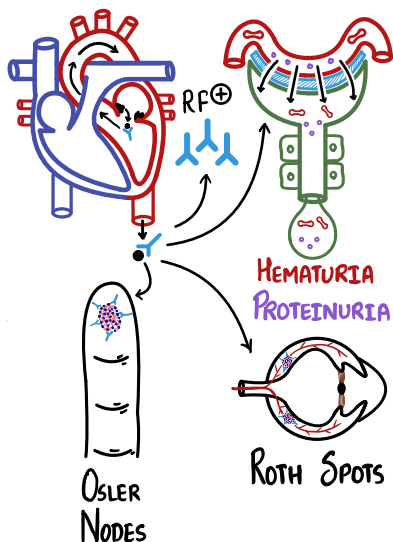


Figure 13. Increased immune complex deposition forming different clinical manifestations.

- Immune complexes can be distributed to the systemic circulation and can be deposited to the following:
 - Pulp of the digits producing painful lesions called **Osler's nodes** (Figure 15)
 - Mnemonic: Osler ouch!
 - Retina leading to hemorrhagic lesions called **Roth spots** (Figure 14)
 - Symptom: Visual changes
 - Glomerulus and glomerular tissue leading to their erosion once immune system attacks → leakage of blood (RBC) and plasma proteins (hematuria and proteinuria) → **glomerulonephritis**
- Specific antibodies for Ab-Ag deposition process: **rheumatoid factor (RF)**

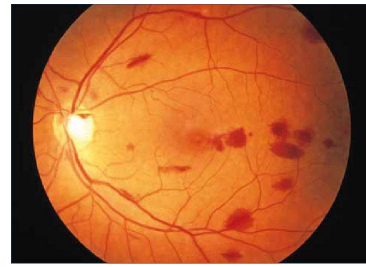


Figure 14. Roth spots [Arora et al, 2012].



Figure 15. Osler's nodes [Dermnet NZ].

Table 5. Summary of clinical findings in IE.

↑Cytokines	Fever Leukocytosis ↑Acute phase reactants (CRP and ESR)
↑Valve destruction	L >>>> R ◦ Mitral > Aortic > Tricuspid > Pulmonary MV or aortic valve regurgitation murmur Pulmonary edema Hypotension
↑Perivalvular destruction	Abscess Aortic valve: ◦ Murmur ◦ AV blocks and bundle branch blocks Mitral valve: ◦ Pericarditis ± pericardial effusion Prosthetic valves: ◦ Prosthetic valve dehiscence → prosthetic valve dysfunction
Septic emboli	Right-sided ◦ Pulmonary embolism ◦ Lung abscess Left-sided ◦ Acute ischemic stroke ◦ ICH, subarachnoid hemorrhage ◦ Brain abscess ◦ Splinter hemorrhage ◦ Janeway lesions ◦ Discitis or spondylitis → osteomyelitis ◦ Septic arthritis ◦ Splenic infarct, splenic abscess ◦ Renal infarct
Immune complexes	Osler's nodes Roth spots Glomerulonephritis Specific antibodies: Rheumatoid factor

III) DIAGNOSIS

(A) ECHOCARDIOGRAPHY

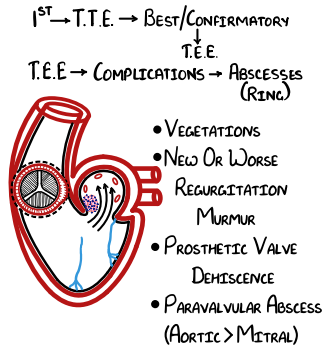


Figure 16. Diagnosis of IE with echocardiogram.

• Transthoracic Echocardiogram (TTE)

- Looking at different views: subxiphoid, parasternal long axis, short axis, apical, etc.
- Provides a global visualization of the heart
- However, it's difficult to have a good look at the AV and MV using this

• Transesophageal Echocardiogram (TEE)

- High specificity and sensitivity (>90%)
- Probe is swallowed allowing visualization of the posterior aspect of the heart
- Another advantage is the visualization of other complications such as ring abscesses

• Look for the following:

- **Vegetations**
- **New or worse regurgitation murmur**
 - Using Color Doppler
- **Prosthetic valve dehiscence**
 - Prosthetic valve rocking back and forth with perivalvular leak
- **Perivalvular abscess (ring abscess)**
 - More common in aortic than mitral valve

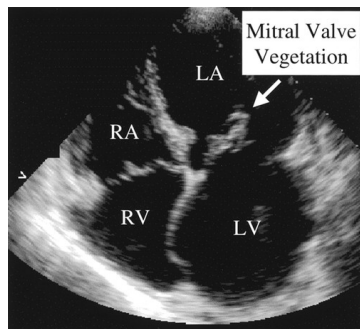


Figure 17. Mitral valve vegetation shown on echocardiogram

[Cabell et al, 2003].

(B) BLOOD CULTURES

- FIND BACTEREMIA → TYPICAL PATHOGENS
- 3 SETS OF CULTURES

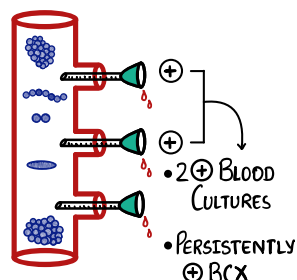


Figure 18. Diagnosis of IE with blood cultures.

• Purpose:

- To prove that bacteremia is present
 - Looking for typical pathogens + *Coxiella burnetii*
- To narrow the antibiotics for specific pathogens

• Three sets of blood culture is obtained

- Draw from different sites at different times
- Get a lot of blood to get a good number of potential bacteria
- Aerobic, anaerobic and fungal cultures
- Remember that IE is an endovascular infection meaning it's continuous

• Bacteremia is established when:

- ≥2 (+) blood cultures OR
- Persistently (+) blood cultures

(C) TESTS FOR SEPTIC EMBOLI

Table 6. Tests for septic emboli.

Brain MRI	• Assess for presence of infarct, abscess or bleeds ○ For patients with altered mental status
Spinal MRI	• Assess for discitis, osteomyelitis or spinal cord abscess
Splenic UTS or CT of abdomen and pelvis	• Assess for splenic infarcts or abscesses
Renal UTS	• Can show renal vascular emboli • Look for signs of AKI: ○ Basic metabolic panel (BMP) - ↑BUN, ↑Cr ○ ↓urine output
Physical Exam	• Splinter hemorrhages and Janeway lesions
Chest Xray or CT Scan	• <u>CXR</u>: opacities or abnormal nodular vision → proceed to CT scan • <u>CT</u>: look for pulmonary emboli or abscesses

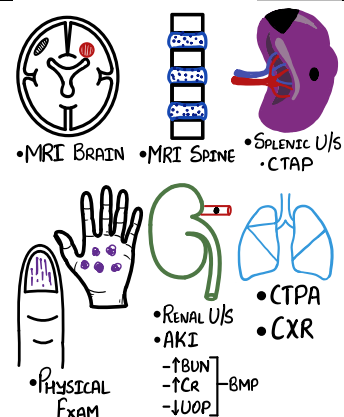


Figure 19. Diagnostic tests and imaging for septic emboli in IE.



(D) TESTS FOR IMMUNE COMPLEXES

Table 7. Tests for immune complexes.

Urinalysis with microscopy	• (+) RBC casts, protein • Look for signs of AKI: ◦ ↑BUN, ↑Cr, ↓urine output
Funduscopy	• Check for presence of lesions (hemorrhages) on the retina
Physical Examination	• Osler's nodes
Rheumatoid Factor	• Positive RF

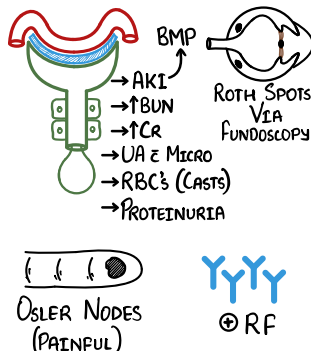


Figure 20. Diagnostic tests for immune complexes in IE.

(E) MODIFIED DUKE'S CRITERIA

- Establishes the diagnosis of infective endocarditis when the following conditions are met:
 - **Two major criteria**
 - **One major criterion + three minor criteria**
 - **Five minor criteria**

(1) Major Criteria

- (+) Echo findings
 - Vegetations, murmur, PV dehiscence, abscess
- (+) Blood culture
 - ≥2 (+) tests OR persistently (+) tests; AND
 - Typical pathogens
 - **EXCEPT for *Coxiella burnetii***
 - Does not need to meet the aforementioned circumstances

(2) Minor Criteria

- (+) Fever ($\geq 38^{\circ}\text{C}$ or $\geq 100.4^{\circ}\text{F}$)
- (+) Predisposing factors:
 - Factors for abnormal valves and/or bacteremia
- (+) Septic emboli
- (+) Immune phenomenon
- (+) Blood cultures not meeting major criteria
 - <2 positive cultures or not persistently positive

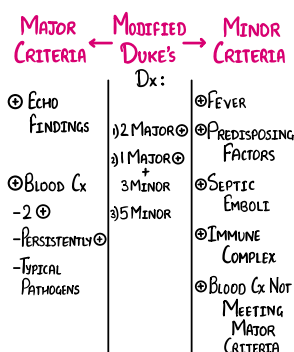


Figure 21. Modified Duke's criteria.

(F) NON-INFECTIONAL ENDOCARDITIS

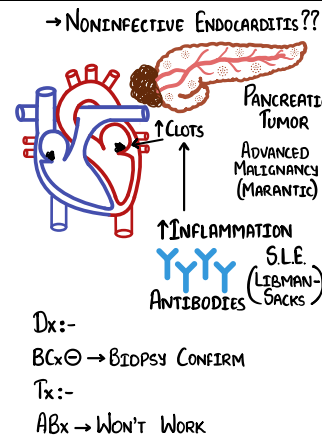


Figure 22. Non-infective endocarditis.

(1) Marantic Endocarditis

- Pancreatic carcinoma
 - Tumor produce cytokines that stimulate clot formation
 - microclots spread to the valves
 - Microclots are non-septic emboli

(2) Libman-Sacks Endocarditis

- Endocarditis from **SLE (systemic lupus erythematosus)**
 - Body produces a lot of auto-Abs that increase inflammation → increases activity of microthrombi that form on the heart valves

(3) Diagnosis

- Manifestations:
 - Low-grade fevers
 - Little vegetations on the valves (on Echo)
 - Valve dysfunction leading to heart murmurs
 - **(-) blood cultures**
 - **Does not improve on antibiotics**
 - It does not always mean non-infective endocarditis; it may also mean IE that needs surgery

(i) Biopsy

- For confirmation

(ii) Look for underlying condition

- More important
- **CT of the abdomen or MRCP** = pancreatic tumors
- (+) SLE antibodies

IV) TREATMENT

(A) ANTIBIOTICS

- To clear the infection that causes problems such as septic emboli, vegetations, etc.
- Patients are sometimes hemodynamically unstable, especially patients with **acute IE**, where cardiogenic shock can occur
 - Immediately start on empiric antibiotics after taking the blood cultures
 - On **subacute IE**, it's possible to hold off the antibiotics after taking the blood cultures unless they are not as hemodynamically stable as possible

(1) Empiric Antibiotics

- Depends upon the valve affected
- When blood cultures come back positive, narrow the types of antibiotics depending the type of pathogens

(i) Native Valve IE

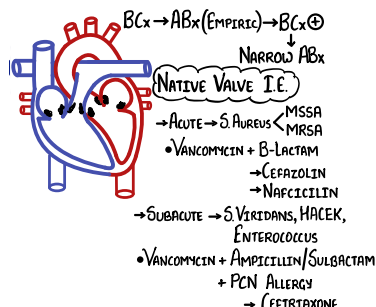


Figure 23. Antibiotics used in native valve IE.

- Vegetations on the mitral, aortic, tricuspid or pulmonary valves
- Establish whether acute or subacute
- **Acute IE**
 - *S. aureus*: either MSSA or MRSA
 - **Vancomycin + Cefazolin/Nafcillin** (β-lactam)
 - Vancomycin: for MRSA
 - Cefazolin/Nafcillin: augments effect of vancomycin covering MSSA

MSSA: Methicillin-susceptible *S. aureus*
MRSA: Methicillin-resistant *S. aureus*

- **Subacute IE**
 - *S. viridans*, *HACEK*, *Enterococcus*
 - **Vancomycin + Ampicillin-Sulbactam (or Ceftriaxone)**
 - Vancomycin: for gram-positive bacteria
 - Ampicillin-Sulbactam: covers HACEK and *Enterococci*
 - Ceftriaxone to replace Ampicillin-Sulbactam if there is penicillin allergy

(ii) Prosthetic Valve IE

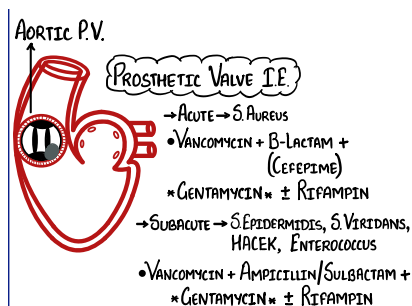


Figure 24. Antibiotics used in prosthetic valve IE.

- **Acute IE**
 - *S. aureus*: either MSSA or MRSA
 - **Vancomycin + Cefepime** (β-lactam) + **Gentamicin ± Rifampin**
 - Cefepime is much more superior than cefazolin/nafcillin in prosthetic valve IE
 - Gentamicin is IMPORTANT for prosthetic valve IE
 - Covers *Staph* species
 - Rifampin can cause bacterial resistance to other Abx so this should be added later on (after 1 week)
- **Subacute IE**
 - *S. epidermidis*, *S. viridans*, *HACEK*, *Enterococcus*
 - Recall that *S. epidermidis* love prosthetic hardware
 - **Vancomycin + Ampicillin-Sulbactam (or Ceftriaxone) + Gentamicin ± Rifampin**

Table 8. Summary of empiric Abx used in native and prosthetic valve IE.

		Native Valve IE	Prosthetic Valve IE
Pathogens	Acute	<i>S. aureus</i> (MSSA or MRSA)	
	Sub-acute	<i>S. viridans</i> , <i>HACEK</i> , <i>Enterococci</i>	<i>S. epidermidis</i> , <i>S. viridans</i> , <i>HACEK</i> , <i>Enterococci</i>
Abx	Acute	Vancomycin + Cefazolin/ Nafcillin	Vancomycin + Cefepime + Gentamicin ± Rifampin
	Sub-acute	Vancomycin + Ampicillin-Sulbactam (or Ceftriaxone)	Vancomycin + Ampicillin-Sulbactam (or Ceftriaxone) + Gentamicin ± Rifampin

(B) SURGERY

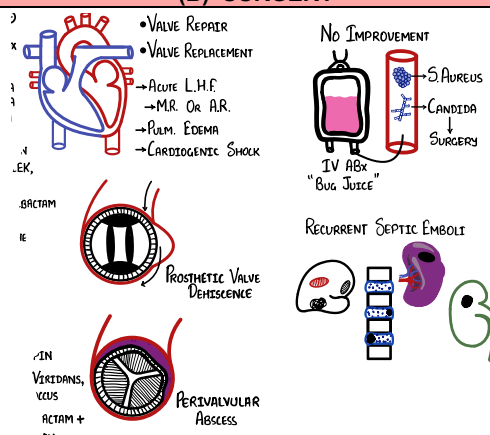


Figure 25. Indications for surgery in IE.

- **Valve repair or valve replacement**
 - Depending on the cardiothoracic surgeon's opinion

(1) Indications

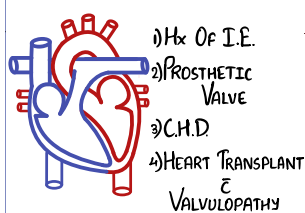
- **(+) Acute left-sided heart failure**
 - Mitral regurgitation or aortic regurgitation
 - Pulmonary edema
 - Cardiogenic shock
- **(+) Prosthetic valve dehiscence**
 - Can lead to acute LHF
- **(+) Perivalvular abscess**
 - Abx cannot adequately clear the infections
- **(-) Improvement on IV Abx**
- **(+) Pathogens that cannot be cleared with antibiotics**
 - *Candida* species
 - Need IV antifungals (amphotericin B and/or caspofungin)
 - *S. aureus*
- **Recurrent septic emboli**
 - Resistant to antibiotics
 - Led to brain abscesses, hemorrhages, mycotic aneurysms, splenic abscess, renal infarcts, discitis



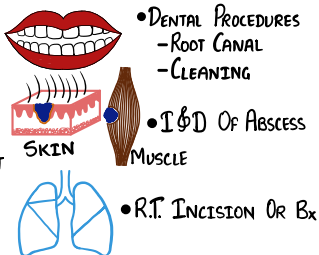
V) ENDOCARDITIS PROPHYLAXIS

ENDOCARDITIS PROPHYLAXIS

CARDIAC CONDITIONS



PROCEDURES



ANTIBIOTIC PRx

PO → AMOXICILLIN

IV/IM → AMPICILLIN



→ 30-60 MIN PRIOR

PCN ALLERGY → AZITHROMYCIN

→ CLINDAMYCIN

Figure 26. Endocarditis prophylaxis.

- For people who are high-risk (cardiac conditions) and are undergoing specific procedures

(1) Indications

(i) Cardiac Conditions

- History of IE
- Prosthetic valve
- Congenital heart defects
- s/p Heart transplant with associated valvulopathy

(ii) Procedures

- Any simple dental procedure
 - Cleaning
 - Root canal
- Incision and drainage (I&D) of skin or musculoskeletal abscess
- Respiratory tract incision or biopsy
- Insertion of cardiac prosthetic hardware (AICD, pacemakers, etc)

(2) Antibiotic Prophylaxis

- PO (per ore): **amoxicillin**
 - Most common
 - 30-60 mins prior the procedure
- IV or IM: **ampicillin**
- Penicillin allergy: **azithromycin** or **clindamycin**



VI) APPENDIX

Table 23-9 Summary

	Acute Infective Endocarditis	Subacute Infective Endocarditis
Definition	- Patients are really septic (hypotensive, high fever, new heart failure symptoms, septic emboli) - Due to <i>S. aureus</i>	- Non-specific symptoms: low-grade fever, dyspnea, fatiguability - Due to <i>S. viridans</i> (most common), <i>HACEK</i>, <i>Enterococci</i>, <i>S. gallolyticus</i>, <i>S. epidermidis</i>, <i>Candida</i>
Causes	Abnormal Valves - Rheumatic heart disease - Hx of IE - Bicuspid aortic valve - Mitral valve prolapse - Congenital heart defects - Prosthetic valves	Bacteremia <i>S. aureus</i> - Skin abscesses, IV drug abuse, prosthetic hardware <i>S. viridans</i> - Dental procedures, poor dentition <i>HACEK</i> - Dental procedures, poor dentition <i>Enterococci</i> - UTI (pyelonephritis), catheters and other urogenitary procedures <i>S. gallolyticus</i> - Colorectal cancers, IBD <i>S. epidermidis</i> - Loves prosthetic hardware; skin flora <i>Candida</i> - Immunocompromised patients
Clinical Manifestations and PE	↑Cytokines - Fever - Leukocytosis Acute Heart Failure Symptoms - Shortness of breath due to pulmonary edema - Dyspnea on exertion - Paroxysmal nocturnal dyspnea - Orthopnea - Hypoxemia - Hypotension - Cold extremities - New aortic and/or mitral regurgitation Left side >>>> Right side ↑Perivalvular Destruction - Murmur - AV blocks and BBB - Pericarditis +/- pericardial effusion - Perivalvular dehiscence → perivalvular dysfunction	Septic Emboli - Pulmonary embolism (right-sided) - Lung abscess (right-sided) - Acute ischemic stroke - ICH/SAH - Abscess - Splinter hemorrhages - Janeway's lesions - Discitis → Osteomyelitis - Septic arthritis - Splenic infarct → splenic abscess - Renal infarct ↑Immune Complexes - Glomerulonephritis = hematuria and proteinuria - Osler nodes - Roth spots (+) Rheumatoid factor
Diagnosis	Echocardiogram - Vegetations - New or worse regurgitation murmur - Prosthetic valve dehiscence - Perivalvular abscesses Blood Cultures - Two positive cultures - Persistently positive BCx Tests for Septic Emboli - Brain MRI - Spinal MRI - Splenic UTS or CTAP - Renal UTS - PE - CXR or CT scan	Tests for Immune Complexes - Urinalysis with microscopy - Fundoscopy - PE - Rheumatoid factor Modified Duke's Criteria - Two major criteria - One major criterium + three minor criteria - Five minor criteria <u>Major criteria</u> (+) Echo findings (+) Blood culture <u>Minor criteria</u> (+) Fever (+) Predisposing factors (abnormal valves and/or bacteremia) (+) Septic emboli (+) Immune phenomenon (+) Blood cultures not meeting the major criteria



Differentials	● Marantic Endocarditis ○ (+) Advanced malignancy such as pancreatic carcinoma ● Libmann-Sacks Endocarditis ○ (+) SLE
	● Clinical Features ○ Low grade fevers ○ Little vegetations ○ Heart murmurs ○ <u>(-) Blood cultures</u> ○ <u>Does not improve on Abx</u> ● Diagnosis ○ Biopsy ○ Look for underlying condition
Treatment	● Empiric Antibiotics ○ Native valve IE ▪ Vancomycin + cefazolin/nafticillin ○ Prosthetic valve IE ▪ Vancomycin + cefepime + gentamicin +/- rifampin ○ Native valve IE ▪ Vancomycin + ampicillin-sulbactam (or ceftriaxone) ○ Prosthetic valve IE ▪ Vancomycin + ampicillin-sulbactam (or ceftriaxone) + gentamicin +/- rifampin ● Surgery ○ Valve repair or valve replacement ○ Indications: ▪ (+) Acute LHF ▪ (+) PV dehiscence ▪ (+) PV abscess ▪ (-) Improvement on IV Abx ▪ (+) Pathogens that cannot be cleared with Abx ▪ Recurrent septic emboli
Prophylaxis	● Cardiac Conditions ○ History of IE ○ PV ○ Congenital heart defects ○ s/p Heart transplant with assoc. valvulopathy ● Procedures ○ Dental procedures ○ I&D ○ Respiratory tract incision or biopsy ○ Insertion of cardiac prosthetic hardware ● Abx Prophylaxis ○ PO: amoxicillin ○ IV: ampicillin ○ Penicillin allergy: azithromycin/clindamycin



VII) REVIEW QUESTIONS

- 1) Which of the following is NOT a pathogen for **subacute endocarditis**?
 - a) *S. aureus*
 - b) *S. viridans*
 - c) *Klebsiella*
 - d) *Haemophilus*
- 2) The following are causes of damaged heart valves **EXCEPT**:
 - a) Infective endocarditis three years ago
 - b) Mitral valve regurgitation
 - c) Tetralogy of Fallot
 - d) Prosthetic valves
- 3) The following can cause spread of *S. aureus* into the bloodstream which may cause IE?
 - a) Dental cleaning
 - b) IV drug abuse
 - c) Colorectal cancer
 - d) Pyelonephritis
- 4) Which of the following is TRUE about *S. aureus*?
 - a) One of the pathogens that can damage healthy valves
 - b) Gram-positive
 - c) Most common bacteria causing IE on IV drug abusers
 - d) All of the above
- 5) Which is a clinical manifestation caused by increased immune complexes?
 - a) Janeway lesions
 - b) Roth spots
 - c) Regurgitation murmur
 - d) Shortness of breath
- 6) What diagnostic tests should you order if a patient with IE presented with altered mental status?
 - a) MRI of the brain
 - b) CT scan
 - c) Physical exam is okay
 - d) None of the above
- 7) A 58/F patient with history of IE, presented with fever. Her spinal MRI revealed abscesses on the vertebral discs. Upon fundoscopy, you observed small hemorrhages in the retina. You ordered blood cultures but only one of the cultures are positive. Her echo findings showed vegetations and perivalvular abscesses. Will you establish IE as diagnosis?
 - a) Yes, it met the Duke's criteria.
 - b) No, I will order more tests.
- 8) Aside from vancomycin, what antibiotics will you prescribe for a septic IE patient with prosthetic valves?
 - a) Cefazolin
 - b) Ampicillin-Sulbactam
 - c) Gentamicin
 - d) B and C
- 9) What antibiotic prophylaxis is prescribed PO if the patient has no allergies?
 - a) Ampicillin
 - b) Amoxicillin
 - c) Clindamycin

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