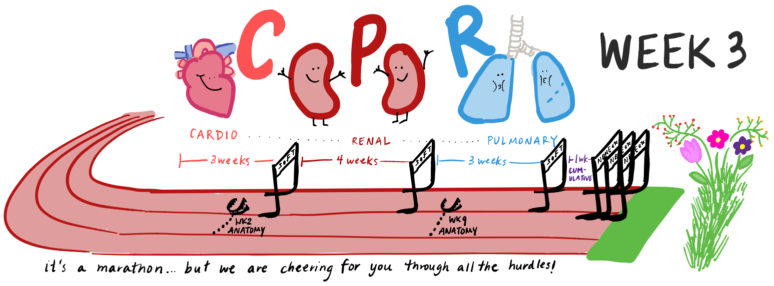


WEEK 3

it's a marathon... but we are cheering for you through all the hurdles!

O_2 supply	metabolic O_2 demand from myocardial cells
DIASTOLIC PERFUSION PRESSURE	WALL TENSION
CORONARY ARTERY VASCULAR RESISTANCE, BLOOD FLOW	HEART RATE
O_2 - CARRYING CAPACITY	CONTRACTILITY

This Week:

- Atherosclerosis + Coronary Artery Disease
- Stable / Unstable Angina
- Acute Myocardial Infarction
- Lytic Therapies
- Bradyarrhythmias
- Tachyarrhythmias
- Anti Arrhythmic Drugs
- Cardiac Hypertrophy
- Valvular Disease I - clinical
- Valvular Disease II - pathology

CARDIO-VASCULAR PRINCIPLES

all we want is adequate O_2 delivery to meet our tissue's metabolic demands! → the heart is very demanding **CARDIAC MUSCLE** cannot tolerate ischemic insults → **ISCHEMIA** - inadequate O_2 supply + impaired metabolite removal → + angina : presenting the clinical sx — cardiac-related chest pain → MYOCARDIAL **INFARCTION** follows coagulative necrosis PATHOPHYSIOLOGY, puts the heart @ risk for future events

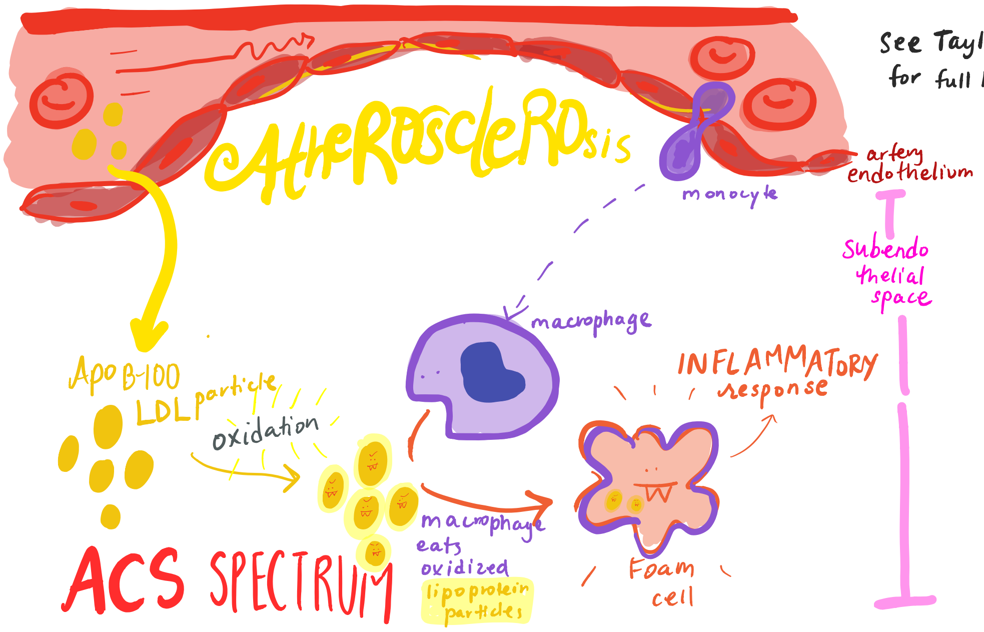
VASCULAR

beds are susceptible to atherosclerotic injury which compromises blood flow + O_2 delivery that meets metabolic demands of the heart

RISK FACTORS

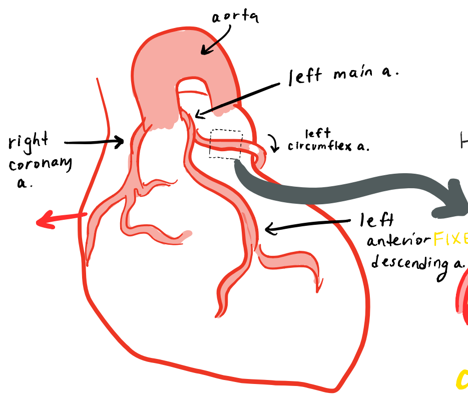
"non modifiable"
- age
- family hx
- ethnicity
- biological sex MALE

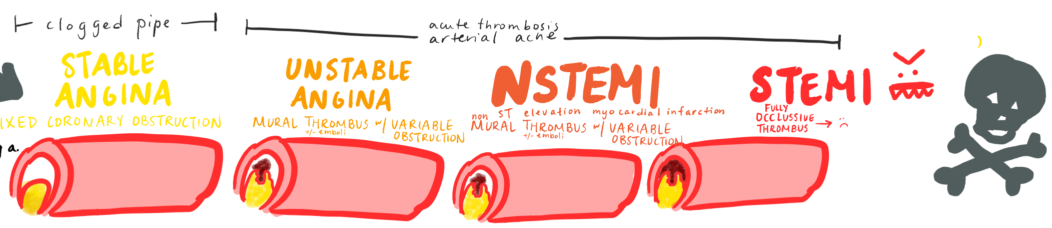
"modifiable"
- smoking
- elevated cholesterol
- sedentary lifestyle
- stress
- obesity
- insulin resistance
- diabetes
- alc. in excess



See Taylor's notes for full breakdown!

ACS SPECTRUM





STABLE ANGINA
- chest pain w/ predictable onset
- known triggers — stress, physical exertion
- relieved w/ nitroglycerin, rest

UNSTABLE ANGINA
- chest pain new onset, unpredictable
- pain occurs while resting — minimal exertion
- accelerating angina
- increasing severity
- no ECG changes / cardiac biomarkers

NSTEMI
- chest pain "white thrombi" (platelets)
- DO NOT GIVE THROMBOLYTICS !!! CAN CAUSE HARM
- · β blockers, nitrates
- · statins
- · anti coag/antiplatelets
- + CARDIAC BIOMARKERS! troponins
- + ECG changes ST depression
- SUBENDOCARDIAL — partial wall thickness, partial artery occlusion

STEMI
- chest pain red thrombi (fibrin + coagulation)
- · β blockers, nitrates
- · tPA + thrombolytics
- · anti coag/antiplatelets
- + CARDIAC BIOMARKERS! troponins
- + ECG changes ST ELEVATIONS
- TRANSMURAL (full wall thickness, full artery occlusion)

- Diffuse intimal thickening
- Extracellular lipid accumulation
- Leukocyte recruitment
- Intracellular lipid accumulation
- Inflammation
- Smooth muscle cell migration + proliferation
- plaque angiogenesis (VEGF)
- plaque mineralization
- cellular necrosis — cap thinning + plaque instability

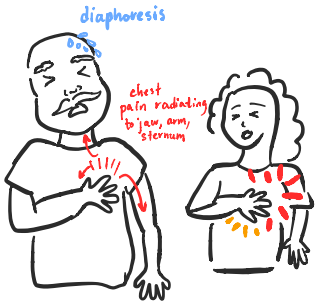
atheroma → OBSTRUCTION, DILITATION

acute events d/t plaque rupture — no clinical test for plaque vulnerability

so you've got

CHEST PAIN...

what's on the differential dx?



CLINICAL CLASSIFICATION

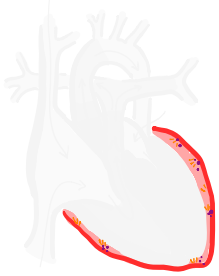
TYPICAL ANGINA (definite)
1) SUBSTERNAL CHEST PAIN w/ CHAR. quality & duration
2) PROVOKED BY EXERTION
3) RELIEVED BY REST/NITROGLYCERIN

atypical ANGINA (probable) — meets 2 of 3 above CRITERIA

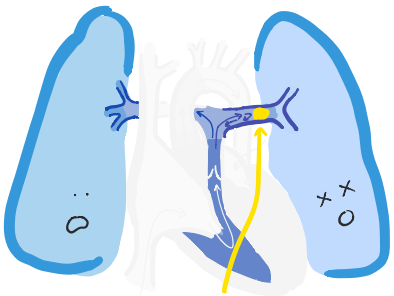
noncardiac CHEST PAIN — meets 1 or less of above CRITERIA

ENDOCARDITIS
often affects valves

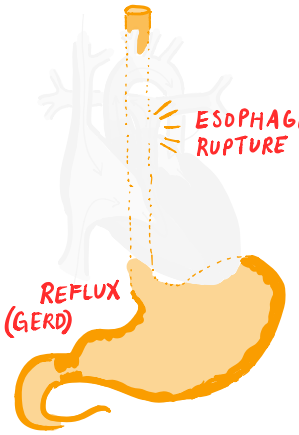
MYOCARDITIS



PERICARDITIS

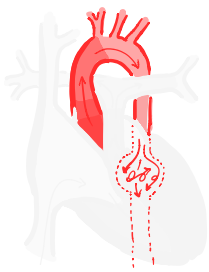


PULMONARY EMBOLISM

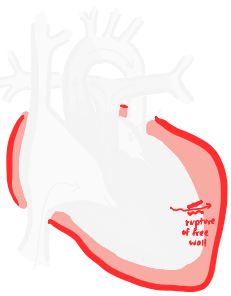


ESOPHAGEAL RUPTURE

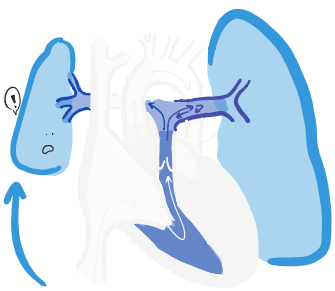
REFLUX (GERD)



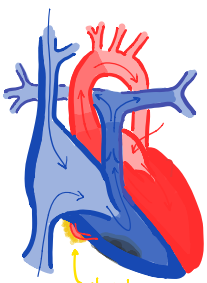
AORTIC ANEURYSM
can be anywhere along aorta!



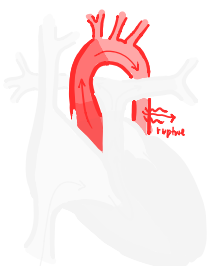
PERICARDIAL TAMPONADE



PNEUMOTHORAX
(collapsed lung d/t air entering pleural cavity)



Acute MYOCARDIAL INFARCTION



AORTIC DISSECTION

PRELOAD-DEPENDENT
bringing fluid into other interstitial space
offload filling pressures

NSTEMI Type II
lactate 2.5 poor tissue perfusion

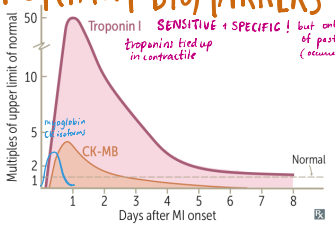
KEY POINT

Since MI's are extremely common + often have classic presentation, be expected to know detailed pathophysiology and/or given histological/EKG findings, estimate the onset of MI, so you can anticipate potential RISKS.

YOU DO NOT WANT TO MISS THIS DIAGNOSIS!

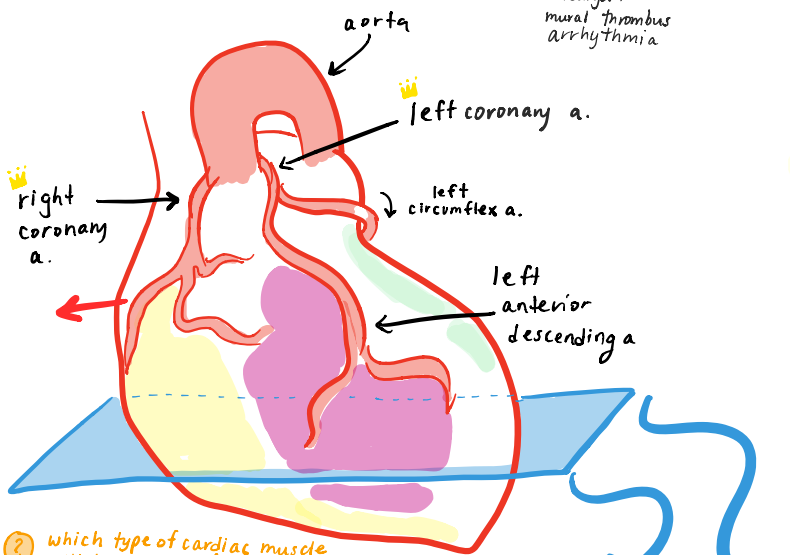
Acute MYOCARDIAL INFARCTION

IMPORTANT BIOMARKERS

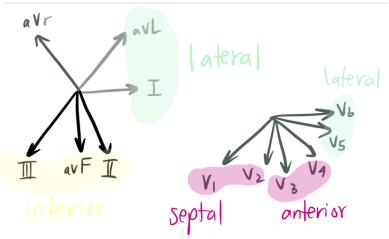


	HISTOLOGICAL changes of CARDIAC MUSCLE	PATIENT is @ risk of...	EKG
normal	—	—	normal
INSULT!	none	arrhythmia cardiogenic shock (if infarct large enough) Congestive heart failure	peaked T wave
minutes (min to <4h)			progression of ST segment elevation
hours (4h-24h)	coagulative necrosis loss of nuclei tissue architecture preserved	arrhythmia	loss of R wave Q WAVE formation
1-3 days	neutrophilic infiltrate	fibrinous pericarditis (chest pain w/ friction rub)	T wave inversion
4-7 days	macrophage infiltrate CARDIAC WALL IS SUPER WEAK	RISK OF RUPTURE to... ✓ CARDIAC MUSCLE free WALL → cardiac tamponade ✓ CHORDAE TENDINAE → mitral regurg ✓ INTERVENTRICULAR SEPTUM → "VSD"-like shunt	T wave normalization + persisting Q WAVE
1-3 weeks	fibroblast proliferation, granulation tissue		T wave normalization + persisting Q WAVE
months onward	connective tissue scar, fibrosis, collagen		

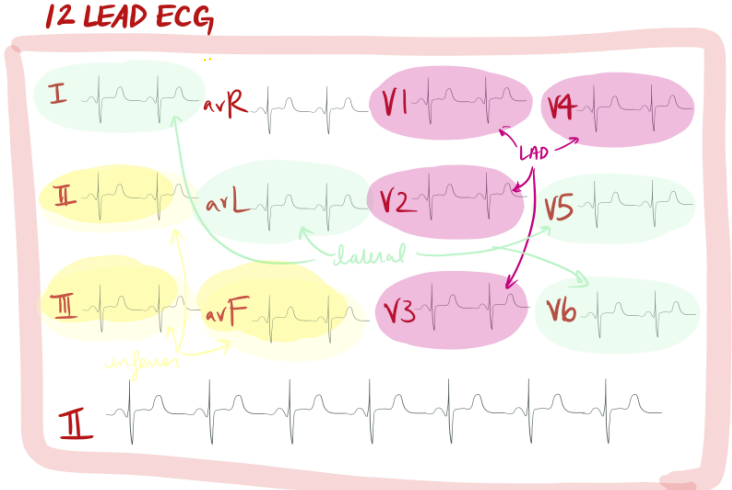
DRESSLER SYNDROME
aneurysm
mural thrombus
arrhythmia



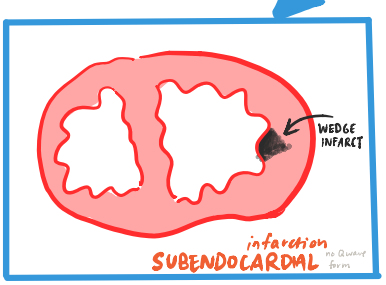
? which type of cardiac muscle will be affected first in AMI?
A. epicardium
B. myocardium
C. endocardium
D. valves



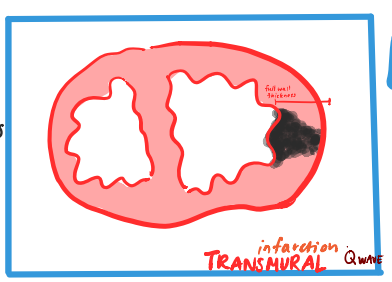
12 LEAD ECG



t = 1 hr



t = ~4-6 hours

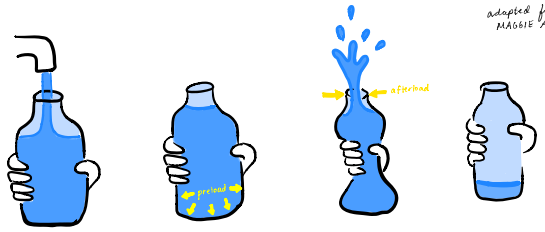


Location of AMI	Coronary artery INVOLVED
anterior	LAD
septal	LAD
lateral	LCx or diagonal
inferior	RCA or LCx
posterior	RCA or LCx

EKG Leads
INVOLVED (ST ELEVATION) → ischemia w/ no flow
ST depression → ischemia w/ partial flow

V1 V2 V3 V4
V1 V2
I, AVL, V5, V6
II, III, AVF
Tall R waves V1, V2
ST depression V1, V2, V3

CARDIAC HYPERTROPHY



adapted from MAGGIE AULET-EDDY '20

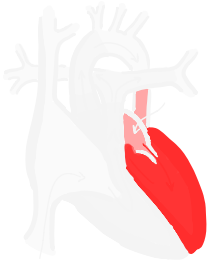
DIASTOLE — EDV — SYSTOLE — ESV

S2 — S1

Laplace's LAW determines wall tension

WALL TENSION = pressure × radius

WALL STRESS = $\frac{\text{pressure} \times \text{radius}}{2 \times \text{wall thickness}}$



isolate left ventricle

✓ normal

volume overload

increased DIASTOLIC pressure

increased DIASTOLIC 6

new sarcomeres added in SERIES to form longer myofibrils

chamber enlargement (a response to offset pressure)

eccentric left ventricle hypertrophy

VOLUME OVERLOAD

↑ incr wall thickness +
↑↑ chamber radius

pressure overload

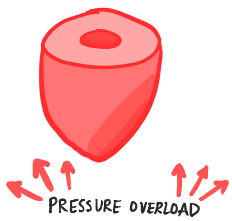
increased SYSTOLIC pressure

increased SYSTOLIC 6

new myofibrils added in PARALLEL

increased wall thickness

CONCENTRIC left ventricle HYPERTROPHY

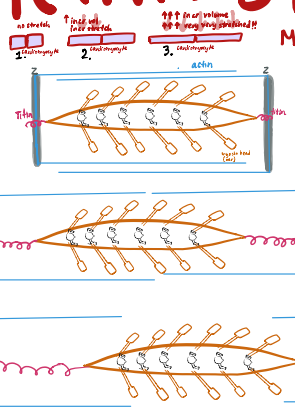


PRESSURE OVERLOAD

↑↑ incr wall thickness

FRANK-STARLING

MECHANISM + CURVES



1. NO ROOM TO MOVE! (NO STRETCH)
   little contraction force
   ✓ myosin crowded
   ✓ myosin already close to Z disk
   ✓ actin overlapping each other

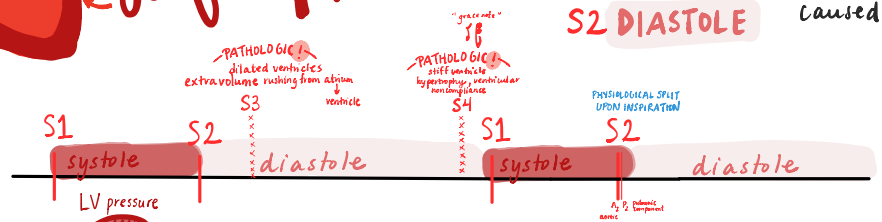
2. ★ OPTIMAL STRETCH / PRELOAD
   lots of contraction force
   ✓ actin within reach of myosin oars

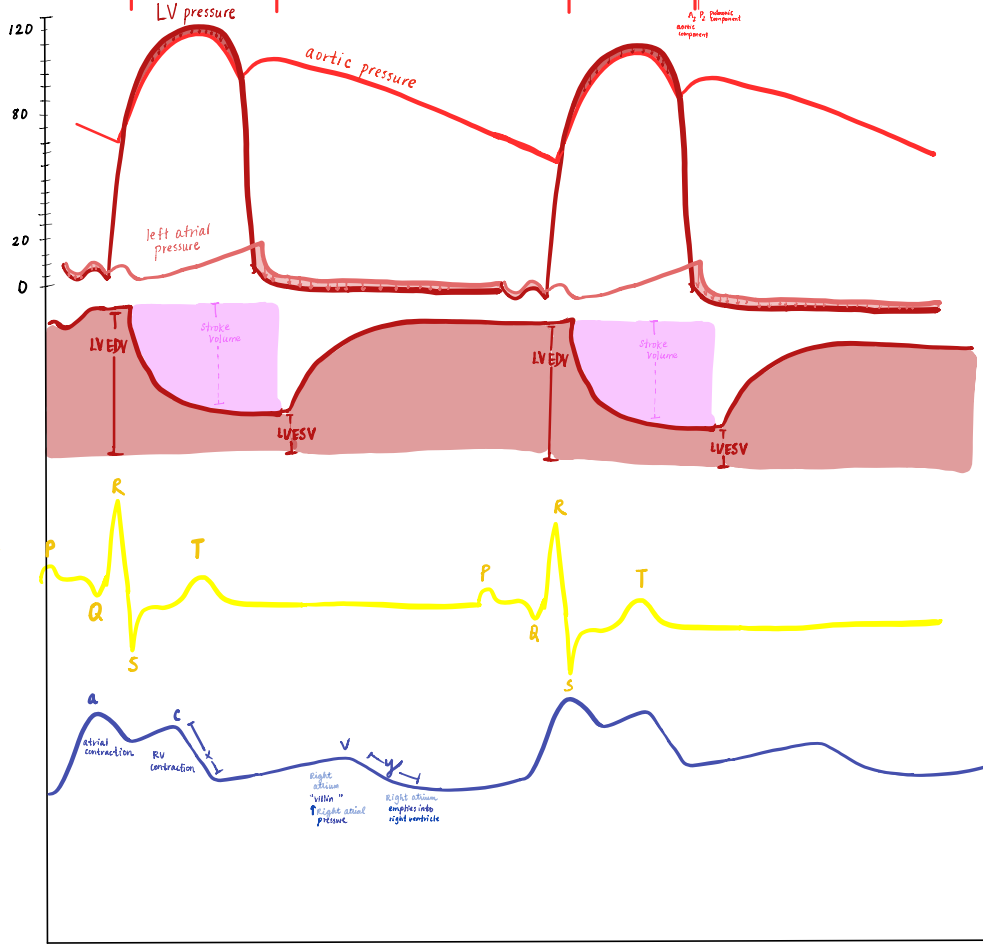
3. TOO SPACED OUT!
   no contraction force
   actin out of reach of myosin oars

Left Ventricular PRESSURE

S1 SYSTOLE caused by closure of _____ and _____

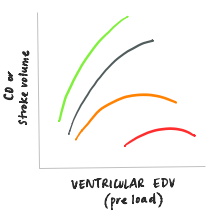
S2 DIASTOLE caused by closure of _____ and _____





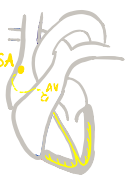
! at what point does the mitral valve close?
aortic valve open?
aortic valve close?
mitral valve open?

? what is isovolumetric contraction and where is it on the graph?



INCREASED CONTRACTILITY
digoxin
catecholamines
NE
Epinephrine

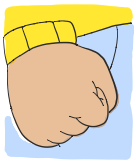
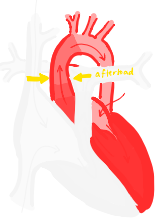
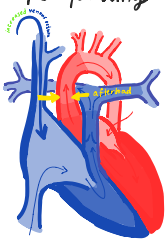
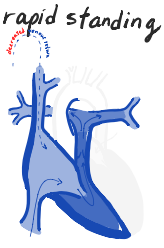
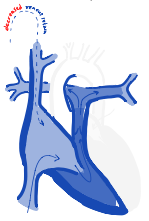
DECREASED CONTRACTILITY
MI → loss of functioning myocardium
β blockers (acutely)
CCBs (non dihydro)
dilated cardiomyopathy



KEY POINT

murmur sounds are NOT FIXED.

CERTAIN MOVEMENTS can increase or decrease murmur intensity

MOVEMENT TYPE	inspiration	expiration	passive leg raise	handgrip	rapid squatting	rapid standing	vasalva (phase II)
							
							
preload	increased	decreased	increased	–	increased	decreased	decreased
afterload	–	–	–	increased	increased	–	–

HEART MURMURS THAT INCREASE in intensity + sound

RIGHT HEART SOUNDS

LEFT HEART SOUNDS

HOCM

MVP

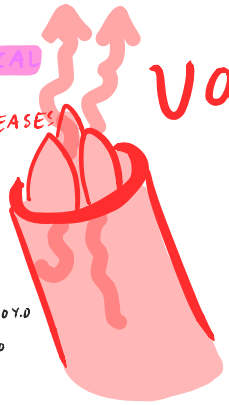
HEART MURMURS THAT decrease in intensity + sound

HOCM

MVP

KEY POINT

APPRECIATE THE GROSS HISTOPATHOLOGICAL CHANGES OF CLINICALLY RELEVANT VALVULAR DISEASES



valvular murmurs (WEEK 2) → valvular DISEASES (WEEK 3)

THE LIST

- Bicuspid aortic valve
- Calcified aortic stenosis
  - degenerative wear & tear >60 Y.O
  - d/t bicuspid aortic valve <60 Y.O
- Mitral valve prolapse
- Rheumatic Heart Disease
- infectious endocarditis
- noninfectious thrombotic endocarditis

STENOSIS (stiff) — valve should be more open

SYSTOLE

PREVALENCE
- aortic stenosis
- HOCM/hypertrophic cardiomyopathy (genetic / environment) ★
- pulmonic stenosis

DIASTOLE

PREVALENCE
- mitral stenosis
- tricuspid stenosis

REGURGITATION (floppy) — valve should be more closed

PREVALENCE
- mitral regurgitation
  - ↳ mitral valve prolapse ★
- tricuspid regurgitation

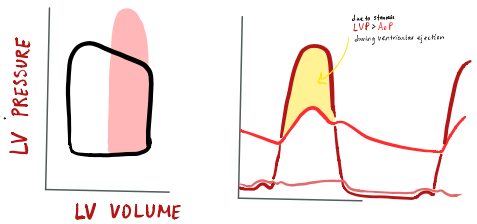
PREVALENCE
- aortic regurgitation
- pulmonary regurgitation

Bicuspid aortic valve ✓ VS Calcified aortic stenosis ✓

Bicuspid aortic valve

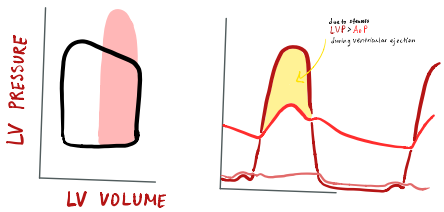
✓ congenital malformation ~1% in population

∴ coarctation of aorta
Turner (XO) syndrome
Thoracic Aortic Aneurysm
Aortic dissection
EARLY degenerative calcific.



Calcified aortic stenosis

✓
- degenerative wear & tear >60 Y.O
- may be d/t mechanical valve
- d/t bicuspid aortic valve <60 Y.O

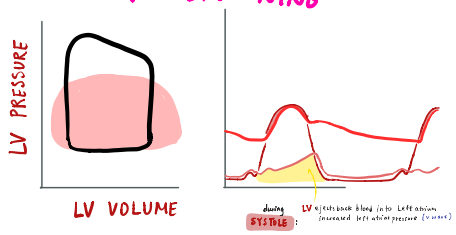


Mitral valve prolapse

HISTOLOGY OF "MYXOMATOUS DEGENERATION"
GROSS PATHOLOGY OF BALLOONING

✓ connective tissue genetic disorders
- Marfan's
- Ehler Danlos
- achondroplasia

✓ increasing regurgitation
Chordae tendinae rupture (!)
endocarditis
arrhythmia
thrombi



Rheumatic Heart Disease

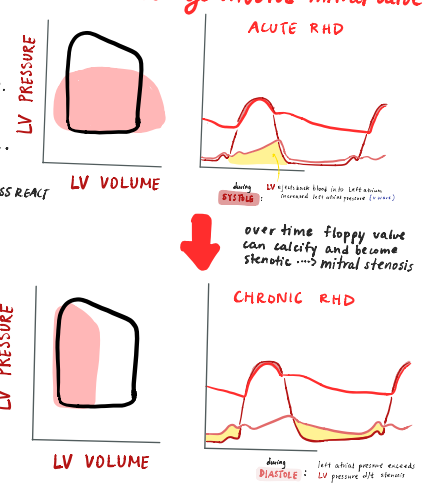
Group A Strep (S. pyogenes) always involve mitral valve

✓ children who do not get treated for strep pharyngitis develop Rheum. Heart D/D.

✓ typically from developing countries / resource-limited settings...

✓ anti-strep Antibodies against bacterial M protein CROSS REACT w/ human tissue (esp. in heart)

- Joints
- Pancarditis
- Nodules (subcutaneous / extensor surfaces)
- Erythema Migrans
- Sydenham Chorea
- Aschoff bodies (inflammatory cells found in cardiac histology)
- Anitschkow cells (modified macrophages "wavy appearance")



infectious endocarditis VS noninfectious thrombotic endocarditis

infectious endocarditis

S aureus — acute & aggressive
S viridans, Enterococcus — subacute, more "indolent"

- d/t mechanical valves
- d/t IV drug use
- damaged valves are EASY TARGETS for bacteria to grow
- dental procedures GONE AWRY

septic emboli travel in blood stream & get lodged in various microvasculature...

- retinal vessels → ROTH spots
- nail beds → SPLINTER HEMORRHAGES (literally can just present as SWOLLEN FINGER...)
- palms/soles → JANEWAY LESIONS
- spleen → SPLENIC INFARCT

fever should be present (+ signs of sepsis)

noninfectious thrombotic endocarditis

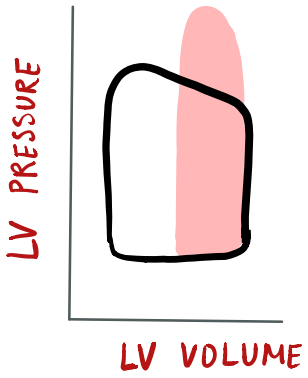
d/t hypercoagulable STATE

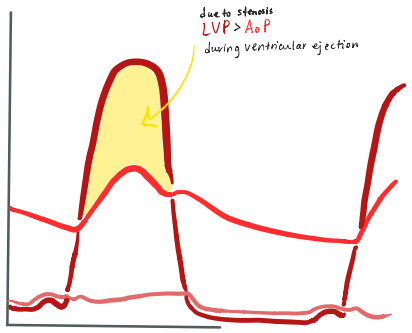
COAGULATION cascade — dysregulated

genetic (1°)
- FACTOR V LEIDEN
- PROTHROMBIN MUTATION

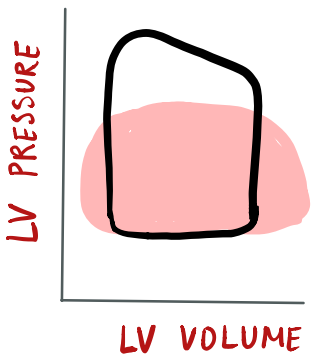
acquired (2°) → VTE, DVT are common complications
- LUPUS, ANTI PHOSPHOLIPID ANTIBODY
- TRAUMA
- MALIGNANCY
- PREGNANCY
- PROLONGED BED REST

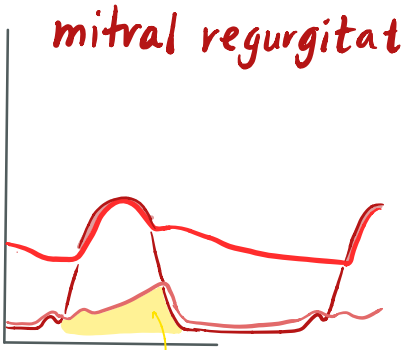
aortic stenosis





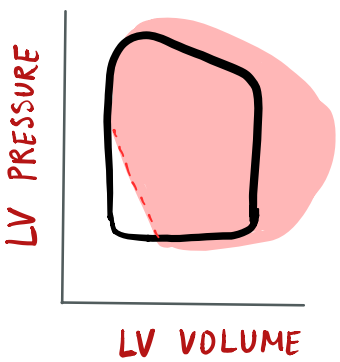
mitral regurgitation

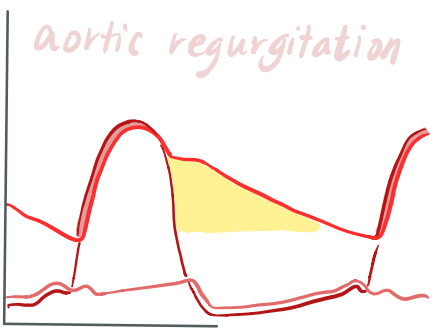




during **SYSTOLE**: LV ejects back blood into Left atrium
increased left atrial pressure (v wave)

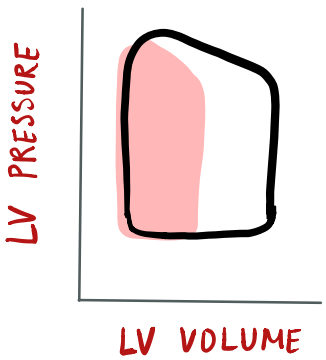
aortic regurgitation

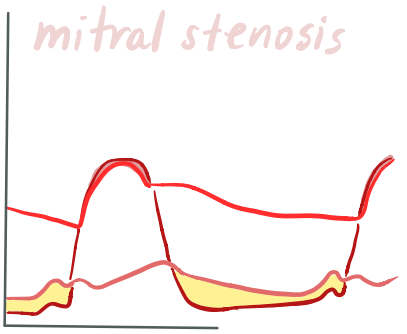




during **DIASTOLE**: blood flows backwards from aorta into LV. Left atrial pressure can increase from backflow
aortic diastolic pressure decreases but aortic systolic pressure increases → WIDE pulse pressure

mitral stenosis





during **DIASTOLE**: left atrial pressure exceeds LV pressure d/t stenosis

NOW ANNOTATE

stroke volume
EDV
ESV
calculate CO, EF!

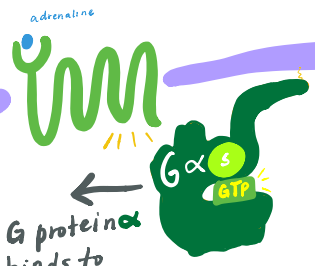
SYMPATHETIC ADRENERGIC aka stress - MOLECULAR PHYSIOLOGY

G_s

↑ cAMP

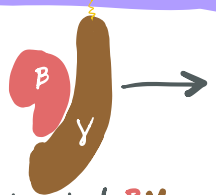
↑ protein KINASE A activity

1. ligand binding activates

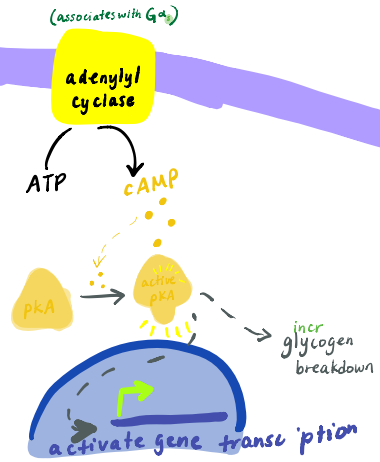


2. G protein α binds to activated GPCR

Gα: inherent GTP (active) to GDP (inactive) activity



3. activated βγ separates & acts on downstream targets

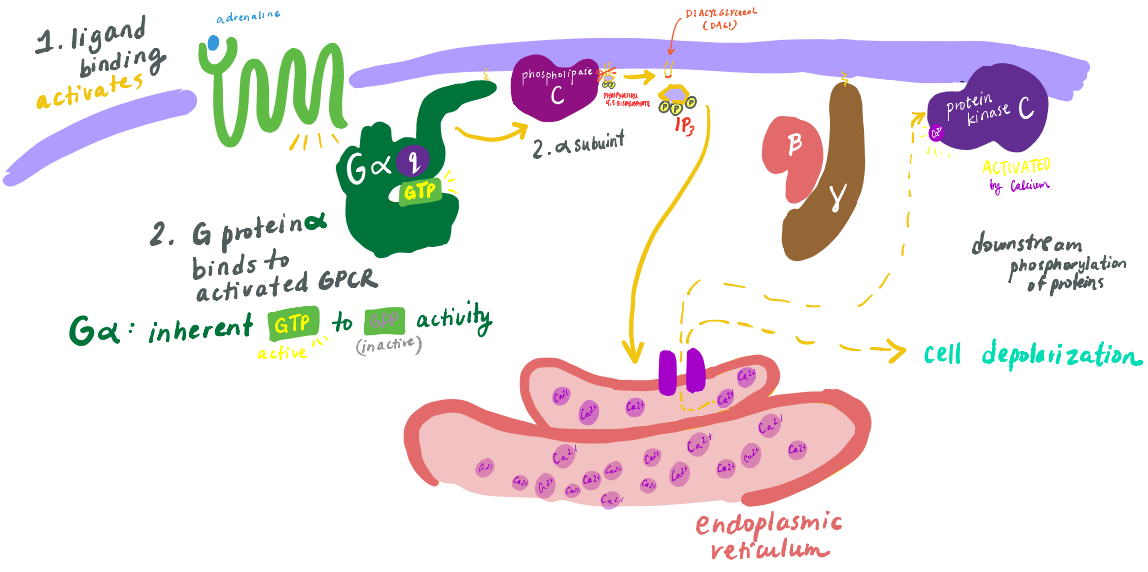


G_i

↓ cAMP

↓ protein KINASE A activity

G_q



↑ IP_3

↑ phospholipase C activity

Catecholamines BIOSYNTHESIS