PULMONARY

Mean Pulmonary Artery Pressure

MPAP - LAP = CO × TPR

Systemic: High Resistance, low compliance
Pulmonary: Low Resistance, high compliance

MAP = CO x TPR
(CO = SV x HR)

PP = SV / compliance = ΔV / ΔP → ★ stiff vessels = ↑systolic ↓diastolic

MAP = Diast. P + ⅓ PP

SV = EDV - ESV EF = SV / EDV

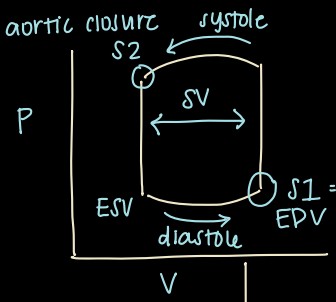
FLOW
Q = Pressure gradient (ΔP) / Resistance = ΔPr⁴ / ηL ← diameter profoundly changes flow

★ if BP ↓ then ↓CO
CO ↓ caused ↓BP
HR ↑ bc MAP = CO×TPR

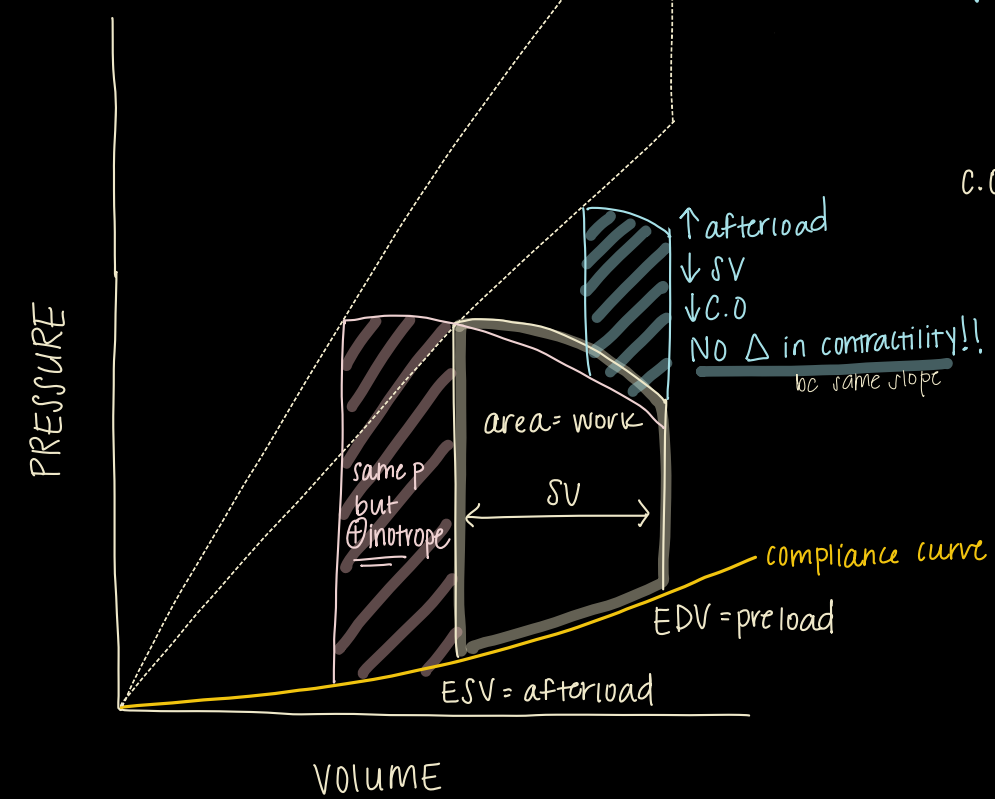
★ if ↑BP & ↑CO
↑BP caused by ↑CO

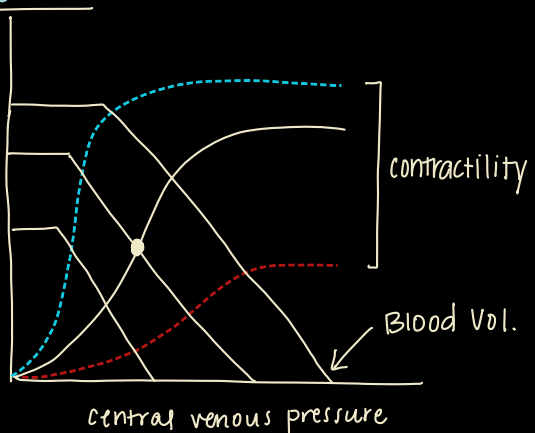
★ if ↓BP, ↓CO, ↑HR
what's compensating for ↓CO?
↑TPR bc MAP = CO×TPR

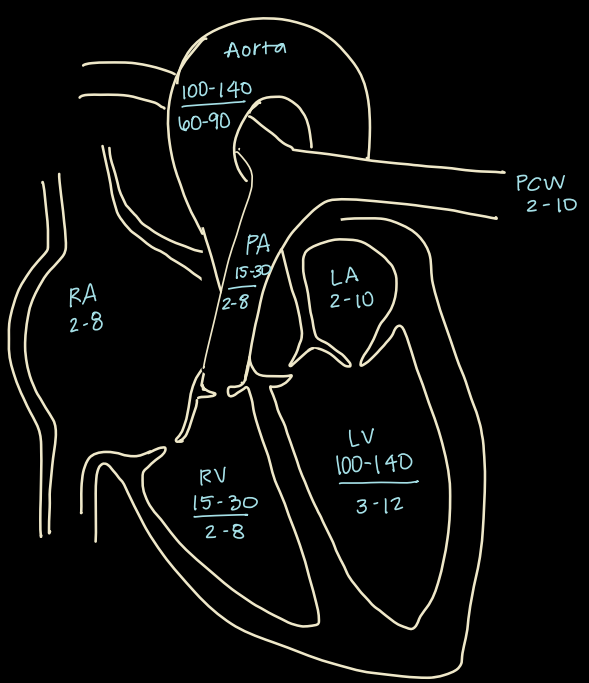
★ if ↑EDP, ↓EDV, ↓MAP
= ↓compliance



PV LOOPS







★ RRP = AP but not normal = WEAK CONTRACTION

HY L2
PCW = LA pressure
S1/S2 Heart Sounds
PV loop
EDV/ESV/SV relationship

↑afterload = ↓SV

Antiarrythmia Drugs

II & IV = rate control

I & III = rhythm control

II = β-blockers → block sympathetic activation of SA & AV

★amio I, II, III & IV — LOW RISK OF TORSADE

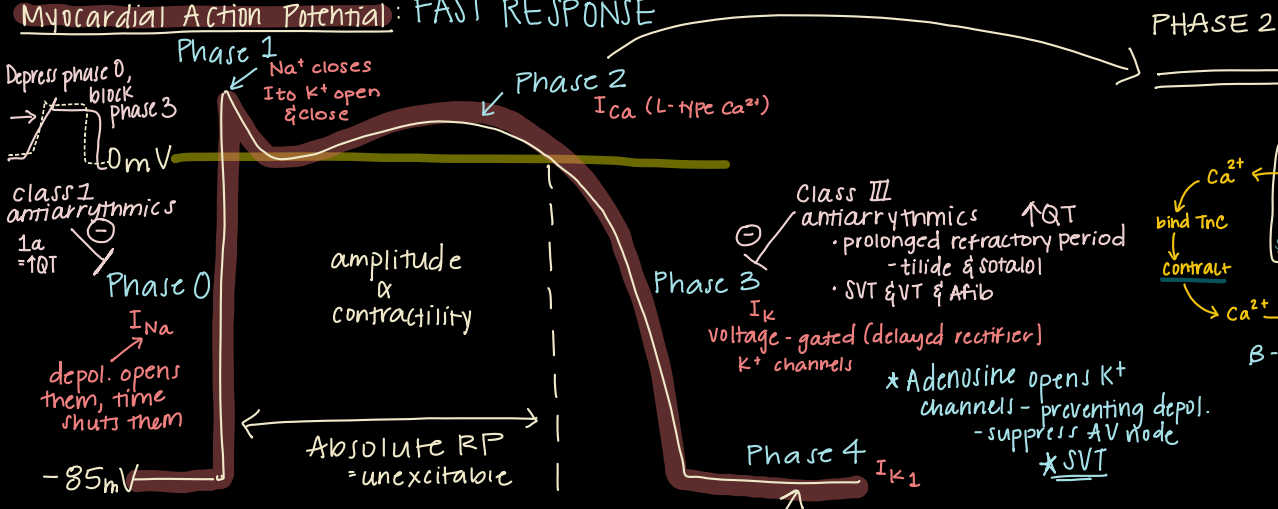
K⁺ channel block + β-block & Ca^{2+} channel block

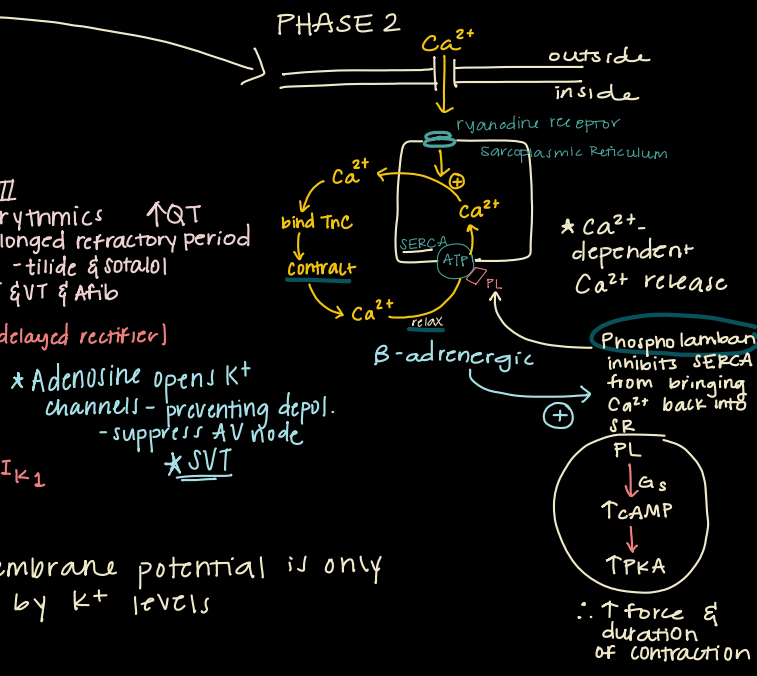
- Neuro toxicity
- grey corneal deposits
- Thyroid problems
- pulmonary fibrosis
- HB ; CI in HF

CP450 inhib.

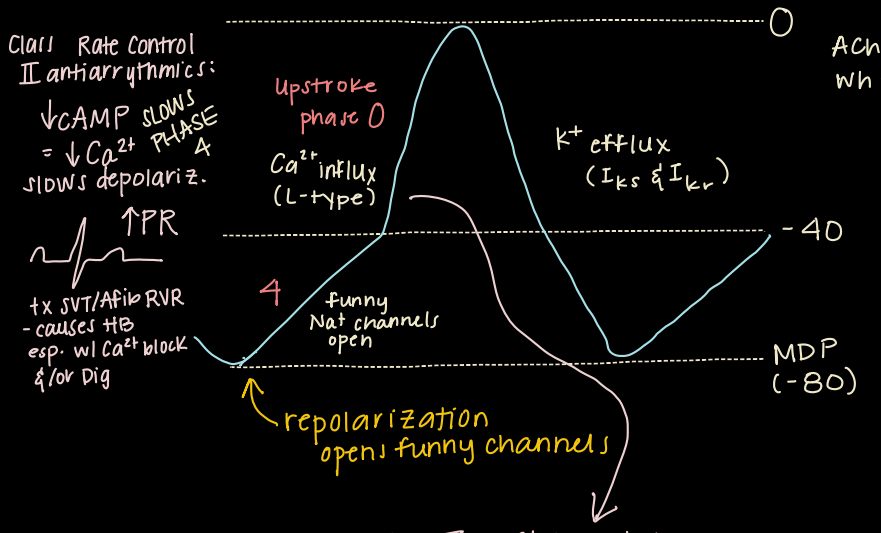
★shellfish allergy★ (iodine)

Myocardial Action Potential: FAST RESPONSE





PACEMAKER CELLS: SLOW RESPONSE



ACh makes MDP more negative, which slows HR

= overdrive suppression via Na^+/K^+ ATPase working harder @ latent pacemakers, making MDP more ⊖

Class III : Ca^{2+} channel blockers

SLOWS PHASE 0

- diltiazem & verapamil
- block L-type Ca^{2+} channels
- prolonging phase 4 = ↓sinus rate
- ↑PR (suppress AV) → can cause HB
- SVT/Afib w/ RVR

TBL:

late phase of vent. repolarization = U-wave

AFIB Tx: Beta-blockers, Ca^{2+} blockers, Amio, Digoxin + anticoag.

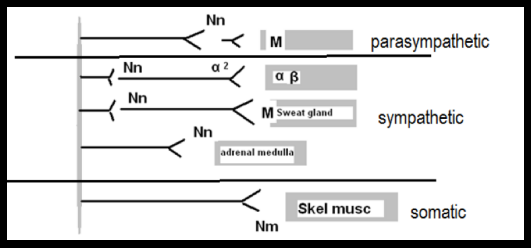
L11 Mechanisms of Arrhythmias

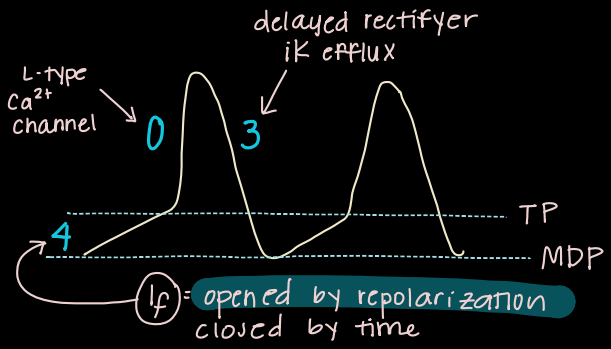
*ischemia @ SA node: ESCAPE RHYTHM

junctional rhythm

*ischemia @ AV node:

1°, 2°, 3° AV Blocks





WBOT

* modulates but DOES NOT create pacemaker

∴ if you stop the funny current, you will NOT stop the heart (not essential)

* (PSNS) cholinergic stimulation → M2 → DECREASE HR

* sympathetic stimulation → β1 → INCREASE HR

* Purkinje cells = slower bc more ⊖MDP

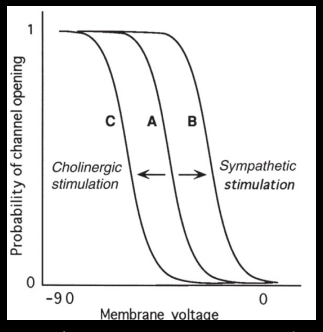
WBOT

* overdrive suppression: due to ↑Na^+/K^+ ATPase pushing cells more ⊖ MDP ∴ can't initiate their own AP

* if you give a pt ACh, their HR will ↓ bc there will be ↑activation of M2 rec.

* EAD = prolonged AP → TORSADES

* DAD: Ca^{2+} overload → VT, dig tox



When myocytes aquire phase 4 depolarization = Ectopic Tach

can be caused by anti-arrhythmic drugs

* Functional conduction block = acute ischemia → polymorphic TORSADES

* Fixed conduction block = scar/fibrosis → monomorphic (vtach) (healed MI)

WBOT

ECGs:

LCA LAD & septal aa. → * Septal: V_1, V_2

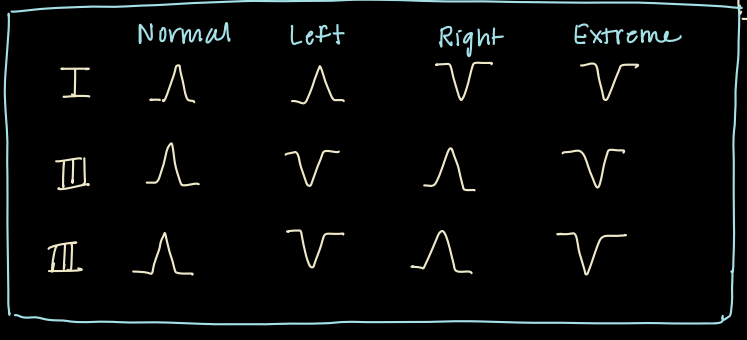
LCA LAD & diagonal aa. → * Anterior: V_3, V_4

LCA Circumflex a. → * Lateral: V_5, V_6, I, aVL

RCA Post. Descending a. → * Inferior: II, III, aVF

HY

I lateral		V1 septal	V_4 Anterior
II inferior	aVL lateral	V_2 septal	V5 antero-lateral
III inferior	aVF inferior	V_3 Anterior	V6 antero-lateral



L12 Atherosclerosis & Thrombosis

* causes of endothelial injury: ① Predisposing factors (HTN, DM) ② Hypercholesterolemia ③ Hemodynamic disturbance
damaged barrier = leaking lipids

* Arteriolosclerosis = small arterioles
① Hyaline: thick pink hyaline surrounding vessel = benign HTN & DM
② Hyperplastic: onion skin, prolif. of smooth muscle = malignant HTN
③ Mockenberg: Medial calcium deposition W/O vessel occlusion
] can cause ischemic injury.

* Predisposition: ** WBOT
↑ Lipoprotein (a) = homolog to plasminogen & inhibits fibrinolysis & ↑ MØ uptake of lipids

* Complications of atherosclerosis:
① stenosis
② Acute Plaque Change (via chemical factors or physical stress)
· Plaque Rupture → THROMBUS
· Erosion / ulceration → THROMBUS
· Hemorrhage
THROMBUS → Proliferate / Embolize / Dissolution / Organize
③ Aneurysm - destruction through vessel wall (media)
④ Vasoconstriction

Only arteries have internal elastic lamina

Normal —(oxidized LDL in intima, foam cells)→ Fixed coronary obstruction (angina)
Fixed coronary obstruction → Plaque Disruption / Severe fixed Coronary obstruction (chronic IHD)
Plaque Disruption → Mural thrombus w/ variable obstruction = unstable angina or acute subendothelial / Occlusive Thrombus = acute transmural MI or sudden death

Atherosclerosis [Response to injury, hypercholesterol, or hemodynamic disturbances]
① injury → LDL accumulates in INTIMA
② endothelial dysfunction (↑permeability)
③ MØ activation
④ MØ eat lipids → foam cells
⑤ sm proliferation, collagen & ECM deposition

* Normal Endothelium = ANTITHROMBOTIC
* - ANTI-platelet = PGI_2, NO, ADP
* - ANTI-coagulant = thrombomodulin, protein C, tPA

* Injured endothelium ↑ischemia via ① vasoconstriction = TXA & serotonin ② vWF exposure

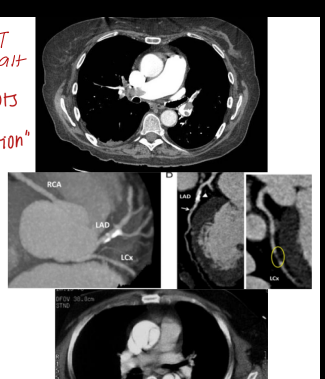
---

L10: Imaging
to determine EF (most accurately) = LV scintigraphy

SPECT Perfusion scintigraphy: know diff. between infarcted & ischemic tissue

WBOT
- If myocardium does not take up the radiotracer in the resting state, it is because there is non-viable myocardium, ie - infarct = dead
- If the myocardium takes up radiotracer at rest, but not during stress, it is because of inadequate blood flow during stress, ie - ischemia

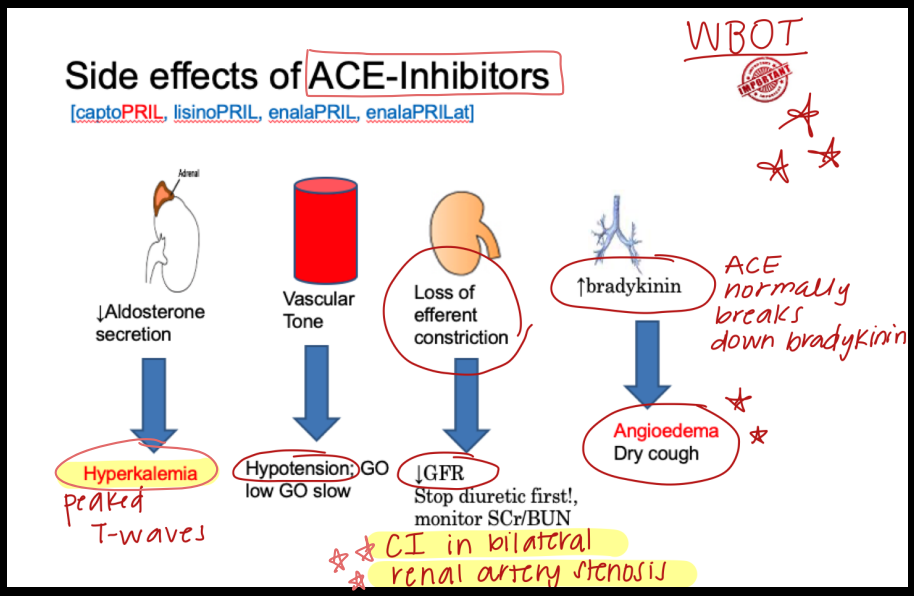
WBOT "Triple rule-out"
use a CT w/ contrast
* "two clots & a dissection"
- CT angiogram thorax (contrast)
  - Pulmonary arteries for embolus
  - Coronary arteries for obstruction
  - Aorta for dissection
- For acute chest pain of indeterminate cause
- Requires immediate reading capabilities by radiologist and/or cardiologist
- Requires on-site reconstruction of coronary artery portion of the exam



PHARM:

When to NOT use β-block

- DM
- CHF
- lung issues (asthma)
- Brady (HB)
- vasospastic angina



VLDL inhibitors:

Mipomersen inhibits ApoB

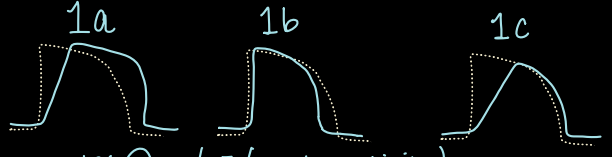
Lomitapide binds MTP

- Homozyg. familial hypercholesterolemia

SE: ↓ADEK
↓LFT (Ø Liver failure)

Fish Oil: ↓TG by regulating TFs SREBP$_{1c}$ & PPARα
may raise LDL, ↑risk of bleeding
Ø in familial hypercholesterolemia

ANTIARRYHTHMICS



Class I

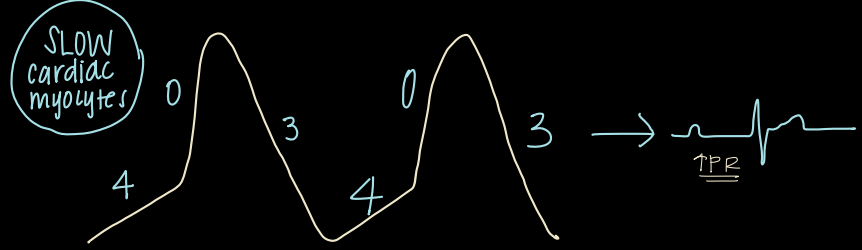
→ Na^+ channel blockers (so also decreases slope in slow myocytes @node = ↓automaticity)

slow phase 0, block phase 3 of fast myocytes = ↑QRS (&QT in 1a)

Class II

→ β-blockers ↓cAMP = ↓Ca^{2+} release

slows phase 4 of slow myocytes = ↑PR

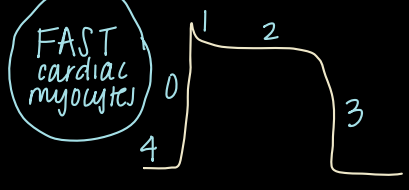


Class III

→ K^+ channel blockers

Prolong phase (3) of fast myocytes = ↑QT → torsades!

class 3 = phase 3

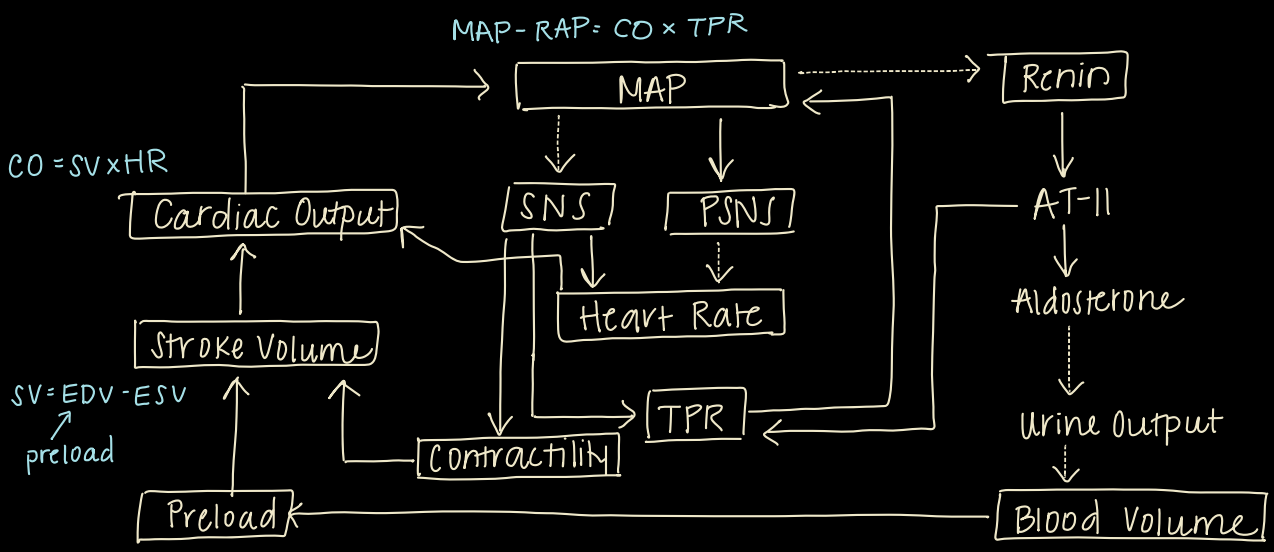


Class IV

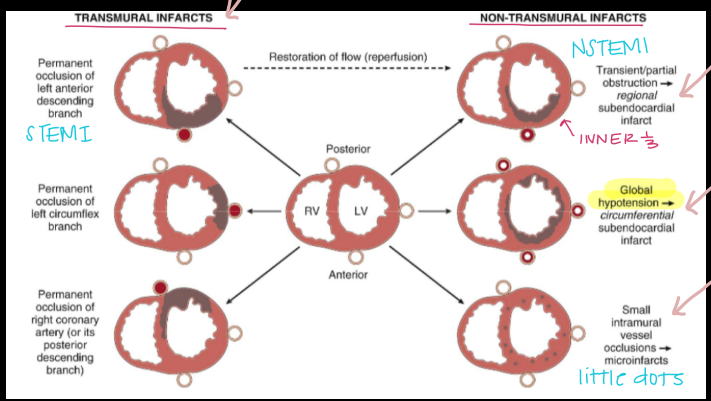
→ Ca^{2+} channel blockers

slows phase 0, prolong phase (4) in SLOW myocytes = ↑PR

class 4 = phase 4



L13 IHD



ST-elevation
+ troponins

ST depression
+ troponins

opioid overdose, ↓BP

emboli
or Syndrome X
(microvascular angina)

MORPHOLOGIC FEATURES of Myocardial infarction (see table 12-5 in Robbins, page 544)

- GROSS (MACROSCOPIC)
  - At autopsy, gross changes may not be seen for up to 12 hours after infarct, 6 at the earliest.
  - 12 to 24 hours: Dark mottling
  - 1 to 10 days: yellow-tan discoloration and softening (necrosis).
    - 1-3 days: mottling with yellow-tan infarct center
    - 3-7 days: Hyperemic border; central yellow-tan softening
    - 7-10 days: maximally yellow-tan and soft, with depressed red-tan margins
  - 10 to 14 days: Red-gray depressed infarct borders
  - 2 to 8 weeks gray-white scar, peripherally to central.
  - Greater than 2 months-white scar.

WBOT · > 24 HRS · variable

Contraction band necrosis (CBN) — Hypercontraction

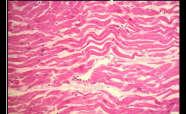
- **Contraction band necrosis**: occurs in myocytes that are **already irreversibly injured** and **then re-perfused** → ↑Ca^{2+} → ↑contract
  - Also seen in sudden cardiac death with V. fib, increased catecholamines
- **Appearance:** Dark eosinophilic stripes across cardiomyocyte
- **Composition:** closely packed sarcomeres due to hypercontraction of myofibrils
- **Pathogenesis:**
  - Irreversibly damaged myocytes have plasma membrane defects
  - during reperfusion, increased amounts of calcium enter the cell causing hypercontraction of myofibrils

12-24 HOURS

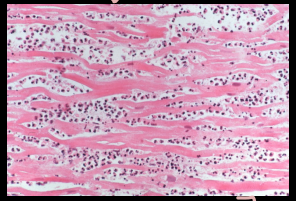
WBOT

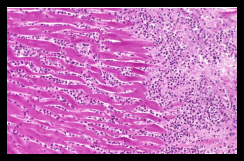
L14 IHD II

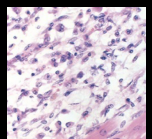
Microscopic changes during MI:

4-12 Hrs
wavy → coag. necrosis (edema & hemorrhage)

eosinophilic & anucleate cells = PINK

12-24hrs
coag. necrosis + NØ = contraction band necrosis ★
irreversibly damaged then reperfused w/ ↑↑Ca^{2+}

1-3 days
↑PMN


3-7days
Dying NØ
MØ lining up


7-10 days
MØ phagocyte = dark (filled w/ hemosiderin)


★ Syndrome X = microvascular → little dots everywhere
- due to vasoconstriction when there should be dilation
- thickened media / fibromuscular dysplasia

No evidence of CAD on angio but spasm when given vasodilators

IHD

Stable Angina: gets better w/ rest/nitro
- >70% stenosis
- NO EKG changes

Unstable Angina (includes prinzmetal variant) ← cigarette smoking
- tx w/ dipines
- >90% stenosis
- ST seg. depression
- NO BIOMARKERS bc NO NECROSIS just ISCHEMIA

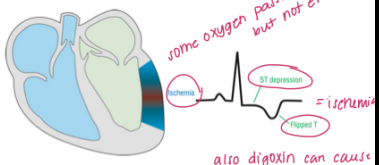
NSTEMI = subendocardial → caused by prolonged hypotension
- ST depression
- ⊕ biomarkers (bc HELLO NECROSIS)

STEMI = transmural
- ST elevation
- ⊕ biomarkers

= injury or infarction
- reversible
- irreversible

Ischemia

Area of ischemia is more negative than surrounding normal tissue
Causes ST depression; T wave is flipped
Causes repolarization to occur along abnormal pathway



also digoxin can cause

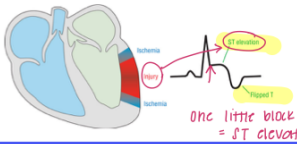
Injury = ELEVATION

Zone of injury does not repolarize completely

Remains more positive than surrounding tissue, leading to ST elevation

T remains flipped (abnormal repolarization paths along injured/ischemic areas of myocardium)

=Reversible damage

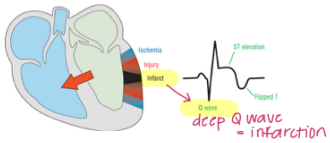


one little black high = ST elevation = injury

Infarction = DEAD

ST Elevation + Q-wave

Dead tissue NECROSIS → irreversible damage
Does NOT generate any action potentials; electrically neutral
Acts like electrical "window" in wall of myocardium
- An electrode can look through and see opposite wall.
- Unopposed, positive vector produces Q wave.



deep Q wave = infarction

L Recurrent = aorta

R Recurrent = subclav

HY L3 Anatomy Review

WBOT

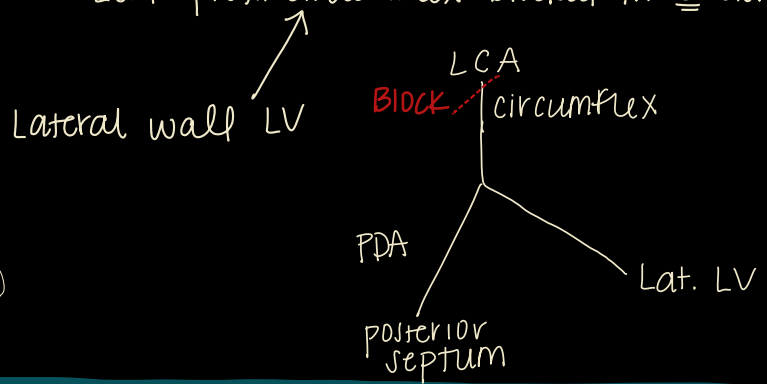
* Recurrent laryngeal (from vagus) "pt has SXS of aortic dissection & hoarseness" = LEFT recurrent around aorta
* Brady / ischemia @ AV/SA = RCA
* RCA → PDA → RV
  - ↑ posterior + post. septum
  - ↓ inferior = leads II, III, aVF

KNOW HOW IT CHANGES IN LEFT DOM HEART

WBOT

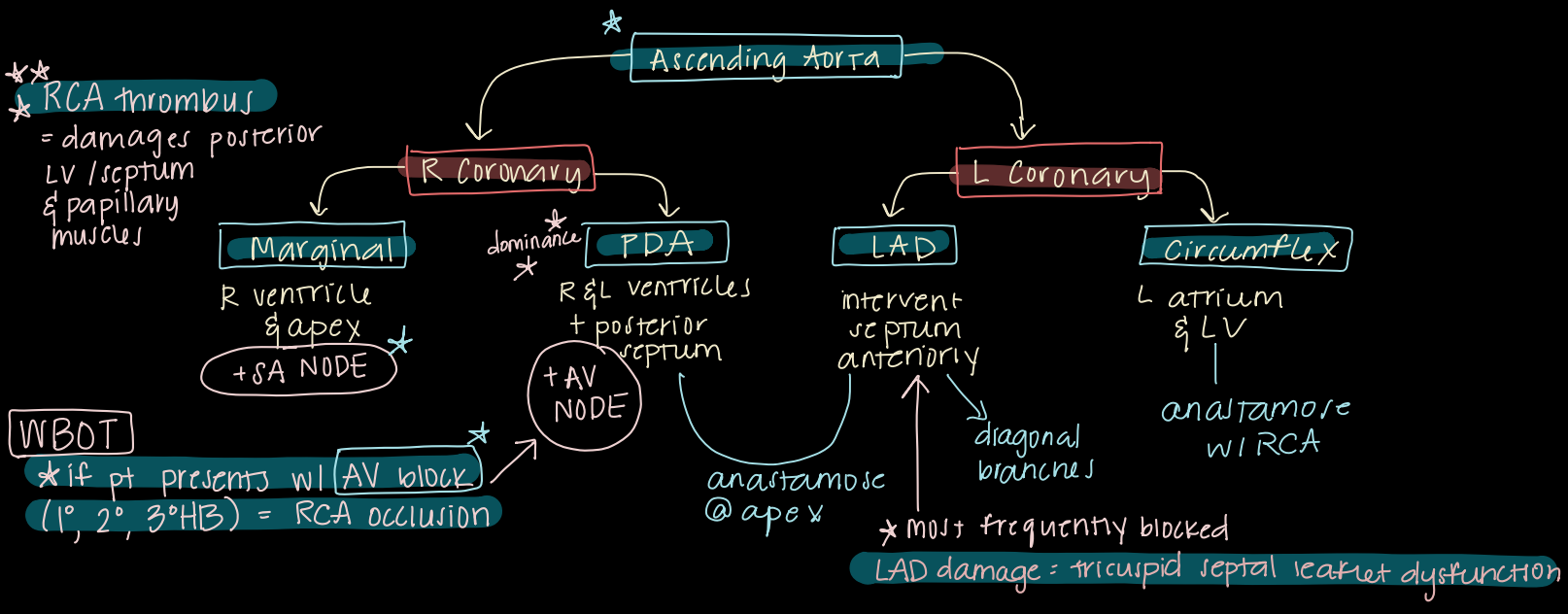
* sympathetics = T1-T6
* parasympathetics = VAGUS

Left prox. circumflex blocked in L dom heart



Normally R Dominant

* RCA = Posterior + septum (includes PDA)
* LAD = Anterior + septum
* circumflex = Lat. LV



RCA thrombus = damages posterior LV / septum & papillary muscles

WBOT

* if pt presents w/ AV block (1°, 2°, 3° HB) = RCA occlusion

LAD damage = tricuspid septal leaflet dysfunction

Tricky PQs:

* IN pts w/ CAD, atherosclerotic plaque begins w/ endothelial damage (INTIMA)
  - → MΦ show up → foam cells
  - → triggers release of cytokines & growth factors
  - → activates smooth muscle cells to produce collagen which forms fibrous cap over the atheroma

L07 Cardio Pharm

→ α_1, q → ↑IP3/DAG/Ca^{2+} = vasoconstrict
→ α_2, i → ↓cAMP = ↓NE release
→ β_1, s → ↑cAMP = ↑renin, ⊕ inotrope/chronotrope
→ β_2, s → ↑cAMP = broncho/vasodilation

WBDT
* β-blockers = CI in COPD
* L-type Ca^{2+} block (VD) CI in CHF & AV blocks

* PHARM PHYSIO REVIEW:
-vasoconstriction on VEINS = ↑ESP
-vasoconstriction on ARTERIES = ↑EDP

* Ca^{2+} Channel Blockers:
* Verapamil & Diltiazem = Class 4 antiarrhythmics (CI in CHF & AV Block)
  - L-type Ca^{2+} channel block @ SA/AV node
  - ↓phase 0 of slow cardiac cells
  - ↓C.O
  (VD brakes your ♡)

* -dipines
  - arteriole dilation SE: peripheral edema
  - ↑C.O.

aldosterone ↑Na^+/K^+ ATP-ase in principle cells (reabsorb Na^+ & H_2O to ↑BP)

* K^+ channel openers (for pts whom ACE-I are CI) Ex: pregnancy
* Hydralazine/Minoxidil (K^+ opening → inhibits Ca^{2+} release from SR)
* SE: reflex tachycardia & edema + postural hypotension

* ACE-inhibitors (-pril)
* peaked T-waves (hyper K^+) + ↓GFR + Hypotension + ↑Bradykinin (Angioedema)

* ANP = ↑GFR ↓BP
* Neprilysin inhibitors Sacubatril inhibit degradation of ANP

* Vasopressin = ADH
* V_2 receptor activation (G_s) ↑cAMP → AQP channels = REABSORB H_2O (NOT Na^+) = ↑BP

L08 Pharm of Hyperlipidemia

* Statins (1st line) ↓↓LDL ↓TG ↑HDL
* HMG-coase inhibitors decreases cholesterol synthesis
* Advantages: ↓inflammation of plaque, ↑stability, ↓thrombosis, reverses endothelial function
* SE: Myopathy & rhabdomyolysis

(Statins improve mortality of CAD)

* Fibrates ↓↓TG (esp >500)
* MOA: ① ↑LPL in muscle // agonist of PPARα
  ② ↑FFA oxidation
* SE: ↓Liver function, gallstones

* Niacin (B_3) ↑↑HDL ↓LDL ↑HDL
* MOA: inhibits HSL in adipose ∴ ↑ApoA clearance
* SE: Flushing, Hyperuricemia (GOUT), hyperglycemia (Diabetes)

* Bile Acid Sequestrants ↓↓LDL (-chol)
* MOA: bind anions in intestine = ↓cholesterol = ↑LDL receptors
* SAFE IN PREGNANCY

* Interactions: ↓absorption of ⊖ charged drugs [Warfarin, Digoxin, Thiazides]
* SE: can ↑TG (CI in pts TG ≥ 400 & familial hypercholesterolemia)

* Cholesterol Absorption Inhibitor: Ezetimide ↓LDL
  * MOA: inhibits uptake by NPC1L1 receptor

* VLDL secretion inhibitors ↓LDL
  * Lomipitapide: binds MTP ↓LDL, ↓ADEK absorption
  * Mipomersen: inhibits ApoB gene exp. = ↓VLDL, ↓ADEK absorp

* Fish oil ↓TG may ↑LDL
  * regulates SREBP-1c & PPARα (↓VLDL synth)
  * SE: bleeding

* PCSK9 inhibitors ↓↓↓ LDL
  * Ab prevent cleavage of hepatic LDL receptors
  * Hetero & homozyg. fam. hypercholesterolemia

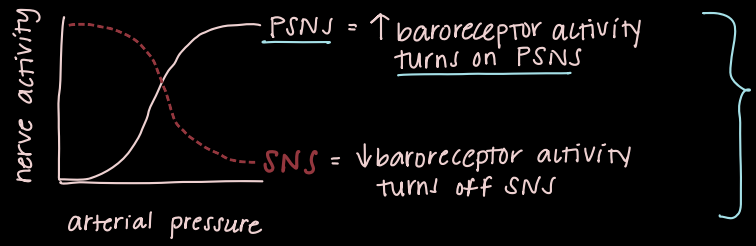
L09 Autonomic Control of Circulation

* Muscarinics = GPCR (M_1 M_3 M_5 = ↑IP_3/DAG) vs (M_2, M_4 = ↓cAMP)
  Nicotinics = ion channels (NOT GPCR)

M_1	Q
M_2	I
M_3	Q

* α_1 = vasoconstrict VASCULAR smooth muscle // RELAXATION of INTESTINAL smooth muscle (decrease motility so you don't pooping while running from a bear)

*



∴ if you volume expand someone you ↑C.O. & BP so HR ↓

* PSNS dominates HR

* postural orthostatic tachycardia syndrome: young female; HR ↑30bpm W/O ↓BP = EXCESS SNS activity
* neurogenic orthostatic hypotension: ↓BP when standing W/O HR reponse
  ↓systolic ≥ 20 mmHg
  ↓diastolic ≥ 10 mmHg
  = predictor of mortality

* ↓SNS = orthostatic hypotension, ↓sweating, ptosis, ejac. dysfunction

Parasympathetic		ORGAN	Sympathetic	
Receptor	Effect	SYSTEM	Receptor	Effect
Nn, M1	Memory/cognition, Balances dopamine for control of movement in nigrostriatal pathway; in nucleus accumbens, Nn increases dopamine release Present in many interneurons	**CNS**	α1?,β(?2) α2	Fear, anxiety Mood, learning Increases signal to noise ratio
M2	Decreases outflow	**Autoreceptor**	α2	Decreases outflow
M3	Miosis, lacrimation Lacrimation Contract (accommodation)	**Eye** **Ciliary musc**	α1 β1	Mydriasis ↑Aqueous humor
M3	Salivation	**Salivary**		
M3	contraction	**Bronchiolar smooth muscle**	β2	relaxation
M2	Decreased rate	**Heart**	β1	↑rate, force, conduction, automaticity
M3	**On vasculature not innervated,** but stimulation by exogenous agonists ↑NO release	**Blood vessels**	α1 β2	Contraction, ↑BP Relax, ↓BP (stimulated by EPI from adrenal)
M3	Secretion, peristalsis (M2) relaxation	**GI Sphincters**	Various* α1	↓secretion, ↓peristal. contraction
		Liver	α1, β2	Glycogenolysis, gluconeogenesis
		Sweat glands	M3	secretion
		Kidney	β1	Renin release (JGA)
M3	Detrusor contract Trigone, sphincter relax (fyi M2 is involved)	**Bladder**	β3 α1	Detrusor relax Trigone, sphincter contract
M3	Erection (via ↑NO)	**Male GU**	α1	ejaculation
		Uterus	α1 β2	gravid contract Relax (gravid & non)
		Fat cells	β3	Thermogenesis, lipolysis, ↓leptin release
		Skeletal	β2	K+ uptake