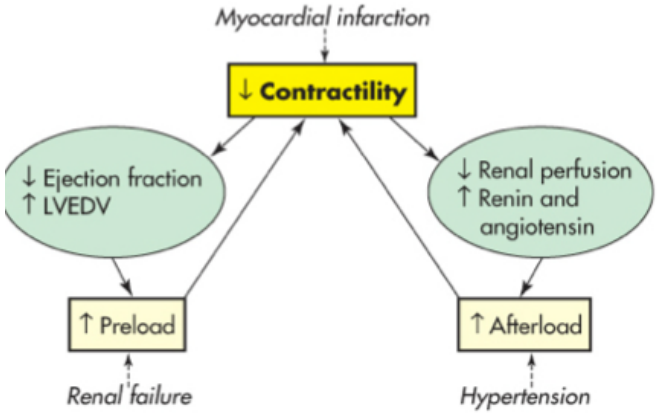
Heart Failure Drugs (Ch. 48)

PATHO REVIEW

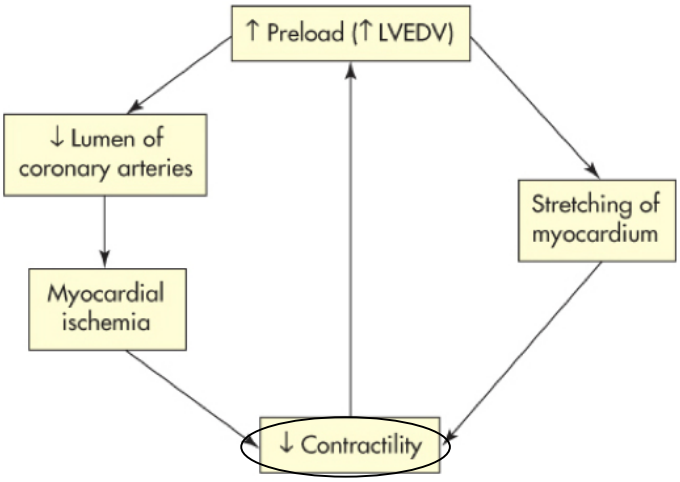


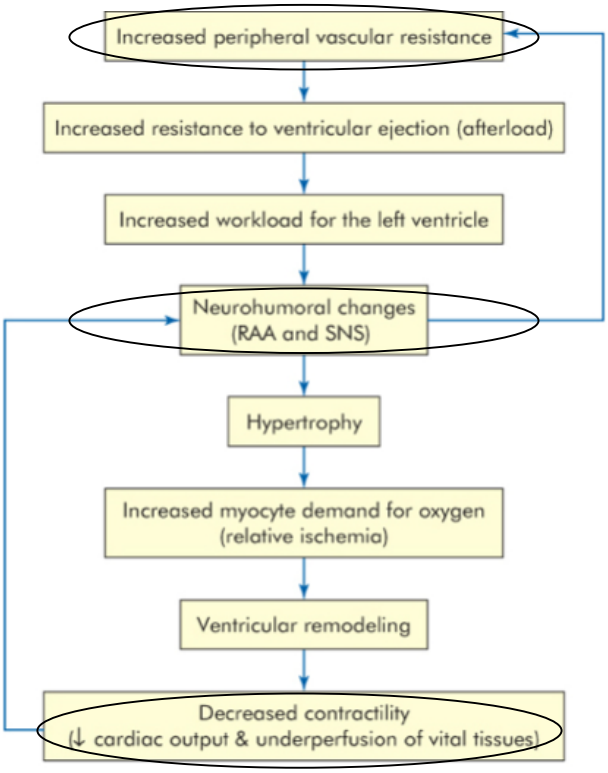
Heart Failure (HF)

- Heart dysfunction → decreased CO < systemic needs
- Congestive HF = left heart failure (LHF)
  - Systolic = HF + decreased ejection fraction (<40%)
- Heart fails to perform its job. It's like a heart attack for the rest of the body.
- Dx: decreased CO + markers of other heart disorders
- Tx:
  - Vasodilators → decrease preload and afterload
  - Diuretics → decrease preload
  - Inotropic drugs → increase contractility
  - ACE inhibitors → decrease preload and afterload
  - Specific to heart disease at origin

Systolic HF

- Heart disease → decreased contractility → decreased SV → decreased CO





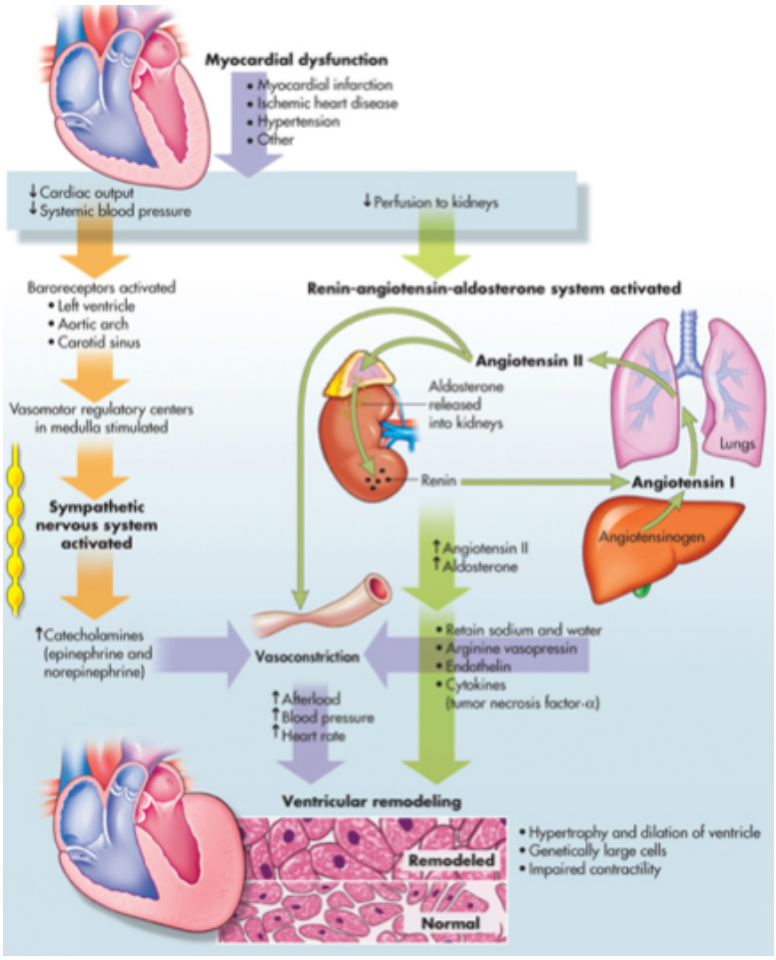
Systolic HF: Key Processes

RAAS & SNS

- Increased catecholamines → myocardial toxicity + hypertrophy
- Increased angiotensin II → increased aldosterone & vasopressin (ADH)
- Ventricular remodeling + increased BP + fibrosis & TPR

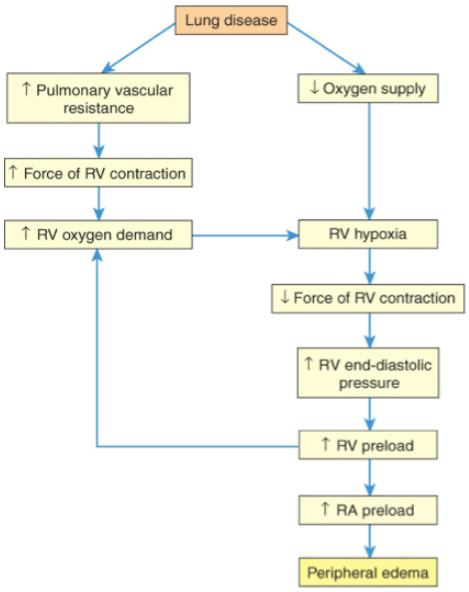
Others:

- Decreased calcium regulation → decreased contractility + arrhythmias
- Diabetes → micro & macrovascular complications → HF



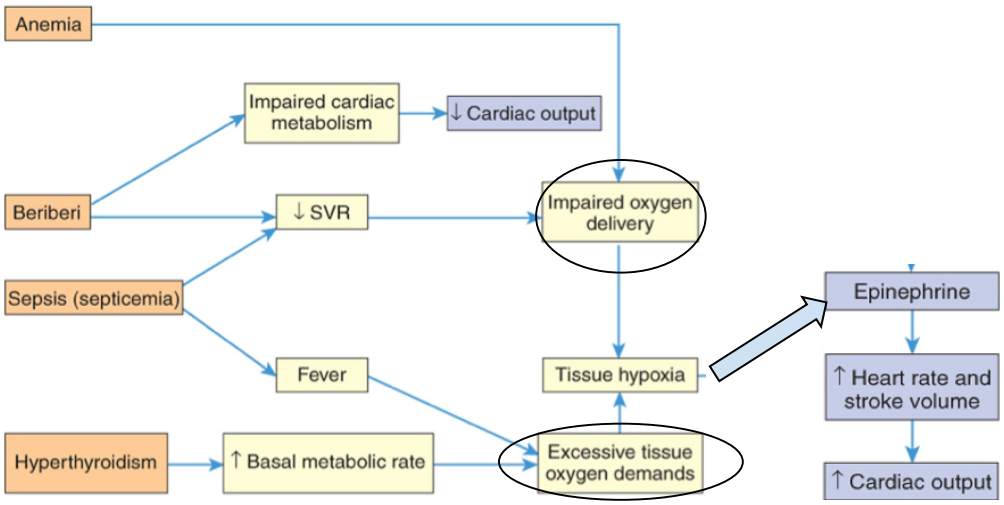
Right Heart Failure

- Decreased right heart CO
- Causes:
  - LHF → increased pulmonary BP
  - Increased pulmonary resistance → decreased CO
  - COPD → see cor pulmonale



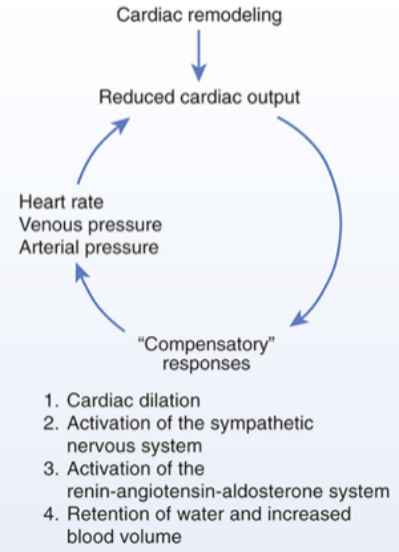
High Output Failure

- Perfusion failure despite increased CO

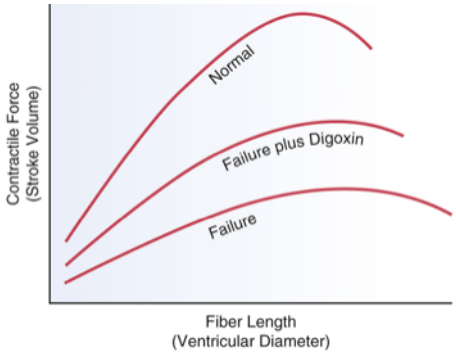


BACK TO PHARM

Heart Failure Vicious Cycle



- The reduced cardiac output sets in motion a bunch of compensatory mechanisms →
- The compensatory mechanisms are trying to counteract and increase the CO. The problem is, even if the body was able to increase the CO, because of the improper remodeling, this would only last a short amount of time. Compensatory mechanisms are very energy demanding.
- Main signs & symptoms
  - Fatigue
  - Short of breath
  - Tachycardia
  - Fluid retention → weight gain
  - Pulmonary edema



- Imagine the heart fibre similar to an elastic. So the harder you pull, the bigger the recoil. Initially, if you stretch the muscle fibre, you'll get an increase in stroke volume (increase in slope).
- There's a point where this relationship breaks (the dip at the end of the curve). If you stretch the fibre so much, causing damage, the recoil will decrease.

HF Classification & Stages

ACC/AHA Stage	NYHA Functional Classification
A At high risk for HF but without structural heart disease or symptoms of HF	
B Structural heart disease but without symptoms of HF	I Asymptomatic
C Structural heart disease with prior or current symptoms of HF	II Symptomatic with moderate exertion
	III Symptomatic with minimal exertion
D Advanced structural heart disease with marked symptoms of HF at rest despite maximal medical therapy. Specialized interventions (e.g., heart transplant, mechanical assist device) required	IV Symptomatic at rest

Heart Failure Drugs

- Routine HF Therapy:

Prototype Drugs

Drugs for Heart Failure

Diuretics

Hydrochlorothiazide
Furosemide

Inhibitors of the Renin-Angiotensin-Aldosterone System

Captopril (ACE inhibitor)
Losartan (angiotensin II receptor blocker)
Entresto (angiotensin receptor neprilysin inhibitor)
Eplerenone (aldosterone antagonist)

Beta Blockers

Metoprolol

Inotropic Agents

Digoxin (a cardiac glycoside)
Dopamine (a sympathomimetic)

Vasodilators

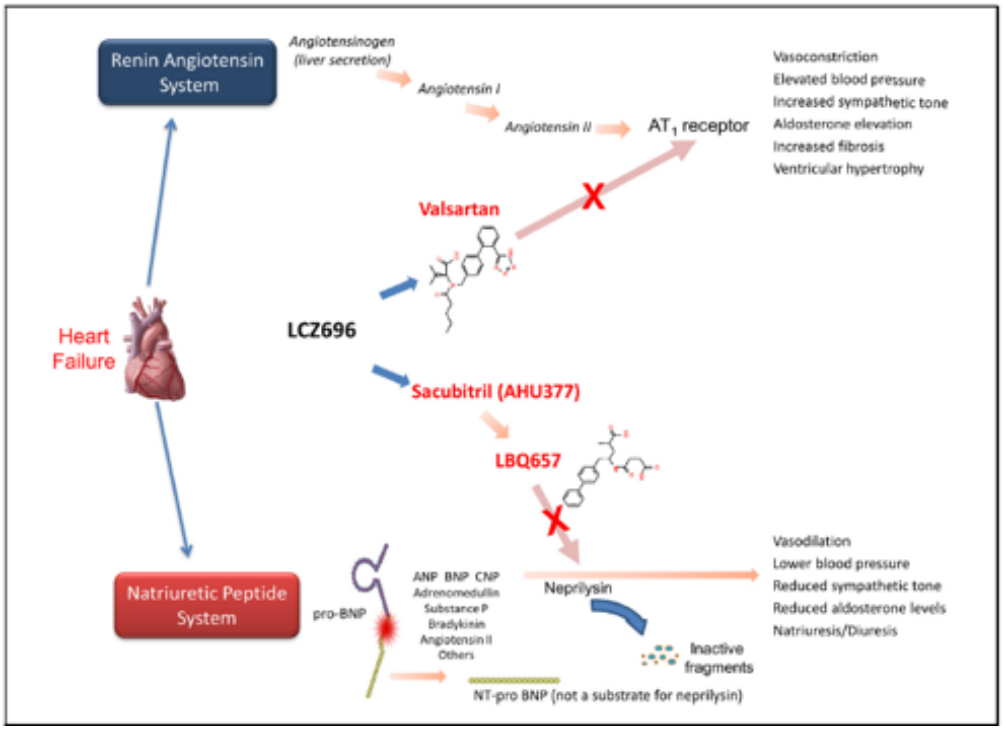
Isosorbide dinitrate plus hydralazine

Main HF Drugs

Drug Class	Diuretics	RAAS inhibitors	Beta-Blockers
General comments	1st-line HF Rx Sx reduction only No ↑ survival	ACE Inhibitors = Best choice for HF ARBs if ACE-I not tolerated	Protect from excessive SNS & Dysrhythmias Start with very low dosage
Beneficial Effects	↓ Blood volume ↓ all of the following: • Cardiac dilation • Pulmonary edema • Venous & Arterial BP	**ACE Inhibitors** Hemodynamic benefits ↑ Kinin → favorable cardiac remodeling **Angiotensin II Receptor Blockers** Equivalent to ACE-I except kinin ↑ **Aldosterone Antagonists** ↑ survival especially in symptomatic patients on ACE-I + Beta-blocker regimen	↑ LV ejection ↑ Exercise endurance ↓ HF progression ↑ Survival
Drug Examples	**Thiazide** Best if GFR is high **Loop Diuretics** Best for severe HF **K+-Sparing** Prevent digoxin toxicity		HF Approved Beta-blockers: **Carvedilol** **Bisoprolol** **SR-Metoprolol**

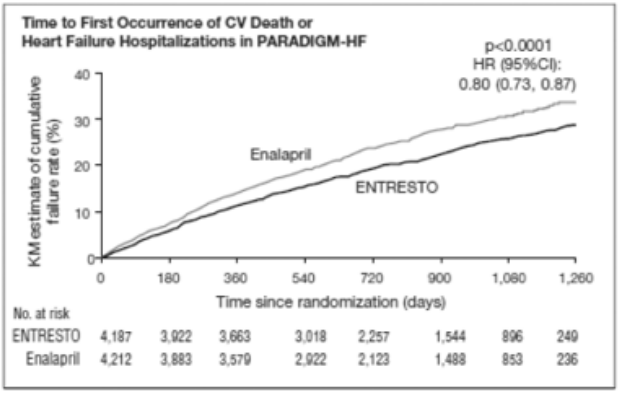
ARB + Neprilysin Inhibitor (ARNI)

- Block angiotensin receptor + increased natriuretic peptides (ANP, BNP)



- Study ended early due to overwhelming advantage of Entresto
- Superior to Enalapril for class II-IV HF:
  - Decreased hospitalization & overall + CV mortality
  - Over time, the gap grew bigger, confirming that Entresto decreases mortality +++

Figure A



Digoxin

Positive Inotropic Agent:

- Increases contractility of the heart
- Alters mechanical & electrical heart activity
- Narrow TI → serious dysrhythmias risk
- Potential increase in female mortality

Indications: HF & Dysrhythmias

- Alleviates HF symptoms but no increase in survival
- 2nd line drug for HF

Kinetics:

- PO or IV administration

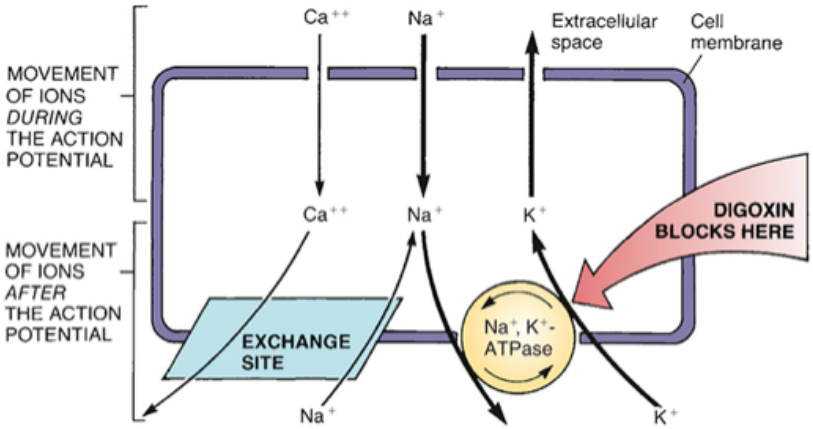
- Very lipid-soluble + 23% albumin-bound
- Almost 100% renal elimination
- Half-life = 1.5 days → 6 days to plateau
- Onset = 30min vs. 5min
- Peak = 4-6h vs. 1-4h

Plasma Digoxin Monitoring:

- Optimal range = 0.5-0.8 ng/mL
- Toxicity increase > 1ng/mL
- Substantial interpatient variability

Digoxin: Mechanism of Action

- Directly blocks the Na+/K+ ATPase pump: K+ levels rise outside the cell, and Na+ levels will rise inside the cell.
- Indirectly blocks at the Ca^{2+}/Na+ exchange site → increases myocyte calcium concentration → **increased contractility**
    - Because in the direct method there is an increase in intracellular Na+, the exchange site will stop pumping Na+ into the cell, to prevent rising levels even more.



Digoxin competes with potassium because they have the same binding site.

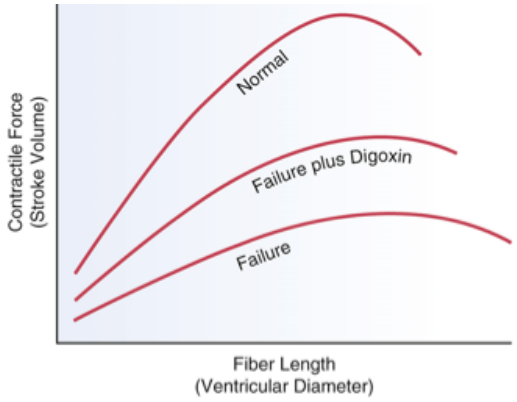
- Hypokalemia → increased digoxin action → toxicity
    - Because K+ levels are lower, Digoxin will bind more easily, it outnumbers K+
- Hyperkalemia → decreased digoxin action → Tx failure
    - K+ outnumbers Digoxin and will bind more easily than Digoxin.
- Must keep [K+] between 3.5-5 mEq/L

Digoxin: Benefits

Hemodynamic benefits:

- Increased cardiac output
- Decreased sympathetic tone → decreased HR & afterload
- Decreased renin release → decreased BP & blood volume

- Increased urine output → decreased BP & edema



Neurohormonal Benefits:

- Initiated at lower dose han inotropy
- Also caused by Na+/K+ ATPase inhibition
- Decreased renin release (decreased fluid retention)
- Increased baroreceptor reflex signalling (decreased SNS tone)

Electrical Effects - Beneficial or Toxic depending on Tx:

- SA node → decreased automaticity (HR)
- AV node → decreased conduction (HR)
- Purkinje fibers → increased automaticity/ectopic heart beats
- Ventricular myocytes → increased automaticity/ectopic heart beats
  ****Yet, no increased survival for HF patients****

<u>Digoxin: Cardiac Dysrhythmias</u>

- Rare if kept in therapeutic range
- Can trigger any type of dysrhythmias
- AV block + escape beats = most common
- Ventricular flutter/fibrillation = most dangerous

Management:

1. Withhold digoxin & diuretics
2. Monitor K+ levels
    a. Administer K+ if low levels
3. Antidysrhythmic drug administration (ex. Lidocaine)
4. If AV block/bradycardia → atropine
5. Severe toxicity → Fab antibody antidote
    a. Very expensive Tx (3-4000$ per injection!!)

Predisposing Factors:

1. Hypokalemia (ex. Diuretics, vomiting, diarrhea)
2. Elevated digoxin levels

   a. Individualization of dose = crucial
3. Heart disease
   a. Toxicity probability is proportional to severity

Digoxin: Other Adverse Effects

- GI ADRs: anorexia, nausea & vomiting
- CNS ADRs: fatigue & visual disturbances

GI/CNS ADRs tend to precede dysrhythmias. Teach patients to use them as warning signs.

Patient Education

- Explain all the toxicity related to digoxin
- Instruct patients to:
  - Take digoxin exactly as prescribed
  - Take K+ supplements/diuretics as prescribed

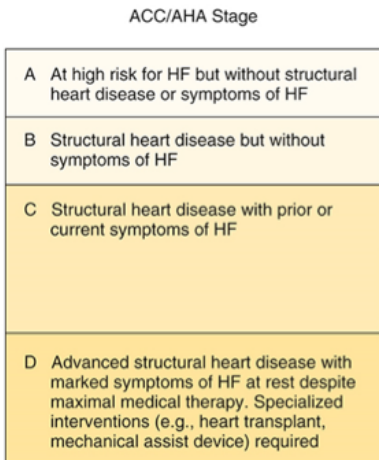
Many drug interactions with digoxin:

Interaction Type	Drug Exampes	Effect
Dynamic	Loop & Thiazide Diuretics	↑ K+ loss → Dysrhytmias
	Beta-blockers / Verapamil	↓ Contractility & HR
	Sympathomimetics	↑ Contractility & HR
Kinetics	Cholestyramine / Neomycin	↓ Absorption or Bioavailability
	Aminoglycosides / Antacids / Omeprazole	↑ Absorption or Bioavailability
	Captopril / Atorvastatin / Verapamil	↓ Excretion or ↑ Distribution or both

Nursing Capsule: Stage A, B & D HF Management

Stage A - asymptomatic

- HF onset risk reduction:
  - Decrease smoking & alcohol
  - Regulate blood glucose & dyslipidemia if present
  - ACE-inhibitor or ARB for diabetic or HTN patients



Stage B - structural heart disease

- Prevent symptomatic HF development
  - Stage A recommendations
  - ACE-I + beta-blocker for patients with decreased ejection fraction

Stage D - advanced HF despite maximal Tx

- Heart transplant = best hope
  - LV mechanical assist can increase life until transplant
  - Regulate fluid retention with diuretics → source of most Sx
  - Avoid ACE-inhibitors or beta-blockers in stage D → worsen state

Nursing Capsule: Stage C HF management

Stage C - structural + functional HF

- Goals = Sx alleviation + increased quality of life + slow cardiac dysfunction + prolong lifespan

Drug therapy

- 1st line = diuretics + ACE-inhibitors + beta-blockers
- Can add digoxin only if Sx management suboptimal with above options
- Can add aldosterone antagonists in moderate to severe HF with well functioning kidneys

Drugs to avoid

- CCBs
- NSAIDs
- Antidysrhythmic drugs - to not amplify the changes in HR

Device therapy

- Implanted cardioverter-defibrillator & cardiac resynchronization pacemakers can decrease mortality

Exercise training

- Recommended in stable patients → improve clinical status & quality of life

Treatment evaluation

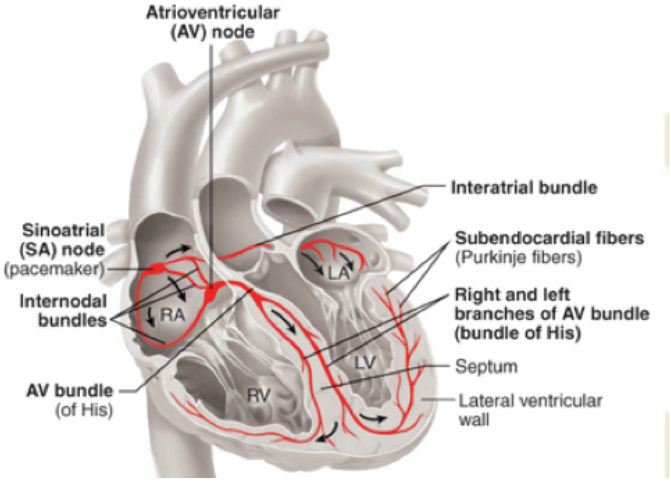
- Based on Sx & physical findings → decrease edema, increase physical endurance, increase sleep & sexual functions
- Decreased BNP levels in blood = survival
- Ejection fraction assessment is not a good measure of success

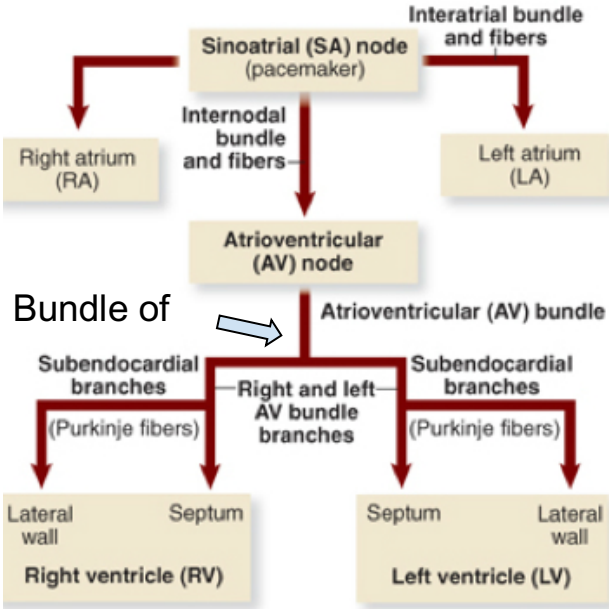
Antidysrhythmic Drugs (Ch. 49)

PATHO REVIEW

Heart Electrical System

- Inside to outside depolarization

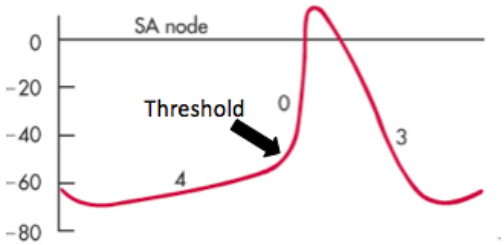




Cardiac Action Potentials

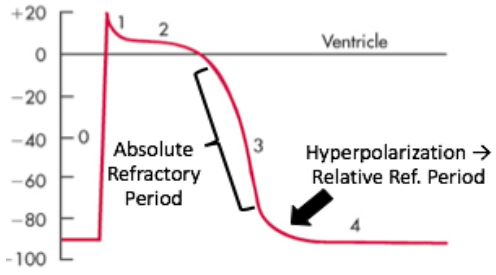
SA node action potential

- 0 = depolarization → T-type Ca^{2+} channels
- 3 = repolarization → K+ leak channels
- 4 = resting potential → leak (funny) Na+ channels & Ca^{2+} channels (calcium clock)



Ventricular action potential

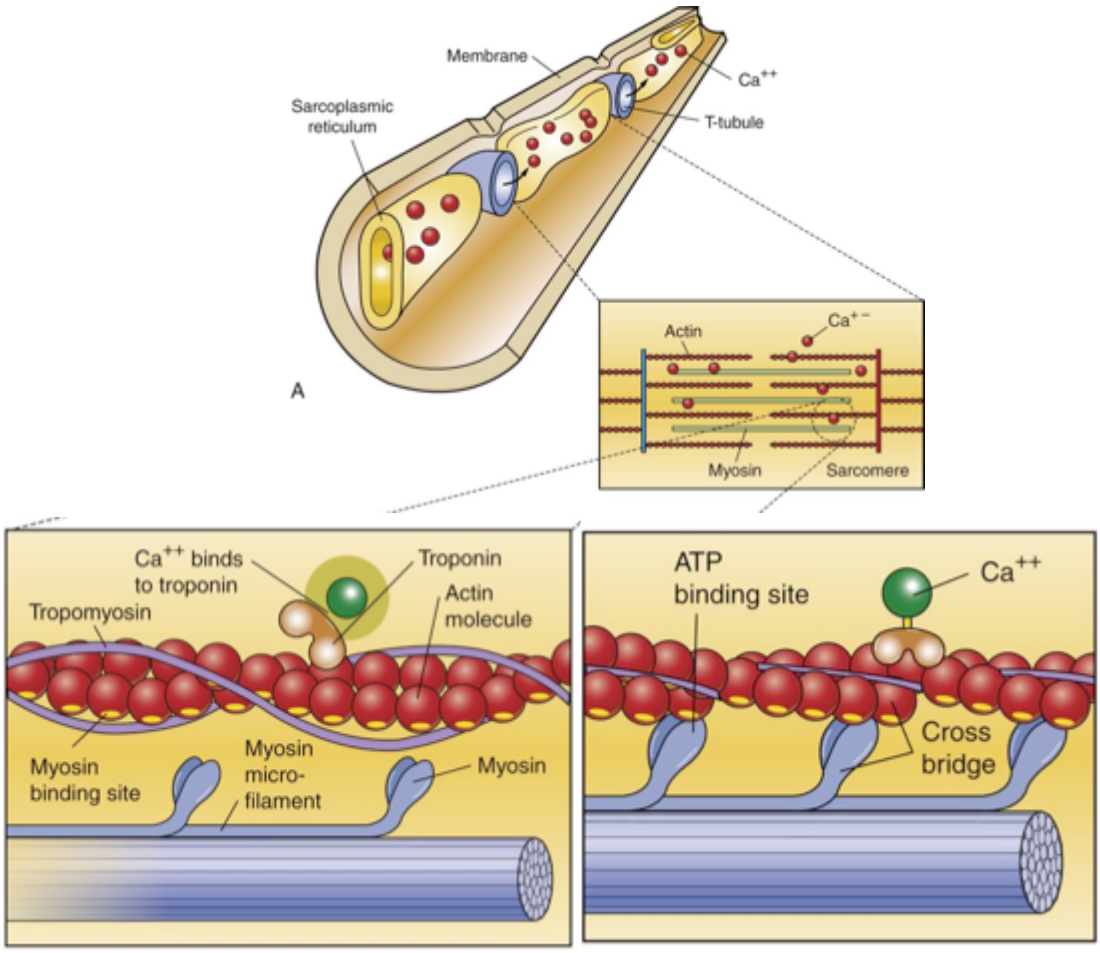
- 0 = depolarization → Na+ channels open
- 1= early repolarization → Na+ channels closure + T-type Ca^{2+} channels open
- 2 = plateau → L-type Ca^{2+} channels
- 3 = repolarization → K+ leak channels
- 4 = resting potential → back to normal



Calcium & Heart Contractions

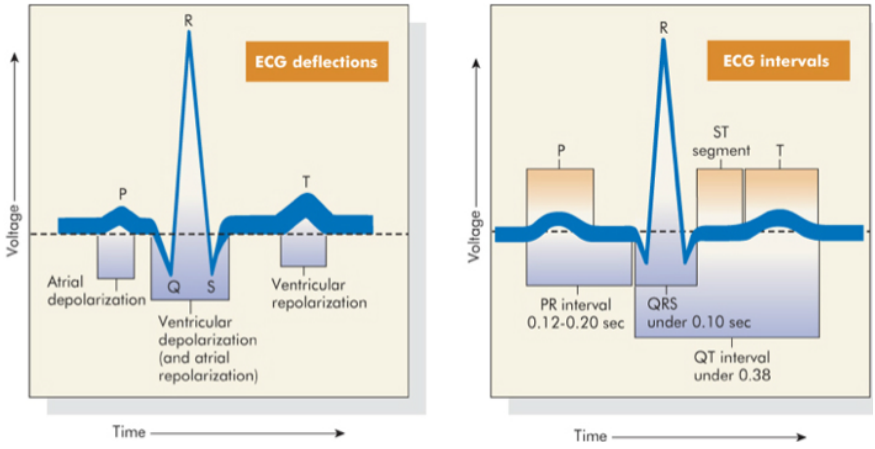
Contraction strength is proportional to calcium concentration

1. Depolarization → opening of plasma membrane calcium channels
2. Interstitial calcium entry → opening of internal calcium channels
3. Release calcium stored in sarcoplasmic reticulum → heart contraction



Electrocardiogram (ECG)

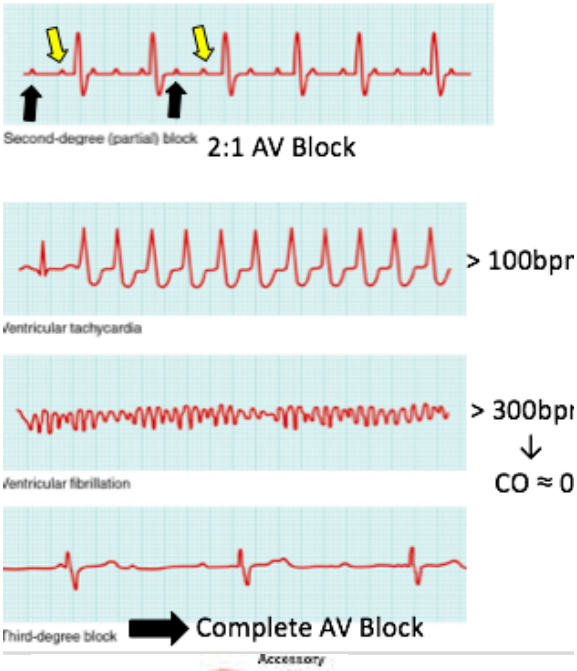
- Automaticity: diastolic (gradual) depolarization → calcium clock
- Rhythmicity: SA node = 60-100/min → AV node = 40-60/min → purkinje fibers = 30-40/min
    - Note: 3 types of cells with automatic properties: SA, AV nodes and purkinje fibers



Dysrhythmias

- Abnormal rhythm (SA node dysfunction) vs. abnormal conduction (circus re-entry)
- Range: single missed beat to fibrillation/cardiac arrest
- Bradycardia: <60 bpm (except athletes)
- Secondary arrhythmias
    - Increased vagal tone → decreased HR
    - Hyperkalemia/calcemia, hypoxia → increased HR

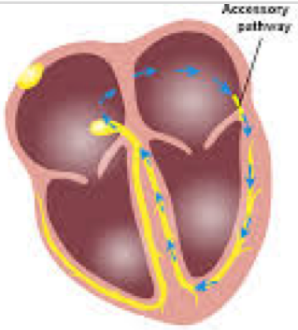
(Only review tables 32-12 & 32-13 for cases discussed in class)



- Yellow arrows = triggers full heart contraction vs. black arrows = atrial contraction only
- Complete AV block → QRS from AV or Purkinje

Circuit Re-entry Tachycardia

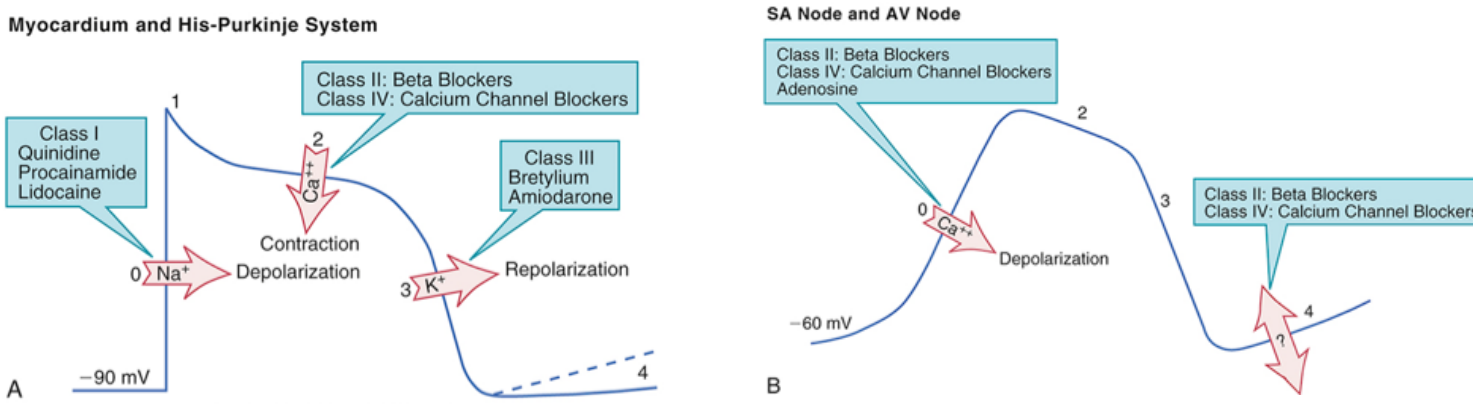
- Aberrant circular conduction
- Form of tachycardia → decreased CO
- Causes:
    - Around scar tissue
    - Accessory pathway



BACK TO PHARM

Antidysrhythmic (ADR) Drugs Classification

Class	Drug examples
Class I = sodium channel blockers	Quinidine (IA) / Lidocaine (IB) / Flecaine (IC)
Class II = beta blockers	Propranolol
Class III = potassium channel blockers (delay repolarization)	Sotalol / Amiodarone
Class IV = calcium channel blockers	Verapamil
Others	Digoxin & adenosine



- Adenosine is used as Dx tool
- Slows down the heart to determine the type of arrhythmia

<u>ADR Drugs: Prodysrhythmic Effects</u>

All ADR drugs can worsen existing dysrhythmias or generate new ones

- Monitor all patients
- Usage when benefits > risk
- Examples:
  - Non-sustained ventricular tachycardia → no major decrease in CO → benefits < risk
  - Serious ventricular fibrillation → risk of death → any Tx is worth it
- Class I & III agents → prolong QT interval → significant risk of Torsade de pointe

<u>Class IB: Lidocaine</u>

Differences vs. Class IA:

- Accelerate repolarization
- No ECG effects

Cardiac effects

- Decrease impulse conduction + ventricle's automaticity
- Accelerate repolarization
- No effect on vagal tone
- Ineffective against. supraventricular dysrhythmias

Other therapeutic use:

- Local anesthetic

Adverse Effects

- Usually well tolerated
- Risk of seizures & respiratory arrest

- IV admin → monitor BP & ECG for toxicity signs

Properties of Antidysrhythmic Drugs

Drug	Usual Route	Effects on the ECG	Major Antidysrhythmic Applications
CLASS IB			
Lidocaine	IV	No significant change	Ventricular dysrhythmias
Phenytoin	PO	No significant change	Digoxin-induced ventricular dysrhythmias
Mexiletine	PO	No significant change	Ventricular dysrhythmias

Class II: Propranolol

* Refresher: non-selective beta-blocker (both beta 1 & 2)

Cardiac & ECG Effects

- Beta1-block = decreased HR, conduction & contractility
- Prolongs PR interval

Other therapeutic use

- Hypertension
- Panic attacks/general anxiety

Adverse effects

- Well tolerated
- Risk of HF, AV block or sinus arrest
- Hypotension
- Bronchospasm - in asthma patients

Properties of Antidysrhythmic Drugs

Drug	Usual Route	Effects on the ECG	Major Antidysrhythmic Applications
CLASS II			
Propranolol	PO	Prolongs PR, bradycardia	Dysrhythmias caused by excessive sympathetic activity; control of ventricular rate in patients with supraventricular tachydysrhythmias
Acebutolol	PO	Prolongs PR, bradycardia	Premature ventricular beats
Esmolol	IV	Prolongs PR, bradycardia	Control of ventricular rate in patients with supraventricular tachydysrhythmias

Class III: Amiodarone

Oral therapy

- Best for atrial fibrillation / last resort
- K+ block = delay repolarization
- Also decreases SA node rate, conduction & contractility
- Metabolism by CYP3A4 → many interactions!

IV therapy

- Initial therapy of recurrent ventricular fibrillation
- Affect AV node: decrease conduction & increase refractoriness

Adverse effects
- Hypotension (15-20%)
- Bradydysrhythmia (5%)

PO adverse effects
- Long half life → prolonged toxicity
- Lung toxicity (ex. fibrosis) = greatest concern
- Pre-treatment chest x-ray is recommended
- Cardiotoxicity: HF, sinus bradycardia
- Thyroid toxicity: hypo or hyperthyroidism
- Hepatotoxicity: LFT recommended & look for signs
- Optic neuropathy or neuritis → rare
- Teratogen & enters breast milk
- Skin photosensitivity: wear sunblock & long clothing
- Some potential CNS impairment & GI distress

Properties of Antidysrhythmic Drugs

Drug	Usual Route	Effects on the ECG	Major Antidysrhythmic Applications
Amiodarone	PO, IV	Prolongs QT and PR, widens QRS	Life-threatening ventricular dysrhythmias, atrial fibrillation*
Dronedarone	PO	Prolongs QT and PR, widens QRS	Atrial flutter, atrial fibrillation
Sotalol	PO, IV	Prolongs QT and PR, bradycardia	Life-threatening ventricular dysrhythmias, atrial fibrillation/flutter

*Very effective but very toxic

<u>Class IV: Verapamil</u>
*Refresher: effects of CCBs = beta-blockers

Cardiac & ECG effects
- CC block = decrease HR, AV conduction & contractility
- Ineffective vs. ventricular dysrhythmias

Other therapeutic use
- Hypertension
- Angina

Adverse effects
- Well tolerated
- Risk of HF, AV block or bradycardia
- Increase vasodilation → hypotension
- Constipation

Drug interactions
- Digoxin: increased levels + additive action
- Beta blockers: additive action

Properties of Antidysrhythmic Drugs

Drug	Usual Route	Effects on the ECG	Major Antidysrhythmic Applications
CLASS IV			
Verapamil	PO	Prolongs PR, bradycardia	Control of ventricular rate in patients with supraventricular tachydysrhythmias
Diltiazem	IV	Prolongs PR, bradycardia	Same as verapamil

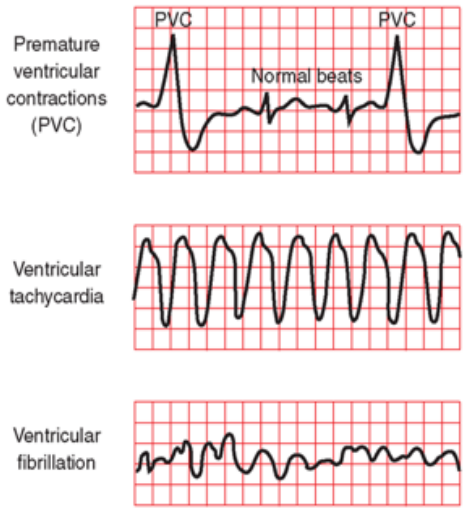
Supraventricular Dysrhythmias

- Anywhere above ventricles
- No major CO impairment
- Biggest concern = spread to ventricles → aim to slow down ventricular rate with cardioversion or class II & IV drugs

Atrial fibrillation	Most common Increased clot risk → stroke risk Anticoagulant prophylaxis Treatment: ● Slow rate via beta-blockers or CCBs = 1st choice ● Or restore rhythm with DC cardioversion
Atrial flutter	Increased stroke risk → anticoagulant prophylaxis Treatment: ● 1st line = DC cardioversion ● 2nd line = slow rate with CCBs or beta-blockers
Sustained supraventricular tachycardia SVT	Treatment: ● 1st line = carotid massage ● 2nd line = beta-blockers or CCBs

Ventricular Dysrhythmias

- Significant CO impairment
- Aim to abolish dysrhythmia
- 1st line = cardioversion
- Preferred ADR drugs = class I or III



Sustained ventricular tachycardia	150-250bpm → emergency intervention Treatment: ● 1st line = cardioversion ● 2nd line = IV lidocaine or amiodarone
Ventricular fibrillation (V.fib)	Multiple ectopic foci → CO drops to almost 0 Treatment: ● Defibrillation to restore rhythm ● Amiodarone for long-term prophylaxis
Premature ventricular complexes (PVCs)	Usually benign, treat only if MI present Treatment: ● 1st line = beta-blockers
Digoxin-induced ventricular dysrhythmia	Treatment: ● 1st line = phenytoin or Lidocaine (class 1B) ● Avoid DC cardioversion → can cause V.Fib
Torsade de pointe	Treatment = IV magnesium + cardioversion

<u>Nursing Capsule: ADR Therapy</u>

Risk-benefit analysis: usually treat only if ventricular pumping impairment

- Sustained or symptomatic dysrhythmias & ventricular dysrhythmias → benefits usually **>** risks
- Non-sustained or asymptomatic dysrhythmias & supraventricular dysrhythmias → risks usually **>** benefits

Phases of treatment

- Acute = terminate dysrhythmia → non drug measures (ex. DC cardioversion, carotid massage)
- Long-term = prevent dysrhythmia resurgence → risks usually **>** benefits
- Drug selection: **trial & error!!!** / use holter ECG monitoring to determine effectiveness & adjust

Minimizing risks

- Low initiation dose → gradual increase
- Holter monitoring of QT prolongation
- Monitor drug plasma concentrations

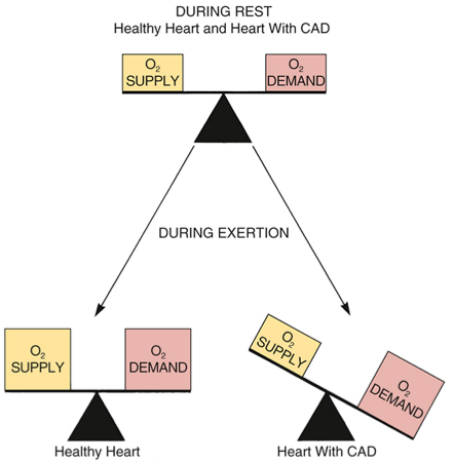
Angina Pectoris Therapy (Ch. 51)

Heart Disease Continuum

- Coronary artery disease (CAD) → myocardial ischemia (MI) → acute coronary syndrome (ACS)
- MI = intermittent imbalance between supply and demand
- Heart attack = acute, complete block of supply

Angina Pectoris

- Oxygen supply/demand imbalance → sudden chest pain
- Imbalance secondary to atherosclerosis development → symptoms vs. disease in itself
- Therapeutic goal = decrease attack intensity & frequency
- Options: increase supply or decrease demand



Types of Angina

Chronic Stable Angina treatment strategy:

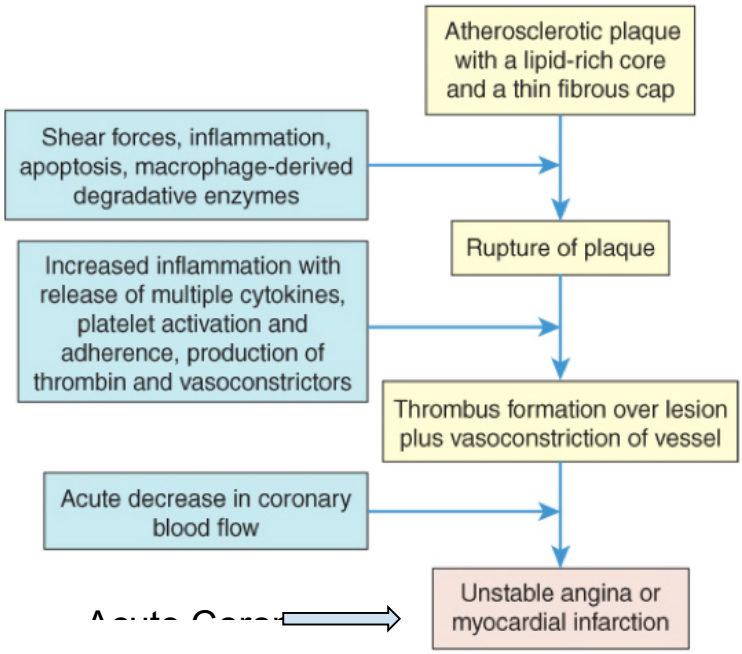
- Stable angina = coronary occlusion → decrease in demand = best option
- Best therapeutic agents:
  - Organic nitrates / beta-blockers / CCBs
  - Ranolazine = adjunct
  - Only Sx relief → no decrease in risk of MI
- Non-drug therapy:
  - Decrease in precipitating factors: stress, overexertion, cold exposure
  - Decrease in risk factors: smoking, HTN, HLD, sedentary lifestyle

Variant angina treatment strategy:

- Variant angina = coronary artery spasms → increase supply = best option
- Best therapeutic agents:
  - Organic nitrates / CCBs
  - Beta-blockers & ranolazine = inefficient
  - Only Sx relief → no decrease in risk of MI

Unstable Angina

**** Medical emergency, closer to MI ****



Antianginal Drugs

Mechanisms of Antianginal Action

Drug Class	Mechanism of Pain Relief	
	Stable Angina	Variant Angina
Nitrates	*Decrease oxygen demand* by dilating veins, which decreases preload	*Increase oxygen supply* by relaxing coronary vasospasm
Beta Blockers	*Decrease oxygen demand* by decreasing heart rate and contractility	Not used
Calcium Channel Blockers	*Decrease oxygen demand* by dilating arterioles, which decreases afterload (all calcium blockers), and by decreasing heart rate and contractility (verapamil and diltiazem)	*Increase oxygen supply* by relaxing coronary vasospasm
Ranolazine	*Appears to decrease oxygen demand,* possibly by helping the myocardium generate energy more efficiently	Not used

*Ranolazine is a new drug that has not been used much yet

Organic Nitrates: Nitroglycerin

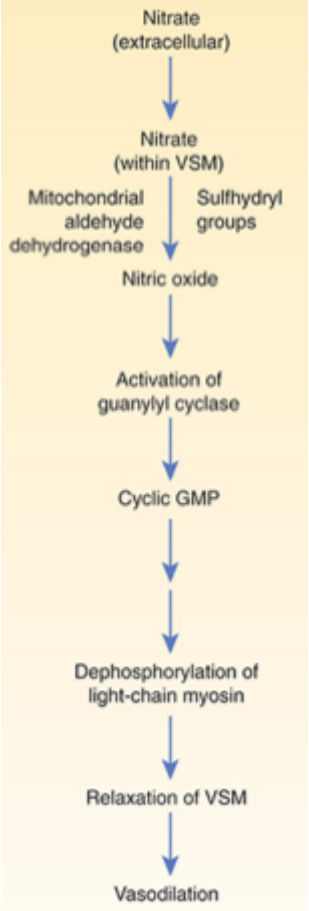
Antianginal effects:

- Stable: decrease venous return → decrease preload
- Variant: decrease risk of coronary vasospasms

November 14th, 2019
William Archambault

Kinetics:

- Very lipid soluble → many formulations
- Rapid hepatic metabolism → half life = 5-7 minutes



Adverse effects:

- Headache → intensity decreases over time
- Orthostatic hypotension
- Baroreceptor activation → reflex tachycardia

Drug Interactions:

- Beta-blockers or CCBs → decreases reflex tachycardia
- Hypotensive drugs/alcohol → potentiation
- PDE5 inhibitors (ex. viagra) → life-threatening hypotension - contraindicated

Tolerance issues:

- Very rapid (over 24h) - your body will quickly realize that the vasodilation is artificial and will build tolerance against it.
- Increase risk with high doses (sulfhydryl depletion)
- Intermittent schedule & smallest effective dose decreases risk

<u>Nursing Capsule: Nitroglycerin Management</u>

Preparation & administration:

- Equivalent efficacy → difference in onset & duration
- Acute therapy: rapid onset → termination of ongoing attack & acute prophylaxis
- Sustained therapy: long-acting preparations
- Intravenous therapy: surgery BP control or when other formulations fail

Discontinuation:

- Gradual for long-acting preparations
- Abrupt → reflex vasospasms

Organic Nitrates: Time Course of Action

Drug and Dosage Form	Onset[a]	Duration[b]
NITROGLYCERIN		
Sublingual tablets	Rapid (1–3 min)	Brief (30–60 min)
Sublingual powder	Rapid (1–3 min)	Brief (30–60 min)
Translingual spray	Rapid (2–3 min)	Brief (30–60 min)
Oral capsules, SR	Slow (20–45 min)	Long (3–8 hr)
Transdermal patches	Slow (30–60 min)	Long (24 hr)[c]
Topical ointment	Slow (20–60 min)	Long (2–12 hr)

Beta-blockers & CCBs

Beta-blockers (metoprolol, propranolol, etc.)

- 1st line for stable/effort angina
- Ineffective for variant angina

Antianginal effects:

- Decrease demand via decreased HR & contractility
- Decrease reflex tachycardia from nitroglycerin

Antianginal administration

- Lowest dose to achieve 50-60 bpm
- Discontinue gradually to avoid rebound MI

Adverse effects

- Classics:
    - Bradycardia
    - Hypotension
    - Bronchoconstriction

CCBs (verapamil, diltiazem, nifedipine)

- Effective for both stable & variant angina

Antianginal effects

- Arteriolar dilation → decrease afterload → decrease demand
- Decrease HR & contractility → decrease demand
- Coronary relaxation → decrease spasms → increase supply

Adverse effects

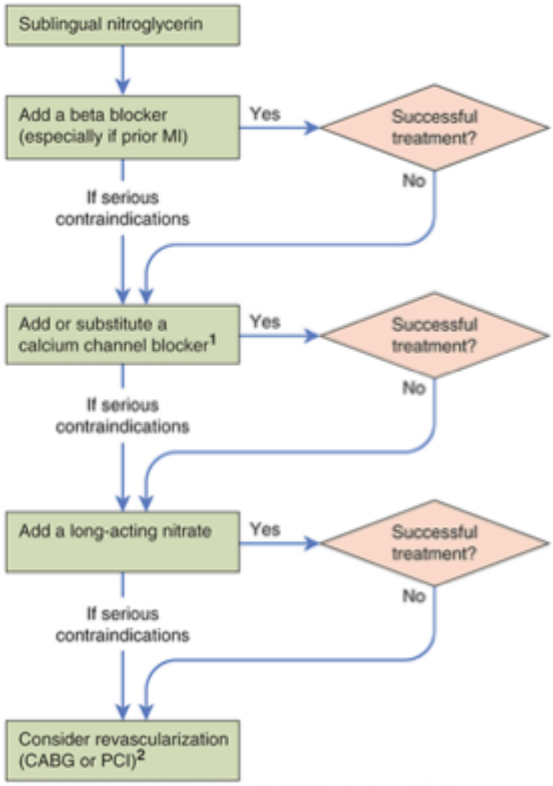
- Classics:
    - Bradycardia
    - Hypotension
    - Beta-blocker interaction

Nursing Capsule: Stable Angina Management

1. Decrease MI risk of death - PRIORITY
    a. Antiplatelet drugs (ex.. Aspirin or clopidogrel)
    b. Cholesterol-lowering drugs (ex. Statins, colesevalam)
    c. ACE-inhibitors (ex. captopril)

2. Decrease ischemic anginal pain
    a. Provide long-term prophylaxis via CCB, beta-blocker
    b. Sublingual nitrate in cases of attacks
    c. Risk factor decrease: exercise, lipid & glucose regulation, decrease stress/anxiety

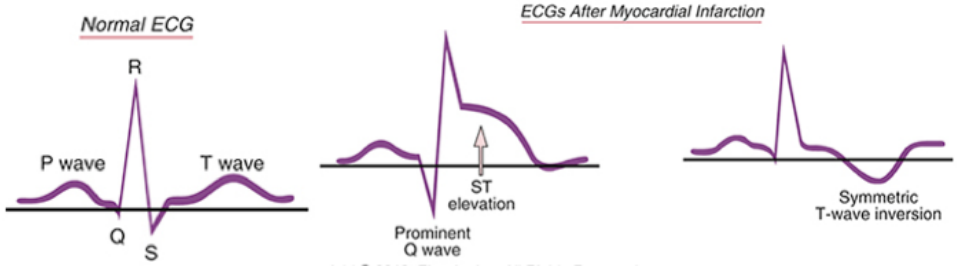
3. Follow algorithm for drug selection
    a. Use nifedipine if combine beta-blocker & CCB
    b. Synergistic actions of 3 class of agents
    c. Ex. contraindication situation: CCB > beta-blocker in asthmatic patients



ST-Elevation Myocardial Infarction (STEMI) (Ch.53)

STEMI

- Complete blockage of coronary blood flow → myocardial infarct → necrosis
- Hallmark signs/symptoms:
    - Chest pain > angina pectoris
    - Cardiac necrosis biomarkers
        - Cardiac troponin I & T = best markers
    - ECG changes



STEMI Management

- From onset to discharge = 6-10 days
- Key goals: reperfusion + decrease O2 demand
- Major threats:
    - Ventricular dysrhythmias
    - Heart failure
    - Cardiogenic shock

Routine Drug Therapy

*Initiate when STEMI suspected until clear diagnosis

- Oxygen supply → intuitive but no concrete evidence of benefits
- Aspirin → decrease in mortality + synergistic with reperfusion therapy
- Discontinue other NSAIDs! → increases mortality
- IV morphine → decrease chest pain + mild decrease in O2 demand
- Beta-blockers → decrease chest pain + infarct size + mortality
    - Oral administration preferred; make sure dosage is adequate
- Nitroglycerin → decrease O2 demand + infarct size + hypertension but not decrease in mortality
    - Sublingual administration followed by IV if necessary

Reperfusion Therapy

- Goal: restore blood flow of blocked coronary
- **PCI preferred to fibrinolytics**

Fibrinolytic therapy (ex. alteplase)

- Try to initiate within 30mins of hospitalization
- Increase ventricular functions + decrease mortality
- More contraindications than PCI
    - Ex. intracranial hemorrhage, severe HTN

PCI (balloon angioplasty + stent)

- Try to install within 90mins
- Adjunct: anticoagulant + antiplatelet drugs
- Success rate & duration > fibrinolytics Tx

Comparison of Fibrinolytic Therapy With Primary PCI

ADVANTAGES OF FIBRINOLYTIC THERAPY
• More universal access • Shorter time to treatment • Results less dependent on physician experience • Lower system cost
ADVANTAGES OF PRIMARY PCI
• Higher initial reperfusion rates • Less residual stenosis • Lower recurrence rates of ischemia/infarction • Does not promote intracranial bleeding • Defines coronary anatomy and LV function • Can be used when fibrinolytic therapy is contraindicated

LV, Left ventricular; *PCI,* percutaneous coronary intervention.

Reperfusion Therapy Adjuncts

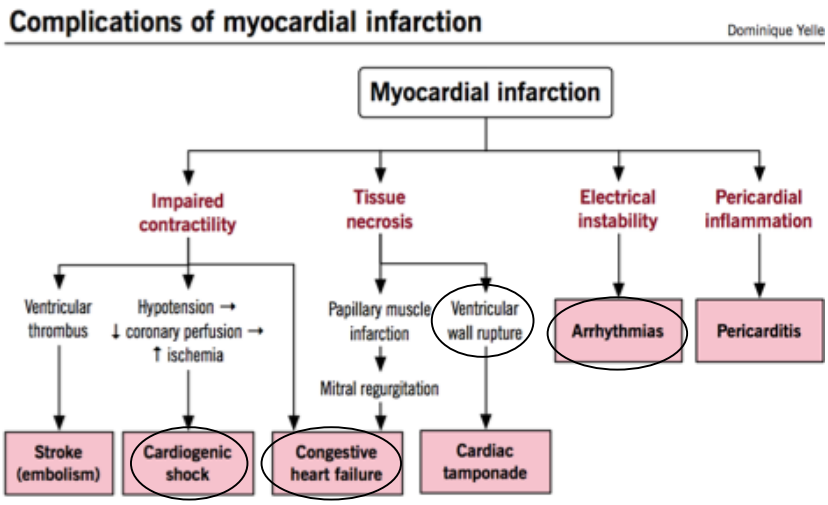
Used with both PCI or fibrinolytics therapy to increase success and decrease mortality

- Heparin → indicated for all STEMI reperfusion patients
    - With PCI: once before procedure
    - With fibrinolytics Tx: before until 72h post therapy
- Fondaparinux → factor Xa inhibitor
    - Alternative for fibrinolytic patients with contraindication for heparin
- Bivalirudin → direct thrombin inhibitor
    - Alternative for PCI patients with heparin-induced thrombosis
- Antiplatelet drugs → clopidogrel + aspirin = preferred combination for stent insertions
    - Watch out for severe bleeding signs & Sx
- ACE inhibitors → decrease in mortality

- Recommended for all STEMI patients unless contraindicated
- ARBs also seem equivalent

STEMI Complications

- Ventricular dysrhythmias
  - Major cause of death
  - Tx: defibrillation + IV Amiodarone for 24h-48h
  - Avoid prophylaxis anti-dysrhythmia Rx → increase mortality!
- Cardiogenic shock:
  - 7-10% of STEMI → large infarct = increase risk
  - Tx: inotropic drugs + vasodilator
  - Sx relief only, no mortality decrease
- Heart failure
  - Best Tx regimen: diuretic + beta-blocker + ACE-inhibitor
- Cardiac rupture
  - Rupture of ventricular wall → shock → rapidly fatal
  - Highest risk: first days of large anterior infarcts
  - Tx: vasodilator + beta-blocker = decrease risk



Secondary Prevention of STEMI

- Complication-free patients → discharge after 72h
  - High risk of reinfarctions (5-15%) & complications
  - Risk reduction Tx + long-term drug regimen decreases mortality
- Risk reduction Tx
  - Exercise, smoking cessation, metabolic syndrome management
- Long-term RX regimen: continue indefinitely
  - Beta-blockers
  - ACE-I or ARB
  - Antiplatelets or anticoagulant
  - Statins