Angina Pectoris

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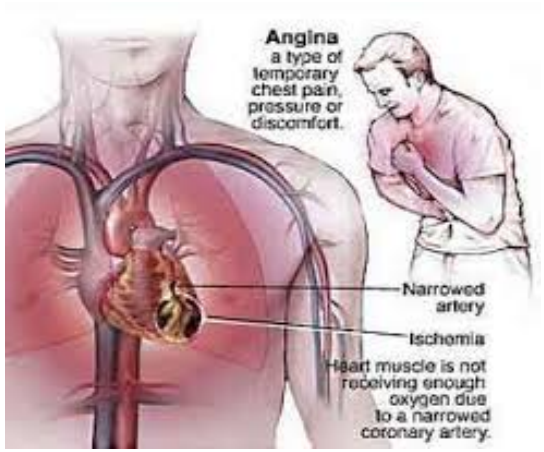
What is Angina Pectoris (AP) ?

- Commonly known as *angina* – is chest pain often due to ischemia of the heart muscle,

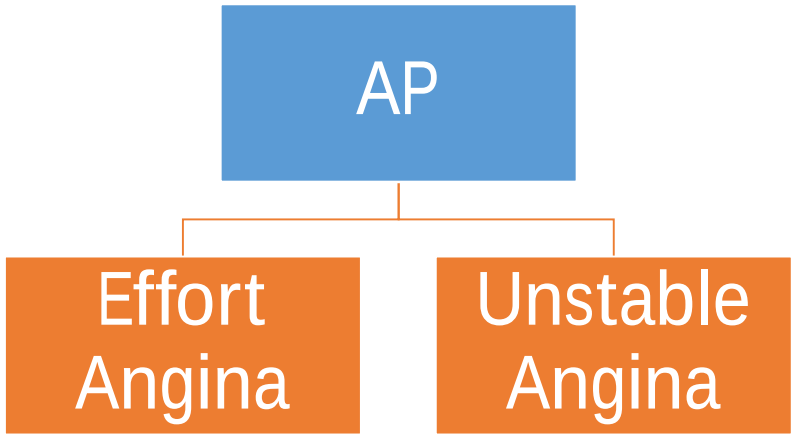
- Because of obstruction or spasm of the coronary arteries



What causes AP ?

- Primary cause: Shortage of oxygen supplied by coronary arteries
- Oxygen deficiency leads to Ischemia (Medical term for what happens when your heart muscle doesn't get enough oxygen)
- Resulting Ischemia leads to pain

Types of AP



- Occurs when heart Oxygen requirement exceeds supply during stress
- Mostly due to obstruction of coronary disease

- Occurs at rest
- Caused by major block in coronary artery caused by platelets around plaque
- High risk of myocardial infarction

How to treat AP ??

Decrease Oxygen Demand

Increase Oxygen Delivery

- Effort Angina: Oxygen demand can be decreased by decreasing cardiac work
- In unstable angina, vigorous measures of both decreasing O_2 demand, decreasing cardiac work

Drug Class to treat AP

Vasodilators

Ca- channel Blockers

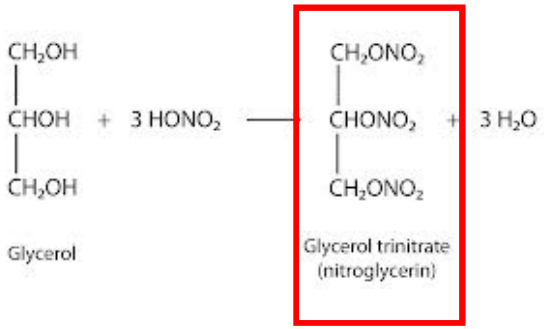
Beta-blockers

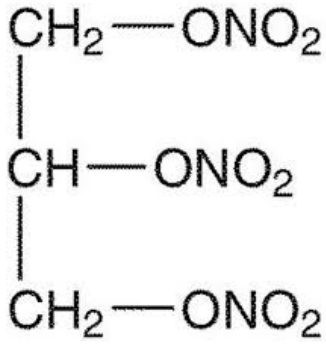
- These drugs *decrease myocardial oxygen* requirement by decreasing

1. Heart rate
2. Ventricular volume
3. Blood pressure
4. contractility

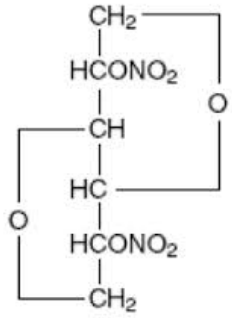
Organic Nitrates (Vasodilators)

- Simple nitric and nitrous acid esters of polyalcohol
- Nitroglycerin : prototype

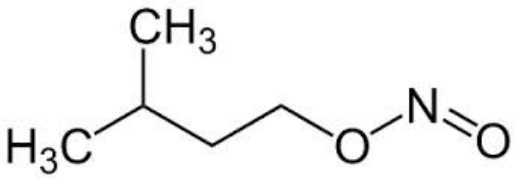




Nitroglycerine



Isosorbide dintrate

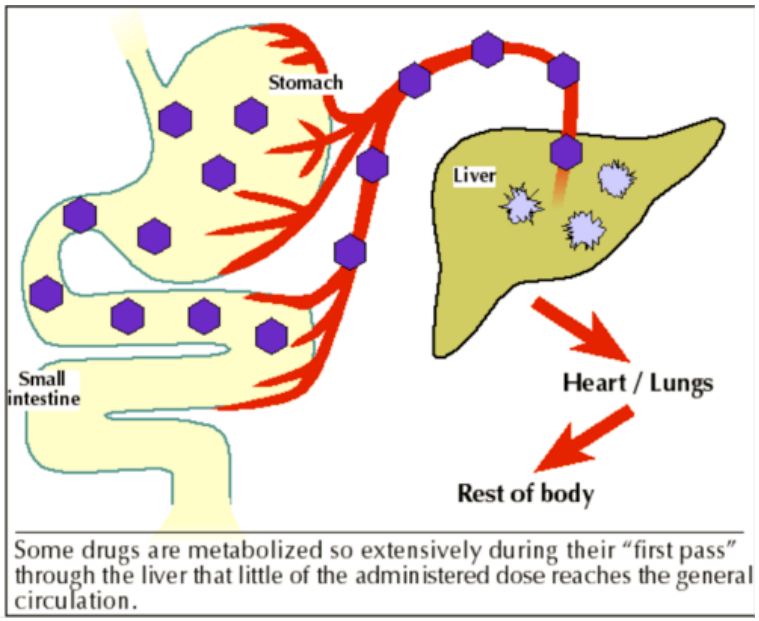


Amyl nitrate

Pharmacokinetics of Nitrates

- Liver rapidly metabolizes nitrates (Active reductases removing nitrate group)
- Oral bioavailability is low (10 – 20 %)
- Sub-lingual route preferred as it avoids first-pass effect
- Rapidly absorbed, effect in minutes
- When larger dose, other administration routes (sustained release oral, buccal)

First Pass Effect



Some drugs are metabolized so extensively during their "first pass" through the liver that little of the administered dose reaches the general circulation.

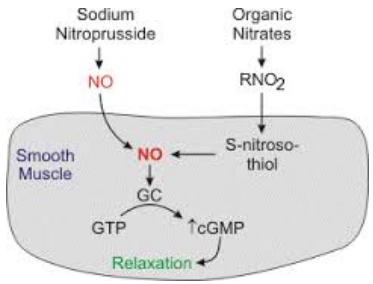
Sublingual or buccal routes by passes Liver & deliver drug directly to blood circulation

Pharmacodynamic Effect of Nitrates

- In general these drugs have to be bio-activated to release nitric oxide (NO)

Nitro-glycerin → Nitric Oxide

Glutathione –s transferase
ALDH2 or ALDH3



Effect of Nitrates on Vascular Smooth Muscle

- All vascular segments (Arteries/Veins) relax in response
- Veins respond to lower conc compared to arteries
- Primary effect: Relaxation of veins with *increased venous capacity & lower ventricular pre-load*
- As a result, pulmonary vascular pressure and heart size reduced

- Some studies suggest nitroglycerin redistributes coronary blood flow from *normal to ischemic region*

Clinical use of nitroglycerin

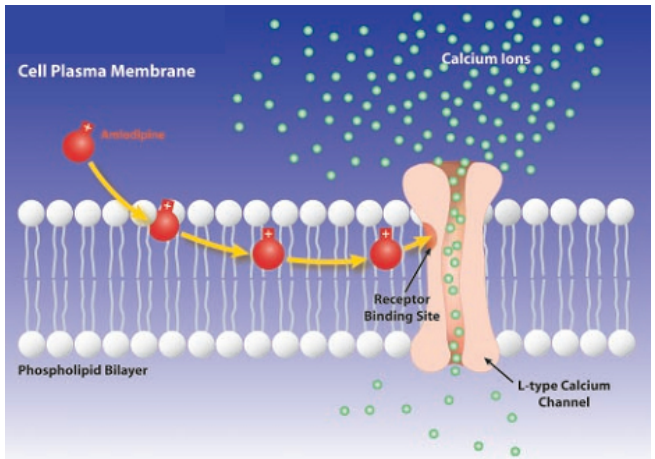
- Sub-lingual most frequently used agent in treatment of AP
- Duration of effect is short so cannot use as maintenance therapy
- IV use only in severe, recurrent rest angina
- Slower release formulations developed (buccal, oral) but risk developing tolerance

Toxicity of Nitroglycerin

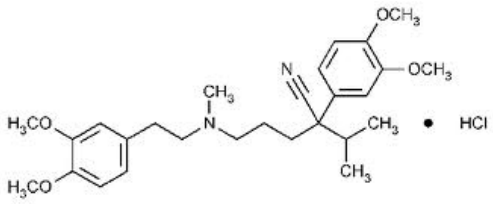
- Acute adverse effect are direct extension on vasodilation
  - Orthostatic hypotension
  - Tachycardia
  - Throbbing headache

Calcium channel blockers

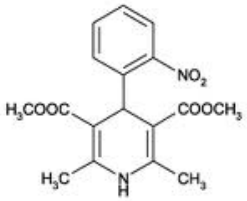
- Drugs bind to Calcium channel, prevent movement of calcium
- Calcium is important for heart muscle, smooth muscle contraction
- Results in vasodilation (smooth muscle relaxation)
- Reduction in heart contractility, decrease AV node activity



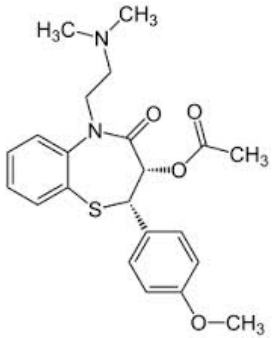
Calcium Channel Blockers



Verapamil



Nifedipine



Diltiazem

- Verapamil, first clinically useful member
- Nifedipine, prototype of dihydro-pyridine class
- These drugs have high first pass, plasma binding, extensive metabolism

Pharmacodynamic effect

Vascular Smooth Muscle:

- Most smooth muscle depend on Calcium
- Blockers relax muscle cells
- Blood pressure is reduced
- Reduction in resistance helps in *Effort Angina*

Cardiac Muscle:

- Cardiac muscle heavily depend on calcium for contraction
- Impulse generation
- Blockers block both effect
- Leads to reduction in cardiac mechanical function

Clinical Effect of Calcium channel blockers

- Calcium channel blockers
  - Decrease myocardial contractile force, reduces heart oxygen requirement
  - Decrease in arterial, venous pressure

- As a result
  - Ventricular wall stress decreases - lower Oxygen requirement
  - Decreased heart rate – lower Oxygen requirement

Clinical use of Calcium channel blockers

- Use of particular Calcium channel blocker based on pharmacology & potential for adverse event
- Nifedipine has no effect on AV conduction so safer than verapamil, diltiazem
- Contraindicated in presence of heart failure
- Verapamil, diltiazem better tolerated in patients with low bp
- Unstable angina patients- immediate release Ca channel blockers might increase risk for AE

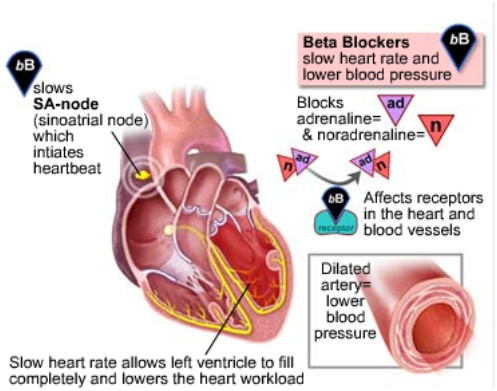
Toxicity of Calcium channel blockers

- Most important toxic effects are direct extension of their therapeutic effect
- Excessive inhibition of Calcium influx can cause
  - Serious cardiac depression
  - Bradycardia
  - Anterioventricular block
  - Cardiac arrest
  - Heart failure

β -blockers

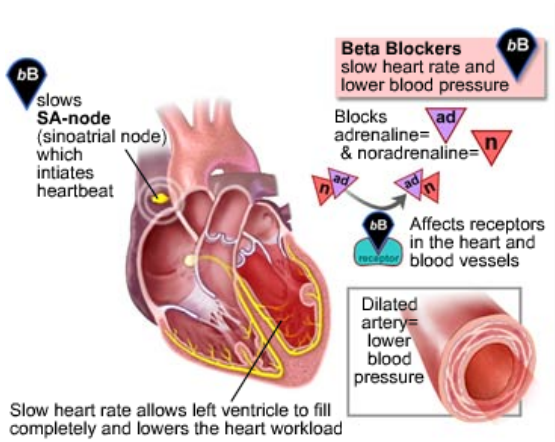
- Beta blockers block the effect of sympathetic nervous system on heart

- Beta blockers prevent binding of catecholamines (adrenaline) on beta receptors (β1) on heart
  1. Resulting is slow heart rate
  2. Decreased contractility of heart



β -blockers

- Lowering of heart rate, contractility *reduces O_2 consumption of heart*
- Most important factor in relief during AP



- Non-selective β -blockers:
  - Carvedilol
  - Nebivolol

- Selective β -blockers:
  - Bisoprolol, metaprolol