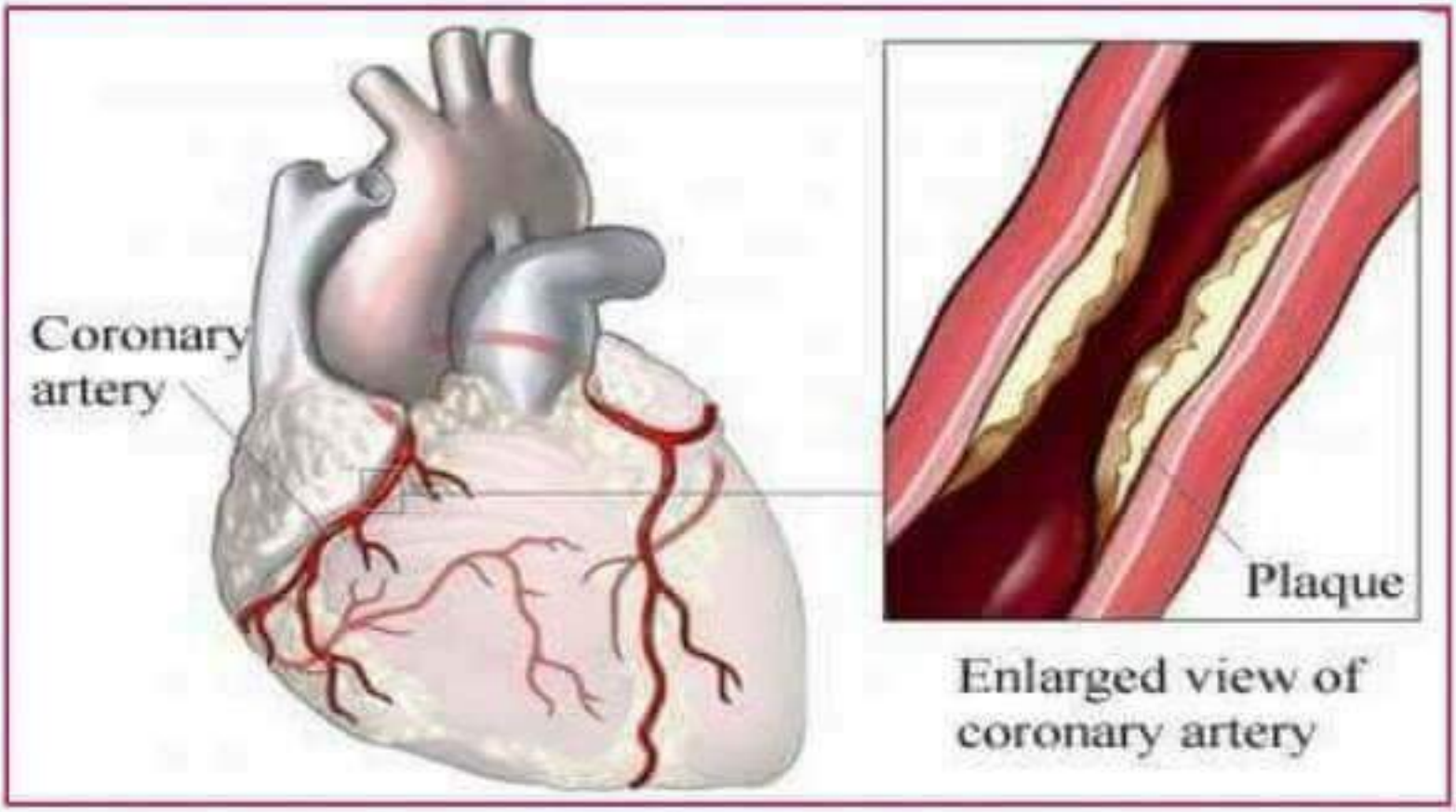

DRUGS USED IN
MYOCARDIAL ISCHEMIA
Share For Others

myocardial ischemia

- **Myocardial ischemia:**
  - Myocardial ischemia also known angina is a heart condition caused by a temporary lack of oxygen-rich blood to the heart.
  - The sudden severe, pressing chest pain occurs, starting from substernal and radiate to left arm.
  - The inadequate blood flow is caused by narrowed coronary arteries, which are the vessels that supply blood to the heart

Myocardial ischemia



Understanding the heart and coronary arteries

- Like any muscle, the heart needs a constant supply of oxygen and nutrients
- Which are carried to it by the blood in the coronary arteries similar to other muscle.
- The harder the heart is working the more oxygen &nutrients it needs
- The coronary arteries can become narrowed or clogged, which can decrease the amount of blood that goes to the heart muscle

➢ **variant MI**

- It is rare and occurs at rest
- Pain associated with this can be severe and usually occurs between midnight and early morning
- Pain relieved by medicines

➢ **unstable MI**

- it is dangerous condition & requires emergency treatment
- it is a sign that heart attack could occur soon
- it does not follow a pattern
- occurs without physical exertion & not relieved by rest & medicine

Conditions that increases o_2 supply

1. Stress
2. Exercise
3. During increased heart rate

Conditions that decrease o_2 supply

1. Coronary arteries diseases
- Accumulation of plaques
- Platelets aggregation
- Stenosis or spasm or constriction or narrowing

2. Reduction in blood flow to heart
- Due to constriction of blood vessels

3. Reduction in $o_2$carrying capacity of blood
- Decrease Hb levels (in anemic conditions)
- Normal blood flow and supply but decrease in o_2 carrying capacity

Risk factors

1. Tobacco
2. Diabetis
3. High B.P
4. High blood cholesterol or triglyceride levels
5. Lack of physical activity
6. Obesity
7. Family history

Complications

- Irregular heart rhythms (arrhythmia)
- Heart attack (myocardial infarction)

Classification

- coronary vasodilators

1. Nitrites & nitrates

according to duration of action

- Shot acting (3 to 60 min)

  Amyl nitrite, nitroglycerin(sublingual), isosorbide dinitrate

- Intermediate acting(3 to 6hrs)

  Isosorbide dinitrate ,nitroglycerin(ointment)

- Long acting(6 to 10 hrs)

  Erythirtyl tetranitrate, nitroglycerin (trans-cutaneous

- Beta adrenergic blocking agents

  Atenolol
  Propranolol
  Nadolol

- Calcium Channel Blockers

  Amlodipine , Bepridil
  Diltiazem , Felodipine
  Isradipine, Nicardipine, Nifedipine
  Nimodipine, Verapamil

- Potassium Channel Activators:
  Nicorandil, Pinacidil
- Antiplatelet Drugs :
  Aspirin Clopidogrel
- Angiotensin-Converting enzyem Inhibitor:

captopril, enalapril, lisinopril

- Cholesterol Lowering Medication :
  Atorvastatin, Fenofivrate

Further treatment

- surgical procedures for MI

1. Angioplasty and stenting
2. Coronary artery bypass surgery

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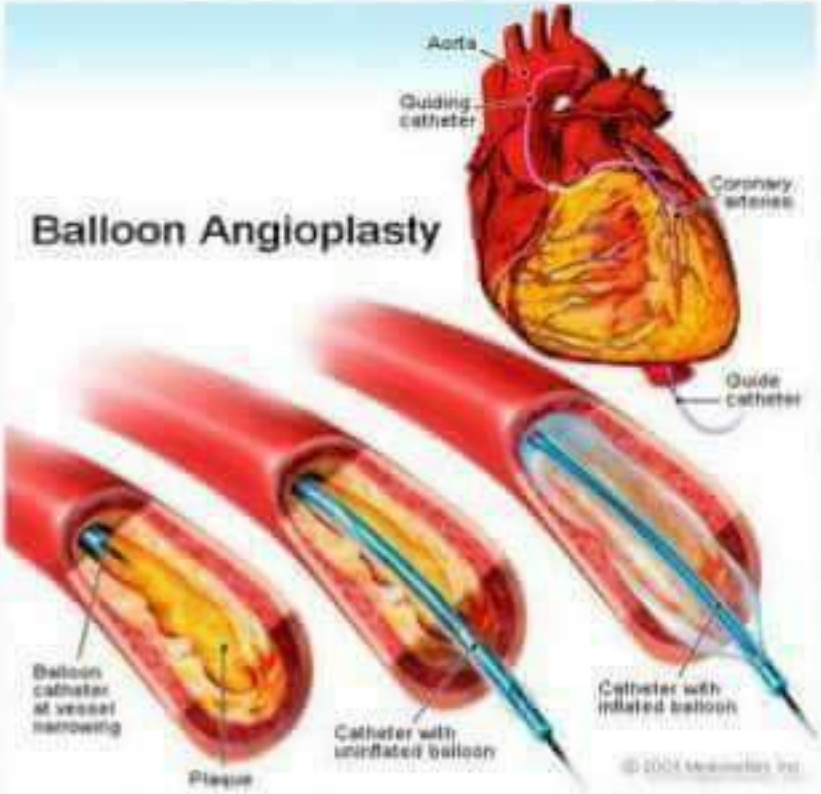
stenting

Angioplasty



Biochemical role of nitrates

Release of Nitric oxide radical

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Activation of Guanylate cyclase

↓

Accumulation of cGMP

↓

Activation of cGMP dependent Kinases

↓

Dephosphorylation of myosin light chain

↓

Vasodilatation of Venules and Arterioles

1. **Hemodynamic role of nitrates**
   1. Venodilatation → ↓ Preload
   2. Arteriolar dilatation → ↓ After load
   3. Redistribution of blood in myocardinm
   4. Increase PGE_1, PGI_2

      Decrease in platelet aggregation

•Pharmacokinetics

-Extensive first pass metabolism.

- Metabolized by denitration & conjugation

-Low bioavailability only 20%

-Unchanged nitrate has half life of 2-8min

-Excretion : renal route.

Clinical uses of Nitrates:

- For treatment & prophylaxis of classical angina pectoris
- Treatment of Variant Angina
- Treatment of Unstable Angina

Adverse effects of Nitrates

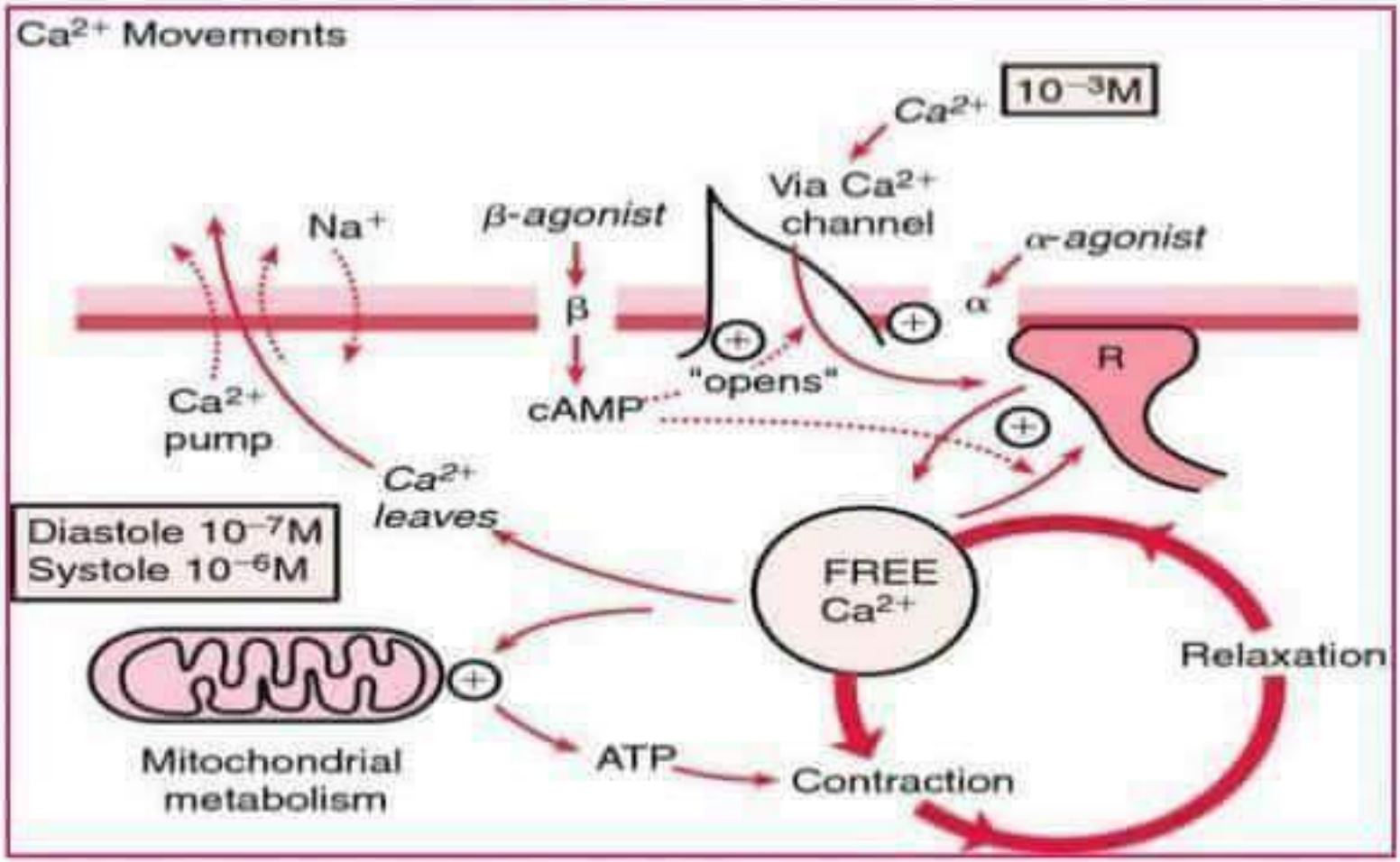
- **In therapeutic doses:-**

1. Throbbing Headache
2. Flushing
3. Syncope
4. Drug rash
5. Tolerance
6. Constipation.

- **In high doses:-**

1. Reflex sympathetic over activity leading to tachycardia which increases work load on heart.
2. Fall in blood pressure
3. Methemoglobinemia

Ca^{+2} Channel Blockers



Ca^{+2} Channel Blockers

- Ca^{+2} channel blockers protect tissue by inhibiting the entrance of Ca^{+2} into cardiac and smooth muscle cells of the coronary and systemic arterial beds.
- All Ca^{+2} channel blockers produce some vasodilatation (↓ PVR)
- Some agents also slow cardiac conduction particularly through the AV node thus serving to control cardiac rhythm.
- Some agents have more effect on cardiac muscle than others but all serve to lower blood pressure.
- They are useful in Prinzmetal angina in conjunction with nitrates.

Potassium channel opener's mechanism

Potassium channel openers

↓

Activate potassium channel

↓

increase potassium permeability in cell

↓

Hyperpolarisation occurs

↓

Closer of L-type calcium channels

↓

Reduced intracellular free calcium

↓

Leads to vasodilatation

Nicorandil

- Administration : orally
- Bioavailability : 75 to 80%
- Protein binding : 25%
- Metabolism : hepatic
- Half life : 1hr
- Excretion : renal

Adverse effect

- Headaches
- Nausea
- Vasodilatation
- Vomiting
- Decrease B.P
- Stomach pain

Antiplatelet drugs

Mechanism of action

- prostacyclin (PGI2) & thromboxane (TXA2) are derived from archedonic acid.
- PGI2 is formed from vascular endothelium
- TXA2 is generated by platelets is a vasoconstrictor
- PGI2 is important for natural resistance to arterial thrombosis
- TXA2 and vascular PGI2regulates the the platelet aggreability
- Collagen form sub endothelial matrix of damaged vessel initiates the attachment
- TXA2 inhibits the adenylyl cyclase and lowers the cAMP concentration
- Low concentration of cAMP accelerates platelets aggregation

-Aspirin inhibits cyclo-oxygenase

-Inhibits the TXA2 synthesis

-Prevention of platelet aggregations

Pharmacokinetics

- Administration : orally
- Bioavailability : rapidly and completely absorbed
- Protein binding : 99.6%
- Metabolism : hepatic
- Half life : 5-9hr
- Excretion : renal

Adverse effects

- Nausea
- Rashes and diarrohea
- Peptic ulceration

Angiotensin converting enzyme inhibitors

Mechanism:

inhibit ACE

↓

low circulating Ang II

↓

decreased PVR

Pharmacokinetics

Bioavailability : 60% (oral)

Metabolism : hepatic

Half life : 11 hrs

Excretion : renal

Main effects: decreased PVR → decreased BP

Adverse effects: skin rash, taste, cough, hyperkalemia

Cholesterol lowering drugs

Mechanism of action

- Competitively inhibiting HMG-CoA reductase first enzyme of HMG-CoA reductase pathway
- Statins are similar to HMG-CoA
- They take the place of HMG-CoA in the enzyme and reduce the rate by which it is able to produce mevalonate which is used in production of cholesterol

- Reduce LDL levels by 30% to40%
- Reduce HDL levels by 2% to 15%
- Reduce triglycerides by 10% to30%

Atrovastatin

- absorption :rapid oral absorption
- T max 1 to 2 hours
- High intestinal clearance &first pass metabolism
- Protein binding >98%
- Excretion: hepatic biliary excretion

Fenofivrate

- absorbtion : oral absorbtion
- Half life :20 hrs
- Protein binding >99%
- Excretion: renalexcretion

Adverse effects

- Mild transient GI disturbances
- Rash headache
- Myopathy (muscle pain)
- Elevation of liver diseases

Contraindication

- Interaction with anti arrhythmic drugs Antidepressants
  - Failure of sublingual tablets of nitrates to dissolve
- Interactions with corticosteroids NSAIDS
  - Hypotensive action is antagonized
- Interaction with beta blockers and calcium channel blockers
  - They can cause the excessive hypotension