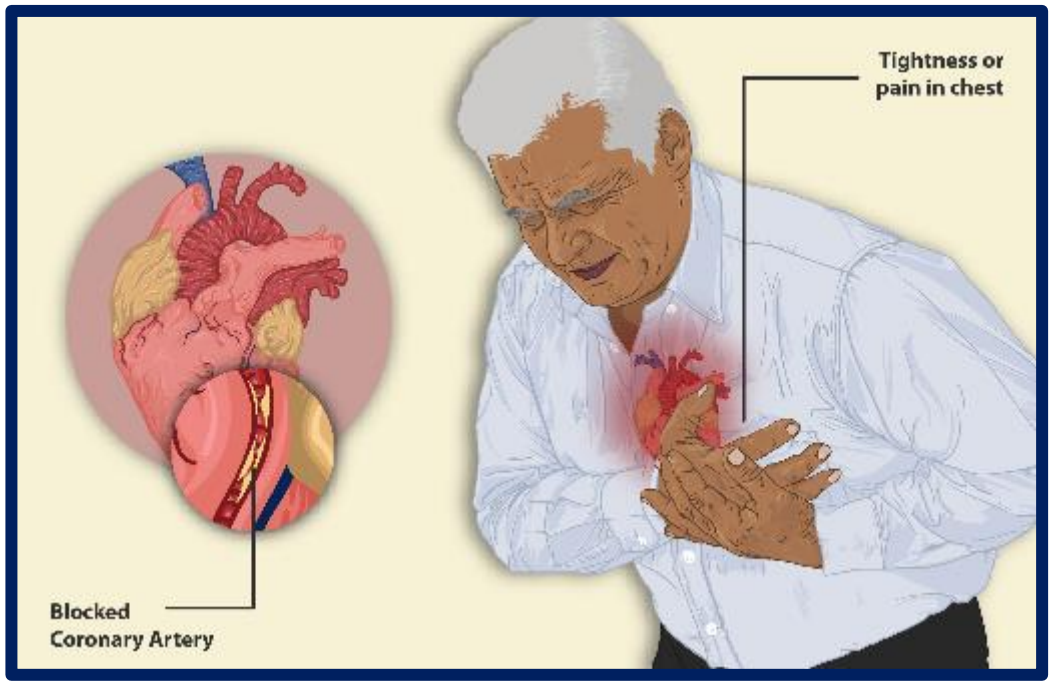
Block CVS-206



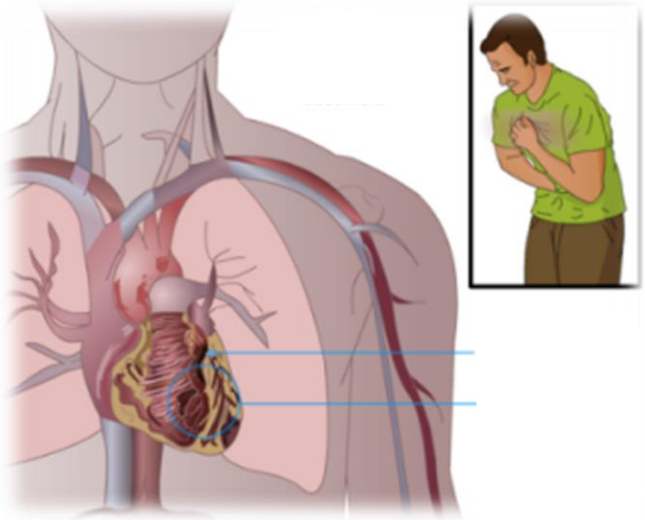
Angina Pectoris

Dr Lobna Aly Abdelzaher

Associate Professor of Pharmacology

Faculty of medicine

Angina Pectoris

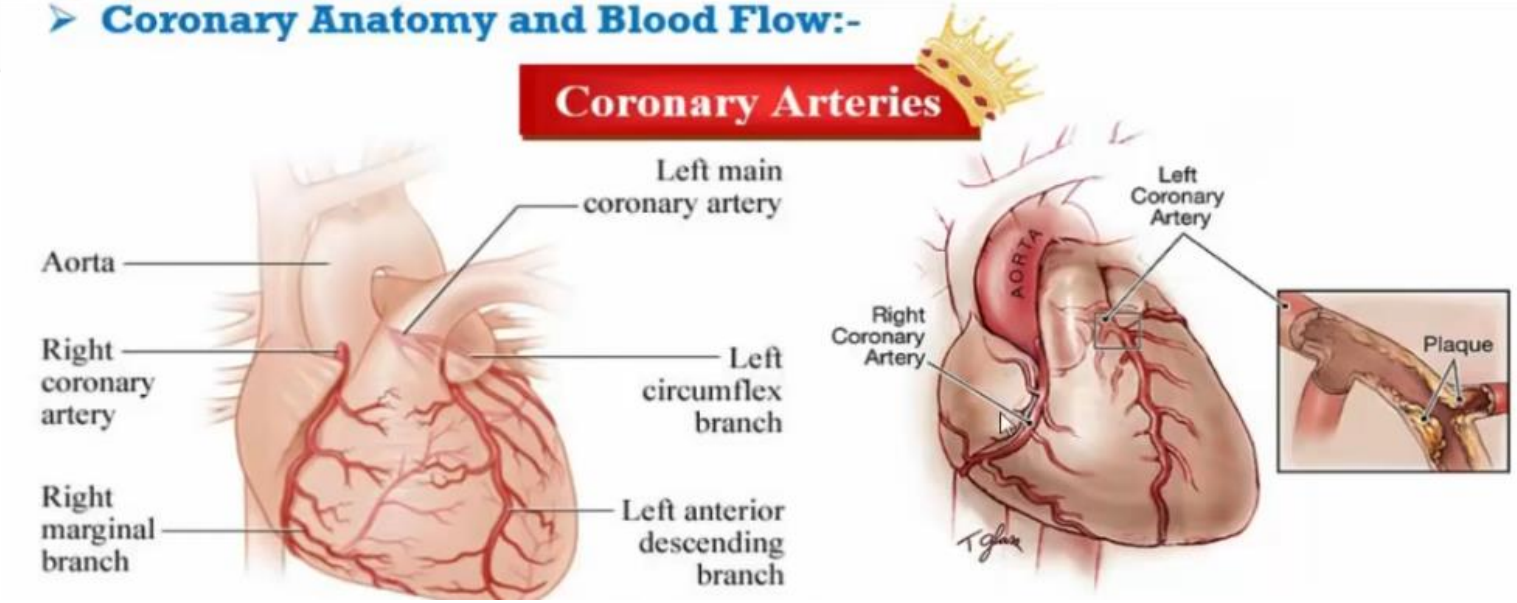


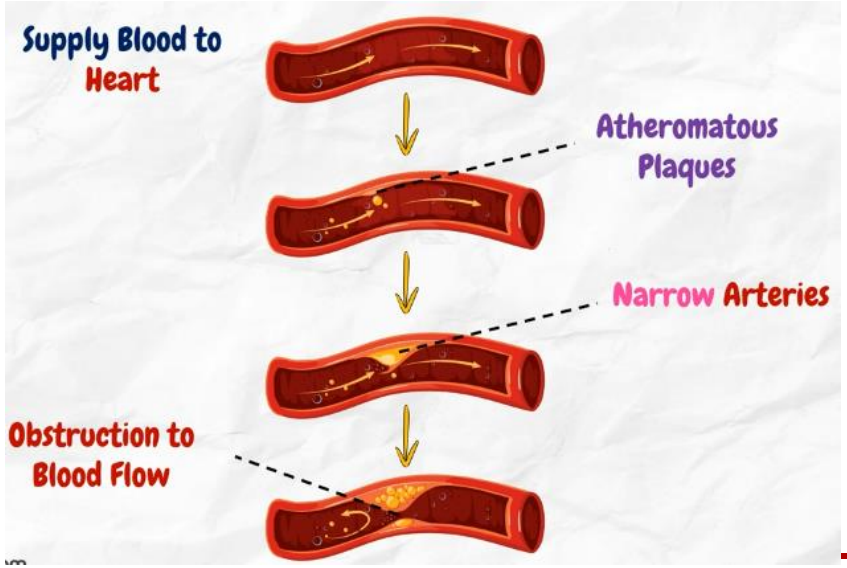
- One of group of diseases known as ***ischemic heart disease (IHD) or Coronary artery disease (CAD)***.
- ***Ischemic heart disease (IHD)*** is defined as **lack of oxygen and decreased or no blood flow to the myocardium resulting from coronary artery narrowing or obstruction** which include:

Angina Pectoris

Myocardial Infarction (MI)

Coronary Anatomy and Blood Flow:-



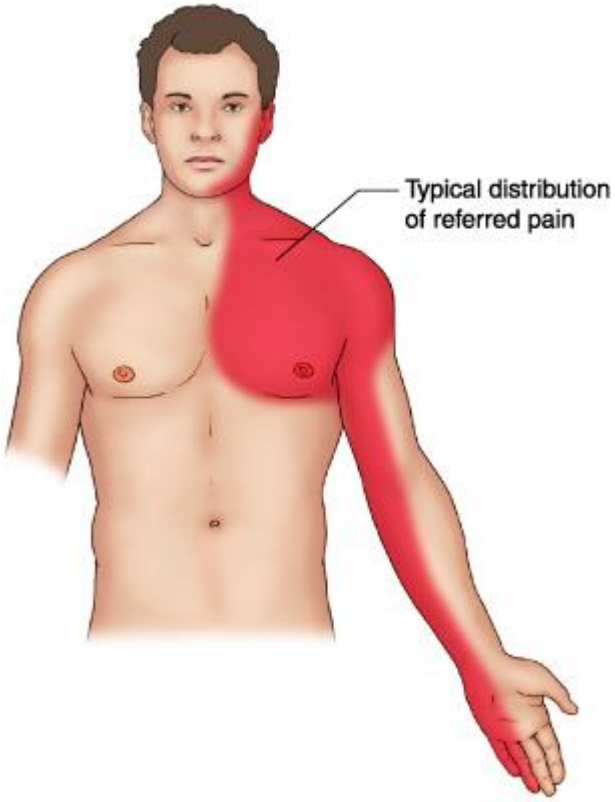


Angina Pectoris

Myocardial Infarction (MI)

Dr Lobna Aly Abdelzaher

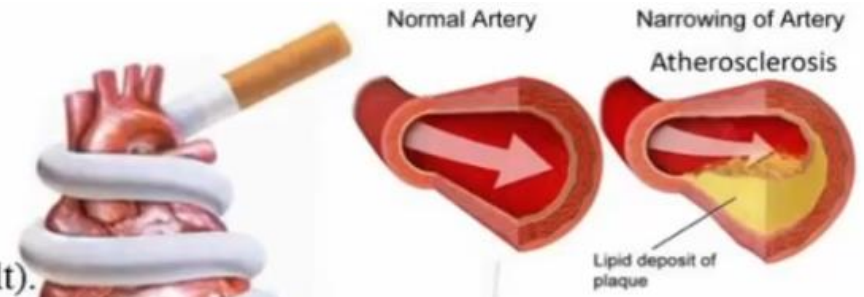
2025-2026



- ***Angina means chest pain due to transient myocardial ischemia due to imbalance in the myocardial oxygen supply–demand.***
- It is experienced as a **sudden severe heavy, pressing substernal discomfort** (rarely described as a "pain"), or **stabbing pain** often **radiating to the left shoulder, flexor aspect of the left arm, jaw, or epigastrium**.

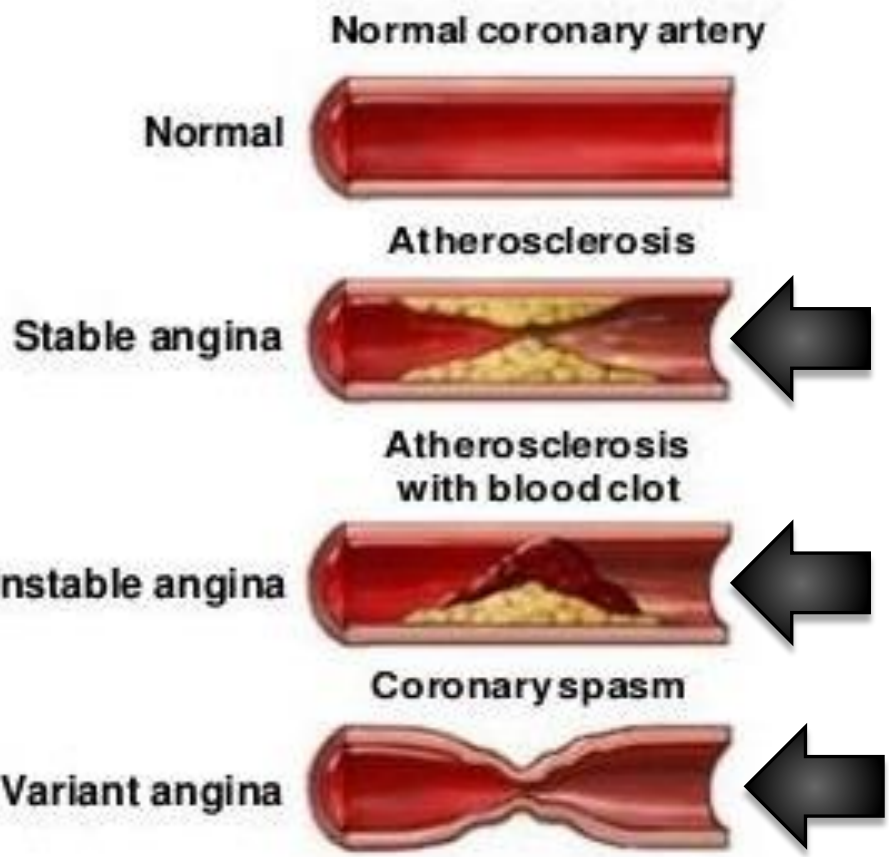
➢ Angina Risk Factors:-

- Coronary heart disease.
- Family history of heart disease.
- Unhealthy cholesterol levels.
- Unhealthy diet (high fat and high salt).
- Smoking.
- Diabetes.
- Inactivity.
- High blood pressure.
- Overweight or obesity.
- Stressful lifestyle.
- Age (Men > 45 years - Women > 55 years).



- *N.B*; **Atherosclerosis**, or **hardening of the arteries**; is a condition in which plaque builds up inside the arteries. Plaque is made of cholesterol, fatty substances, cellular waste products, calcium and fibrin.

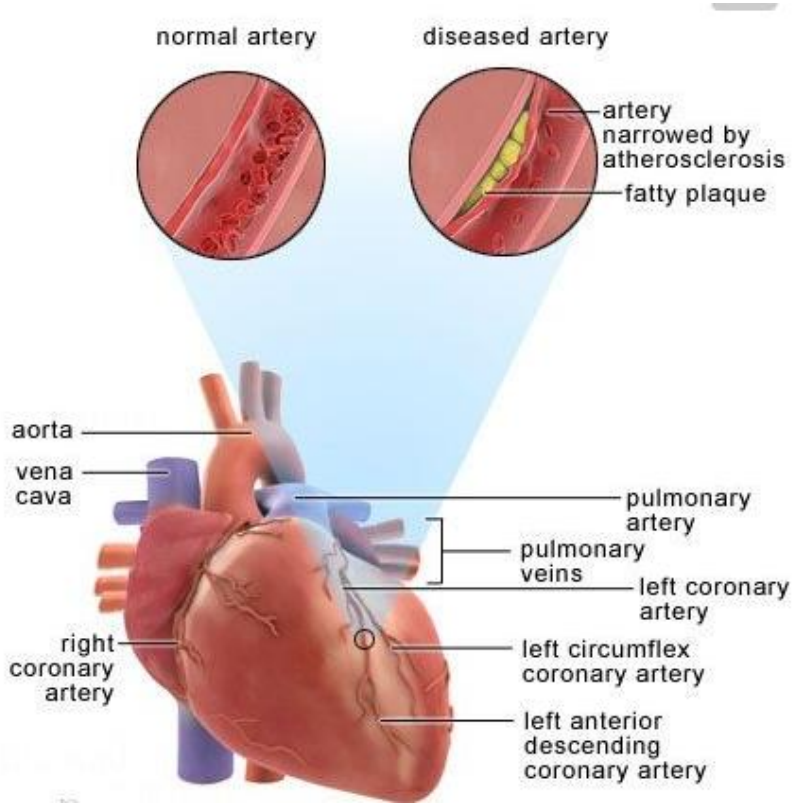
Types



Stable Angina

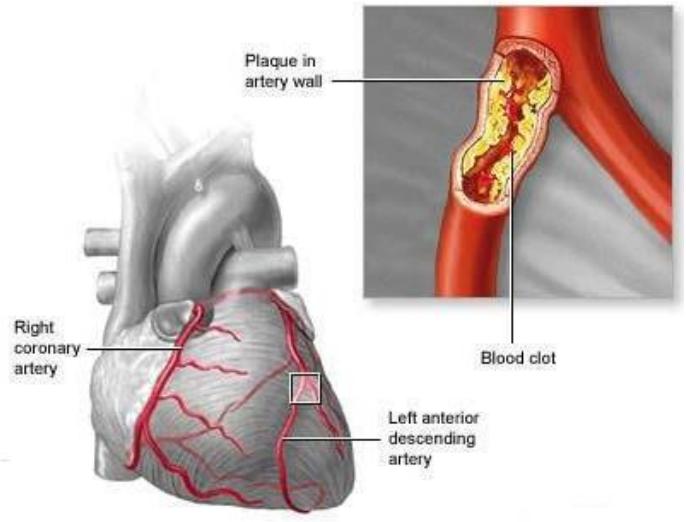
Unstable Angina

Vasospastic angina



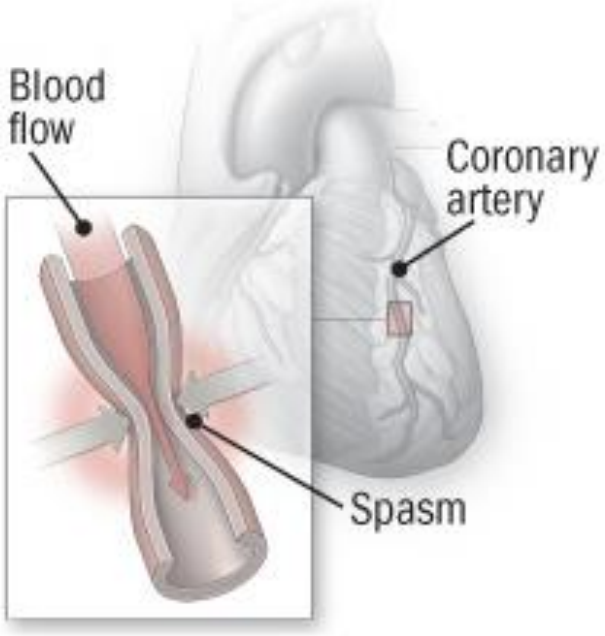
1. Stable (atherosclerotic, angina of effort, exertional, classic or typical angina).

- It is due to **atheromatous plaques that partially occlude one or more coronary arteries**.
- **When cardiac work increases** (e.g., in exercise), **the inadequate oxygen delivery results in the accumulation of metabolites**, e.g., lactic acid, and ischemic changes that **stimulate myocardial pain endings.**
- **Rest** usually **leads to complete relief of the pain within 15 min**.
- **Atherosclerotic angina constitutes about 90% of angina cases**.



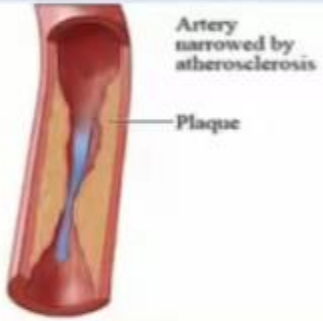
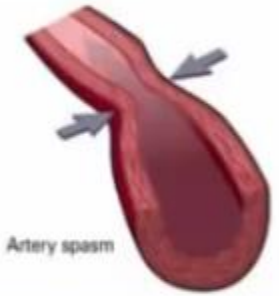
2. Unstable angina (acute coronary syndrome)

- Disruption of a coronary plaque, leading to **local platelet aggregation and thrombosis** at the arterial wall, vasospasm with subsequent partial or total occlusion of the vessel.
- It Is characterized by **increase in severity or frequency of attacks.**
- Unstable angina is **pre-infarction and is treated as a medical emergency**.



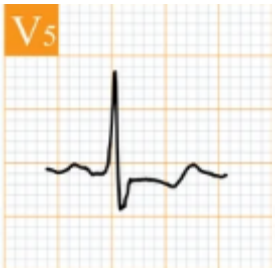
3. Vasospastic angina (rest angina, variant angina, or Prinzmetal's angina)

- It is responsible for less than 10% of angina cases.
- It involves **reversible spasm of coronaries, usually at the site of an atherosclerotic plaque**.
- **Spasm may occur at any time** (usually at midnight between 12 AM and 8 AM; cold weather & stress can cause spasm) .

	Stable Angina	Unstable Angina	Variant Angina
Other Names	- Classical Angina. - Typical Angina. - Exertional or Effort Angina.	- Crescendo Angina. - Pre-infarction Angina. - Acute Coronary Syndrome.	- Vasospastic Angina. - Prinzmetal's Angina. - Angina Inversa.
Causes	- Narrowing of coronary arteries due to atherosclerosis. 	- Narrowing of coronary arteries due to atherosclerosis, transient formation of a blood clot within a coronary artery, result, total or near-total blockage. 	- Results from coronary vasospasm, which temporarily reduces coronary blood flow. 
Distribution	- Most common type.	- Common.	- Rare (2% of angina cases).
Occurs	- Physical exertion. - Emotions. - Exposure to cold weather. - Heavy meals.	- At rest or minimal exertion.	- At rest between midnight (12:00) and early morning (8:00). - Cold weather and stress can cause spasm.
Attack	- Usually lasts a short time (5 minutes or less).	- More severe and lasts longer, maybe as long as 30 minutes.	- Lasts from 5-30 minutes.
Relief	- Decreases at rest. - Relieved by nitroglycerin.	- Not relieved by rest. - Not relieved by nitroglycerin. - Treated as an emergency.	- Relieved by nitroglycerin.

- Myocardial ischemia also may be ***silent***, *with* ***electrocardiographic, echocardiographic***, or radionuclide **evidence of ischemia appearing in the absence of symptoms**.

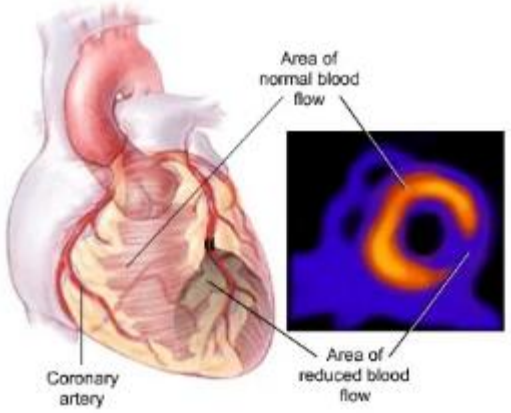
Diagnosis



ST segment depression

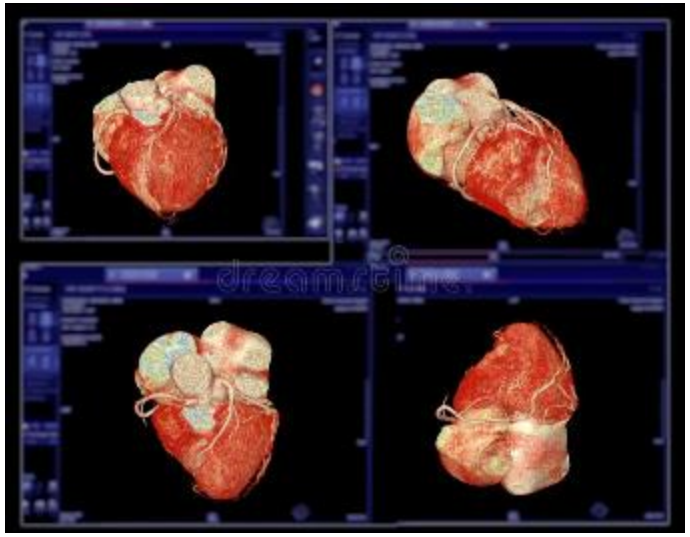
ECG

Stress Test

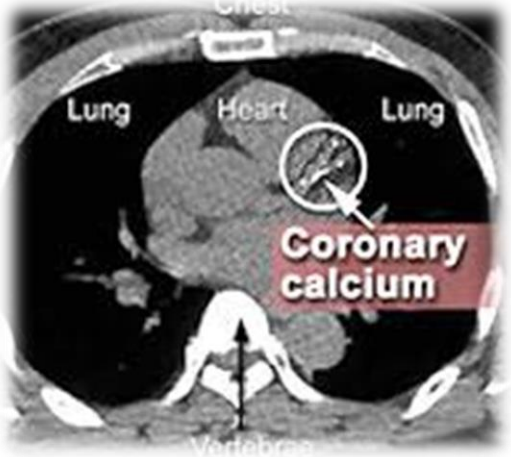


Nuclear Stress Test

Cardiac CT



Coronary CT Angiography



Calcium Score Screening Heart Scan

- **Non Specific:**
  - Blood Pressure,
  - Lipid Profile,
  - Kidney Function Test.

➢ Treatment Goals:-

- ***The main goals*** of treatment in angina pectoris are to **relieve the symptoms**, **slow the progression of disease**, and **reduce the possibility of future events**, especially **myocardial infarction (MI)** and **premature death**.
  - **Increase O_2 Supply**; Vasodilators (Nitrates and Ca^{2+} Channel Blockers).
  - **Decrease O_2 Demand**; β-adrenergic Receptor Antagonists.
  - **Lifestyle modification**.
  - **Treat coronary artery disease**;
    - Decrease bad cholesterol level (LDL) e.g. statins
    - Surgical procedures e.g. angioplasty.

Principles of treatment

- Exertional angina
  - reducing myocardial O_2 demand
  - Increase the coronary flow
  - Both
- Unstable angina
  - Correction of tendency to intracoronary thrombosis
- variant or Prinzmetal angina
  - Prevention of coronary spasm with coronary vasodilation

Dr Lobna Aly Abdelzaher

2025-2026

Antianginal Drugs

- Four types of drugs, used either alone or in combination, are commonly used to manage patients with stable angina.
- Antiplatelet therapy and lipid-lowering therapy are needed to prevent clot formation and decrease atherosclerosis plaque formation.

Organic Nitrates

β-Blockers

Ca^{2+} Channel Blockers

New Antianginal Drugs

Surgical treatment

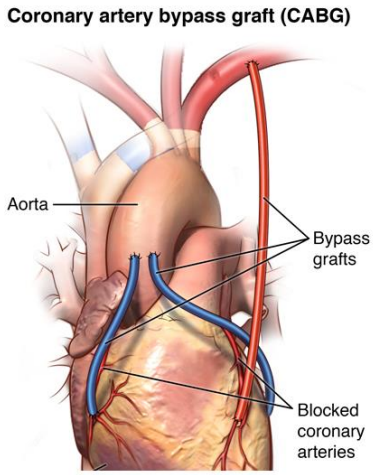
(if medical treatment failed)

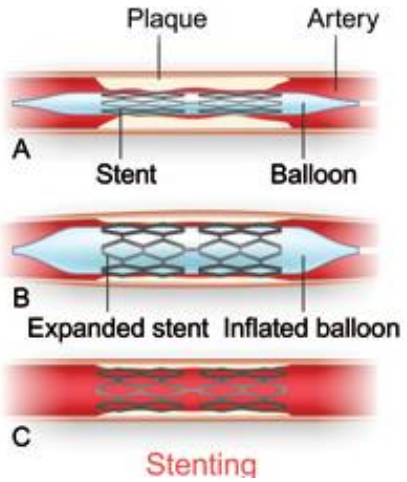
- **Coronary angioplasty** (ballon dilatation).
- **Stent placement Atherectomy**.
- **Coronary bypass grafting.**

Myocardial revascularization corrects coronary obstruction

Bypass grafting
(CABG)

Angioplasty (PTCA)
(enlargement of the coronary lumen by means of a special catheter)





Treatment Of Exertional Angina

General management

- **Fat diet restriction.**
- **Mental & physical rest.**
- **Correction of any predisposing factors** (smoking, diabetes, hypertension & obesity).

Specific drug therapy

- **Organic nitrates.**
- **Ca++ channel blockers.**
- **Beta-adrenergic blockers.**
- **New drugs** (ranolazine).

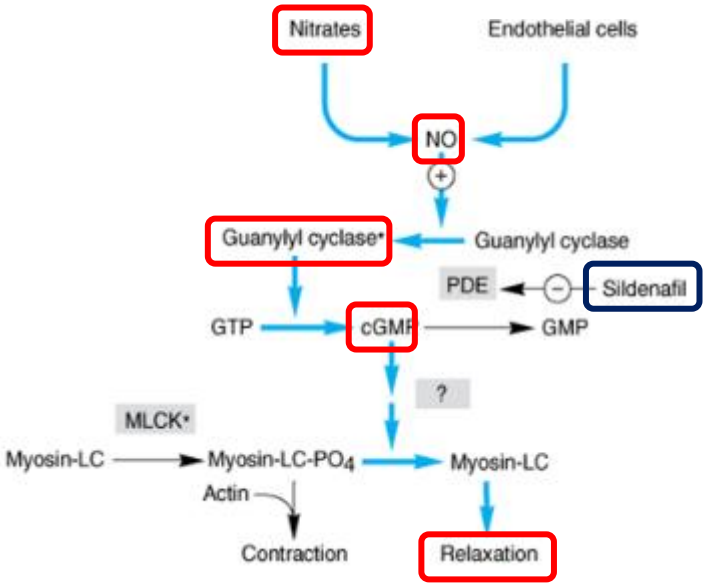
I- ORGANIC NITRATES

Sublingual Nitroglycerin

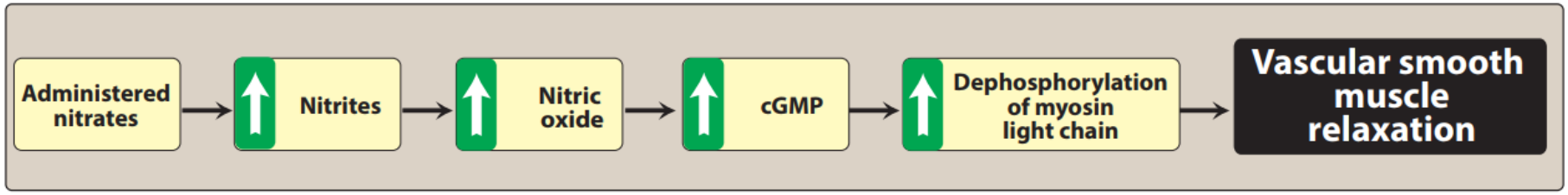
Transdermal Nitroglycerin

- ***Nitroglycerin*** is considered the prototype of this group. Other members include ***isosorbide dinitrate*** and ***isosorbide mononitrate***. **Amyl nitrite** is not used now.
- **Nitroglycerin** (glyceryl trinitrate) (the active ingredient in dynamite) **is the most important of the therapeutic nitrates.**
- It is available in forms that provide a range of durations of action from **10–20 min** (sublingual for relief of acute attacks, onset 1-3 minutes) to **8–10 h** (transdermal for prophylaxis).

Mechanism of Action



- They are **exogenous sources of NO**.
- **Nitrates release nitric oxide (NO) within smooth muscle cells**, probably through the action of the **mitochondrial enzyme aldehyde dehydrogenase-2** (ALDH2)
- **NO can activate guanylyl cyclase and thereby increase the cellular level of cyclic GMP**, the latter results in **smooth muscle relaxation by stimulating the dephosphorylation of myosin light-chain phosphate**.
- **This NO-mediated pathway leads to relaxation of smooth muscle in the vasculature, bronchi, and GI tract, and inhibition of platelet aggregation**.

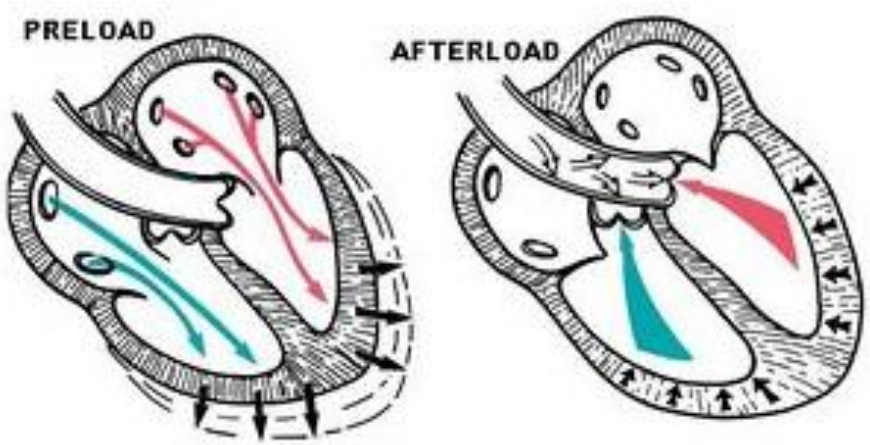


Pharmacological actions

I-Antianginal effect

II-Other effects

Important terms



Preload is determined by the diastolic pressure that distends the ventricle (ventricular end diastolic pressure).
Preload = venous return

Afterload is the impedance against which the ventricle must eject.
Afterload = arterial resistance

I- Antianginal effect

- ***Dilatation of veins*** which **decreases the cardiac preload *(main action in angina)*, *dilatation of arteries*** (but less than veins) which **decreases the afterload**.
- The **decrease in preload and afterload causes decrease in myocardial work and oxygen demands**.
- **Relaxation of arterial smooth muscle** may **increase flow through partially occluded epicardial coronary vessels**.
- ***Dilatation of collateral coronary channels*** with redistribution of coronary blood flow from the normal to ischemic areas.
- **Nitrates are effective in dilating non-atherosclerotic coronary arteries**.

II- Other organs

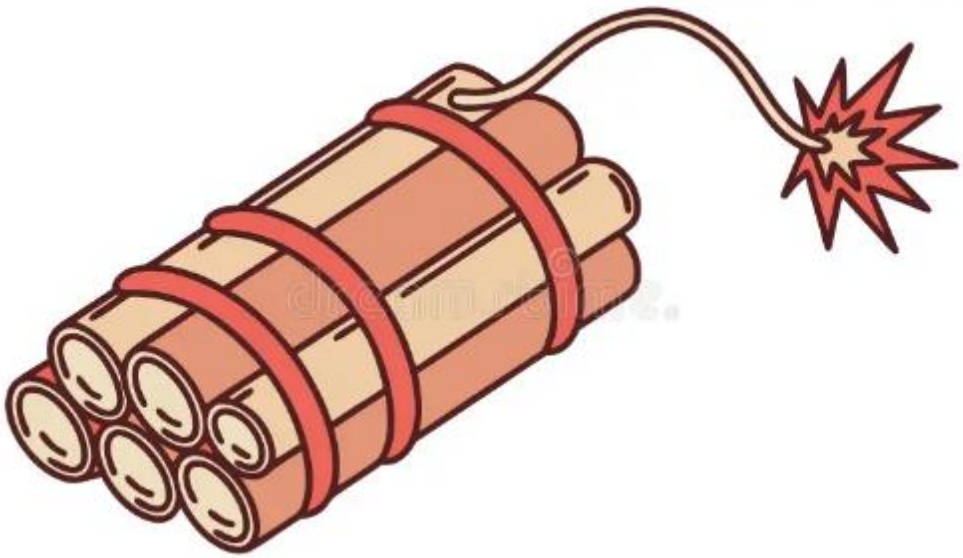
- Nitrates **relax the smooth muscle of the bronchi, gastrointestinal tract, and genitourinary tract, but these effects are too small to be clinically significant.**

Nitrate tolerance

- **Repeated or continuous exposure to high doses** of organic nitrates leads to a marked **attenuation in the magnitude of most of their pharmacological effects**.
- An effective approach **to restoring responsiveness** is to **interrupt therapy (Nitrate Holiday or Nitrate Free Period) for 8-12 h each day, which allows the return of efficacy (omit dosing at night in patients with exertional angina** either by adjusting dosing intervals of oral or buccal preparations or by removing cutaneous nitroglycerin).

Monday Syndrome

(Monday Morning Sickness)



Toxicity and adverse effects

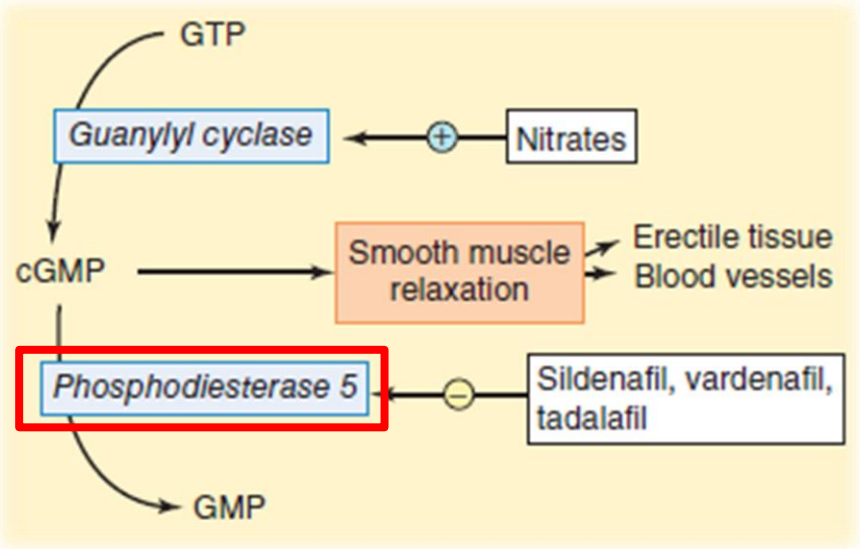
The most common toxic effects of nitrates are the **responses evoked by vasodilation**. These include **tachycardia** (from the baroreceptor reflex), **orthostatic hypotension** (a direct extension of the venodilator effect), **nitrate flush** and **throbbing headache** from meningeal artery vasodilation.

- **Headache is common and can be severe.**

- **Postural hypotension & nitrate syncope** (positioning and other measures that facilitate venous return are the only therapeutic measures required).

- **Transient episodes of dizziness, weakness & drug rash.**

Interaction with PDE5 inhibitors



- The combination of **nitrates** (through increased production of cGMP) and a PDE5 inhibitor as **sildenafil and similar drugs** (through decreased breakdown of cGMP) causes a **synergistic relaxation of vascular smooth muscle with potentially dangerous hypotension and inadequate perfusion of critical organs**.
- **PDE5 inhibitors are contraindicated for patients taking organic nitrate.**

Therapeutic uses

1) Angina pectoris *(effective in all types of angina)*

a) Treatment of acute attacks:

- **Nitroglycerin sublingual is the drug of choice**; it acts within 1-2 minutes and lasts for 15 minutes (Sublingual tablets can be repeated but if pain is not relived by 3-4 tablets or lasts for more than 20 minutes, myocardial infarction may be suspected, and the patient should be transferred to ICU.).
- It is used also by **IV injections in severe cases**.

b) Prevention of attacks:

- Using either short acting drugs just before activity or Long acting nitrates as sustained release tablets or capsules.

2) Acute heart failure with pulmonary edema

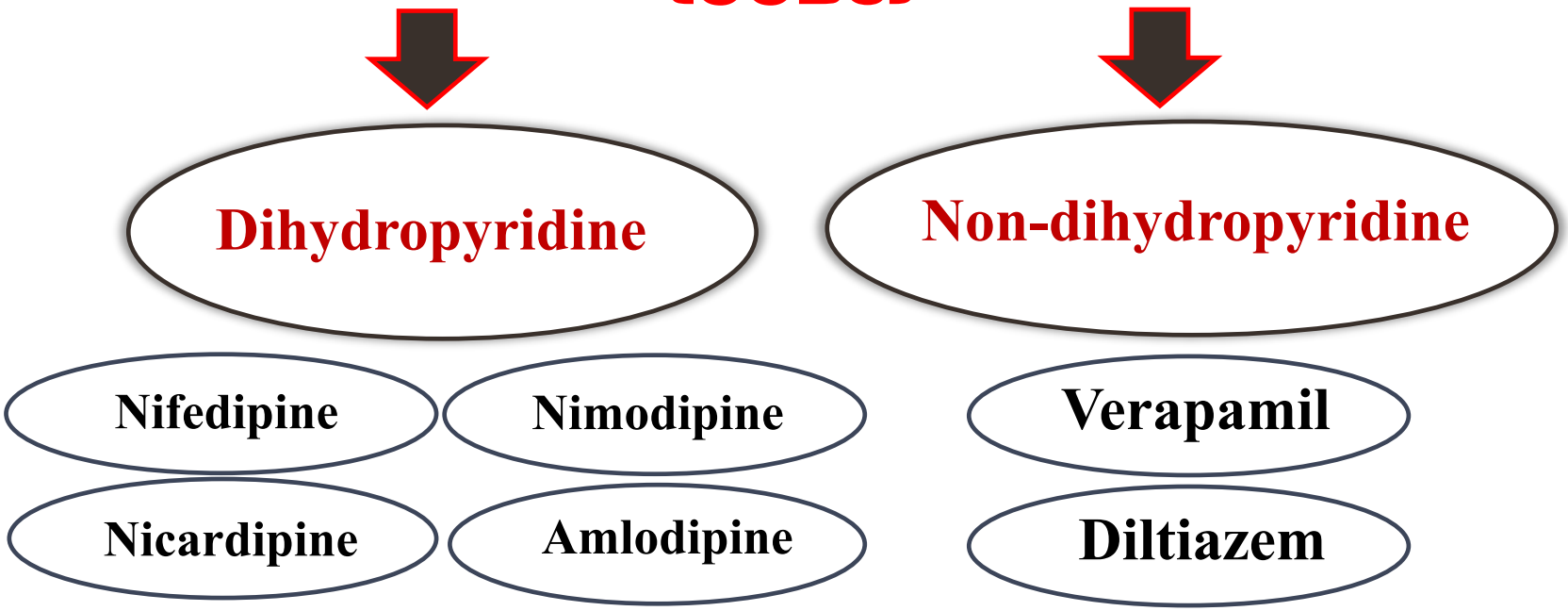
- They act by dilating the veins, so they decrease the preload.

3) Hypertensive emergencies: I.V. nitroglycerin is used in hypertensive crisis with acute ischemic syndrome.

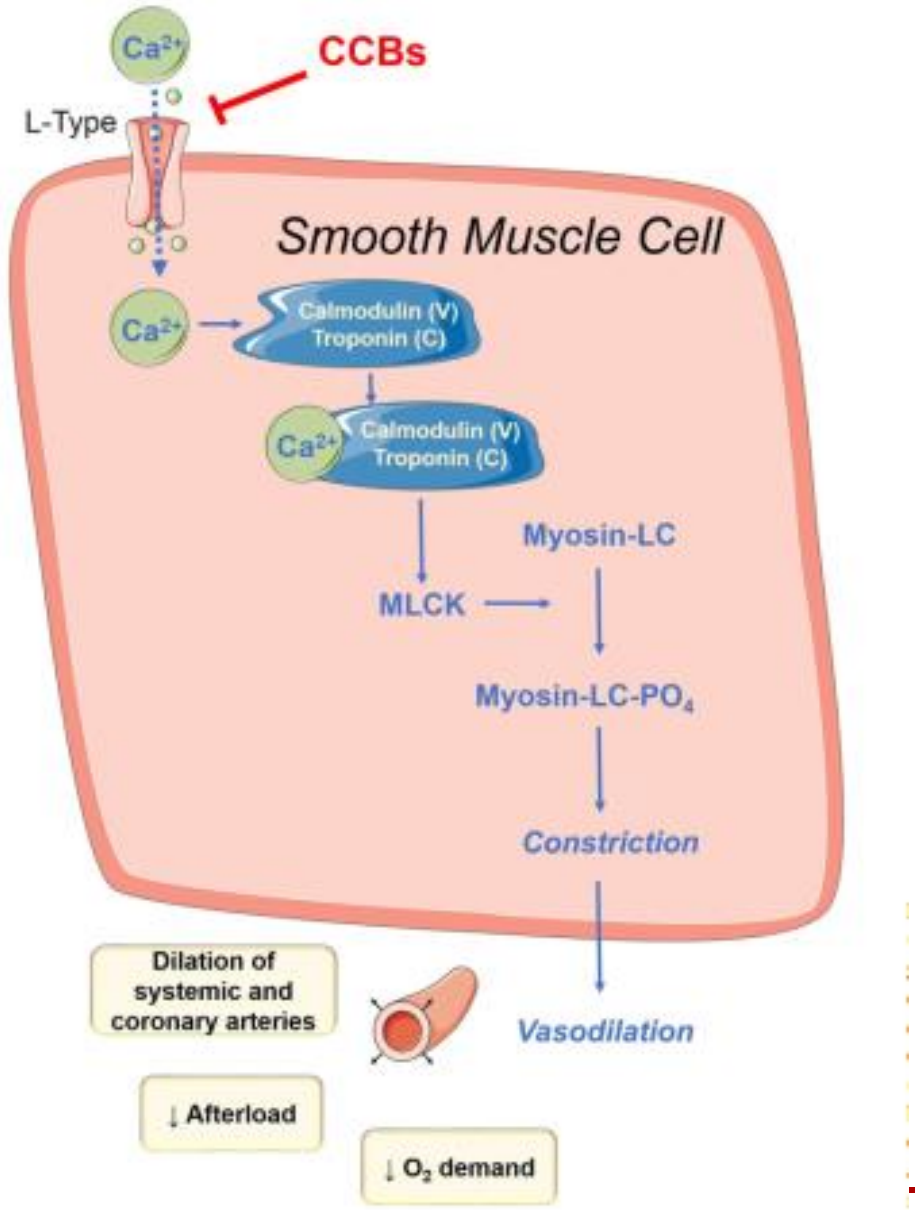
4) Diffuse esophageal spasm:

- relief the spasm during the acute attack

II- Calcium channel-blockers (CCBs)



- All are orally active and most have half-lives of 3–6 h.
- They **block voltage-gated L-type calcium channels (cardiac and smooth muscles), and reduce intracellular calcium concentration and muscle contractility**.


Ca2+
CCBs
L-Type
Smooth Muscle Cell
Ca2+
Calmodulin (V)
Troponin (C)
Ca2+
Calmodulin (V)
Troponin (C)
Myosin-LC
MLCK
Myosin-LC-PO4
Constriction
Dilation of systemic and coronary arteries
Vasodilation
↓ Afterload
↓ O2 demand

Pharmacological actions

- All Ca^{2+} channel blockers **relax arterial smooth muscle, but they have a less pronounced effect on most venous beds (do not affect cardiac preload significantly).**
- Nifedipine and other **dihydropyridines** are more potent **vasodilator** resulting **sympathetic reflex (from dihydropyridines vasodilator effect) that may actually increase heart rate**.
- **Non-dihydropyridines as Verapamil** and **diltiazem depress the rate of the sinus node pacemaker and slow AV conduction.**

Role in Angina

1-Variant angina

- **Drug of choice**

2- Exertional angina

- Their utility may result from:
  - **Increase in blood flow owing to coronary arterial dilation,**
  - **Decrease in myocardial oxygen demand (secondary to a decrease in arterial blood pressure, heart rate, or contractility),**
  - **or both.**

Toxicity and adverse effects

- **Headache, flushing, dizziness, and peripheral edema (pretibial edema).**
- More serious adverse effects include **heart failure, AV blockade, and sinus node depression (most common with verapamil and least common with the dihydropyridines)**.

Contraindications

- The use of **intravenous verapamil with an intravenous β adrenergic receptor antagonist is contraindicated because of the increased propensity for AV block and/or severe depression of ventricular function**.
- Patients with **ventricular dysfunction, SA or AV nodal conduction disturbances, and systolic blood pressures < 90 mm Hg should not be treated with verapamil or diltiazem**, particularly intravenously.

III- Beta-blocking drugs

Role in Angina

- Timolol, metoprolol, atenolol, and propranolol exert cardioprotective effects.
- Beta blockers with ISA as pindolol should be avoided
- Because they **reduce cardiac work by decreasing heart rate, cardiac force, blood pressure**, **all β blockers are effective in the prophylaxis of atherosclerotic angina attacks**.
- Beta blockers are used only **for prophylactic therapy of angina; they are of no value in an acute attack.**
- **They decrease risk of death in patients with myocardial infarction.**
- They are **ineffective against the vasospastic form** (if used in isolation, may worsen the condition).
- The **combination of β blockers and nitrates is useful** because **the adverse undesirable compensatory effects evoked by the nitrates (tachycardia and increased cardiac force) are prevented or reduced by β blockade.**
- **Withdrawal of beta blockers should be gradual over 2 or 3 weeks.**

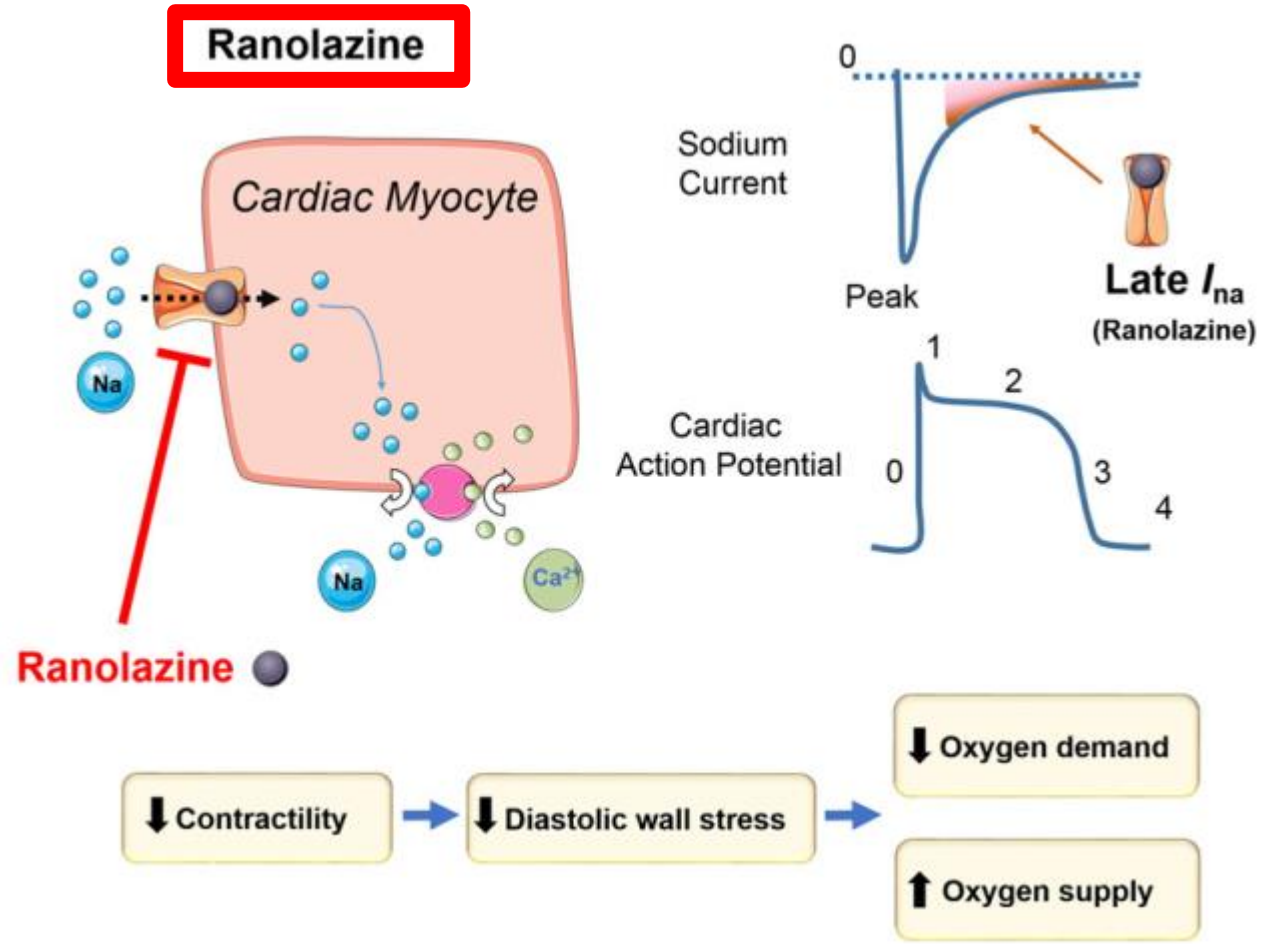
IV-Newer Antianginal Drugs

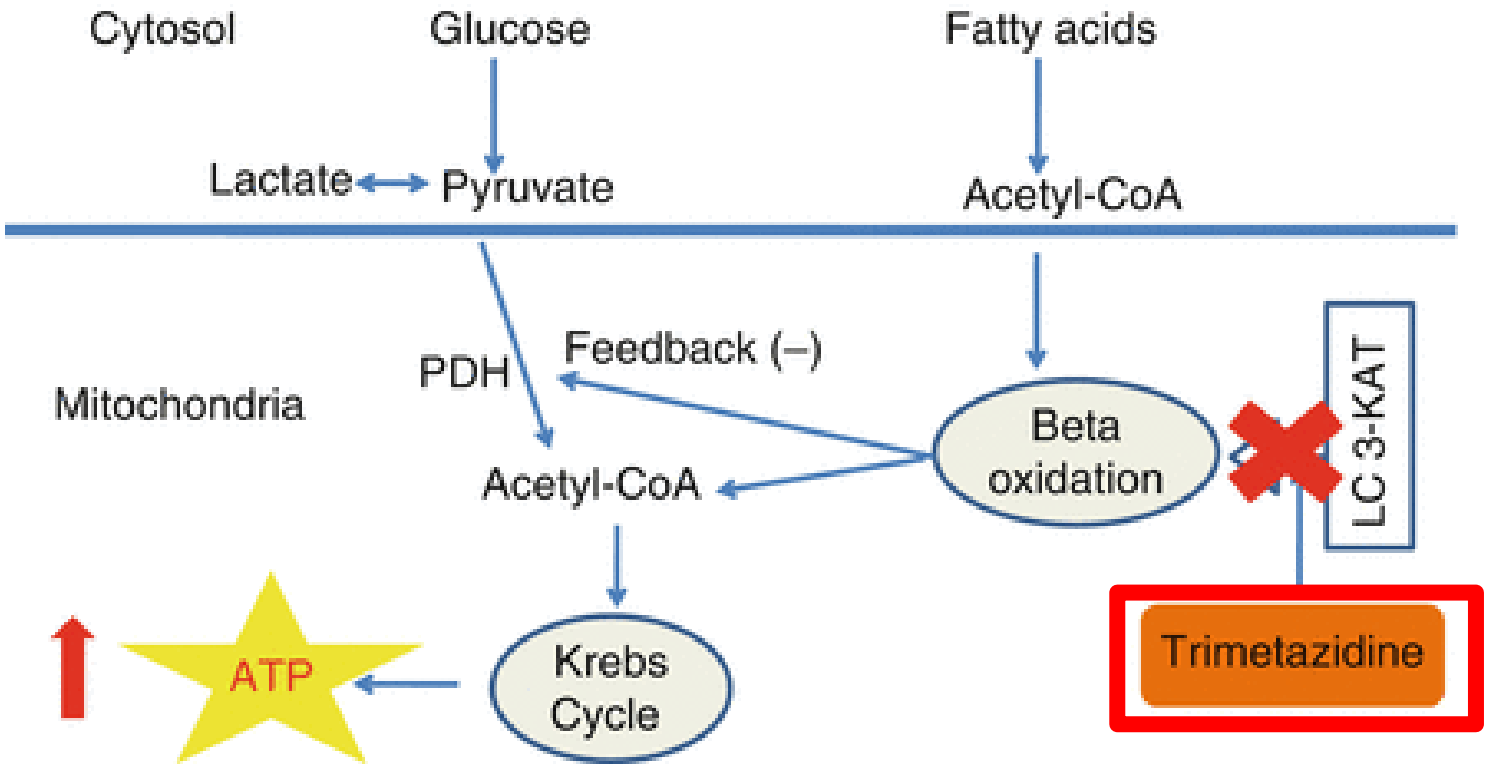
Ranolazine

- It can be used in chronic angina if **it is resistant to other drugs (used alone or in combination)**.
- It acts by **reducing a late sodium current** (I Na) in the cardiac cells, decrease calcium entry via the sodium-calcium exchanger (decrease intracellular calcium) **decrease cardiac contractility and work & decrease oxygen demand.**

Trimetazidine

- It acts by partial **inhibition of fatty acid oxidation pathway in myocardium**.
- They are known as **pFOX inhibitors** because they partially **inhibit the fatty acid oxidation pathway** in myocardium, so **oxygen requirement is decreased**.


Ranolazine
Cardiac Myocyte
Na
Na
Ca2+
Ranolazine
0
Sodium Current
Peak
Late I_{na}
(Ranolazine)
1
2
Cardiac Action Potential
0
3
4
Oxygen demand
Contractility
Diastolic wall stress
Oxygen supply

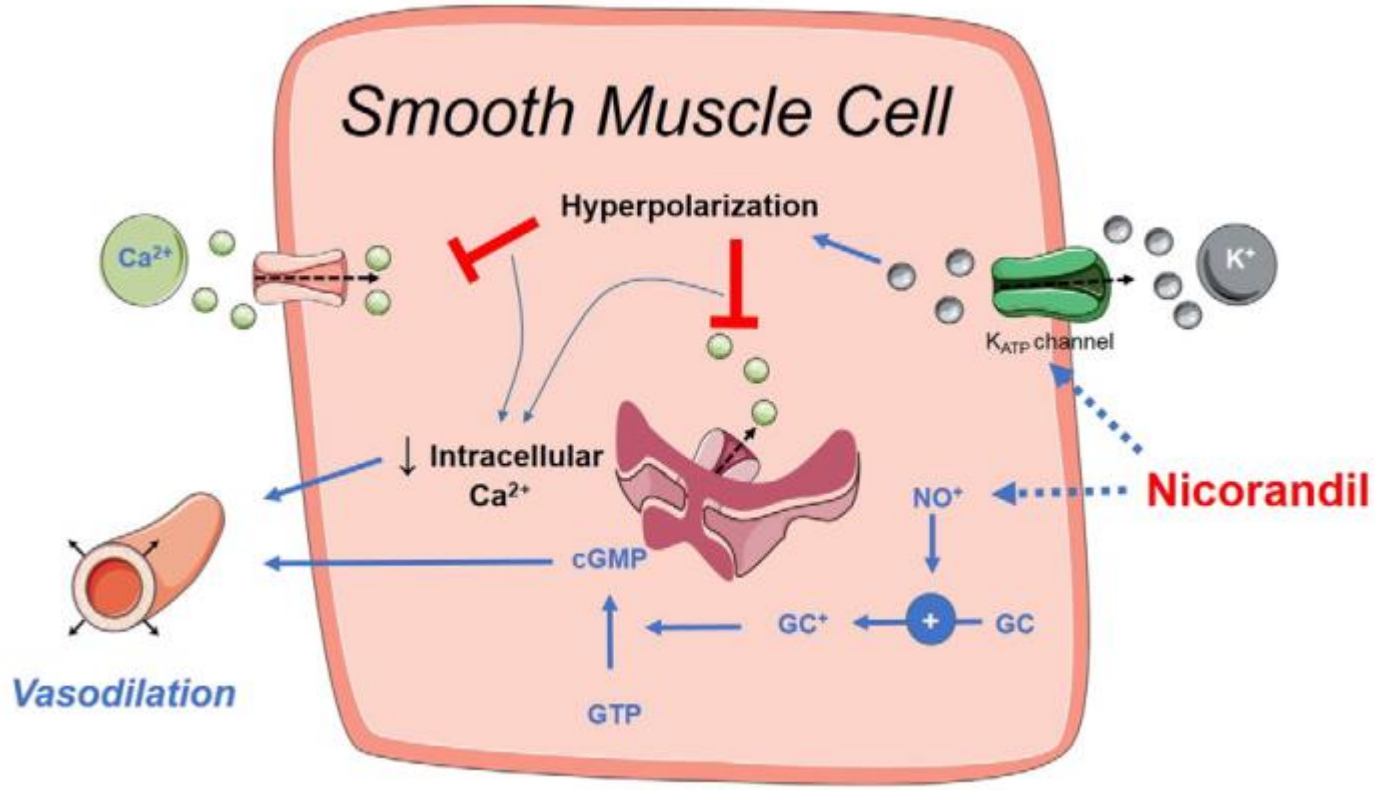

Cytosol
Glucose
Fatty acids
Lactate
Pyruvate
Acetyl-CoA
Mitochondria
PDH
Feedback (–)
Beta oxidation
LC 3-KAT
Acetyl-CoA
Trimetazidine
ATP
Krebs Cycle

Nicorandil

- It **acts as nitrate.**
- It provides some myocardial protection by **activation of cardiac K channels**.

Ivabradine

- **It acts by inhibition of the sinoatrial pacemaker current resulting in decreased heart rate and consequently decreased cardiac work** (if beta blocker is not effective)**.**


Smooth Muscle Cell
Hyperpolarization
Ca2+
K+
KATP channel
↓ Intracellular Ca2+
Nicorandil
NO+
cGMP
GC+
GC
GTP
Vasodilation

Combination Therapy

- It is **better to use single drug** for prophylaxis to decrease the side effects.
- **If no response to single drug one of the following combinations can be used**:

Long acting nitrates with B-blockers

Ca++ channel blockers and B-blockers

Ca++ channels blockers and Nitrates

Ca ++ channel blockers, Nitrates & B-blockers

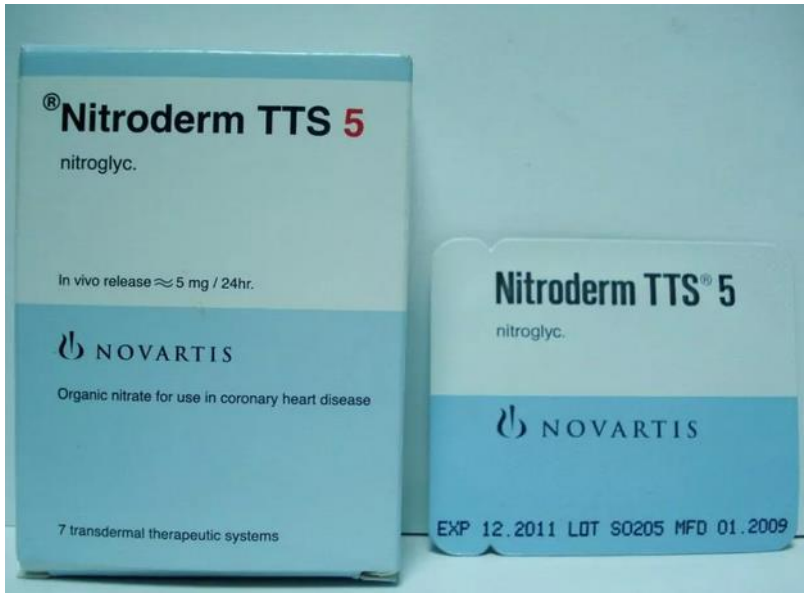
Treatment of Unstable Angina

- **Anti-ischemic drugs**: IV nitroglycerin, and I.V. beta-blockers.
- **I.V. heparin** to dissolve the thrombus and prevent infarction.
- **Antiplatelet drugs** as low dose of aspirin to reduce platelet aggregation.

Treatment of Myocardial Infarction

- **Thrombolytic drugs** or percutaneous coronary intervention.
- **Morphine** to control pain.
- **Anti-ischemic drugs**: I.V. nitroglycerin, and I.V. beta-blockers
- **Antiplatelet drugs** as abciximab.
- **Treatment of any complications** as arrhythmia, heart failure, shock.

Organic Nitrates & Nitrites



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Calcium Channel-Blockers (CCBs)

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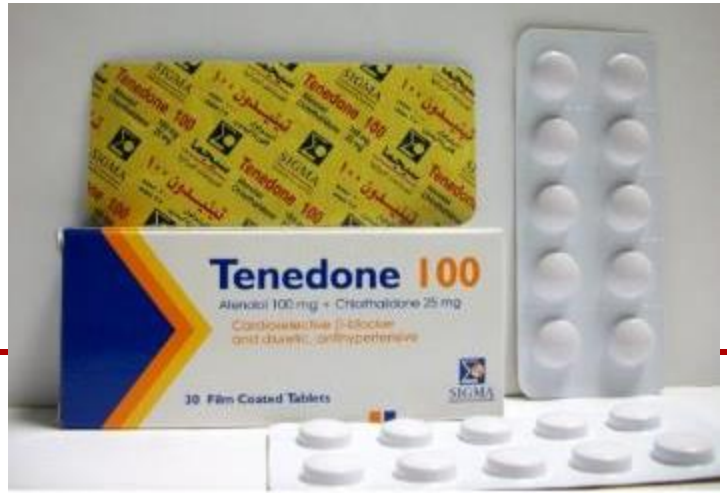
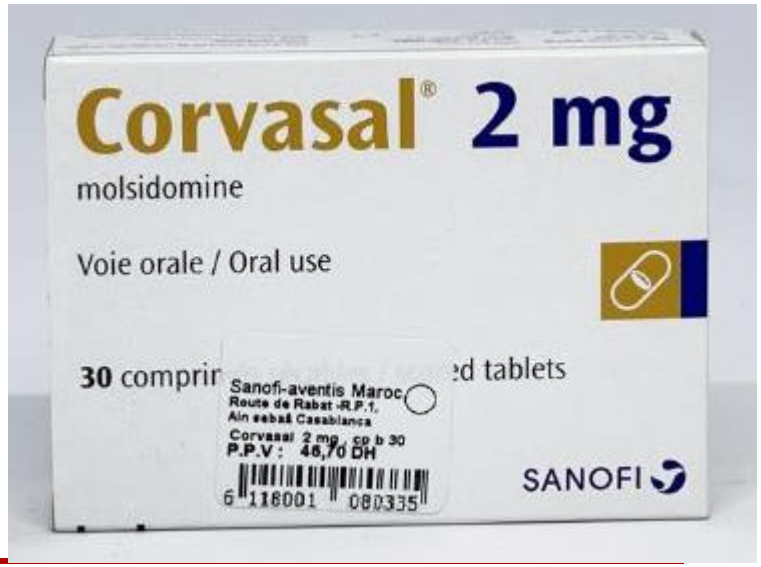
Beta-blocking drugs



Newer Antianginal Drugs



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thank
you!