

ANTIANGINAL DRUGS

LEARNING OUTCOMES

Recognize variables contributing to a balanced myocardial supply versus demand

Differentiate between drugs used to alleviate acute anginal attacks and those meant for prophylaxis & improvement of survival

Detail the pharmacology of nitrates and other drugs used as antianginal therapy



Calcium channel blockers

Classification

Selectivity

Dihydropyridines:-

Nifedipine ,

Nifedipine, Nisoldipine, Amlodipine

Vascular smooth muscle

Verapamil

es:-

Cardiomyocytes

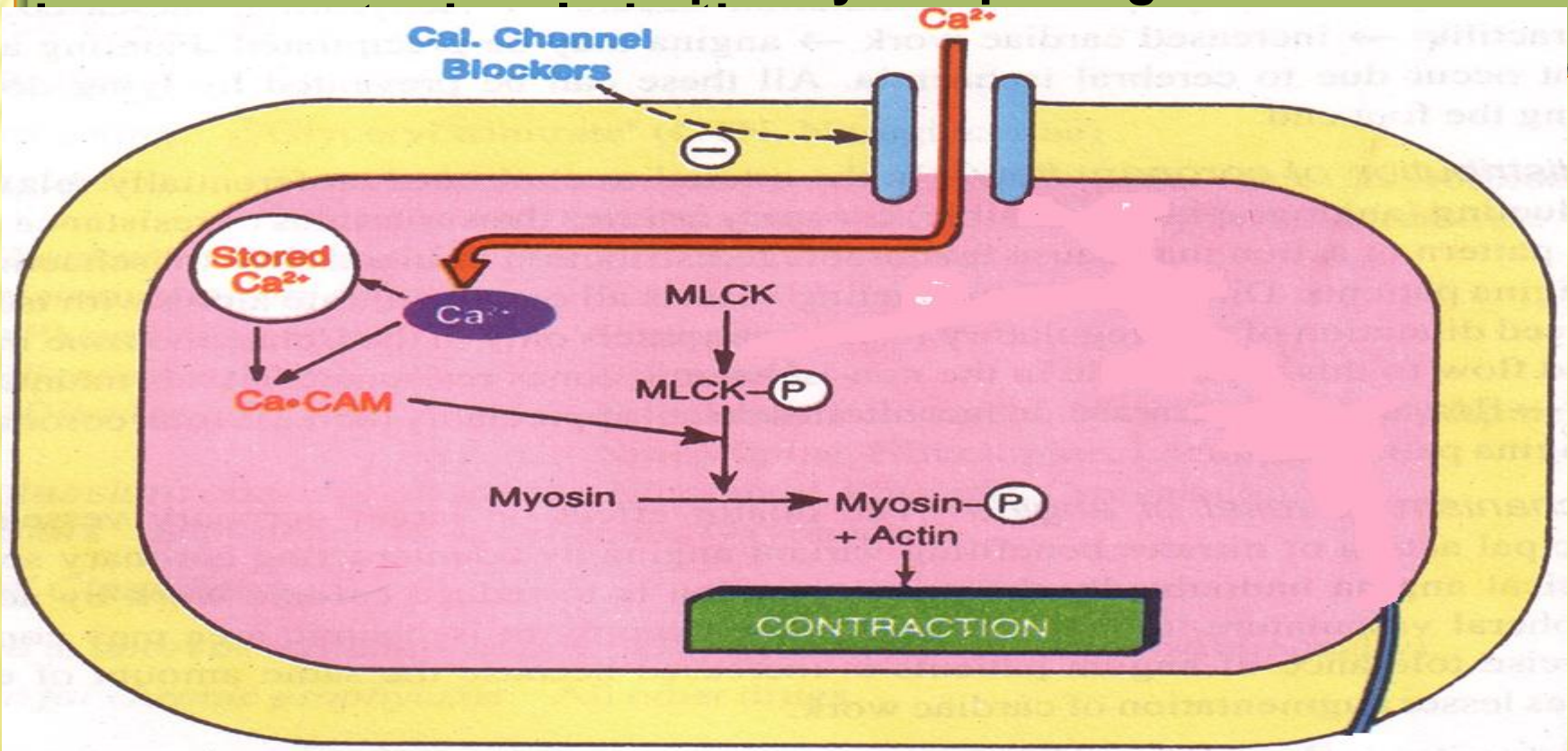
Diltiazem

:-

Intermediate

Mechanism of Action

Binding of calcium channel blockers [CCBs] to the L-type Ca channels ↓ their frequency of opening



Antianginal Action

↓ **Cardiomyocyte Contraction** → ↓ cardiac work through their –ve inotropic & chronotropic action (verapamil & diltiazem) → **↓ myocardial oxygen demand**

↓ **VSM Contraction** → ↓ After load → ↓ cardiac work → **↓ myocardial oxygen demand**

Coronary dilatation → **↑ myocardial oxygen supply**

Therapeutic Uses

IN VARIANT ANGINA

→ Attacks prevented

Short acting dihydropyridine should be avoided ??

Can be combined to β -adrenoceptor blockers???

IN UNSTABLE ANGINA

Seldom added in refractory cases

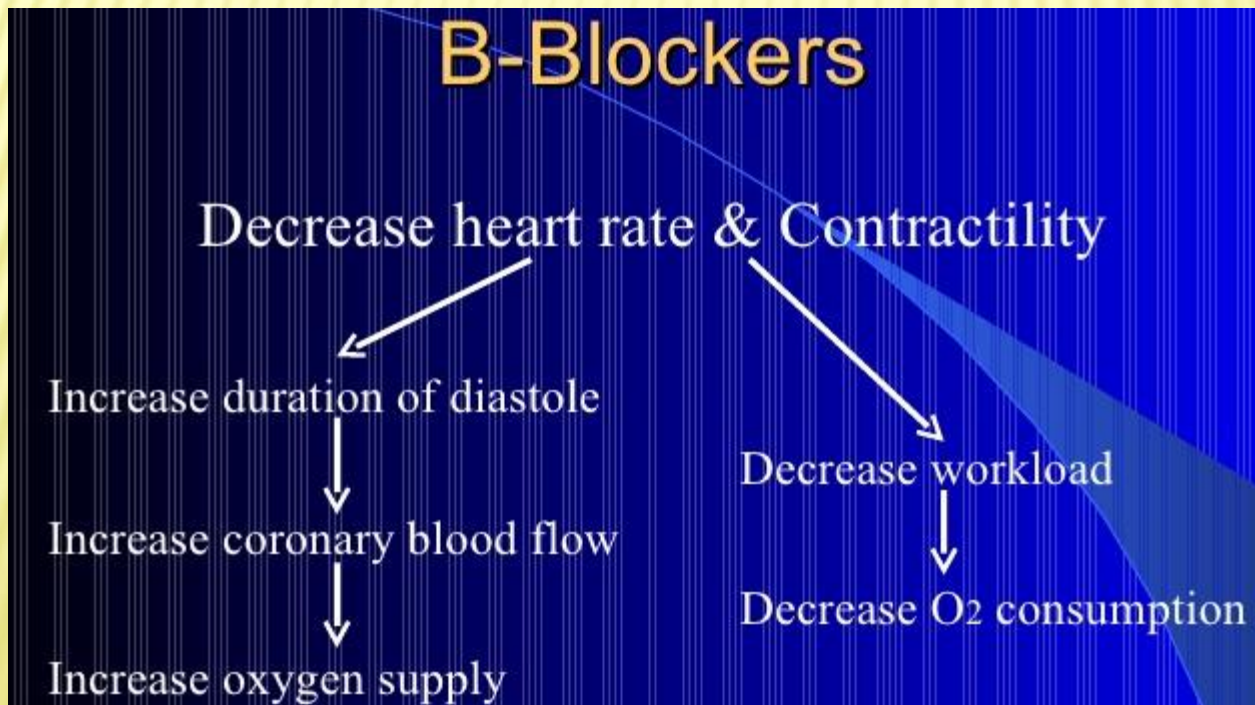
Can be combined with nitrates???

Dihydropyridenes useful antianginal if with CHF??

Beta Adrenoceptor Blockers

Examples Atenolol, Bisoprolol, Metoprolol (β_1 - Selective)

Antianginal Mechanism



Indications in Angina pectoris

IN STABLE ANGINA

Cardioselective are preferred?

Prolong use reduces incidence of sudden death?

IN UNSTABLE ANGINA

Halts progression to AMI, improves survival

IN VARIANT ANGINA

Contraindicated?

IN AMI

Reduce infarct size, reduce morbidity & mortality

Beta Adrenoceptor Blockers

β - blockers should be withdrawn gradually?

Given to diabetics with ischemic heart disease?

MINICASE



Which antianginal drug is the best choice for the case of Helmi? And Why?

MINICASE



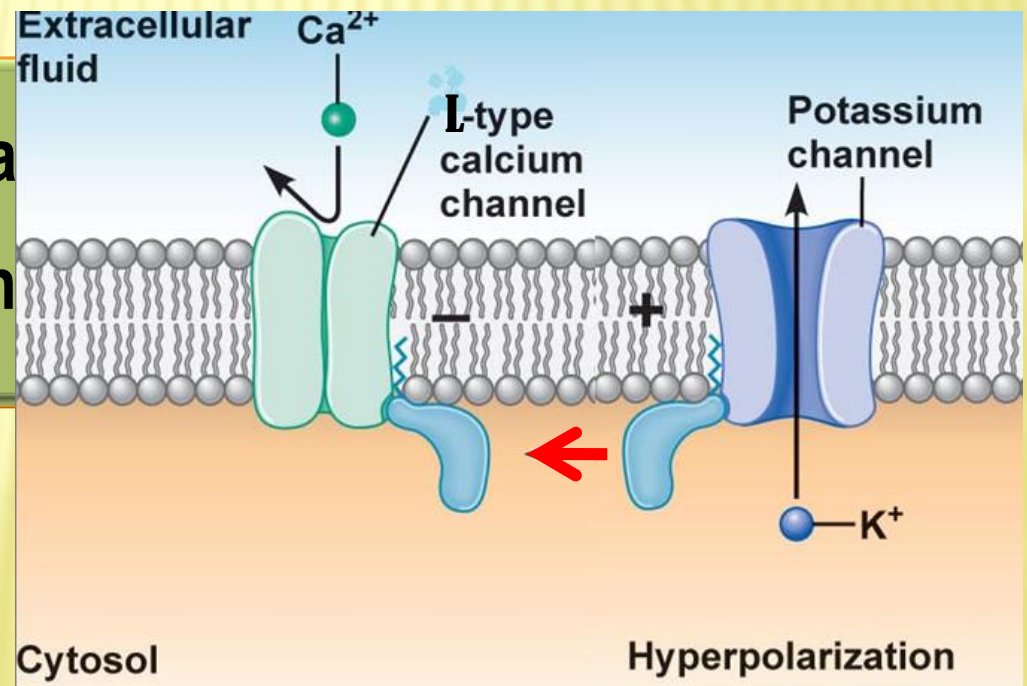
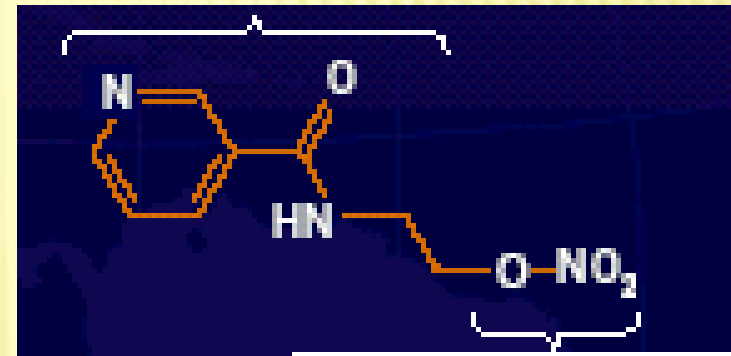
If Helmi dose not respond to monotherapy, what other drug should be added to his regimen?

Potassium channel openers

Nicorandil

Mechanism

It has dual mechanism of
1. Opens K_{ATP} channels (a dilator)
2. NO donor as it has a nitro moiety (venular dilator)



Pharmacodynamic Effects

As K channel opener

As nitric oxide donor → opening of K channels

→ hyperpolarization → vasodilatation

NO ↑ cGMP/PKG → vasodilatation

On cardiomyocytes opening of K channels → repolarization

→ ↓ cardiac work

Indications

- 1-Prophylactic 2nd line therapy in stable angina**
- 2-Refractory variant angina**

ADRs

**Flushing, headache,
Hypotension, palpitation, weakness
Mouth & peri-anal ulcers, nausea and vomiting.**

THINK-PAIR-SHARE

A 55-year-old woman complained to her physician of palpitations, flushing of the face, and vertigo. The woman, suffering from diabetes mellitus, was giving herself three daily doses of insulin. She had been recently diagnosed with exertional angina for which nitrate therapy was started with transdermal nitroglycerin and oral isosorbide mononitrate. After 3 weeks of therapy, her anginal attacks were less frequent but not completely prevented. Which would be an appropriate next therapeutic step for this patient?

Metabolically Acting Agents

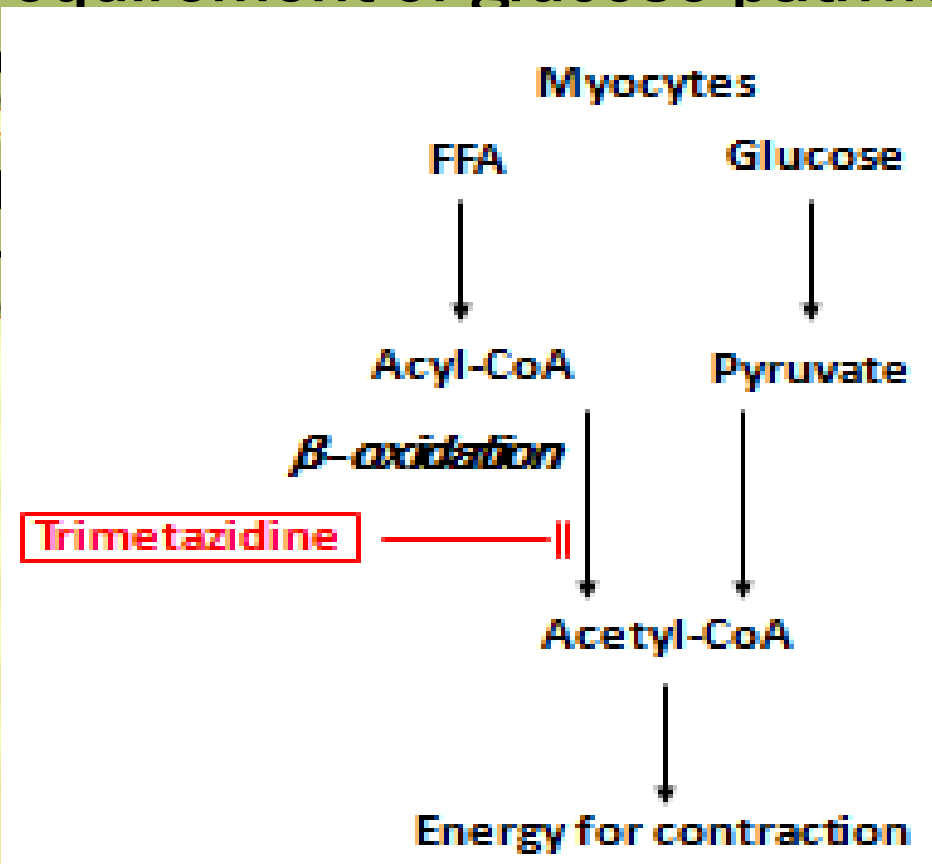
e.g. Trimetazidine

O₂ requirement of glucose pathway is

low

During
blunt

is rise,



Reduces O₂ demand without altering hemodynamics

Trimetazidine

Indications

Used as an add on therapy

ADRs

GIT disturbances

Contraindications

Hypersensitivity reaction

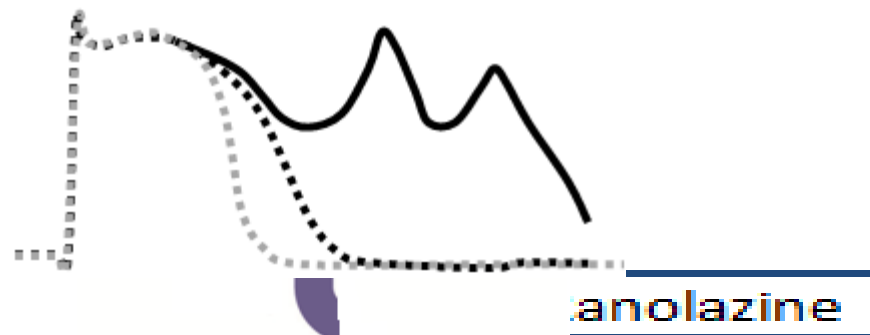
Pregnancy & lactation

Ranolazine

Inhibits the late sodium current which increases during ischemia

It prolongs
Class Ia &

Toxicity develops as;
diltiazem
antibiotics,



Diastolic Wall Tension

Impaired Diastolic Relaxation

Diastolic Extension

h;

inhibitors

MINICASE

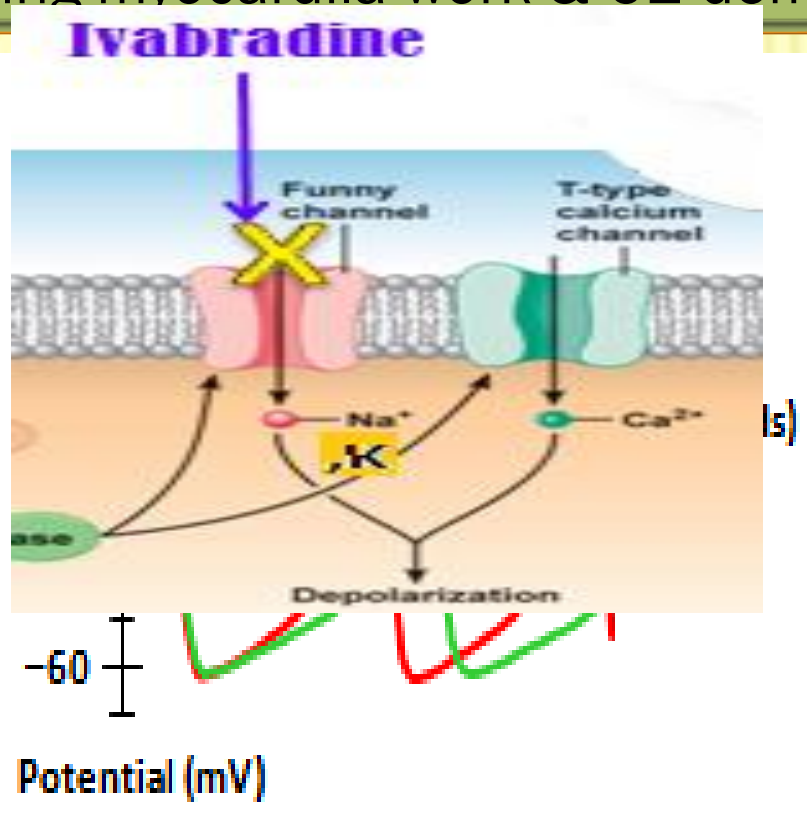


Which antihyperlipidemic drug should be prescribed to Helmi?

Ivabradine

Ivabradine Selectively blocks I_f

Ivabradine reduces slope of depolarization, slowing HR, reducing myocardial work & O₂ demand



I_f current is a pacemaker

that activates

Agents that improve prognosis

- Aspirin / other antiplatelet agents
- ACE inhibitors
- Statins
- β -blockers

Halt progression
Prevent acute insult
Improve survival

MINICASE



Which antihypertensive drug should be prescribed to Helmi?

MEMORY MATRIX

In the following table indicate increase, decrease or no effect with signs \uparrow , \downarrow , $-$ respectively

Drug/Class	HR	BP	Wall Tension	Contractility	O ₂ Supply
Beta-blockers					
CCBs					
Verap/Dilt					
Dihydropyridines					
Nitrates					
Ranolazine					