ANTIANGINAL DRUGS

LEARNING OUTCOMES

Recognize variables contributing to a balanced myocardial supply versus demand

Expand on the drugs used to alleviate acute anginal attacks versus those meant for prophylaxis & improvement of survival

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

Calcium channel blockers

Classification

Selectivity

Dihydropyridines:-

Nifedipine , Nicardipine , Amlodepine

Nifedipine ,

Vascular smooth muscle

Verapamil

es:-

Cardiomyocytes

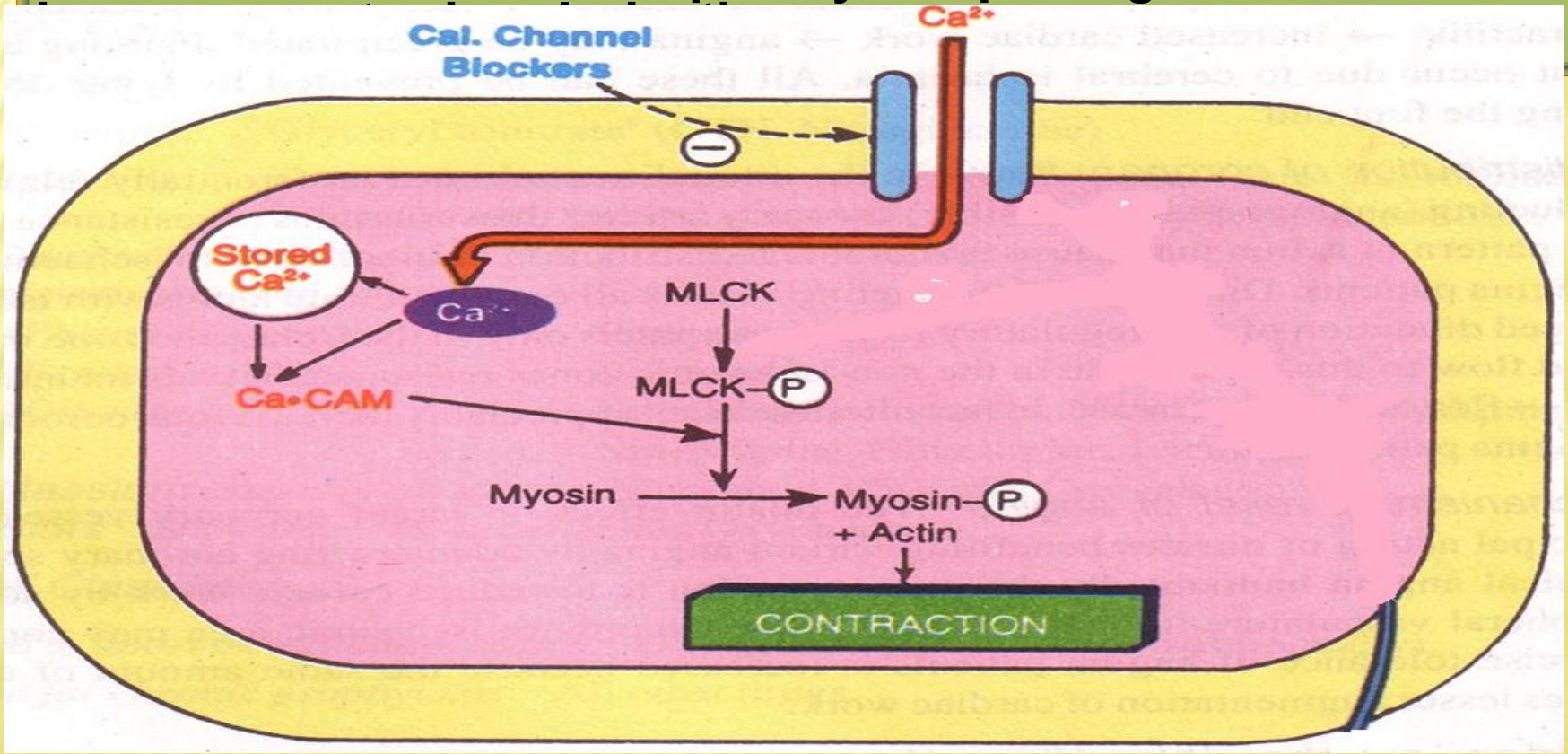
Diltiazem

:-

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

↓VSMC Contraction → ↓ After load → ↓cardiac work → ↓myocardial oxygen demand

Coronary dilatation → ↑myocardial oxygen supply

Therapeutic Uses

IN VARIANT ANGINA

- Attacks prevented (> 60%) / sometimes variably aborted

Short acting dihydropyridine should be avoided ??

Can be combined to β-AR blockers???

IN UNSTABLE ANGINA:

- Seldom added in refractory cases

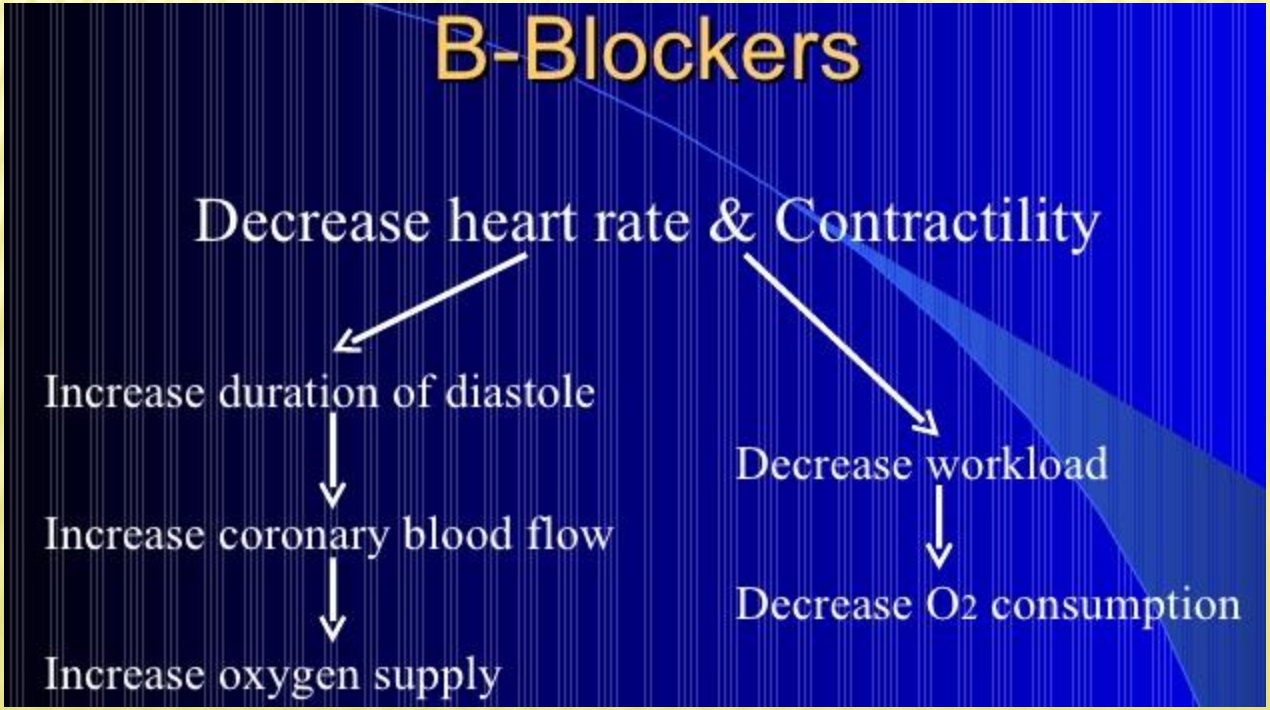
Can be combined with nitrates???

Dihydropyridenes useful antianginal if with CHF??

Beta Adrenoceptor Blockers

Examples Atenolol, Bisoprolol, Metoprolol (β_1 – Selective)

Antianginal Mechanism



Beta Adrenoceptor Blockers

Indications in angina

In stable angina

Regular prophylaxis, selective are prefered?

First choice for chronic use?

Can be combined with nitrates?

Can be combined with dihydropyridine CCB?

Verapamil?

In variant angina

Contraindicated?

Beta Adrenoceptor Blockers

Indications in angina

In Unstable angina

Halts progression to MI, improve survival

In Myocardial infarction

Reduce infarct size

Reduce morbidity & mortality

→reduce **O2 demand**

→reduce **arrhythmias**

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β- blockers should be withdrawn gradually?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?

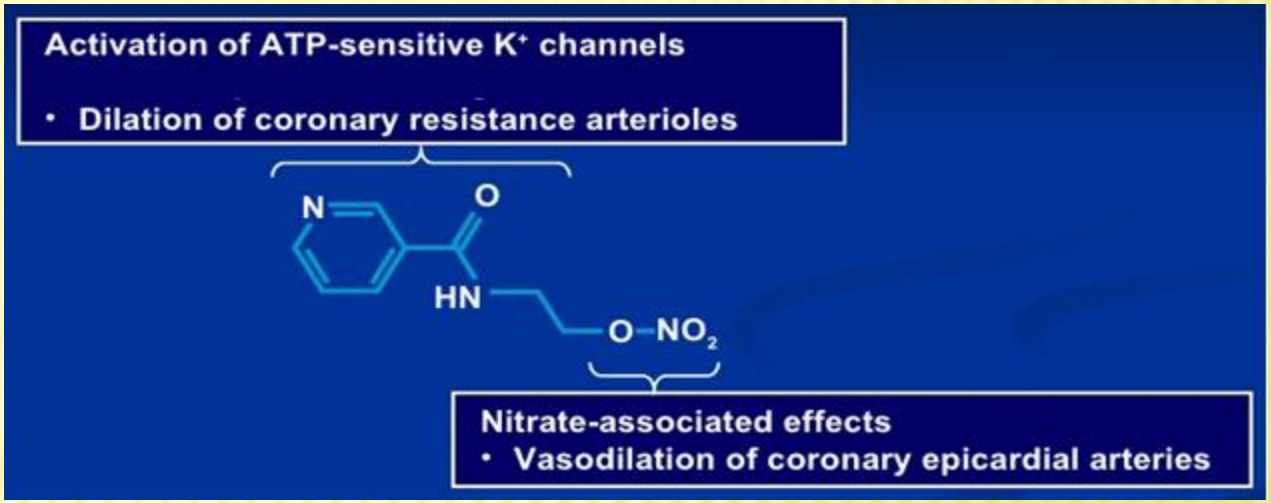
MINICASE

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

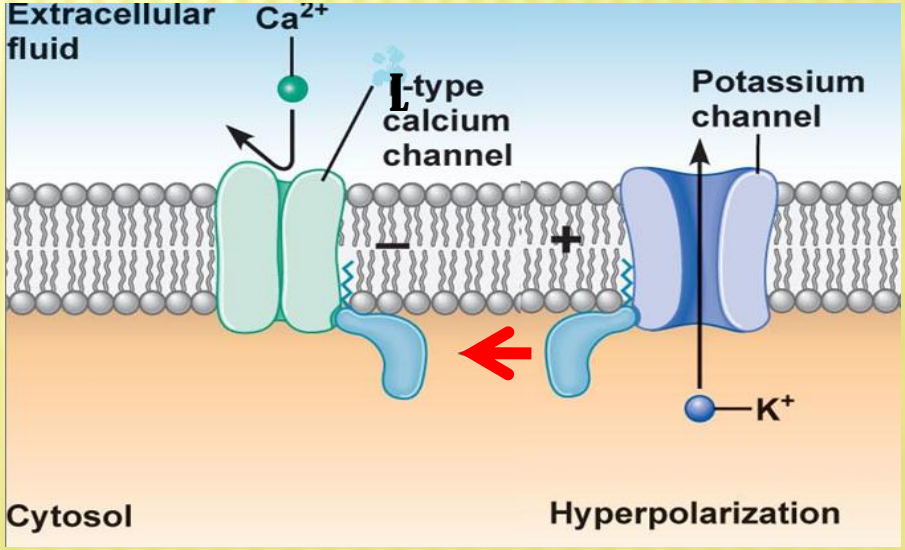
Potassium channel openners

Nicorandil

Mechanism



It has dual mechanism of action;
1. Opens K_{ATP} channels (> arteriolar dilator)
2. NO donner as it has a nitrate moiety (> venular dilator



Pharmacodynamic Effects

As K channel openner

As nitric oxide donor

s opening of K channels

➔hyperpolarization ➔ vasodilatation

NO ↑ cGMP/PKG ➔ vasoditation

On cardiomyocytes opening of K channels ➔repolarization

➔↓ cardiac work

Indications

Prophylactic 2nd line therapy in stable angina & refractory variant angina

ADRs

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

THINK-PAIR-SHARE

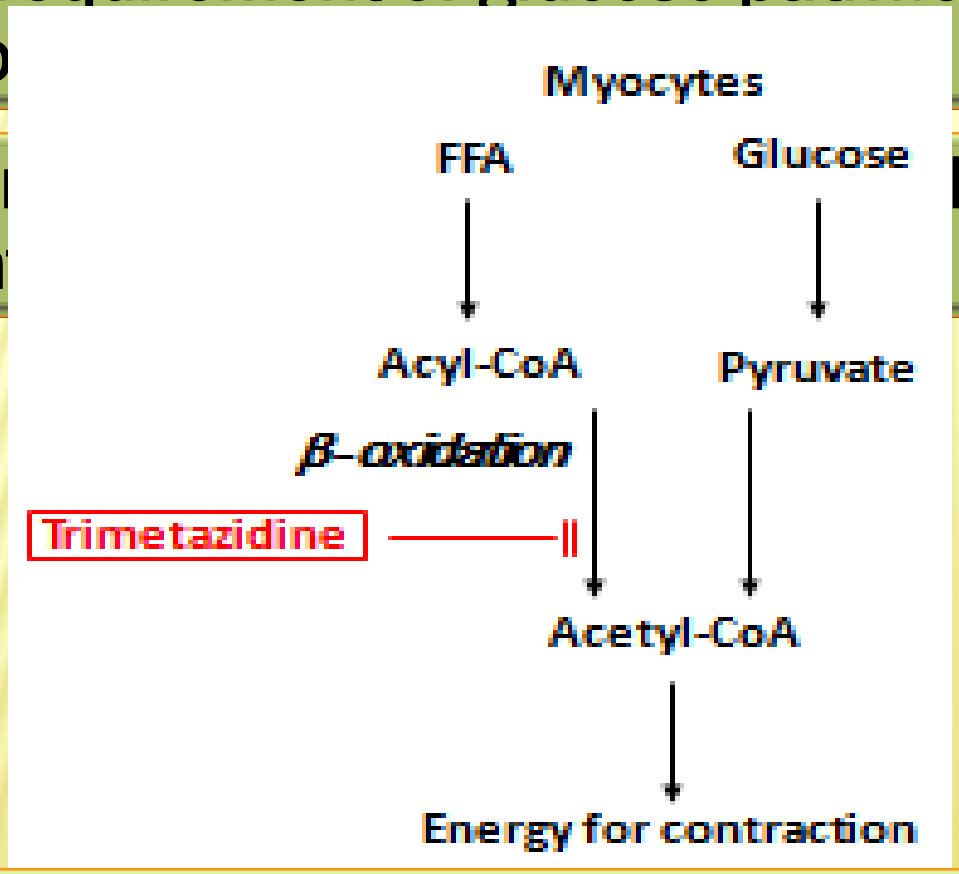
A 5 5 - year - old woman complained to her physician of palpitations, flushing of the face, and vertigo. The woman, suffering from diabetes mellitus, was giving herself three daily doses of insulin. She had been recently diagnosed with exertional angina for which nitrate therapy was started with transdermal 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 lo

Duri ls rise, blun



Reduces O2 demand without altering hemodynamics

Trimetazidine

Indications

Used as an add on therapy

ADRs

GIT disturbances

Contrindications

Hypersensitivity reaction

Pregnancy & lactation

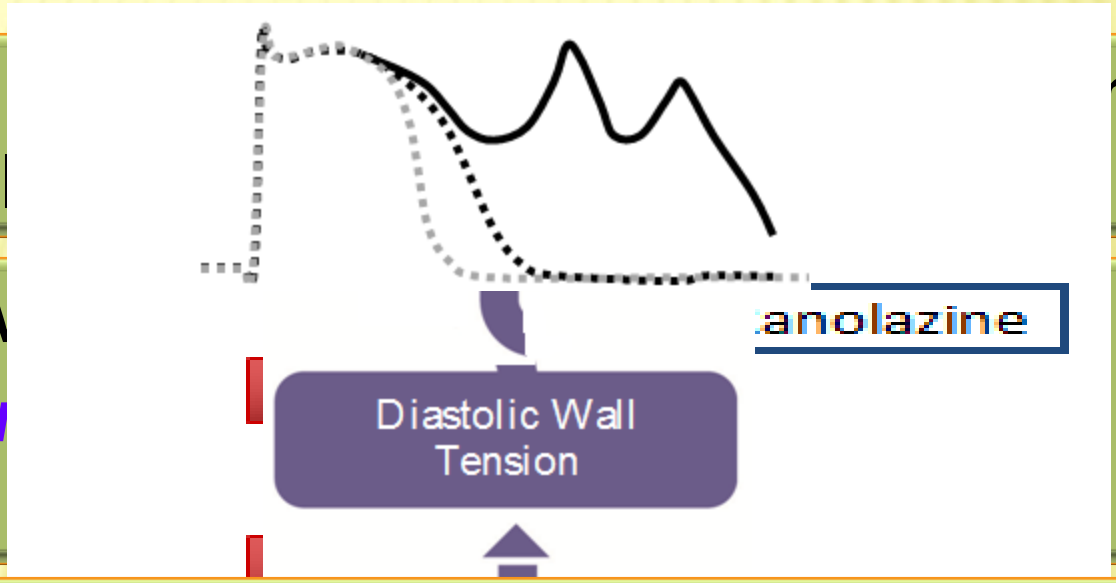
Metabolically Acting Agents

Ranolazine

Inhibits the late sodium current which increases during ischemia

It prolongs **n;**
Class Ia & I

Toxicity dev **inhibitors**
as; ***diltiazer***
antibiotics,



ADRs:- dizziness , constipation

Used in chronic angina concommitanly with other drugs

MINICASE

Which antihyperlipidemic drug should be prescribed to Helmi?

Ivabradine

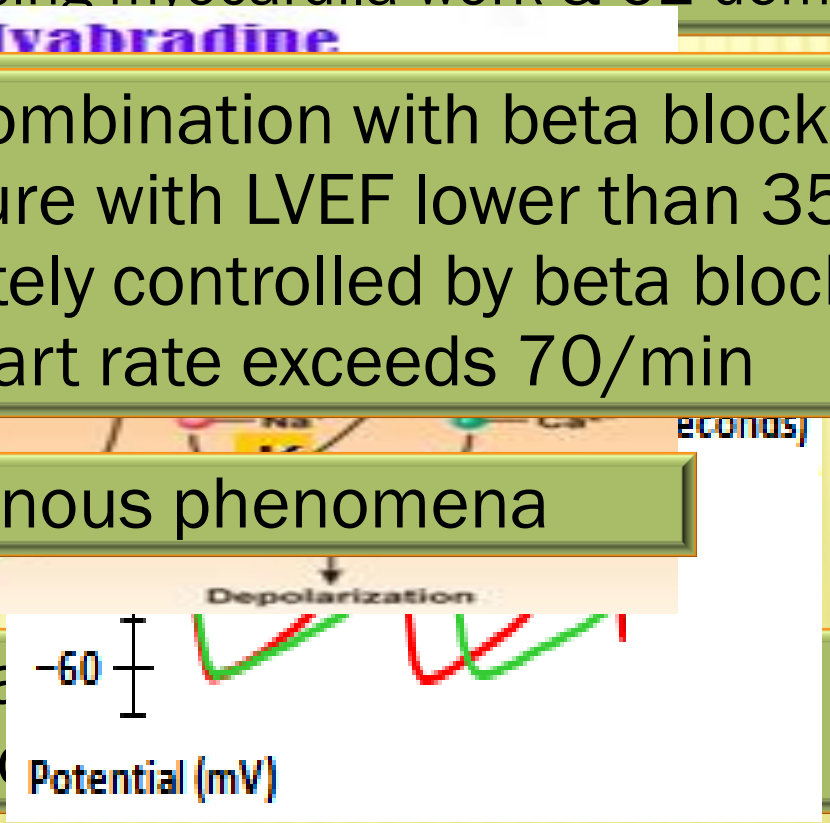
Ivabradine Selectively blocks I_f

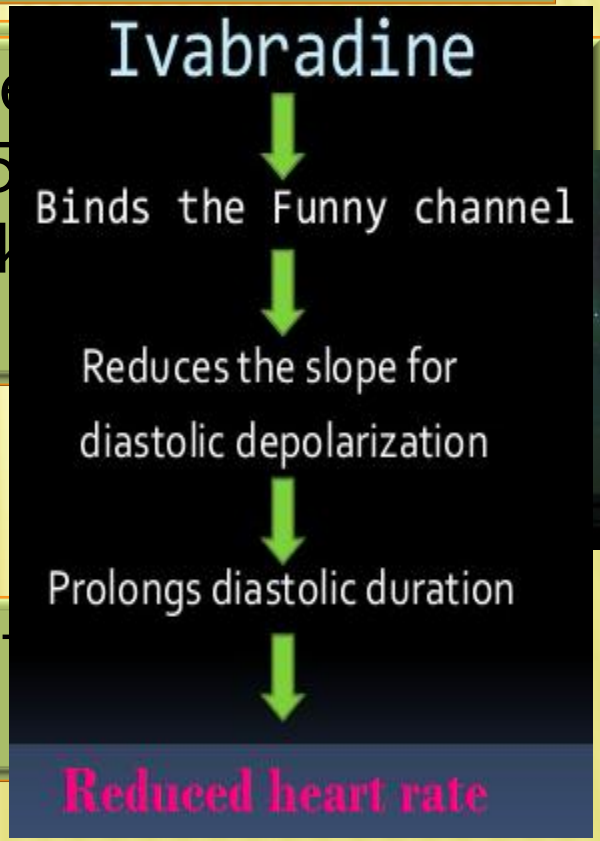
Ivabradine reduces slope of depolarization, slowing HR,reducing myocardila work & O2 demand

Used in combination with beta blocke
heart failure with LVEF lower than 35
inadequately controlled by beta block
whose heart rate exceeds 70/min

ADR:- luminous phenomena

I_f current is a
pacemaker





Agents that improve prognosis

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

Halt progression
Prevent acute insult
Improve survival

MEMORY MATRIX

In the following table indicate increase, decrease or no effect with signs ↑, ↓, – respectively

Drug/Class	HR	BP	Wall Tension	Contract-ility	O_2 Supply
Beta-blockers					
CCBs					
Verap/Dilt					
Dihydropyridines					
Nitrates					
Ranolazine					