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

MINICASE

Helmi, a 62-year-old male smoker with type 2 diabetes mellitus and hypertension presents with a 4-month history of exertional chest pain. Physical examination shows a blood pressure of 152/90 mm Hg but is otherwise unremarkable. The ECG is normal, and laboratory tests show a fasting blood glucose value of 110 mg/dL, glycosylated hemoglobin 6.0%, creatinine 1.1 mg/dL, total cholesterol 160, LDL 120, HDL 38, and triglycerides 147 mg/dL. He exercises for 8 minutes, experiences chest pain, and is found to have a 2-mm ST-segment depression at the end of exercise.

MINICASE

WHAT LIFE STYLE MODIFICATIONS SHOULD HELMI CARRY OUT?

Which signs or symptoms of Helmi suggest diagnosis of Angina Pectoris?

A **Pain is caused either by obstruction**
severity) due to ischemia of heart muscle

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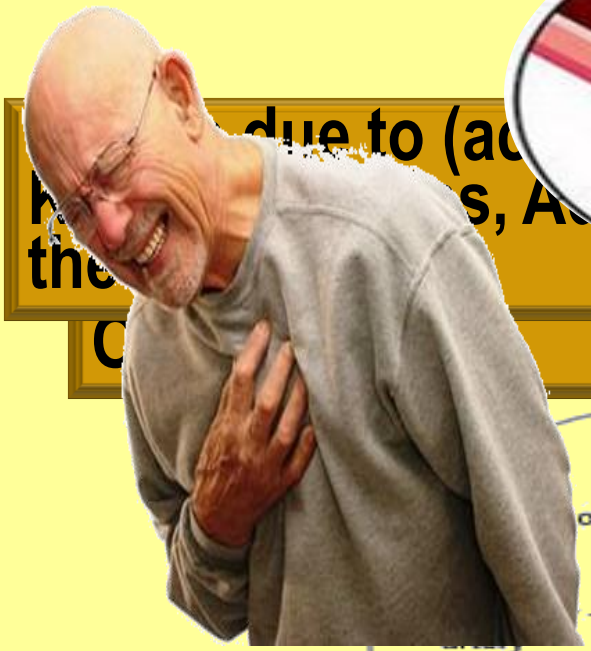
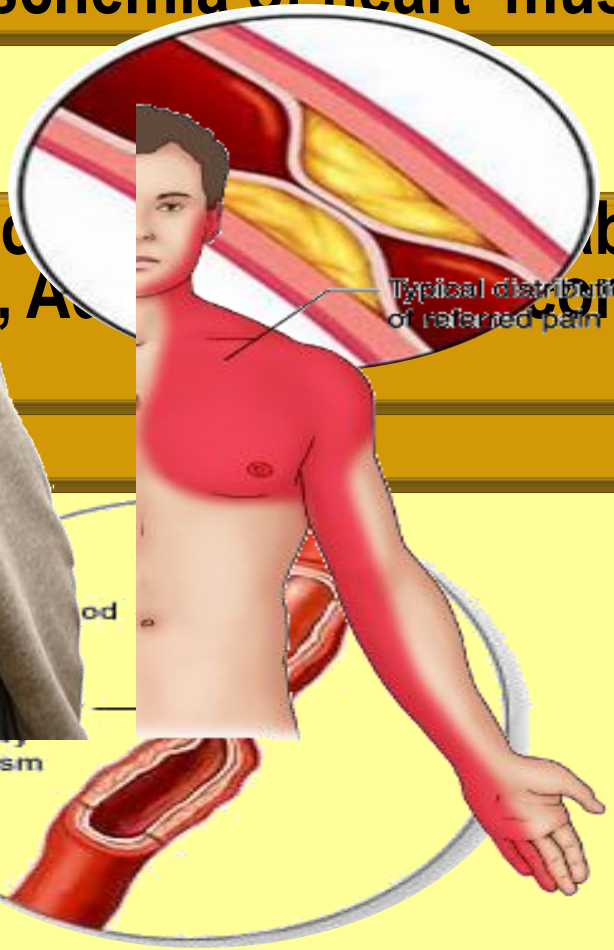


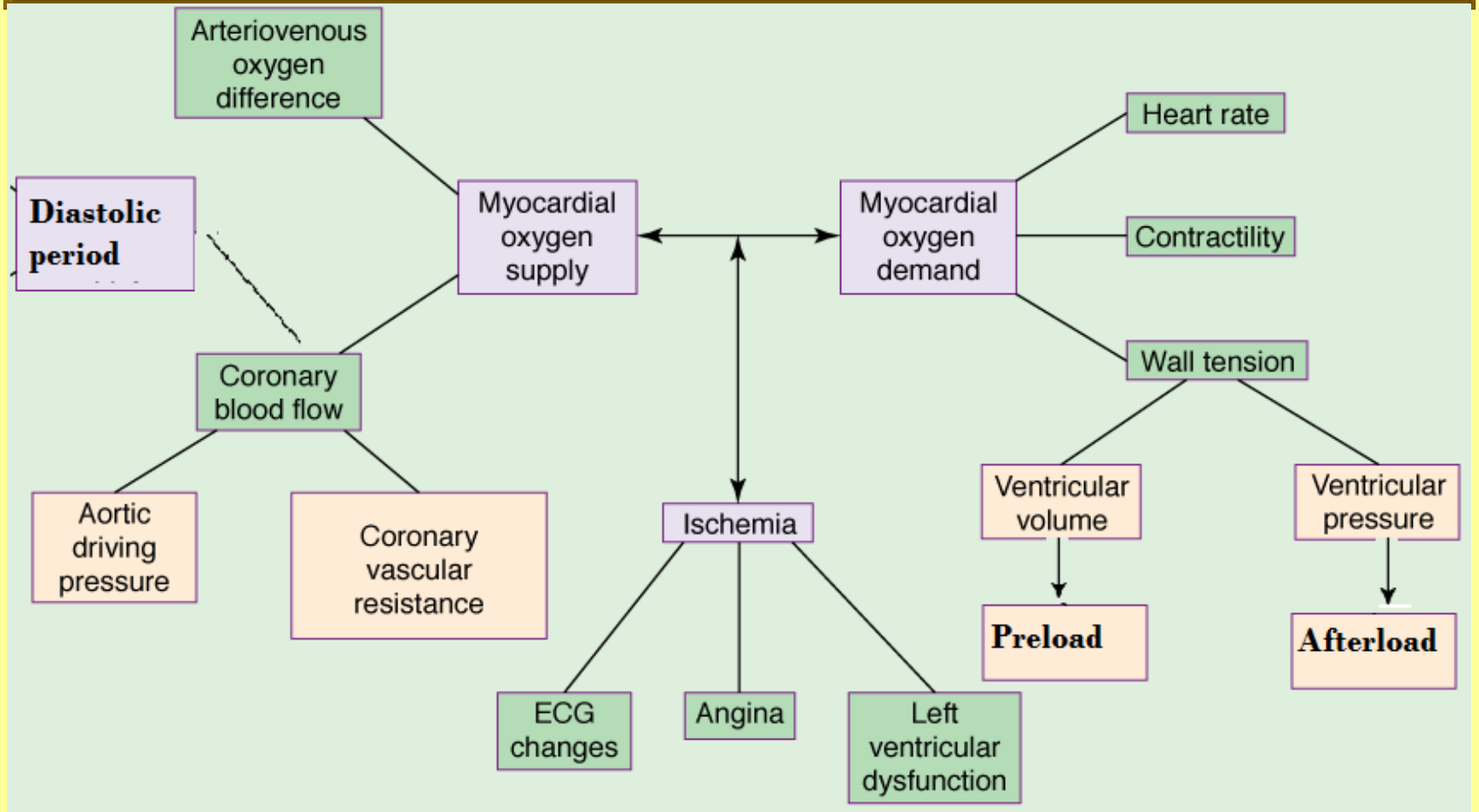


MINICASE

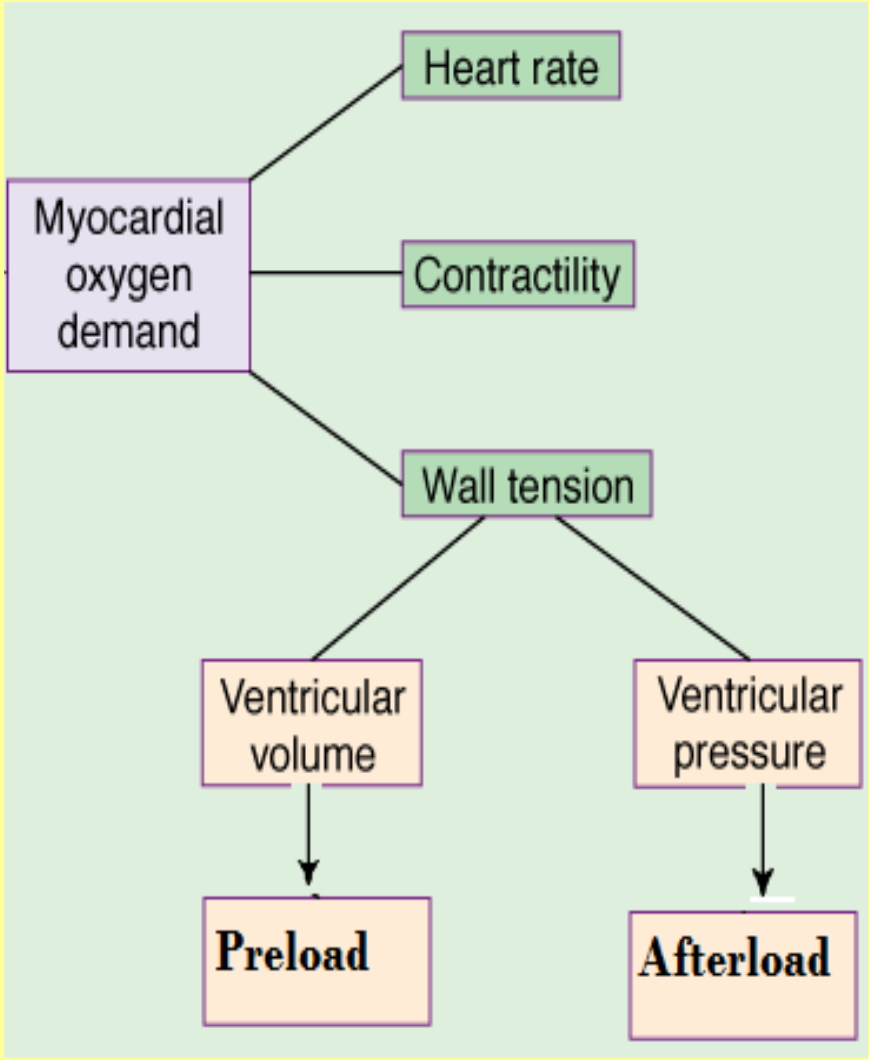
WHAT IS THE POSSIBLE UNDERLYING CAUSE OF HELMI'S EXERTIONAL PAIN?

WHAT IS BASIC MECHANISM OF ANGIA PECTORIS?

WHAT ARE THE DETERMINANTS OF OXYGEN DEMAND AND SUPPLY?



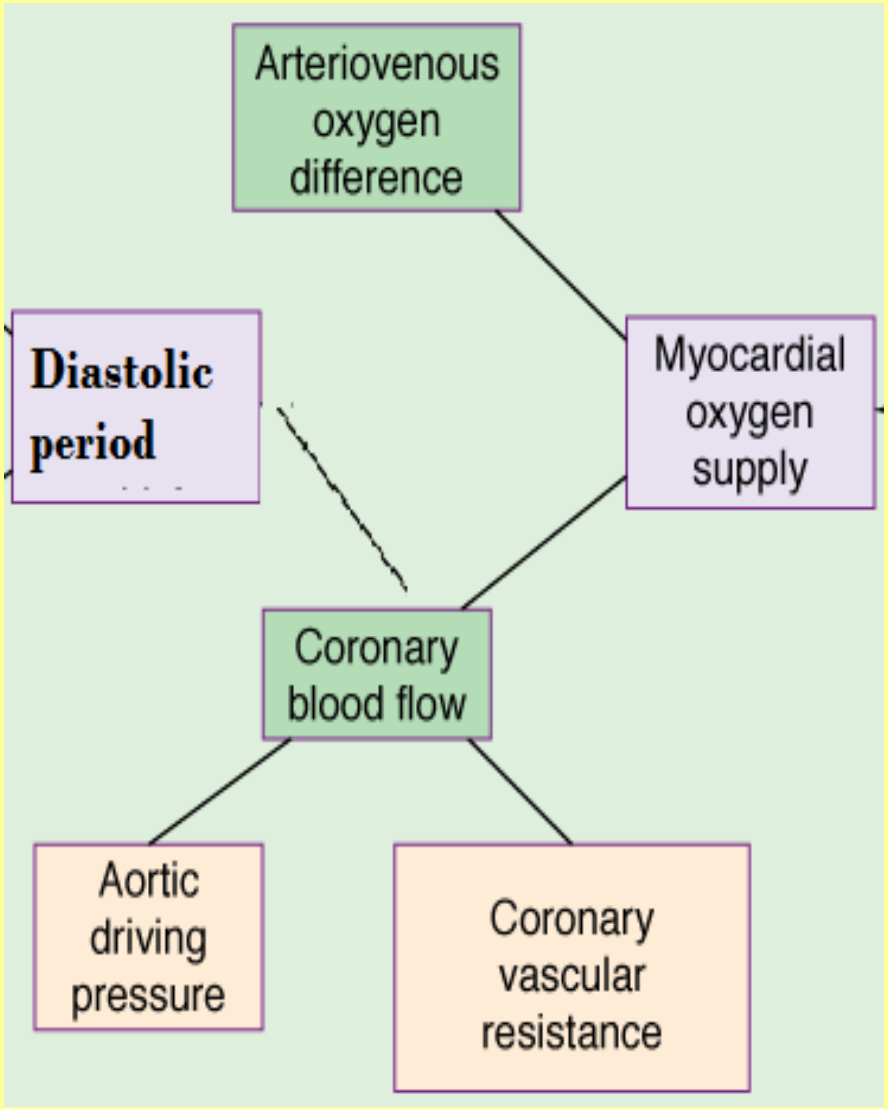
MYOCARDIAL OXYGEN DEMAND IS DETERMINED BY:-



MYOCARDIAL OXYGEN DEMAND IS DIMINISHED BY:-

Reducing contractility
Reducing heart rate
Reducing the preload
Reducing the afterload

MYOCARDIAL OXYGEN SUPPLY IS DETERMINED BY:-



MYOCARDIAL OXYGEN SUPPLY IS ENHANCED BY:-

Reducing coronary vascular resistance
Prolonging diastolic period
Reducing external compression
Dilating collateral vessels

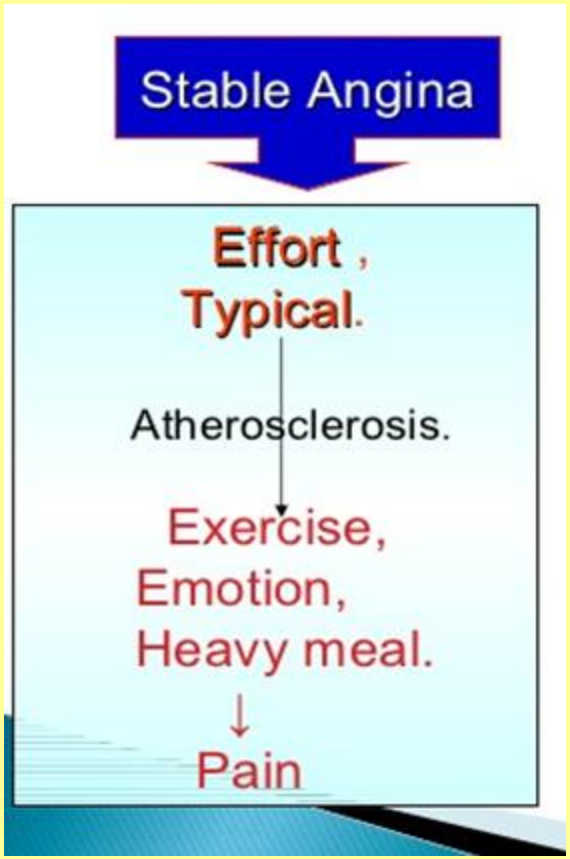
MINICASE

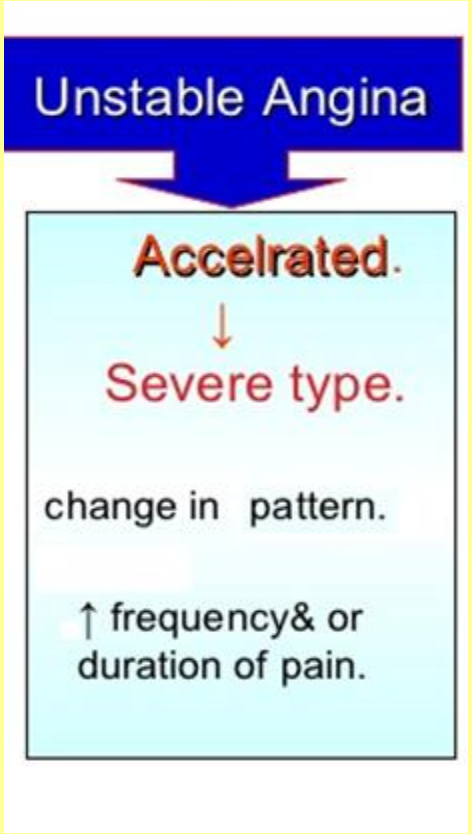
WHAT TRIGGERS THE ONSET OF SYMTOMS IN HELMI?

WHAT FACTORS WORSEN THE SYMPTOMS IN CASE OF HELMI?

WHAT IS THE POSSIBLE UNDERLYING CAUSE OF ANGINA IN HELMI?

Types of Angina Pectoris

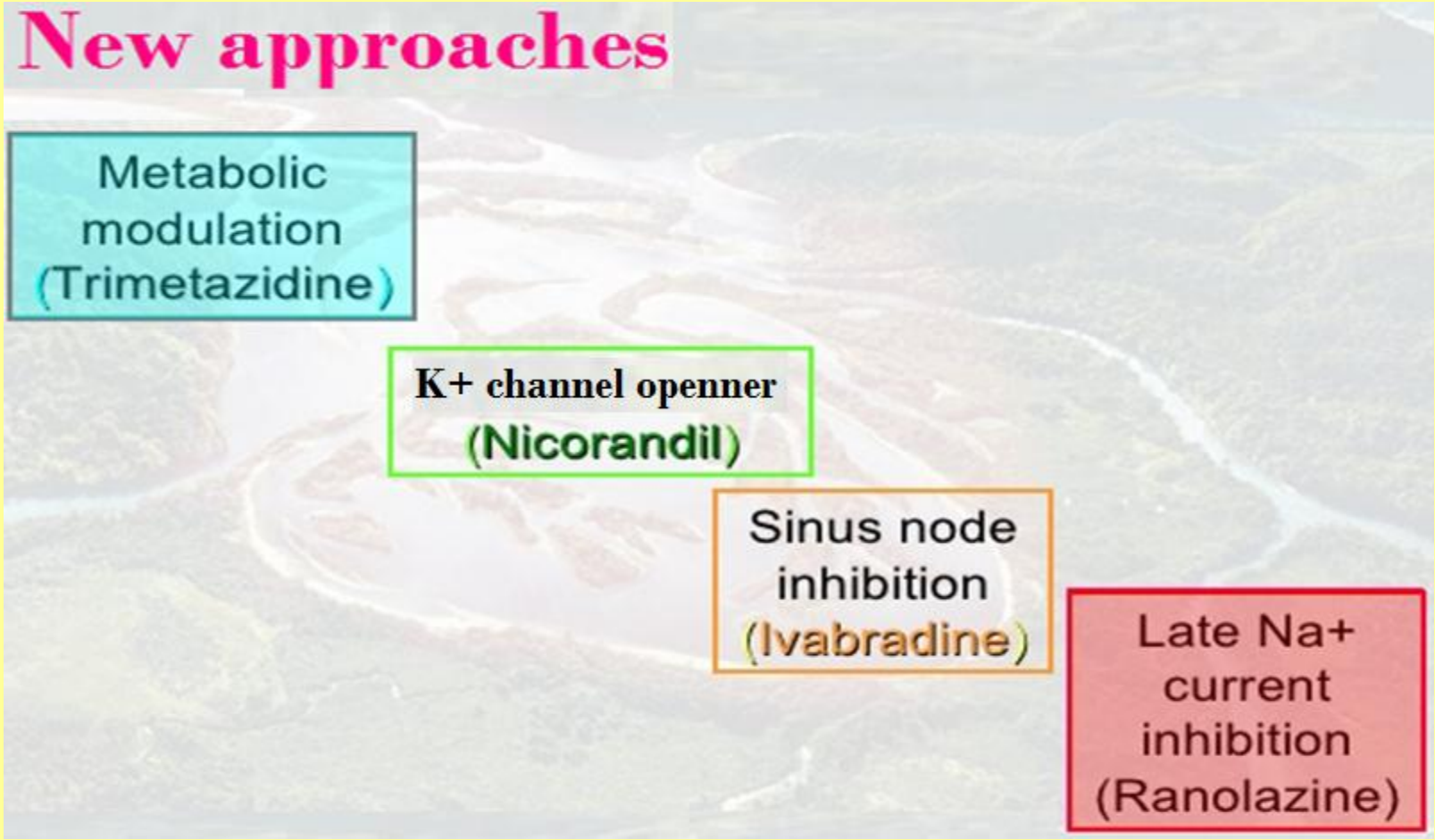




TREATMENT OF ANGIA PECTORS

1-Agents that improve symptoms & ischemia

Traditional Approach



TREATMENT OF ANGIA PECTORS

2-Agents that improve prognosis

- Aspirin / Other antiplatelets
- Statins
- ACE Inhibitors
- β-AD blockers

ORGANIC NITRATES

MECHANISM OF ACTION

LONG ACTING

- ISOSORBIDE MONONITATE

SHORT ACTING

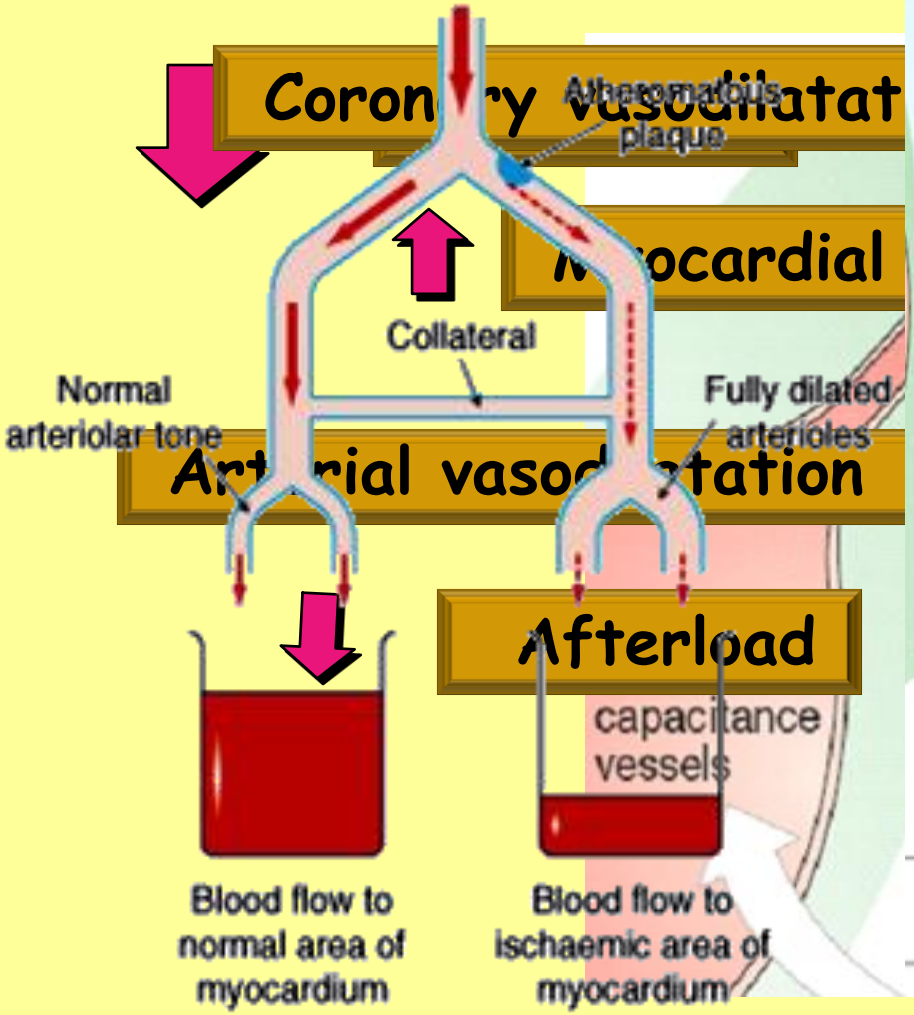
- NITROGLYCERINE

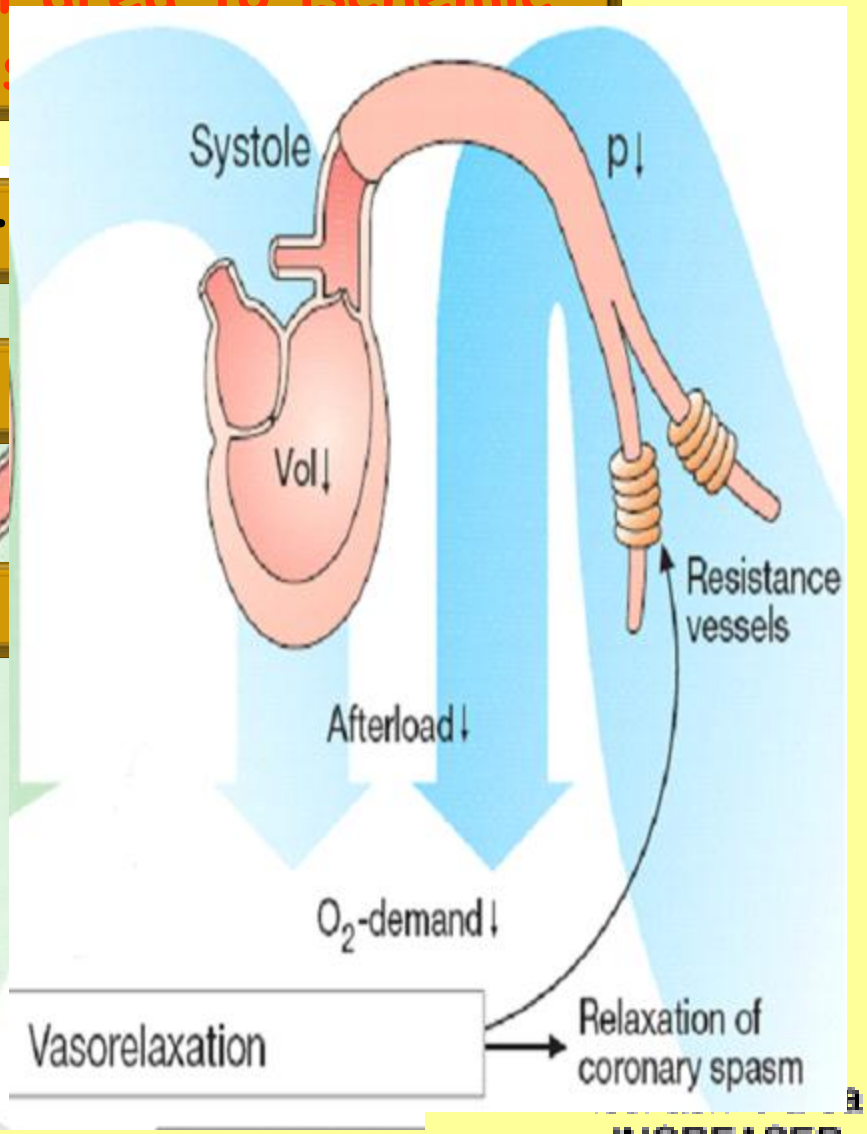
Nitric ate
vasc ell t

cGM duces relaxation

HEMODYNAMIC EFFECTS OF NITRATES

Shunting of flow from normal area to ischemic area by dilating collateral ves





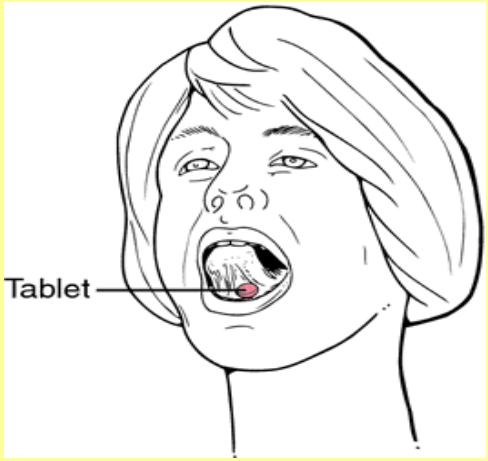
INCREASED

THINK-PAIR-SHARE

Match the effects of nitrates in treatment of angina with their results

Effects	Results
1-↓Ventricular volume	
2-Reflex ↑ in contractility	A-↓ O2 demand
3-↓Arterial pressure	B-↑ O2 demand
4-↑Collateral flow	C-Relief of coronary artery spasm
5-Reflex tachycardia	
6-↓Left ventricular diastolic pressure	D-Improved perfusion to ischemic myocardium
7-↓Diastolic perfusion time due to tachycardia	E-Improve subendocardial perfusion
8-Vasodilation of epicardial coronary arteries	F-↓ myocardial perfusion

PHARMACOKINETICS



Oral isosorbide dinitrate & mononitrate

Very well absorbed & 100% bioavailability

the liver (10-20%) bioavailability

The dinitrate undergoes denitration to two mononitrates➔ both possess antianginal activity

enteral

($t_{1/2}$ 1-3 hours)

Further denitrated metabolites conjugate to glucuronic acid in liver. Excreted in urine.

INDICATIONS

IN STABLE ANGINA;

IN VARIANT ANGINA ➔ sublingual GTN

Prevention; Persistant prophylaxis ➔ Isosorbide mono or dinitrate

Heart Failure

Refractory AHF ➔ IV GTN

CHF ➔ Isosorbide mononitrate + hydralazine
[if contraindication to ACE Is]

AMI ➔ IV GTN

CONTRAINDICATIONS

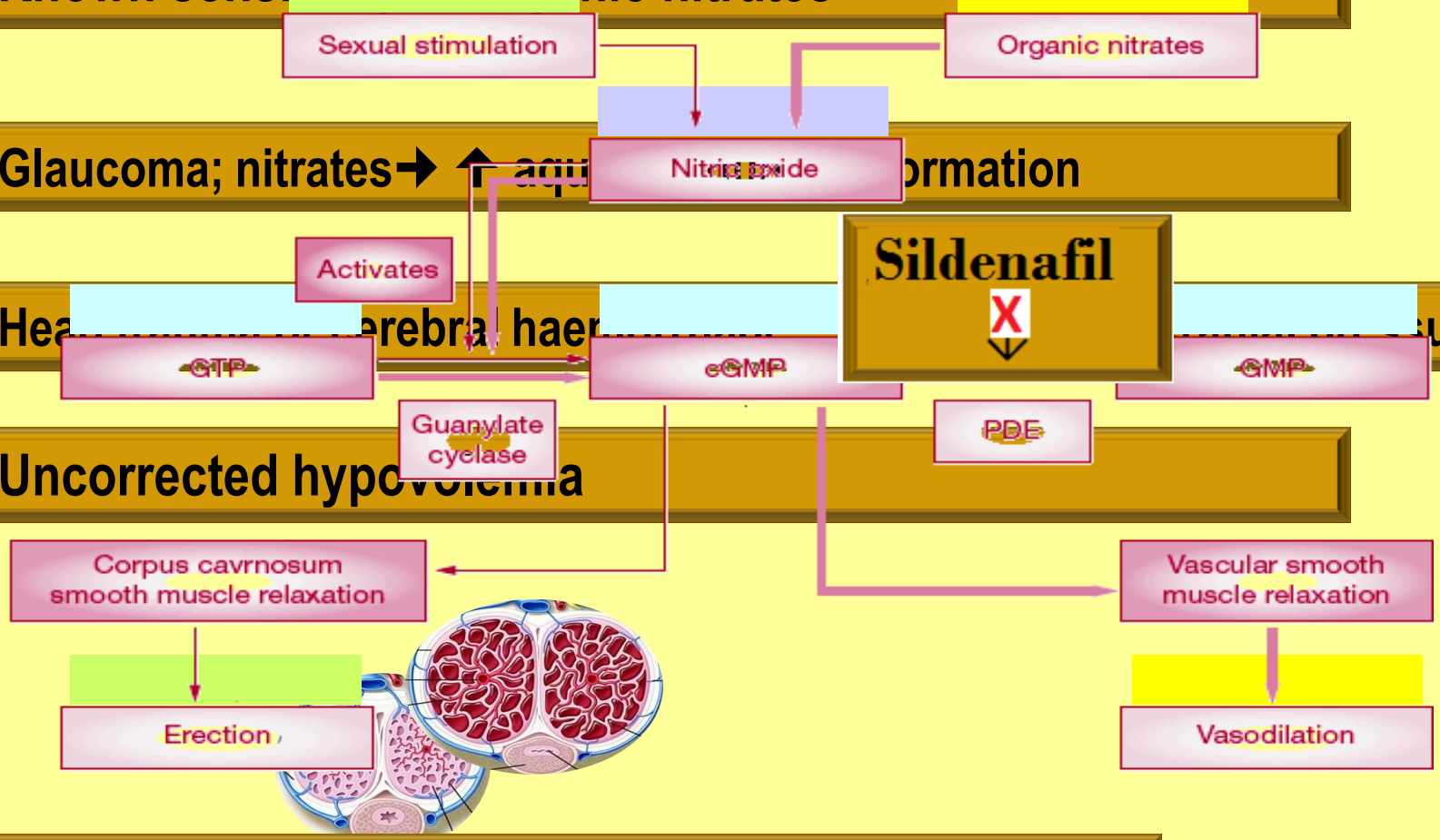
Concomitant administration of PDE_5 Inhibitors

Known sensi nic nitrates

Glaucoma; nitrates → aqu ormation

Hea erebra haer ure.

Uncorrected hypovolemia



Sildenafil + nitrates → Severe hypotension & death

ADVERSE DRUG REACTIONS

THROBING HEADACHE

FLUSHING IN BLUSH AREA

TACHYCARDIA & PALPITATION

POSTURAL HYPOTENSION, DIZZINESS & SYNCOPE

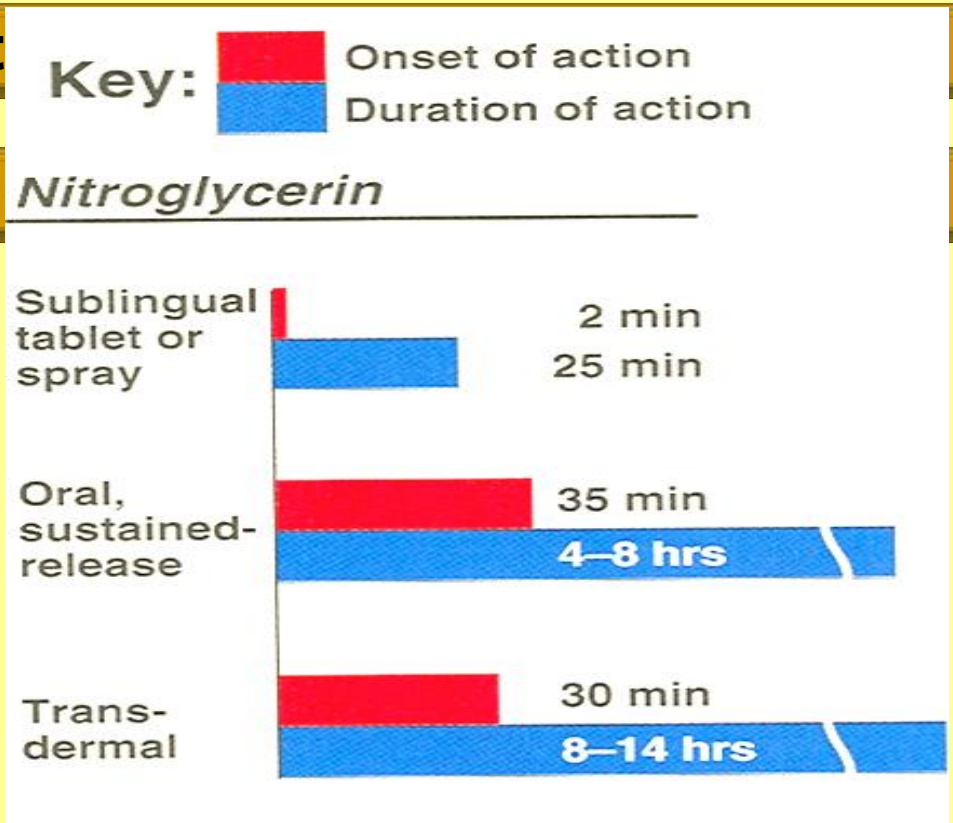
RARELY METHEMOGLOBINEMA

PREPARATIONS

Nitroglycerine

Sublingual t

Transderma



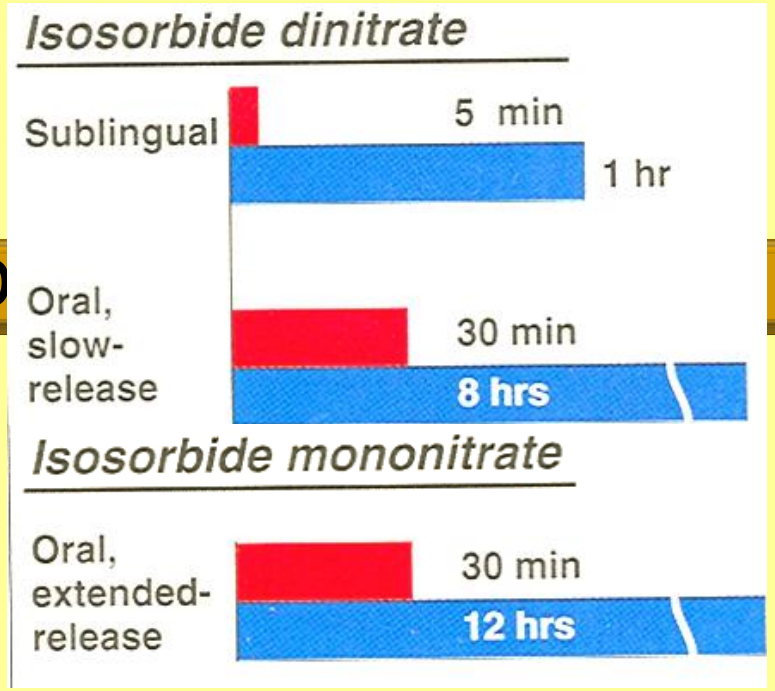
Oral or bucal sustained release
I.V. Preparations

PREPARATIONS

Isosorbide dinitrate

- Dinitrate Sublingual tablets
- Dinitrate Oral sustained release
- Infusion Preparations

- Mononitrate O



NITRATES TOLERANCE

Loss of vasodilator response of nitrates on use of long-acting preparations (oral, transdermal) or continuous intravenous infusions, for more than a few hours without interruption.

MECHANISM

1-Compensatory neurohormonal counter-regulation

2-Depletion of free-SH groups

MINICASE

If Helmi was prescribed nitrates & tolerance developed to its effect, how to overcome tolerance to nitrates?

Nitrate tolerance can be overcome by:

Smaller doses at increasing intervals (Nitrate free periods twice a day).

Giving drugs that maintain tissue SH group e.g. Captopril.

TASK- SELECTION OF A P-DRUG

Instructions:

1- Select a leader for your group

2- Discuss the case according to the steps shown in the sheet

3- Use your internet access to obtain evidence for efficacy, toxicity, convenience & cost.

4- Due to time constrains divide yourself into groups of five, each doing one search e.g. evidence for efficacy.

5- You have 10 minutes to do this and 1 minute to report to the class.