Treatment of ischemic heart disease – coronary artery disease (CAD)

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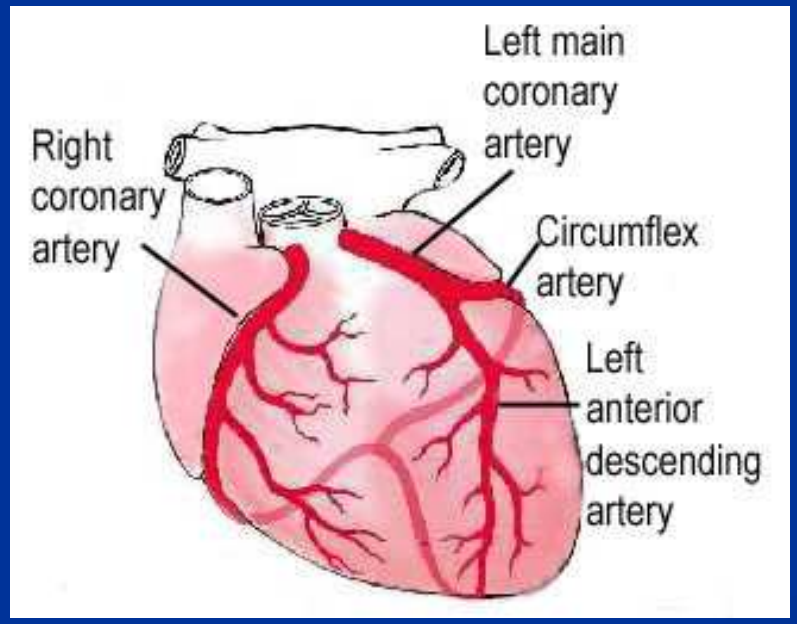
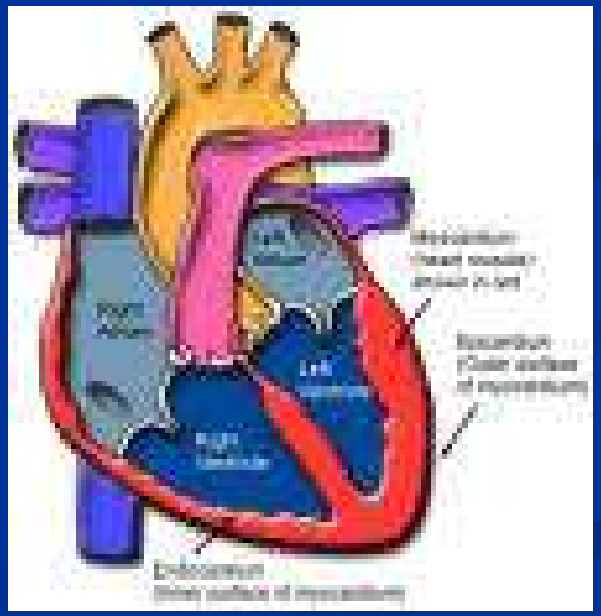
Ischemic heart disease

Group of diseases with the presence of myocardial ischemia, which occurs on the basis of the pathological process in the coronary vessels.

Reducing the flow in coronary arteries>>> ischemia



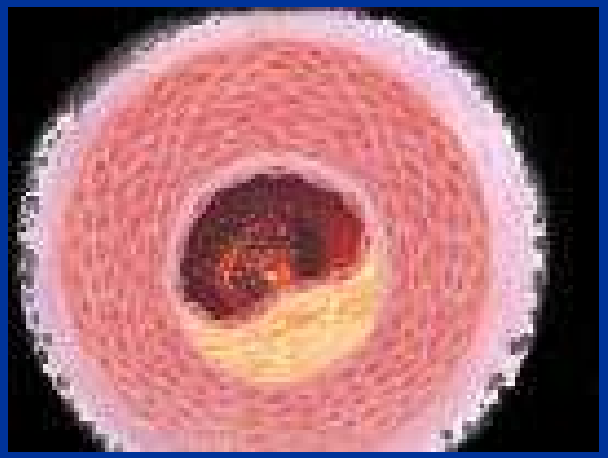


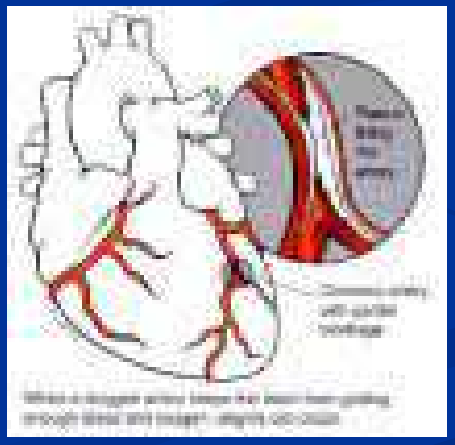
Ischemic heart disease

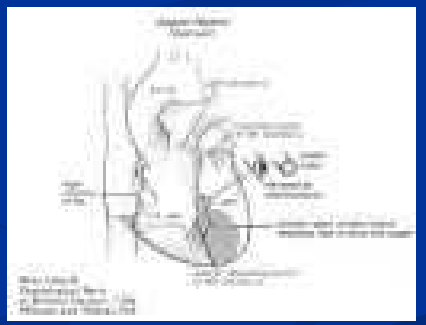
The cause

- Organic - atherosclerosis (95%), thrombus, embolism, arteritis, etc.
- Functional - coronary spasm
- Combined

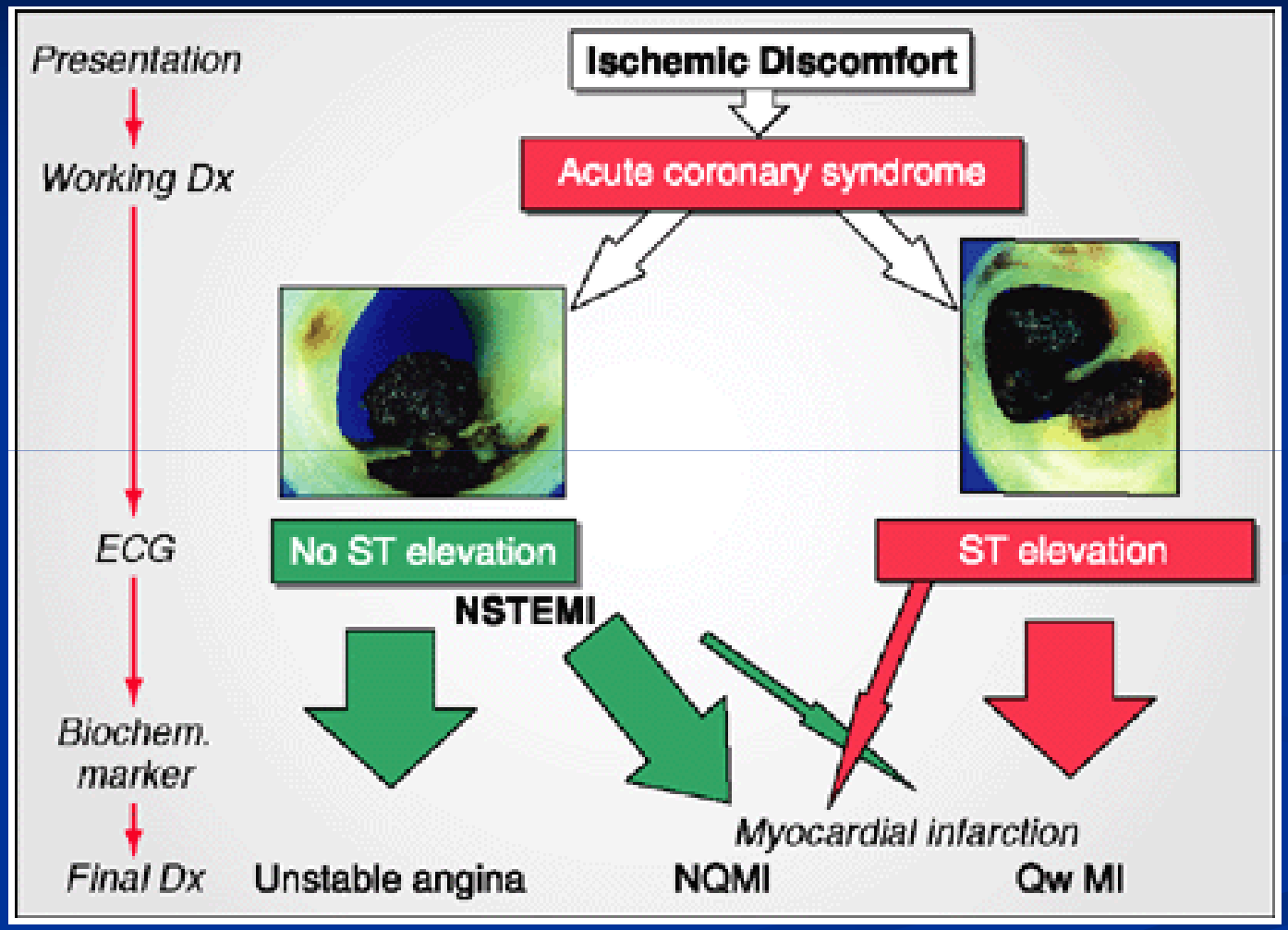
Atherosclerotic plaque>> reduce the flow>> ischemia







Ischemic heart disease



unstable AP (cTnI $\leq$ 0,4 ug/l)

nonQIM (cTnI >0,4 ug/l)

QIM (cTnI > 0,4ug)

Ischemic hearth disease

Risk factors:

- Should not be influenced - age, gender, family history
- Should be influenced - hypertension, hyperlipoproteinaemia, smoking, stress, obesity, physical inactivity, dietary habits

Ischemic hearth disease

Classification:

- acute (unstable) - acute myocardial infarction, unstable angina, sudden death
- chronic (stable) - **angina pectoris** (exertional, mixed, variant), silent ischaemia, arrhythmic forms
-

Ischemic hearth disease

Angina pectoris:

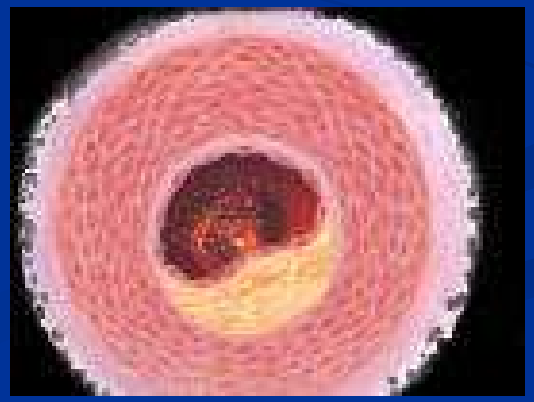
- Most frequent clinical manifestations of IHD - caused by the myocardial ischemia, in which the patient has chest pain (stenocardia).
- Imbalance between myocardial oxygen supply and demand

Angina pectoris

Main cause:

- atherosclerotic plaque in coronary artery

lumen stenosis lower than 50% - insignificant
lumen stenosis above 50% - a significant
lumen stenosis above 95% - critical



Angina pectoris

Classification of severity:

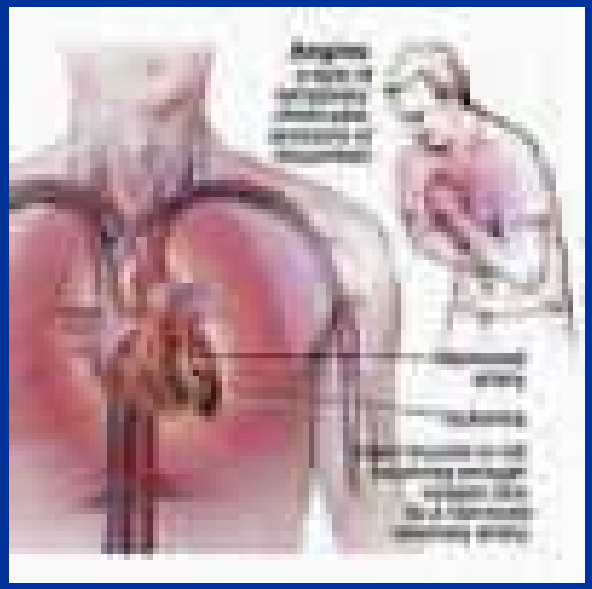
I. stenocardia provoked by extraordinary exertion
II. stenocardia provoked more than usual exertion
III. stenocardia provoked by regular exertion stenocardia
IV. stenocardia provoked by minimal exertion or at rest

Angina pectoris

Clinical picture:

constringent pain with / without feeling a lack of breath, pain with the propagation to the back, neck, shoulders, upper extremities.

Usually it is a link to the previous load (walking, stress, food, ...)
Typically takes a few minutes and gradually subsides after removal causing torque.



Angina pectoris

Diagnosis:

History - family, personal, pharmacological, social..

Problems - duration, time from first occurrence of pain, frequency, repetition, connection to the load, etc.

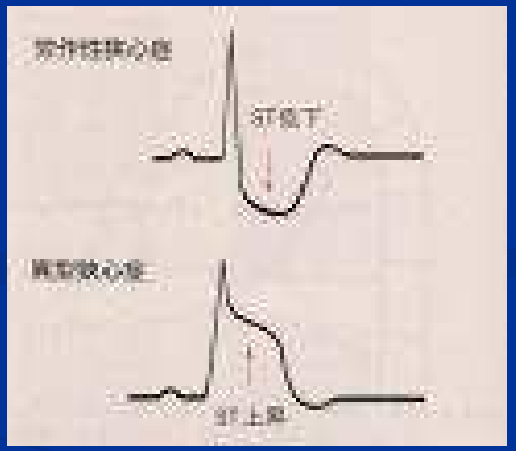
Complete clinical examination, exclusion of non-cardiac etiology problems (nerve, muscle, gastrointestinal, pulmonary, other ... ..)

Laboratory signs - Troponin-I, CK-MB

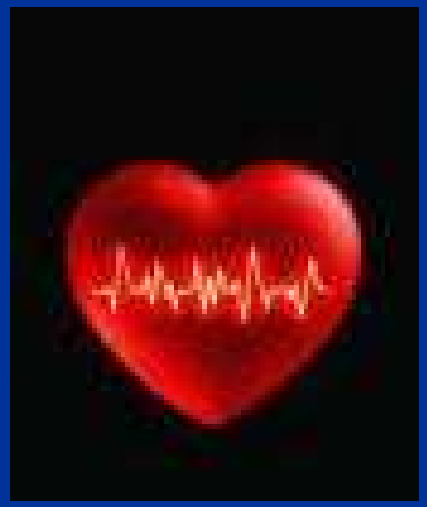
Angina pectoris

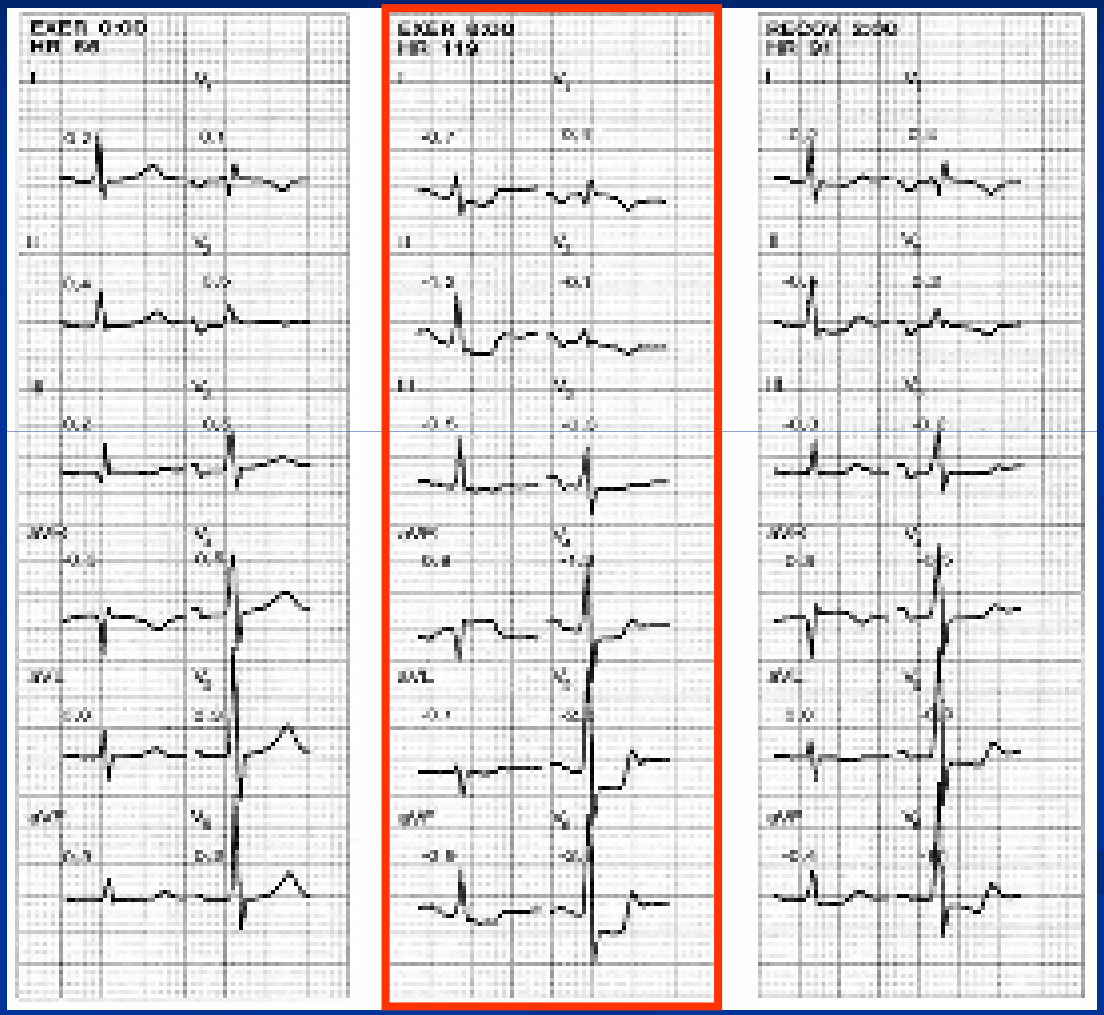
Diagnostic procedures:

ECG – at rest and during exercise, 24-hour ambulatory monitoring, during of angina found in a typical case of ECG changes (depression / ST segment elevation), between angina symptoms ECG is negative.



Ergometer stress test

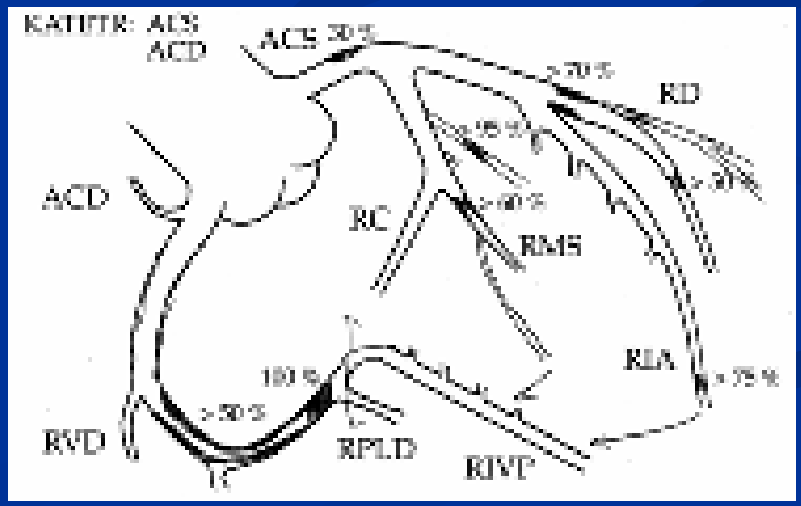




Angina pectoris

Diagnostic procedures:

- Echocardiography: at rest and during the exercise
- Coronary angiography – used to directly view the coronary field using a contrast agent injected into coronary arteries, allowing accurate identification of narrowing or occlusion vessel, its significance, may be determined by the residual flow of the affected artery



Treatment of CAD

Objective:

- to improve the quality of life
- to improve patient prognosis

Methods:

1st: stopping or slowing progress of atherogenesis
2nd: improve the flow of ischemic myocardium
3rd: prevention of vascular thrombus occlusion

Treatment of CAD

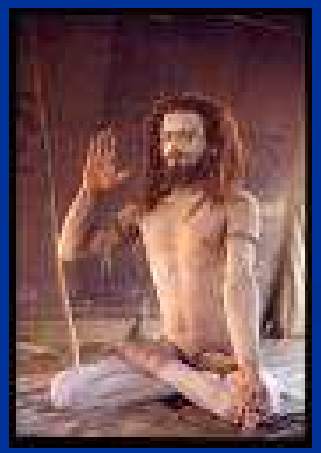
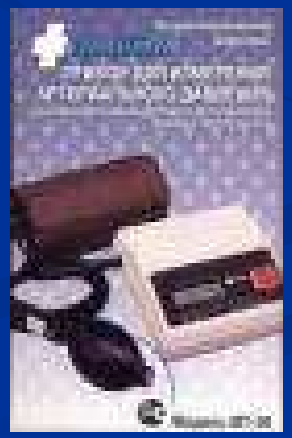
- nonpharmacologic - lifestyle changes
- pharmacological - drug therapy
- intervention - PTCA with / without stent - surgical revascularization

Treatment of CAD

Non-pharmacological:

Motion mode - aerobic (running, swimming, cycling, ...)
Dietary measures - change in eating habits (limit saturated fats, increase the proportion of unsaturated fats, fish, vegetables, fruits)
Abstinence of smoking, alcohol in moderation
Mental relaxation - sports, culture, yoga, psychotherapy
Control of diabetes and hypertension




Treatment of CAD

Interventions:

- Percutaneous transluminal coronary angioplastic (PTCA)

The principle consists from delivery of a catheter (thin tube - at the end of the cylindrical balloon) into the narrowed or closed coronary artery and the balloon expands narrow blood vessels.

The next step may be followed by stent (metallic reinforcement) in place of the previous narrowing.

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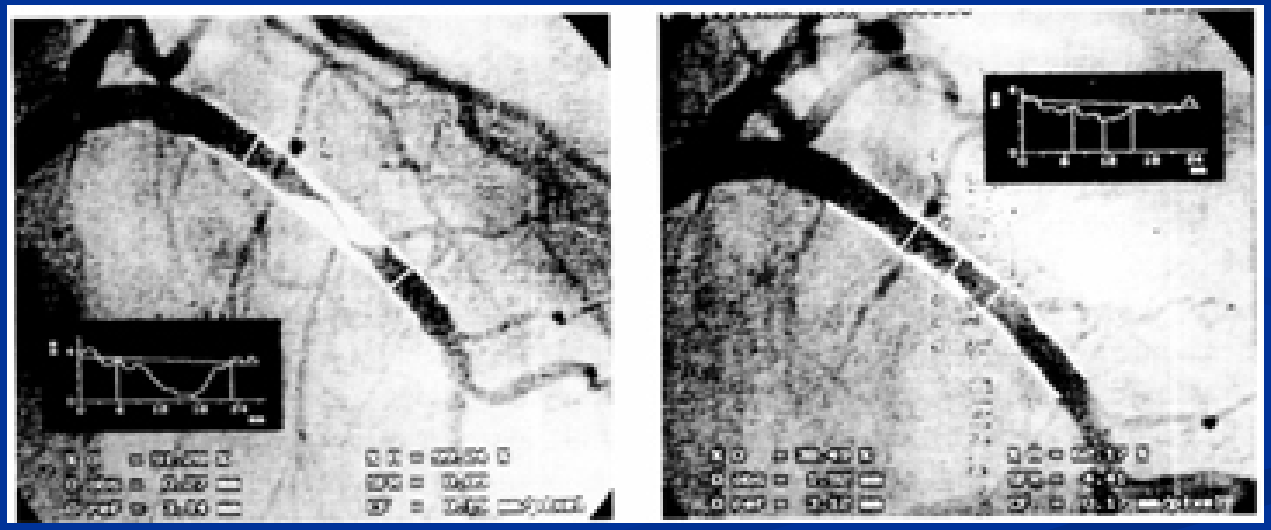
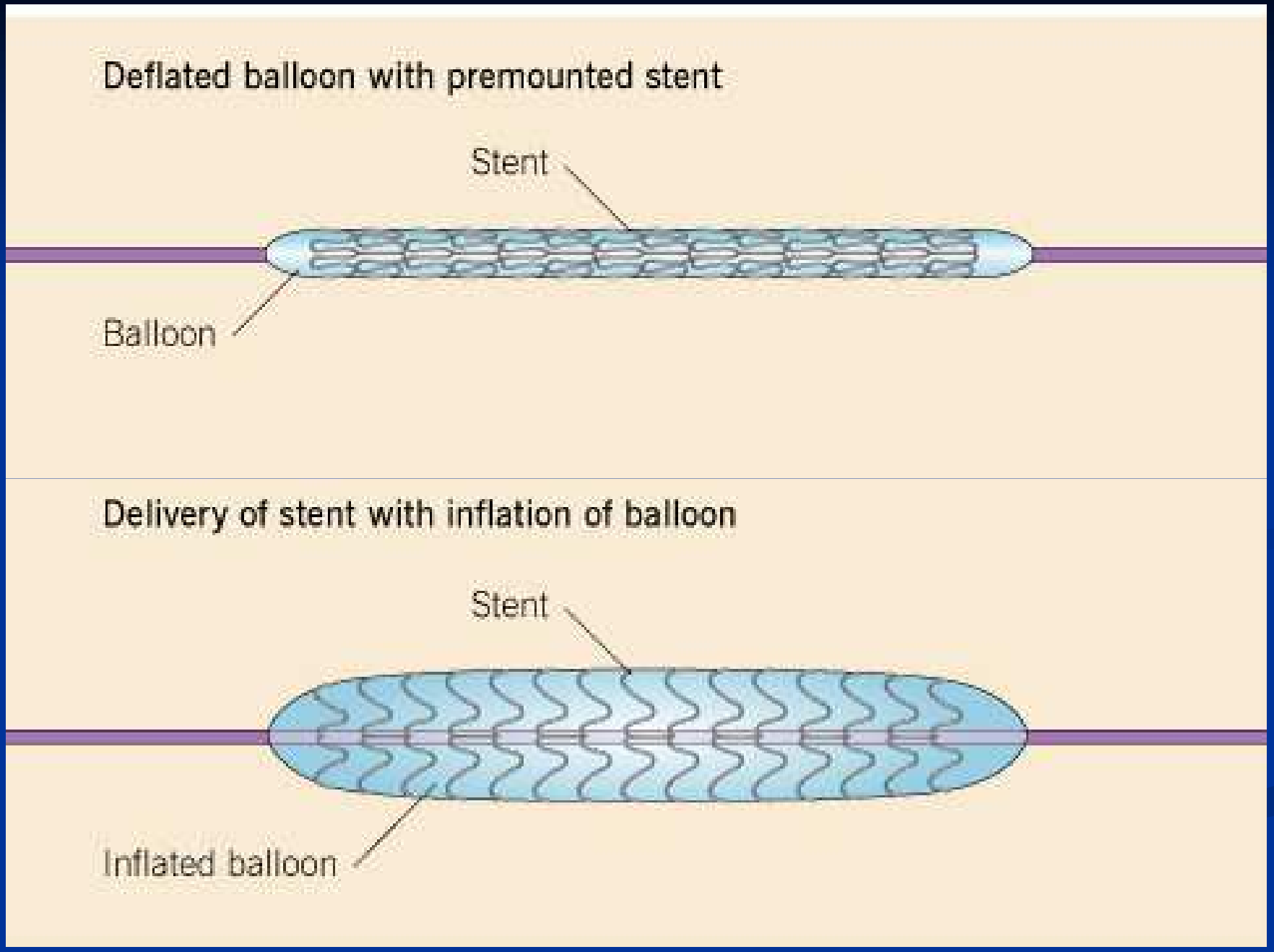
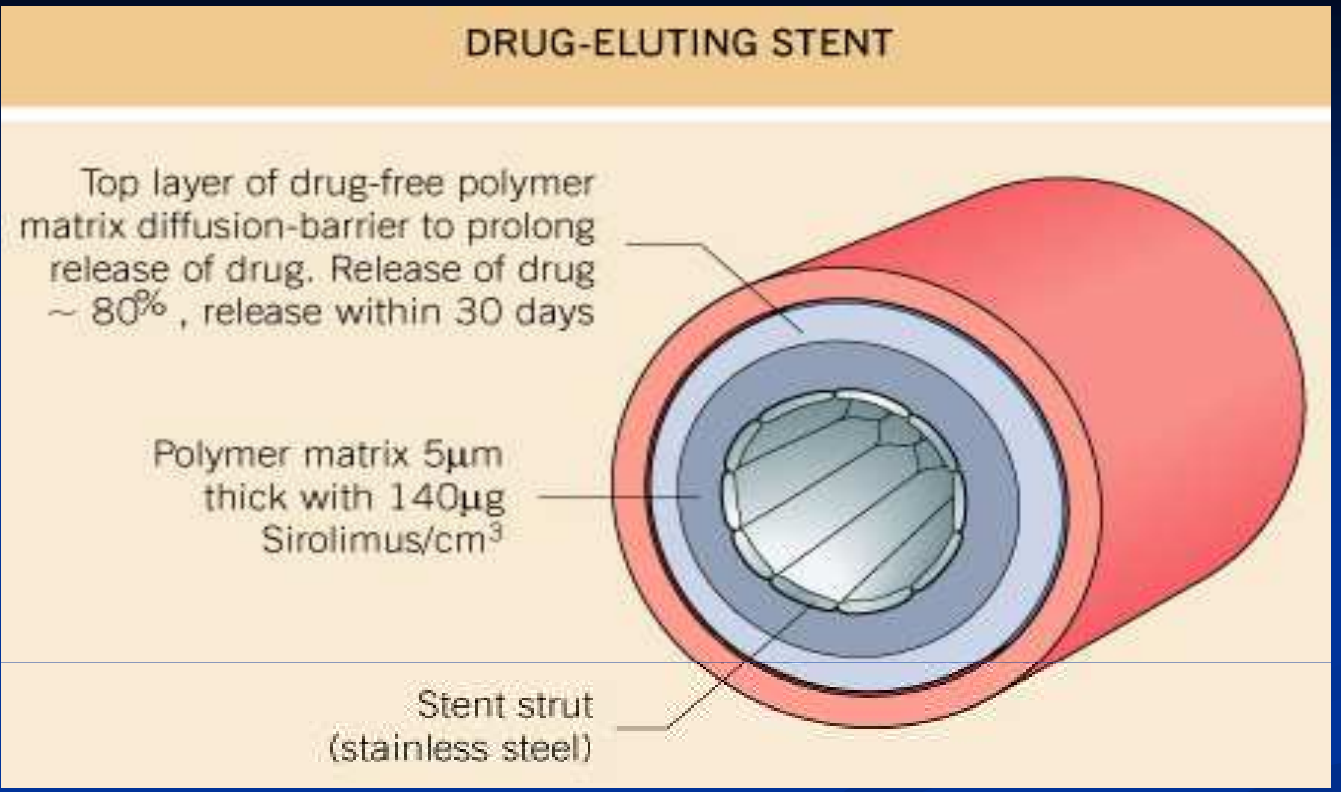
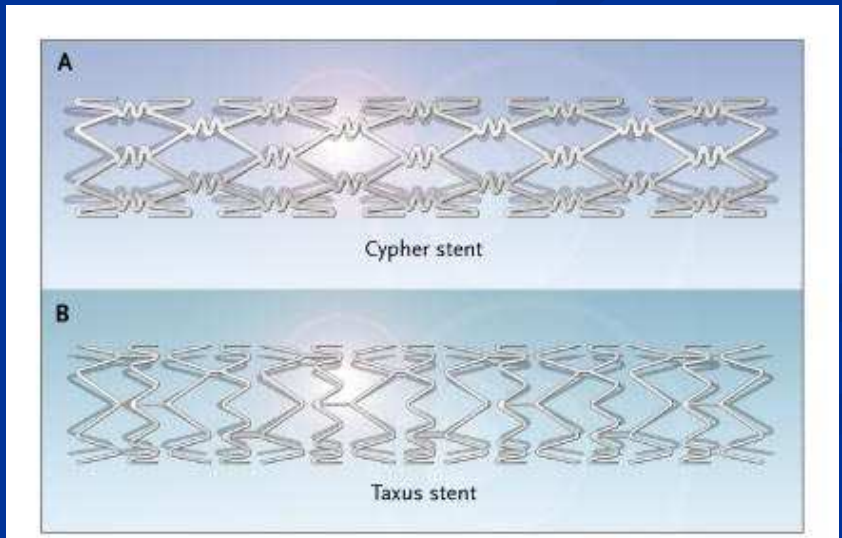
Critical stenosis of the left coronary artery solved successfully by PTCA with stent implantation.




Deflated balloon with premounted stent
Stent
Balloon
Delivery of stent with inflation of balloon
Stent
Inflated balloon

DRUG-ELUTING STENT





Drug-eluting stents – DES

- a peripheral or coronary stents (a scaffold) placed into narrowed, diseased peripheral or coronary arteries that slowly releases a drug to block cell proliferation.

- The stent is usually placed within the peripheral or coronary artery by an Interventional cardiologist or Interventional Radiologist during an angioplasty procedure.

Drug-eluting stents – DES

Cypher	sirolimus
Taxus	paclitaxel
Biomatrix, Nobori	biolimus
Xience	everolimus
Endevour	tacrolimus

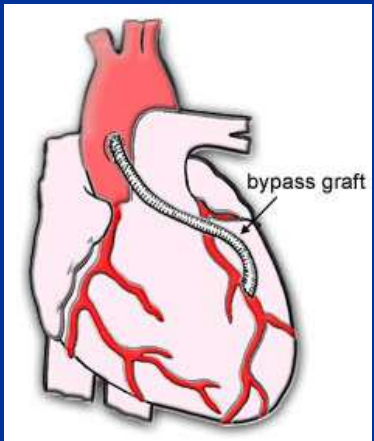
Treatment of CAD

Methods of interventional treatment:

- Surgical revascularization

Coronary artery bypass is the process of restoring the flow of blood to the heart. The surgical procedure places new blood vessels around existing blockages to restore necessary blood flow to the heart muscle.

Critical stenosis of the left coronary artery bypass solved successfully by surgery.



Treatment of CAD

Methods of pharmacological treatment:

1st: stopping or slowing progress of atherogenesis
2nd: improve the flow of ischemic myocardium
3rd: prevention of vascular thrombus occlusion

Methods of pharmacological treatment:

1st:
stopping or slowing progress of atherogenesis

control of risk factors:

- correction of BP – antihypertension th.
- corrections of lipids – hypolipidemics
- DM – glucose control - antidiabetics

Methods of pharmacological treatment:

2nd:
improve the flow of ischemic myocardium

smooth muscle relaxation of coronary artery stenosis
slowing the heart rate - a reduction of metabolic demands
reduction of myocardial contractility - improving coronary perfusion

nitrates, beta-blockers, Ca-channel blockers, If-channel blockers

Methods of pharmacological treatment:

3rd:

Prevention of vascular thrombus occlusion

Antiplatelet/anticoagulants, such as aspirin or warfarin

Treatment of CAD

Methods of pharmacological treatment:

1st: stopping or slowing progress of atherogenesis
2nd: improve the flow of ischemic myocardium
3rd: prevention of vascular thrombus occlusion

Hypolipidemics

- Statins: inhibition of HMGCoA (3-OH-3 CH3 glutaryl coenzyme A) reductase.
- Fibrates: activate lipoprotein lipase, reduces VLDL and increase HDL
- Ezetimibe: blocks absorption of Cholesterol in the intestine
- Niacin: blocking the breakdown of adipose tissue (inhibition of lipolysis)
- Resin: inhibiting resorption of bile acids

Treatment of CAD

Methods of pharmacological treatment:

1st: stopping or slowing progress of atherogenesis
2nd: improve the flow of ischemic myocardium
3rd: prevention of vascular thrombus occlusion

Methods of pharmacological treatment:

2nd:

I . improve the flow and perusion of ischemic myocardium - smooth muscle relaxation of coronary artery stenosis

II . Reduce its metabolic demand -
slowing the heart rate
reduction of myocardial contractility

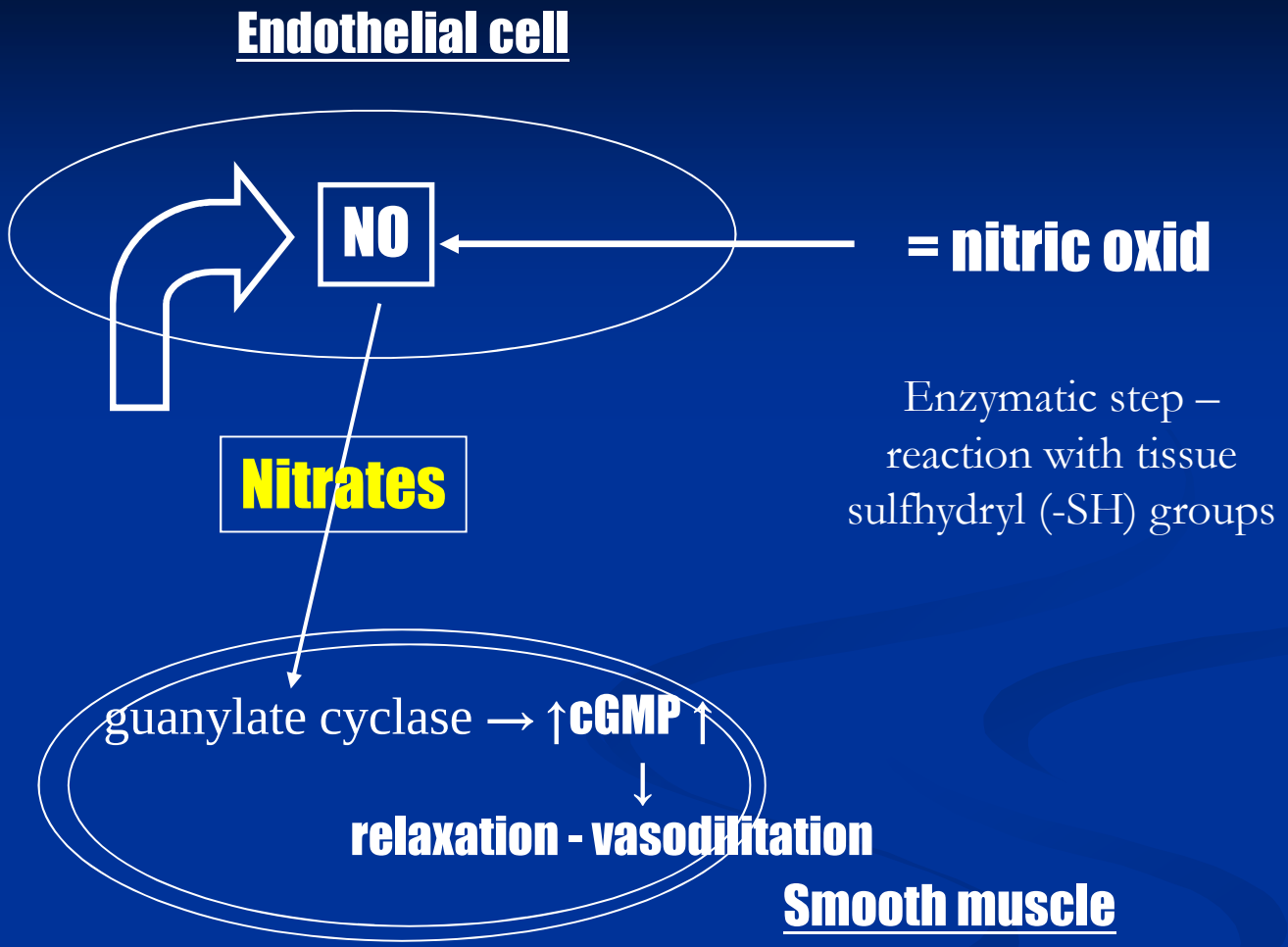
- **I+II : nitrates, Ca-channel blockers**
- **II : beta-blockers + If-channel blockers**

Nitrates

Nitroglycerin was synthesized by the chemist Ascanio Sobrero in 1847

Nitroglycerin is converted to nitric oxide in the body by mitochondrial aldehyde dehydrogenase

NO - nitric oxide - identical to the 'endothelium-derived relaxing factor' (EDRF) -
is a natural vasodilator (stimulation of guanylate cyclase of smooth muscle - relaxation-vasodilatation)


Endothelial cell
NO
= nitric oxid
Nitrates
Enzymatic step – reaction with tissue sulfhydryl (-SH) groups
guanylate cyclase → ↑cGMP ↑
↓
relaxation - vasodilitation
Smooth muscle

Nitrates

- Effects: local x systemic

LOCAL: the direct effect on coronary artery tone - dilation of coronary arteries

SYSTEMIC:
venorelaxation – consequent reduction in central venous pressure – reduce preload

Relaxation of lareger muscular arteries – reduce afterload

Nitrates

- Adverse reactions:
- headache, orthostatic hypotension,
- onset of tolerance (possibly partly because of depletion of free –SH groups), mainly longer-acting drugs

Nitrates

- Representatives:

Nitroglycerin (glyceryl trinitrate)

- rapidly inactivated by hepatic metabolism
- well absorbed from the mouth – is taken as a tbl. under the tongue or sublingual spray – effects within few minutes
- Effectiveduration of action app. 30 minutes
- Well absorbed through the skin – transdermal patch

Nitrates

- Representatives:

Isosorbite 2-mononitrate (ISMN) longer acting – half-life app. 4 hours , the same farmacological action I: prophylaxy twice daily (morning, lunch time – to avoid tolerance)
Isosorbit 2,5-dinitrate (ISDN) - iv
Molsidomin (does not produce tolerance, use of overnight)

Beta - blockers

- **Prophylaxis of angina**
- **Treating the patients with unstable angina**

slowing the heart rate and reduction of myocardial contractility

Beta - blockers

- **Competitive antagonists** (intrinsic activity = 0) or **partial agonists** (ISA - intrinsic sympathomimetic activity)

- **Non-selective** or **cardioselective** (primary blocs of b_1 receptors)

classification

Non-selective ($\beta_1 + \beta_2$) propranolol

(Cardio)selective (β_1) metoprolol

Non-selective with ISA (β1 + β2) S ISA pindolol

(Cardio)selective (β_1) with ISA acebutolol

Combining α + β blocade =
β-blockers of II.generation labetalol

Beta blockers

Indication: angina pectoris, hearth failure with titration tacharrhytmia, glaukom

Contraindication:

absolute: AV block (grade 2 or 3), asthma,

Adverse events

- Bronchoconstriction
- Bradycardia
- Hypoglycaemia
- Fatique

I_f blockers –SA node

Heart rate is determined by spontaneous electrical pacemaker activity in the sinoatrial node controlled by the I_f current (*f* is for "funny", so called because it had unusual properties compared with other current systems known at the time of its discovery)

I_f blockers –SA node

Ivabradine acts on the I_f ion current, which is highly expressed in the sinoatrial node. I_f is a mixed Na^+–K

I_f is one of the most important ionic currents for regulating pacemaker activity in the sinoatrial (SA) node.

Ivabradine (PROCORALAN)

- selectively inhibits the pacemaker I_f current in a dose-dependent manner. Blocking this channel reduces cardiac pacemaker activity, slowing the heart rate and allowing more time for blood to flow to the myocardium.

Ivabradine – indication :

I: Symptomatic treatment of chronic stable angina pectoris in coronary artery disease adults with normal sinus rhythm.

- in adults unable to tolerate or with a contra-indication to the use of beta-blockers

- or in combination with beta-blockers in patients inadequately controlled with an optimal beta-blocker dose and whose heart rate is > 60 bpm.

Calcium-channel blockers (CCB)

- works by blocking voltage-gated calcium channels in cardiac muscle and blood vessels.
- ↓ intracellular calcium leading to ↓ cardiac contractility
- In blood vessels ↓ vascular smooth muscle and therefore ↑ vasodilation. Vasodilation decreases total peripheral resistance.

Calcium-channel blockers (CCB)

- **3 chemically distinct classes:**

- Phenylalkylamines
- Benzothiazepines
- Dihydropyrimidines

Non DHP CCB

Phenylalkylamine: verapamil

Preferentially affects Ca-channel in hearth
Indications: antiarrhytmics

Contraindications:

absolute: AV block (grade 2 or 3), heart failure

relative: bradycardia below 50/min, concomitant with BB

Non DHP CCB

Benzithiazepiny : diltiazem

Affects both Ca-channel in hearth and in vessels
Indications: angina pectoris

Contraindications:

absolute: AV block (grade 2 or 3), heart failure

relative: bradycardia below 50/min, concomitant with BB

DHP CCB

Dihydropyridine CCB

Indications: elderly - angina pectoris, coronary disease of lower extremities, atherosclerotic carotid disability

Contraindications:

relative: tachyarrhythmias, heart failure

Calcium-channel blockers (CCB)

Class	1st generation	2nd generation
Fenylalkylamines	Verapamil	Verapamil SR
Benzothiazepines	Diltiazem	Diltiazem SR
Dihydropyridines	Nifedipin	Nifedipin GITS
		Isradipin SRO
		Felodipin
		Nitrendipin
		Nilvadipin
		Nisoldipin
		Nimodipin
		Amlodipin
		Lacidipin

Calcium-channel blockers (CCB)

ADRs: results from vasodilation and the effect on the conduction system

- headache, orthostatic hypotension, palpitations, swollen ankles,
- AV block non-DHP in combination with beta-blockers, significant bradycardia

Combination of antianginous drugs

- **Nitrates + beta-blockers** – a suitable combination
- **Nitrates + CCB** – need BP corrections
- **Beta-blockers+ CCB –** a suitable, but ! AV block non-DHP in combination with beta-blockers, significant bradycardia