

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

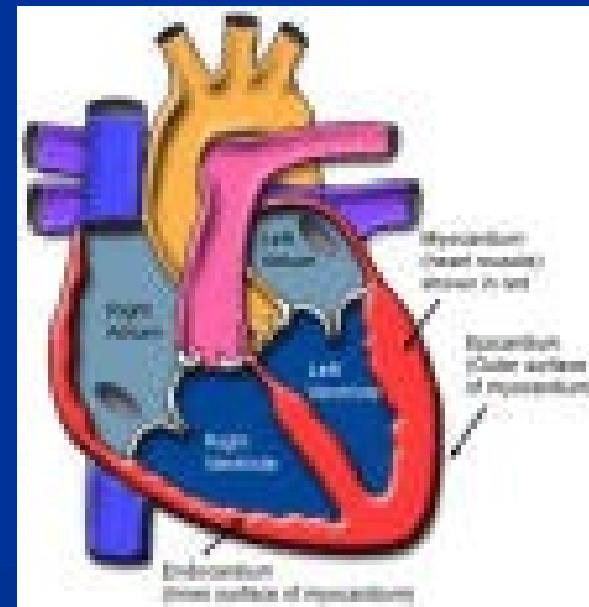
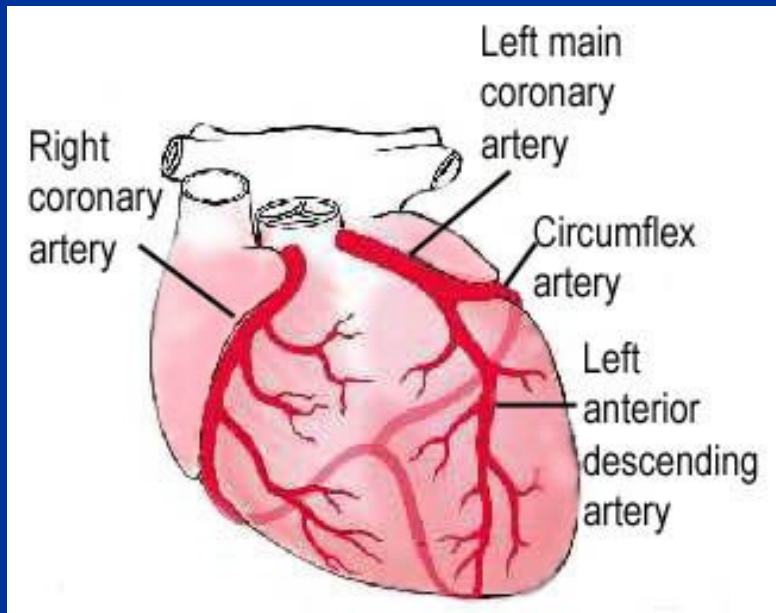
Regina Demlova



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

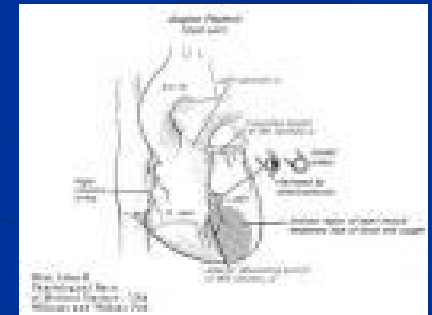
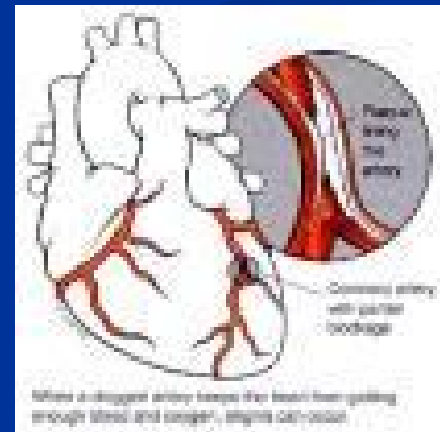
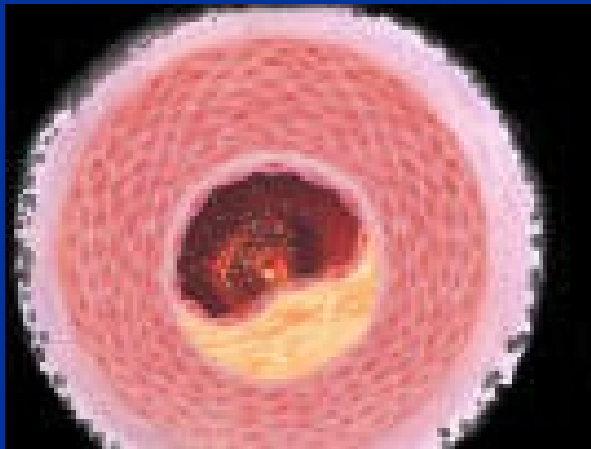


Ischemic heart disease

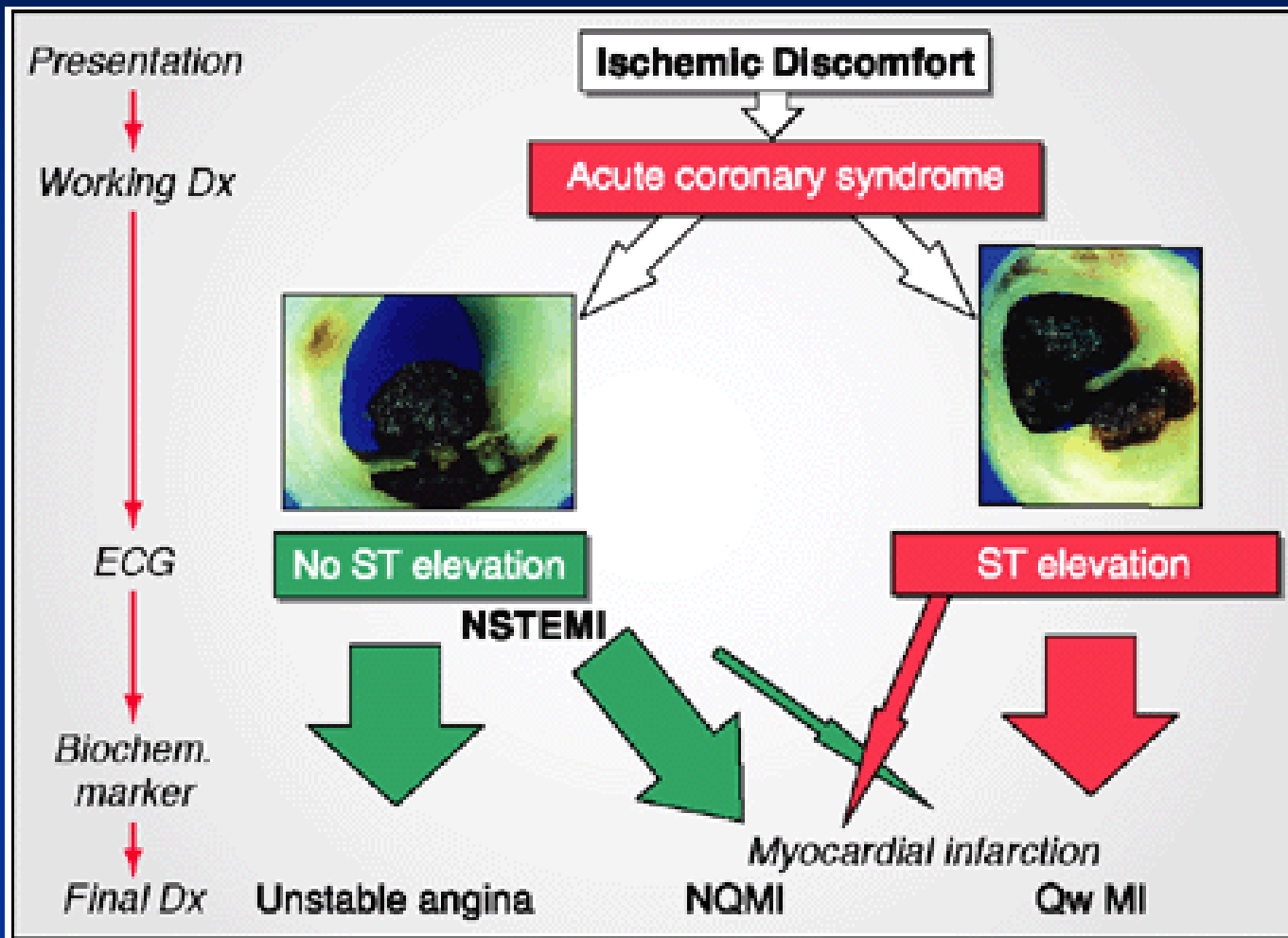
The cause

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

Atherosclerotic plaque >> reduce the flow >> ischemia



Ischemic heart disease



unstable AP
(cTnI ≤ 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

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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

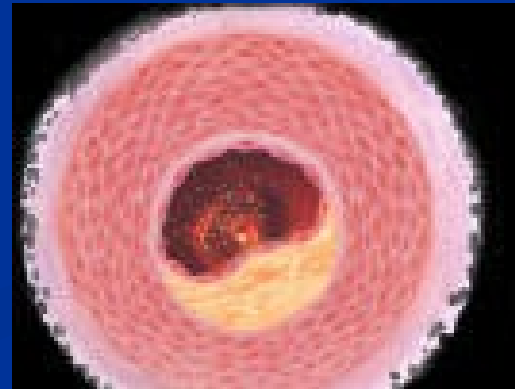
Main cause:

- 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

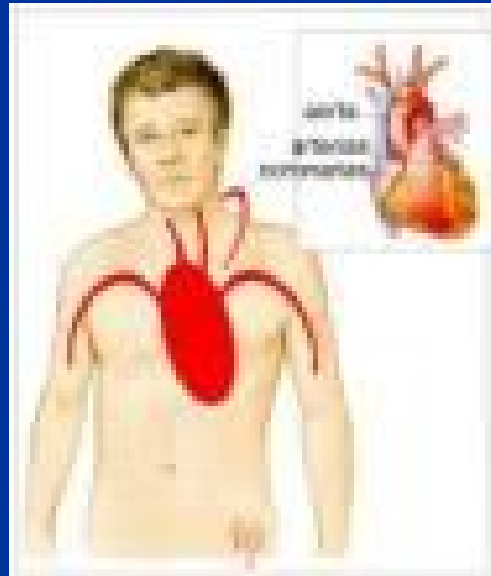
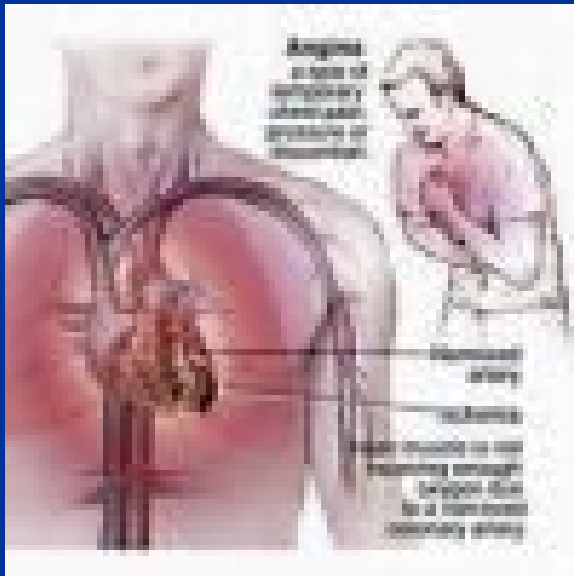


Angina pectoris

Clinical picture:

constricting 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)

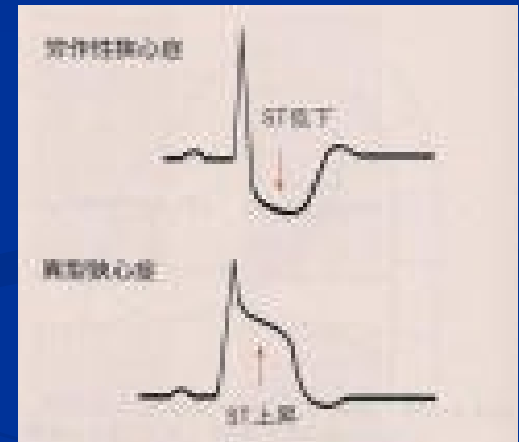
Laboratory signs - Troponin-I, CK-MB



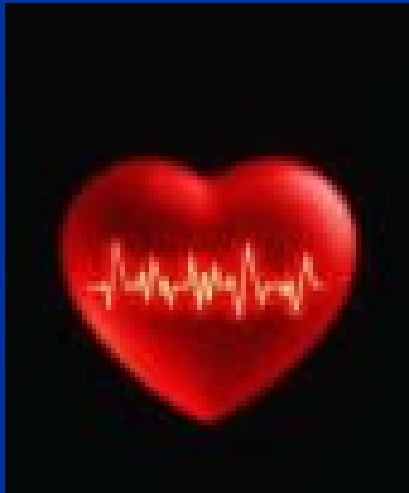
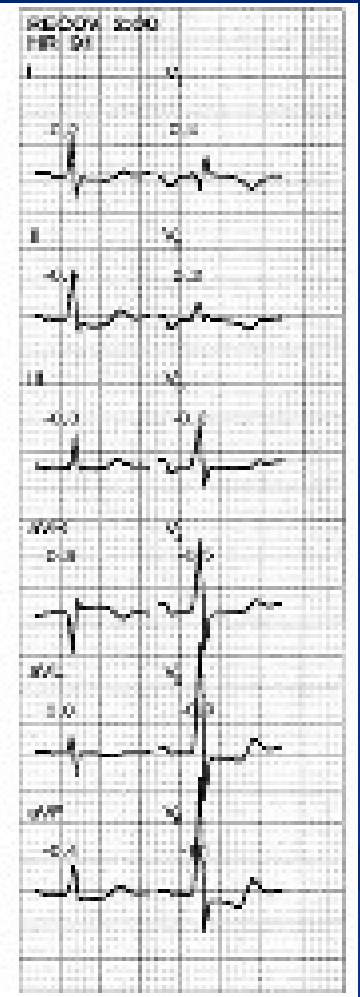
Angina pectoris

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.



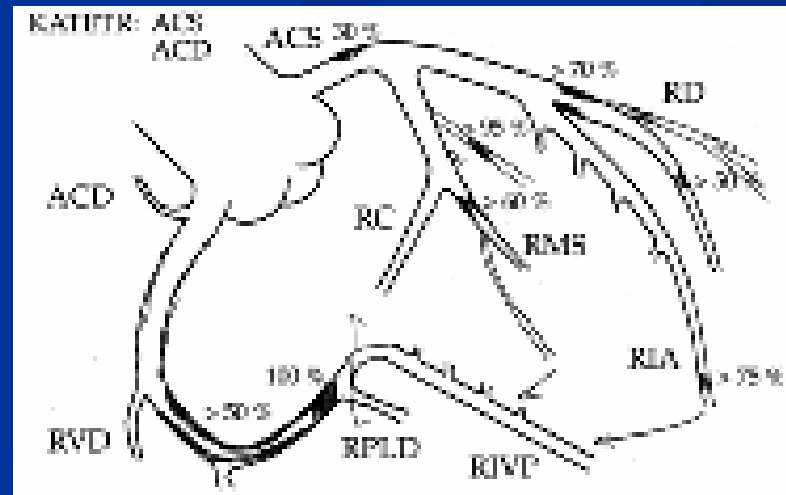
Ergometer stress test



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:

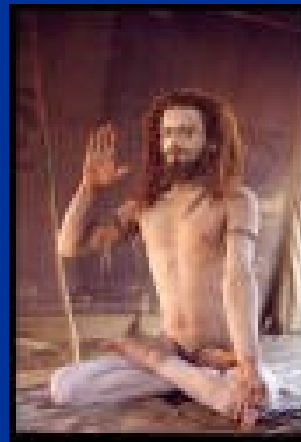
Motion mode - aerobic (running, swimming, cycling, ...)

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 angioplasty (PTCA)

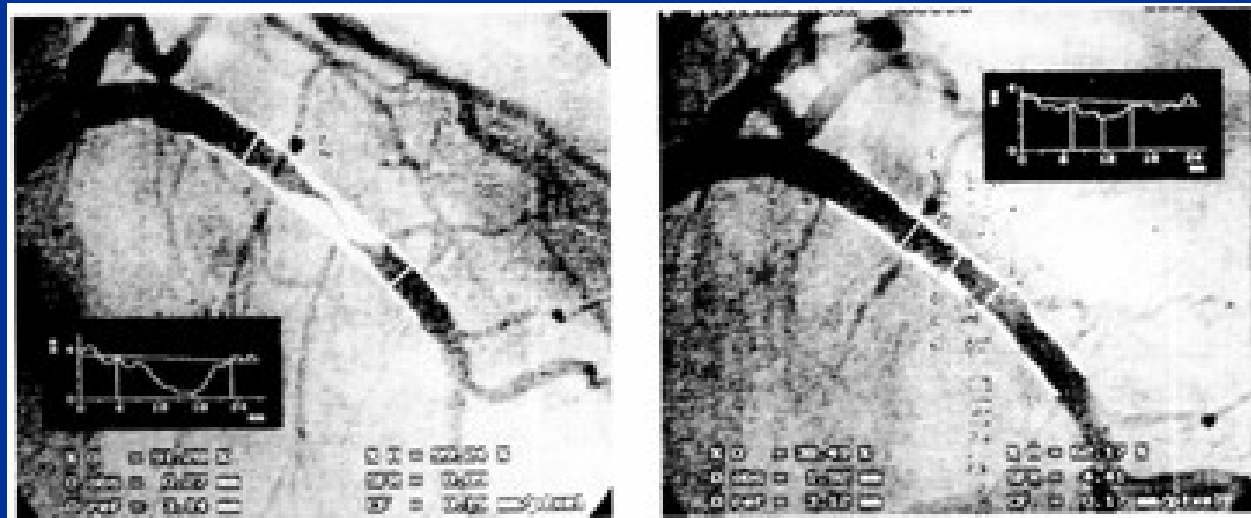
The principle consists from delivery of a catheter (thin tube - at the end of the cylindrical balloon) into the narrowed or closed coronary artery and the balloon expands narrow blood vessels.

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

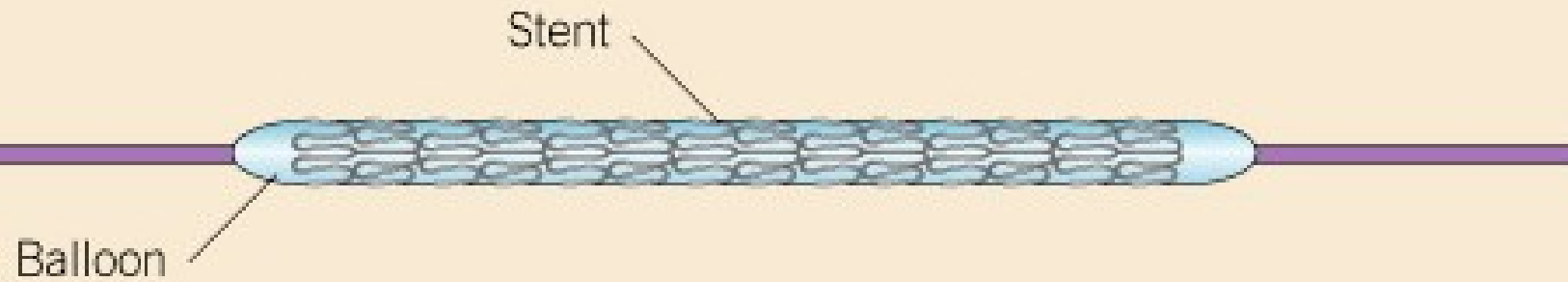
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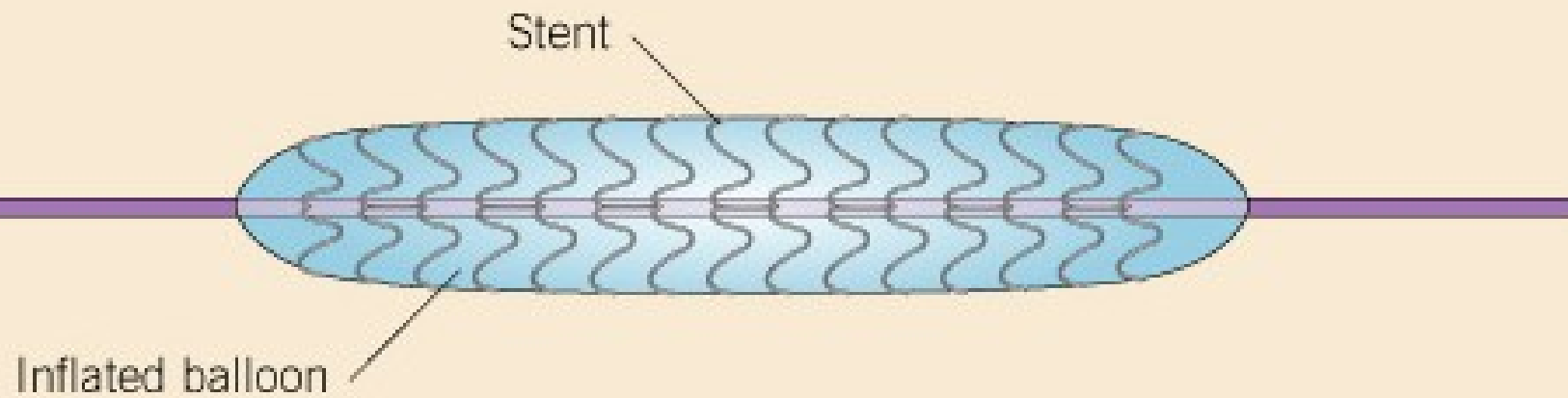
Critical stenosis of the left coronary artery solved successfully by PTCA with stent implantation.



Deflated balloon with premounted stent



Delivery of stent with inflation of balloon

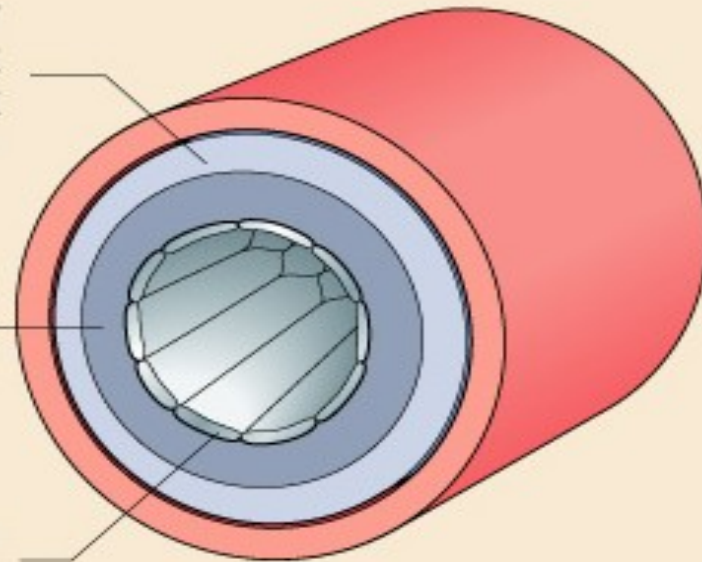


DRUG-ELUTING STENT

Top layer of drug-free polymer matrix diffusion-barrier to prolong release of drug. Release of drug ~ 80% , release within 30 days

Polymer matrix 5 μ m thick with 140 μ g Sirolimus/cm³

Stent strut (stainless steel)



A



Cypher stent

B



Taxus 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
- Endeavour tacrolimus

Treatment of CAD

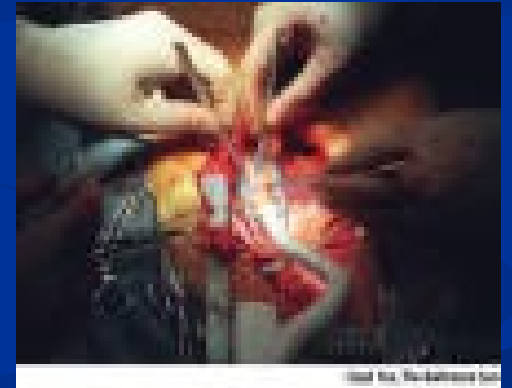
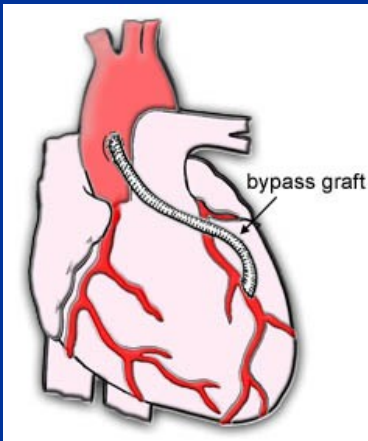
Methods of interventional treatment:

- 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

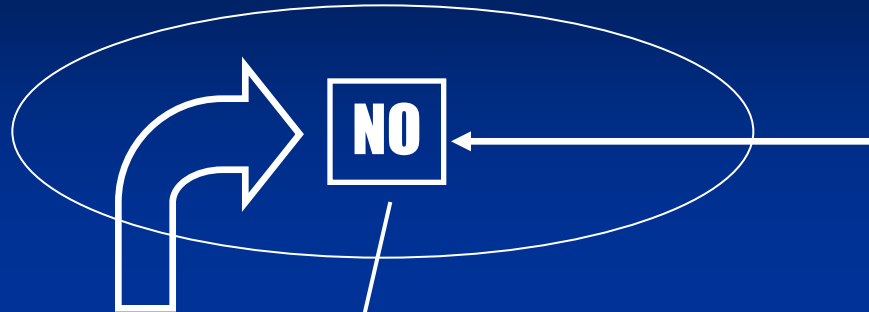
Nitroglycerin was synthesized by the chemist Ascanio Sobrero in 1847

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)

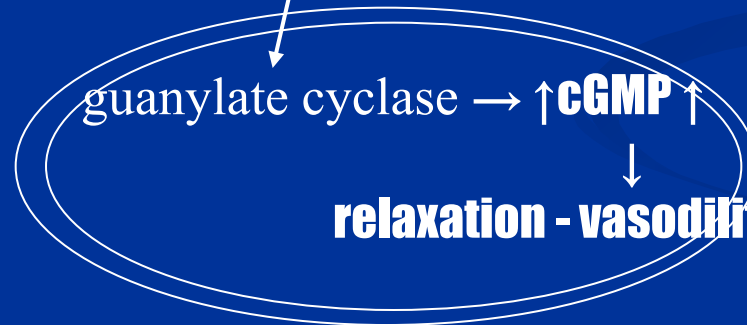
Endothelial cell



= nitric oxid

Enzymatic step –
reaction with tissue
sulfhydryl (-SH) groups

Nitrates



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 larger 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 β_1 receptors)

classification

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

(Cardio)selective (β_1) **metoprolol**

Non-selective with ISA ($\beta_1 + \beta_2$) S ISA **pindolol**

(Cardio)selective (β_1) with ISA **acebutolol**

Combining $\alpha + \beta$ blockade =

β -blockers of II.generation **labetalol**

Beta blockers

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

Contraindication:

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

Adverse events

- Bronchoconstriction
- Bradycardia
- Hypoglycaemia
- Fatigue



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: antiarrhythmics

Contraindications:

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

relative: bradycardia below 50/min, concomitant with BB

Non DHP CCB

Benzothiazepiny : diltiazem

Affects both Ca-channel in heart 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

