Cardio-Vascular Disease

ISCHEMIC HEART DISEASE: Atheroscelorsis, Angina, Myocardial Infarction

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DNB INTERNAL MEDICINE

Ischemic heart disease

- Also known as **Coronary Artery Disease (CAD)**
- **Ischemic heart disease (IHD)** is a condition in which there is an **inadequate supply** of blood and oxygen to a portion of the myocardium
- Imbalance between **myocardial oxygen supply** and **demand**.
- Caused mainly by **Atherosclerosis of Coronary Artery**
- It includes
  - **Angina: Stable** & **Unstable**
  - **Myocardial infarction**
  - **Heart failure** & **Arrhythmia**

Ischemic Heart Disease (IHD): *Pathogenesis of the various types of IHD*

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High serum LDL → *↑ availability of lipids that deposit in arterial wall*

Low Serum HDL → *↓ removal of LDL from coronary artery walls (transport of LDL to liver is impaired)*

Endothelial dysfunction → *Compromise of endothelial barrier → vessel wall vulnerable to infiltration by LDL and cells of the immune system*

Atherosclerosis
Arterial wall degeneration, characterized by fat deposition in and fibrosis of the inner layer of arteries

Note: For a full description of the pathogenesis and complications of atherosclerosis, check out the relevant slides on the topics.

Occurring in the coronary arteries:

If the atheromatous plaque is stable:
The fibromuscular cap overlying fatty plaque contents remains intact, and plaque contents are not released into vessel lumen

Plaque serves as a fixed lumenal obstruction to blood flow

If vessel stenosis is significant (≥70%), myocardial oxygen demand starts to exceed supply, especially with exertion

Predictable, transient myocardial ischemia

Stable Angina

If the atheromatous plaque is unstable:
The fibromuscular cap overlying fatty plaque ruptures

Thrombogenic plaque contents (especially tissue factor) are exposed to the coagulation factors in the vessel lumen

Activation of platelets and the clotting cascade at the site of rupture

Thrombus forms over already partially occlusive plaque → occludes lumen → ↓ perfusion of myocardium

Transient ischemia of cardiomyocytes → **Unstable Angina**

Infarction (death) of cardiomyocytes → **Myocardial Infarction (MI)**

Acute Coronary Syndromes (ACS)

Legend: Pathophysiology | Mechanism | Sign/Symptom/Lab Finding | Complications

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Atherosclerosis

- Can affect any artery in the body
- **Heart**: angina, MI and sudden death;
- **Brain**: stroke and transient ischaemic attack;
- **Limbs**: claudication and critical limb ischaemia.

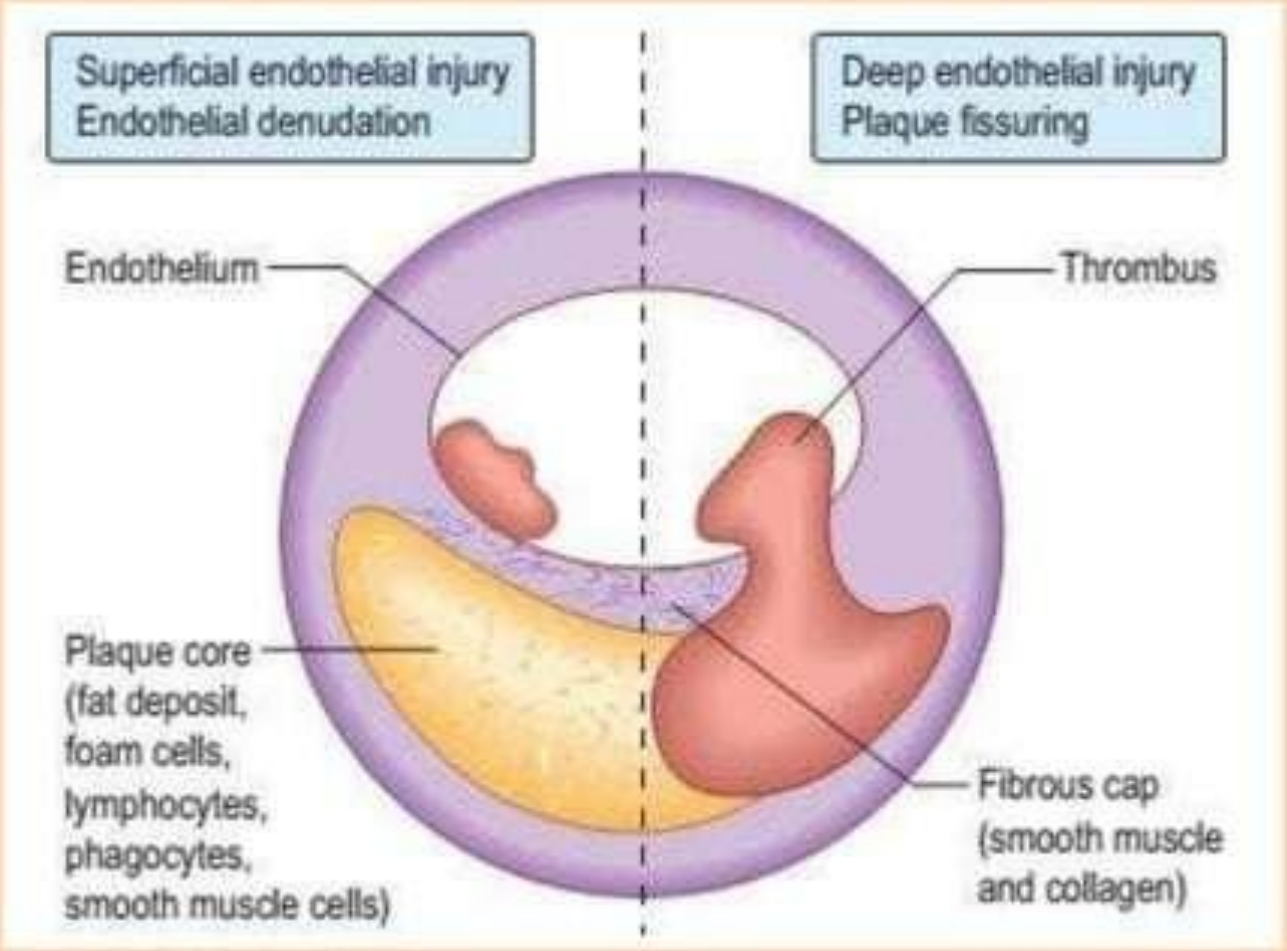
Atherosclerosis

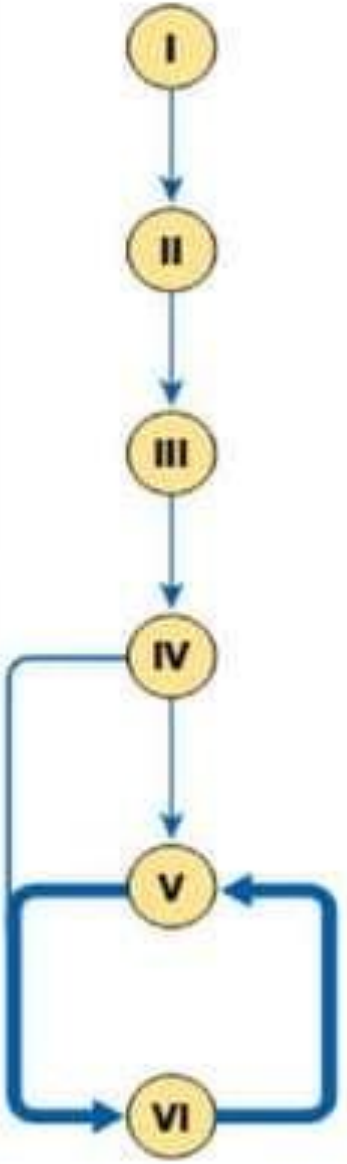
- Progressive **inflammatory disorder** of the arterial wall characterised by focal lipid rich deposits of **atheroma**
- Remain clinically assymptomatic until
  - large enough to impair tissue **perfusion**,
  - Ulceration and disruption of the lesion result in **thrombotic occlusion**
  - **Distal embolisation** of the vessel.
- Clinical manifestations depend upon the **site of the lesion** and the **vulnerability** of the organ supplied

Early Atherosclerosis

- Second and third decades of life
- Tend to occur at sites of **altered arterial shear stress** such as bifurcations
- Starts with any abnormal endothelial function
- Inflammatory cells, predominantly **monocytes**, bind to receptors expressed by endothelial cells,
- Migrate into the **intima**
- Take up oxidised **low-density lipoprotein (LDL)** particles
- Become **lipid-laden macrophages** or **foam cells**.
- As Foam cells dies, it releases its lipid pool in intimal space with **cytokines** and **growth factor**
- In response, smooth muscle cells migrate from the media of the arterial wall into the intima
- Lipid core will be covered by smooth muscle cells and matrix
- Forms **stable atherosclerotic plaque** that will remain asymptomatic until it becomes large enough to obstruct arterial flow

Early Atherosclerosis

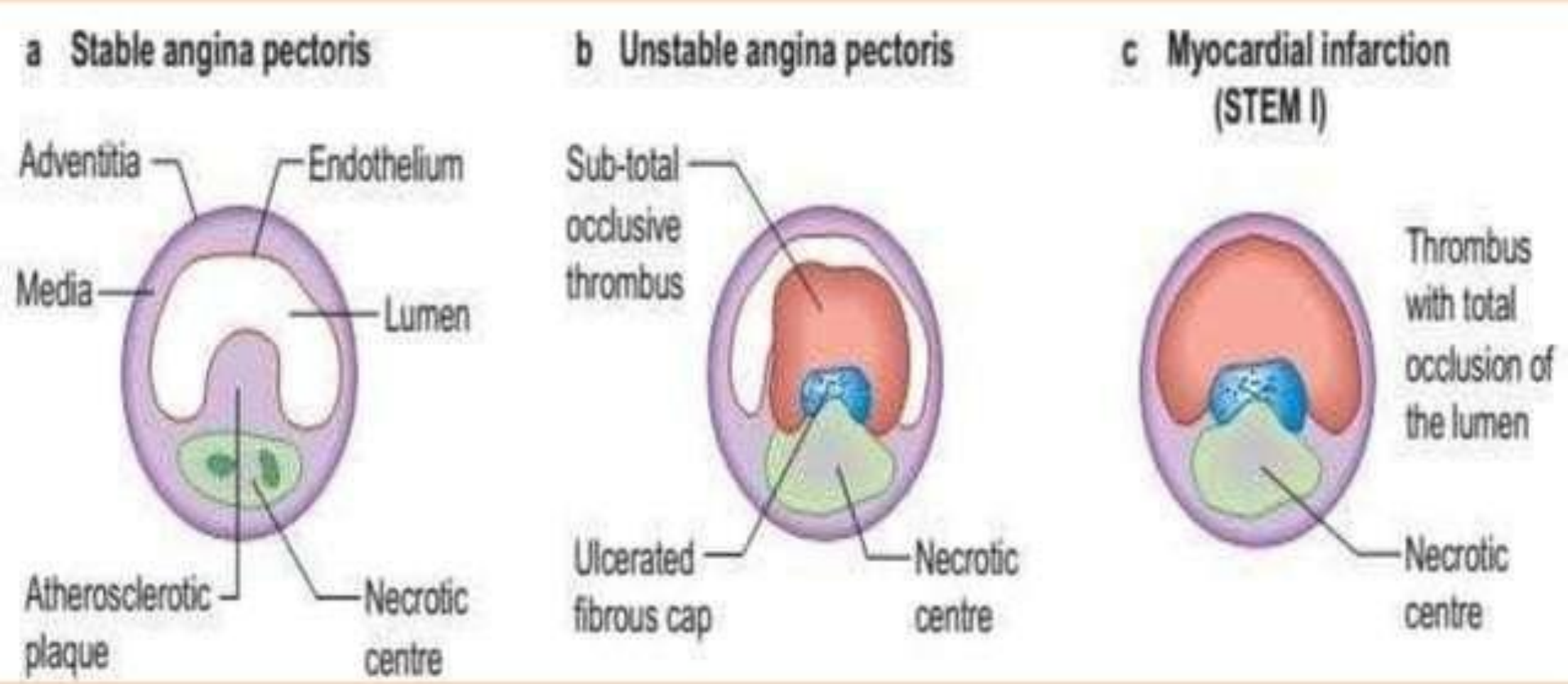


Nomenclature and main histology	Sequences in progression	Main growth mechanism	Earliest onset	Clinical correlation
Type I (initial) lesion Isolated macrophage foam cells 		Growth mainly by lipid accumulation	From first decade	Clinically silent
Type II (fatty streak) lesion Mainly intracellular lipid accumulation 				
Type III (intermediate) lesion Type II changes and small extracellular lipid pools 			From third decade	
Type IV (atheroma) lesion Type II changes and core of extracellular lipid 				Clinically silent or overt
Type V (fibroatheroma) lesion Lipid core and fibrotic layer, or multiple lipid cores and fibrotic layers, or mainly calcific, or mainly fibrotic 		Accelerated smooth muscle and collagen increase	From fourth decade	
Type VI (complicated) lesion Surface defect, haematoma-haemorrhage, thrombus 		Thrombosis, haematoma		

Advanced Atherosclerosis

- In established atherosclerotic plaque, **macrophages** mediate inflammation and **smooth muscle cells** promote repair
- Cytokines released by macrophage starts **degrading** smooth muscle layered over plaque
- Now lesion remains vulnerable to mechanical stress that ultimately causes **erosion, fissuring or rupture** of the plaque surface.
- Any breach in the integrity of the plaque will expose its contents to blood
- Trigger platelet aggregation and thrombosis
- That extend into the atheromatous plaque and the arterial lumen.
  - cause partial or complete obstruction at the site of the lesion
  - distal embolisation resulting in infarction
  - ischaemia of the affected organ

Advanced Atherosclerosis



Atherosclerosis: *Pathogenesis*

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Family History
(genetic predisposition for dyslipidemia, hypertension, and Type II Diabetes)

Dyslipidemia ***(high LDL, low HDL)***

HDL aids in transport of LDL from the periphery back to the liver for breakdown

Worsens dyslipidemia via unclear mechanisms

Smoking

Hypertension

Diabetes Mellitus

Inhaled free radicals enter blood

Chronic, high-pressure forces act on the artery wall

Glucose excess alters endothelial cell metabolism

Direct damage to arterial endothelium

Low levels of HDL allow for more rapid accumulation of LDL in vessel walls

More LDL diffuses across damaged endothelium, & accumulate in the intima layer of the artery wall

LDL in the intima is oxidized into lipids that trigger chronic inflammation in the vessel wall

Elevation of systemic markers of inflammation

Elevated serum CRP
(can be evaluated as an independent predictor of atherosclerosis)

Inflammation recruits monocytes into the vessel wall, which then differentiate into macrophages

Macrophages phagocytose the oxidized LDL and become filled with fat (henceforth, these cells are termed "foam cells")

Streaks of fatty tissue can be observed between the endothelium and the smooth muscle layer (media) of the artery

Fatty Streaks
(Seen on pathological specimens, early indicator of developing atherosclerosis)

Over time, foam cells accumulate in the intima to form an enlarging "**lipid core**". Fibrous connective tissue accumulates around the lipid core, forming a "**fibrous cap**"

Foam cells also release many inflammatory mediators, which ↑ proliferation of media smooth muscle cells

Cells detach, enter the lipid core, and further enlarge it

Development of an "**atheroma**" (lipid-filled plaque that can enlarge and eventually impinge on vessel lumen) in the artery wall **(atherosclerosis)**

The atheroma can calcify and further enlarge, and can either remain stable (not rupture) or rupture

Complications of Atherosclerosis
(see relevant slide)

Legend: Pathophysiology | Mechanism | Sign/Symptom/Lab Finding | Complications

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Atherosclerosis: *Complications*

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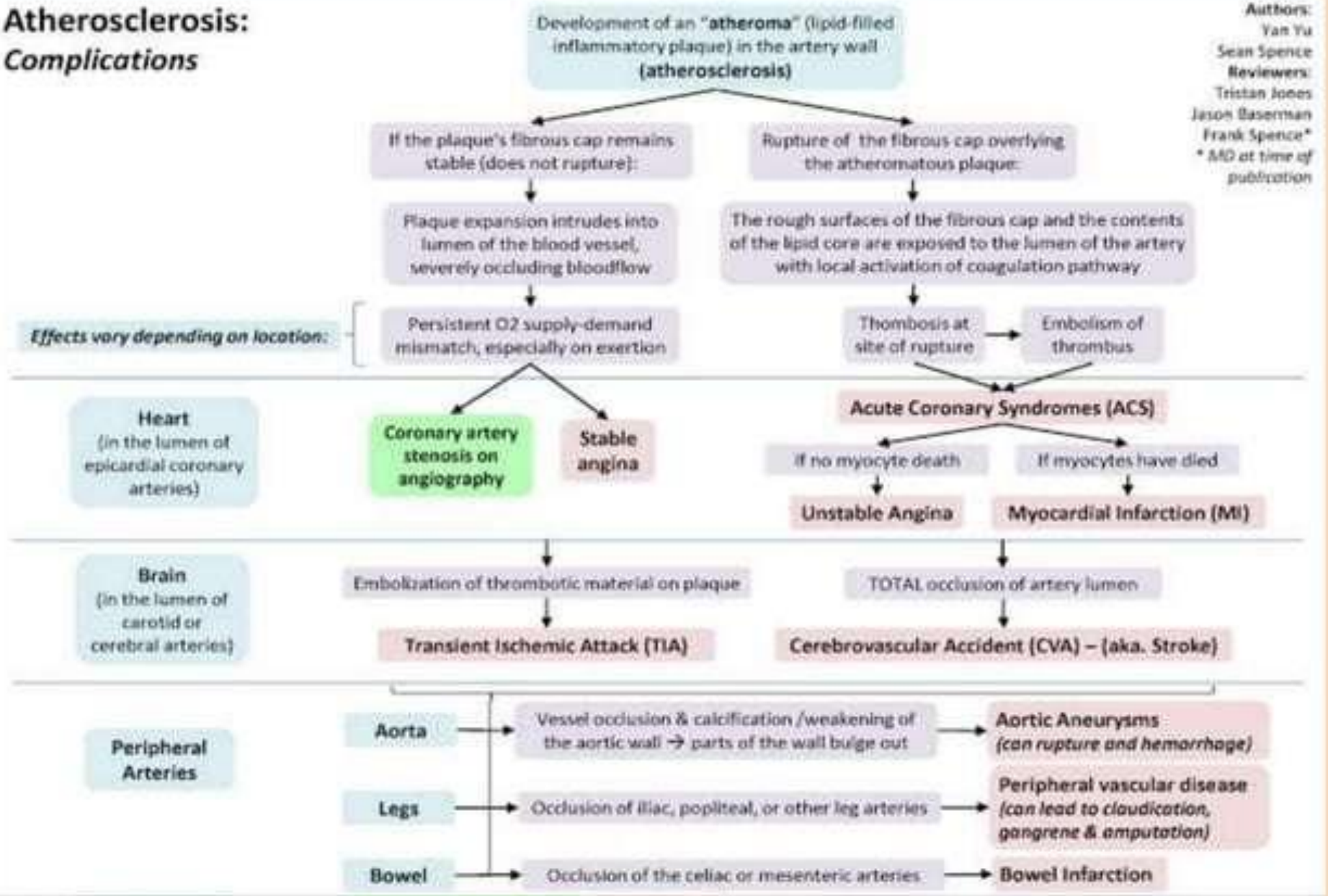

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Risk factor of Atherosclerosis

- Effect of risk factors is **multiplicative** rather than **additive**.
- It is important to distinguish between **relative risk** and **absolute risk**.
- **Absolute Risk**
  - Age
  - Male sex
  - Positive family history

Risk factor of Atherosclerosis

- **Relative Risk**
  - Smoking
  - Hypertension
  - Diabetes mellitus
  - Haemostatic factors.
  - Physical activity
  - Obesity
  - Alcohol
  - Other dietary factors
  - Personality
  - Social deprivation

Risk factor: Absolute Risk

- **Age & Sex**
  - **Premenopausal** women have **lower** rates of disease than **men**
  - Although this sex difference disappears after the **menopause**
- **Positive family history**
  - Runs in families,
  - Due to a combination of shared genetic, environmental and lifestyle factors.

Risk factor: Relative Risk

- **Smoking**
  - strong consistent
  - Dose linked relationship between cigarette smoking and IHD, especially in younger (< 70 years) individuals
- **Hypertension:** directly proportional
- **Hypercholesterolaemia:** directly proportional to **serum cholesterol concentrations (LDL)**
- **Diabetes mellitus:** potent risk factor for all forms of atherosclerosis
  - **Men with type 2 diabetes**: two- to four-fold greater annual risk of CAD,
  - **Women with type 2 diabetes:** (3–5-fold) risk

Risk factor: Relative Risk

- **Haemostatic factors**
  - **Platelet activation** and high levels of fibrinogen
  - **Antiphospholipid antibodies** - recurrent arterial thromboses
- **Physical activity**
  - Physical **inactivity** roughly **doubles** the risk of coronary heart disease
  - Regular exercise
    - Increased serum HDL cholesterol concentrations,
    - Lower BP,
    - Collateral vessel development
- **Obesity:** often associated with HTN and cardiovascular disease

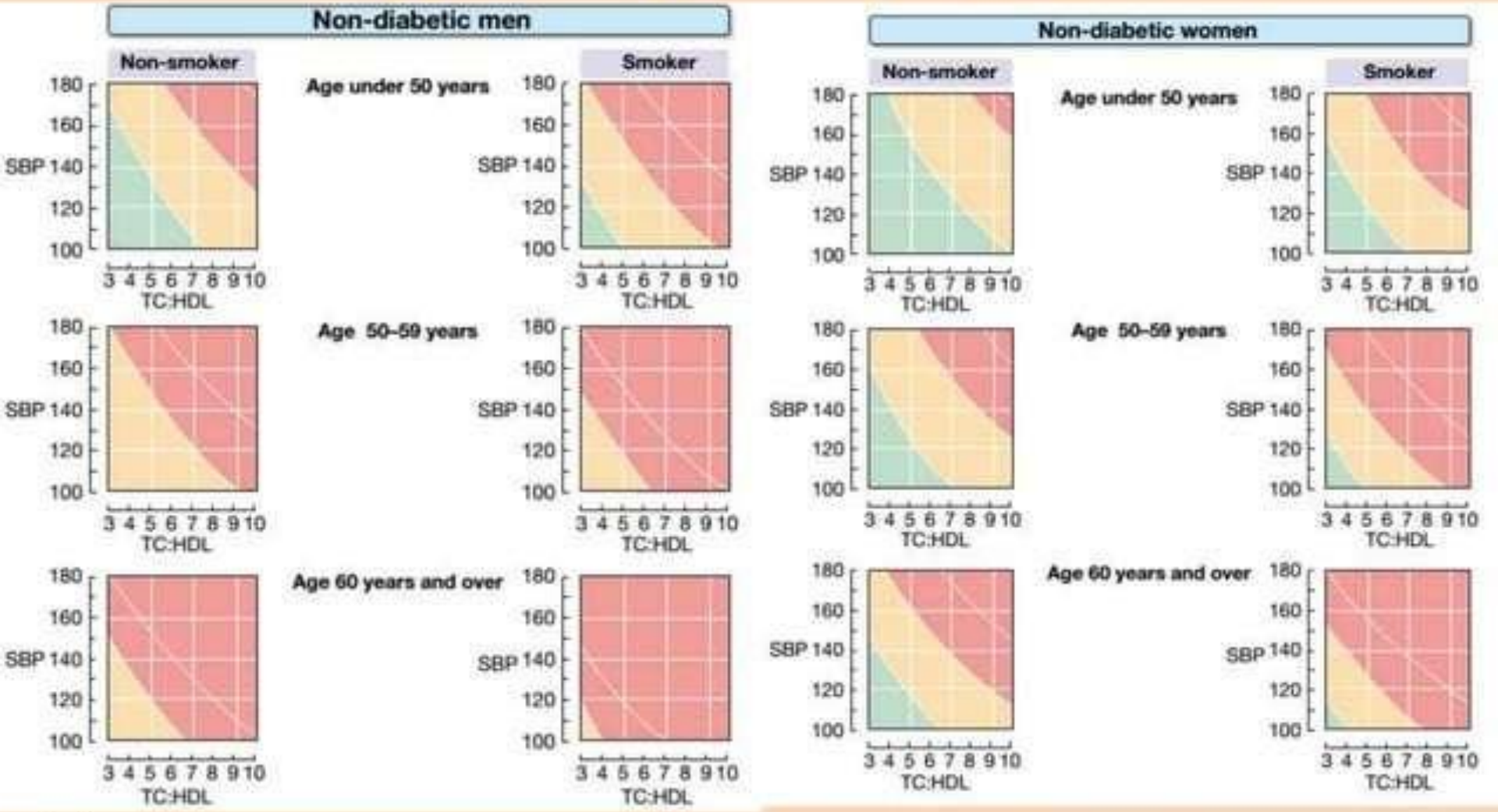
Risk factor: Relative Risk

- **Alcohol:** excess consumption
- **Other dietary factors**
  - Diets deficient in fresh **fruit, vegetables** and **polyunsaturated fatty acids (PUFA)**
- **Personality:** little or no evidence to support the popular belief that stress is a major cause of CAD
- **Social deprivation**

Primary Prevention

- Strategies taken before onset of disease in high risk individual.
- Two complementary strategies
- **Population strategies**
  - modify the risk factors of the whole **population**
  - through diet and lifestyle advice
  - For ex: Public restricting of smoking
- **Targeted strategies**
  - identify and treat high risk **individuals** who usually have a **combination of risk factors**
  - can be identified by using **composite scoring system**

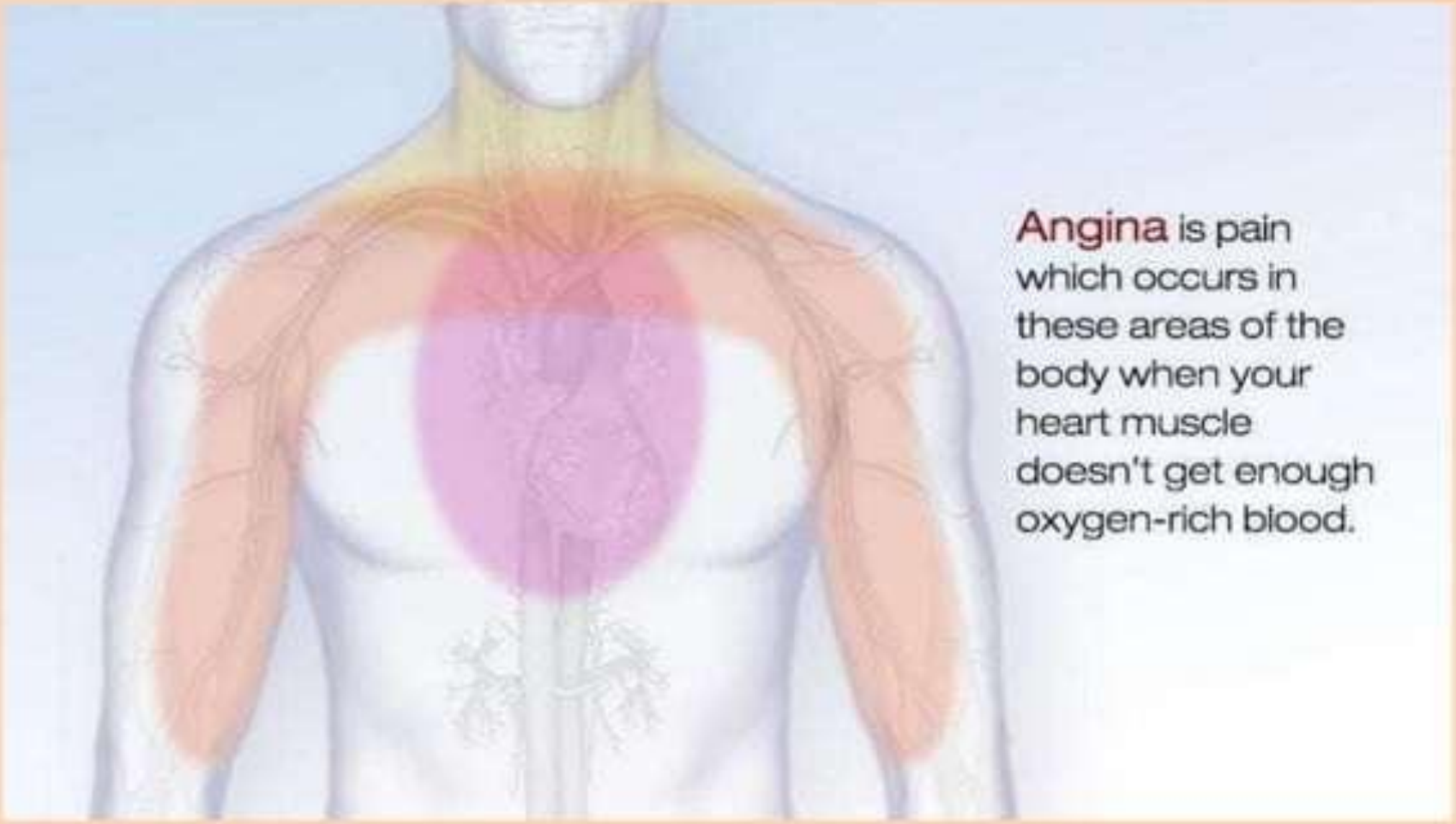
Composite Scoring System



Secondary Prevention

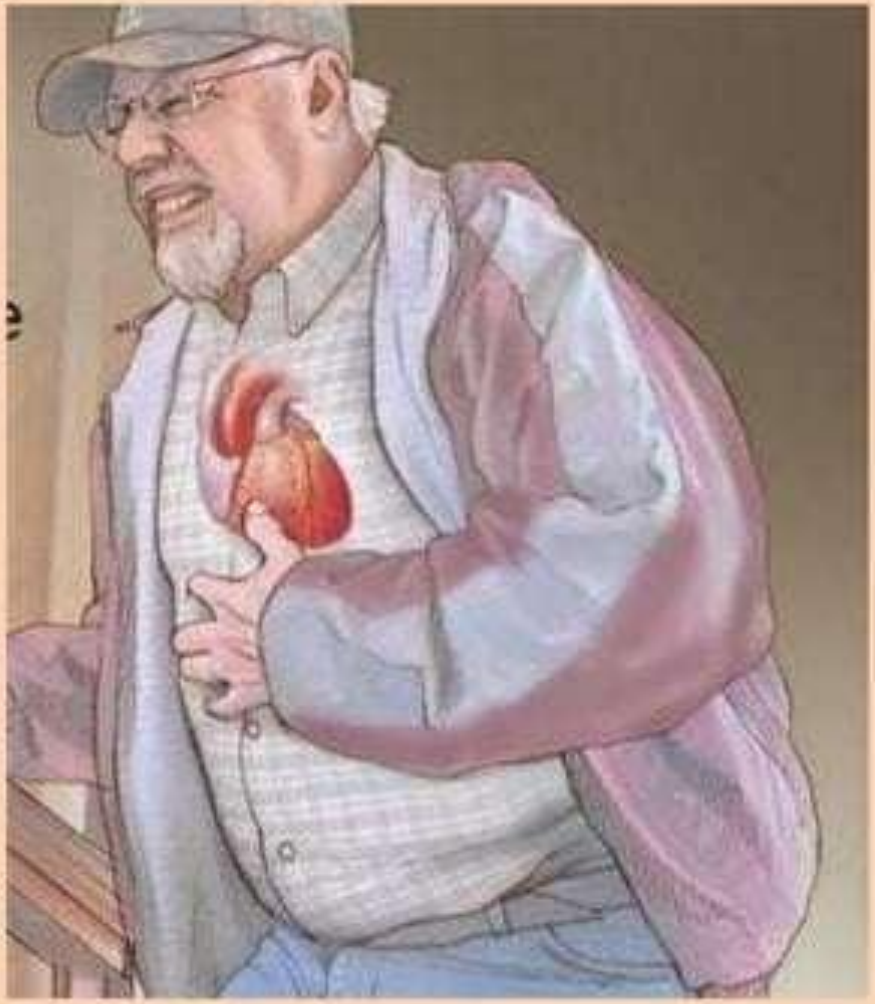
- Already have evidence of **atheromatous vascular disease** are at **high risk** of future cardiovascular events.
- Various secondary measures in this case
  - energetic correction of modifiable risk factors,
    - Smoking
    - Hypertension
    - Hypercholesterolaemia,
  - **Statin therapy** irrespective of their serum cholesterol concentration
  - Target BP of ≤ 140/85 mmHg
  - **Aspirin** and **ACE inhibitors**
  - **Beta-blockers**: h/o MI or heart failure.

Angina


Angina is pain which occurs in these areas of the body when your heart muscle doesn't get enough oxygen-rich blood.

Introduction

- A type of chest pain
- Not a disease, its a symptom of an underlying heart problem specially IHD
- Described as ‘heavy’, ‘tight’ or ‘gripping’.
- Typically, central/retrosternal
- Mild ache to most severe that provokes sweating and fear
- Associated breathlessness.



Canadian cardiovascular society functional classification of angina

CLASS	Characteristic
Class I	No angina with ordinary activity. Angina with **strenuous activity**
Class II	Angina during ordinary activity, e.g. walking up hills, walking rapidly upstairs, with **mild limitation** of activities
Class III	Angina with low levels of activity, e.g. walking 50–100 yards on the flat, walking up one flight of stairs, with **marked restriction** of activities
Class IV	Angina at **rest** or with any level of exercise

Classical or Exertional Angina Pectoris

- Characterized by
  - **constricting discomfort** in the front of the chest, arms, neck, jaw;
  - **provoked** by physical exertion, especially after meals and in cold, windy weather or by anger or excitement and
  - **relieved** (usually within minutes) with rest or glyceryl trinitrate. Occasionally, it disappears with continued exertion ('walking through the pain').
- **Typical angina**: all three features,
- **Atypical angina**: two out of the three,
- **Non-anginal chest pain:** one or less of these features

Types of Angina

- **Stable Angina**: episodic clinical syndrome where there is no change in severity of attacks.
- **Unstable angina: D**eterioration(24 hrs) in previous stable angina with symptoms frequently occurring at rest, i.e. **acute coronary syndrome**
- **Refractory angina:** patients with **severe coronary disease** in whom revascularization is not possible and angina is not controlled by medical therapy.
- **Variant (Prinzmetal's) angina:** occurs without provocation, usually at rest, as a result of coronary artery spasm, more frequently in women

Stable Angina

- Characterised by central chest pain, discomfort or breathlessness that is precipitated by exertion or other forms of stress and is promptly relieved by rest
- **Activities precipitating angina**
  - **Common**
    - Physical exertion
    - Cold exposure
    - Heavy meals
    - Intense emotion
  - **Uncommon**
    - Lying flat (decubitus angina)
    - Vivid dreams (nocturnal angina)

Clinical Features

- History is by far the most important factor in making the diagnosis
- Physical examination is frequently unremarkable
- But careful search for evidence of
  - valve disease (particularly aortic),
  - left ventricular dysfunction (cardiomegaly, gallop rhythm)
  - arterial disease (carotid bruits, peripheral vascular disease)
  - unrelated conditions that may exacerbate angina (anaemia, thyrotoxicosis).
- Important assessment of risk factors e.g. hypertension, diabetes mellitus

Angina Pectoris/Stable Angina: *Pathogenesis and clinical findings*

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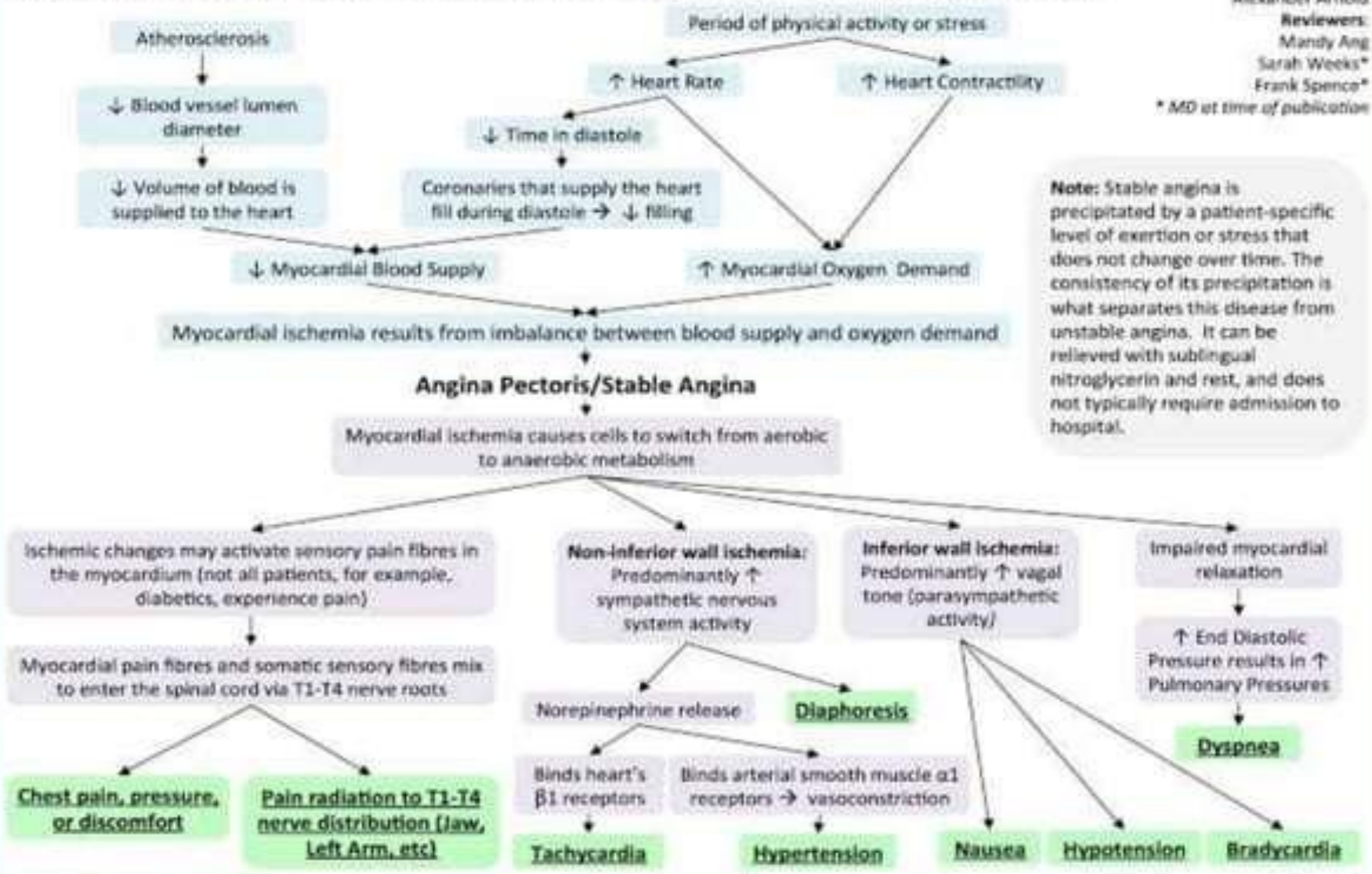

Note: Stable angina is precipitated by a patient-specific level of exertion or stress that does not change over time. The consistency of its precipitation is what separates this disease from unstable angina. It can be relieved with sublingual nitroglycerin and rest, and does not typically require admission to hospital.

Legend: Pathophysiology | Mechanism | Sign/Symptom/Lab Finding | Complications

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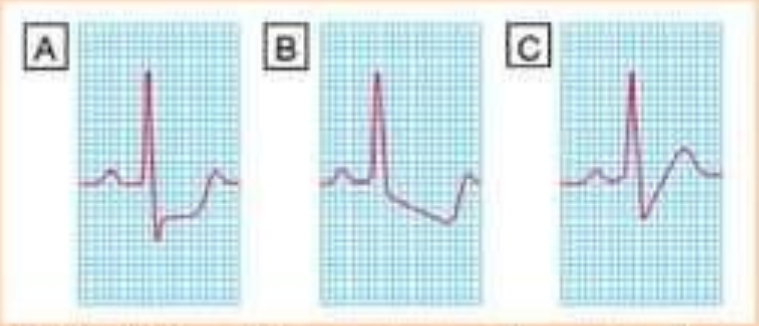
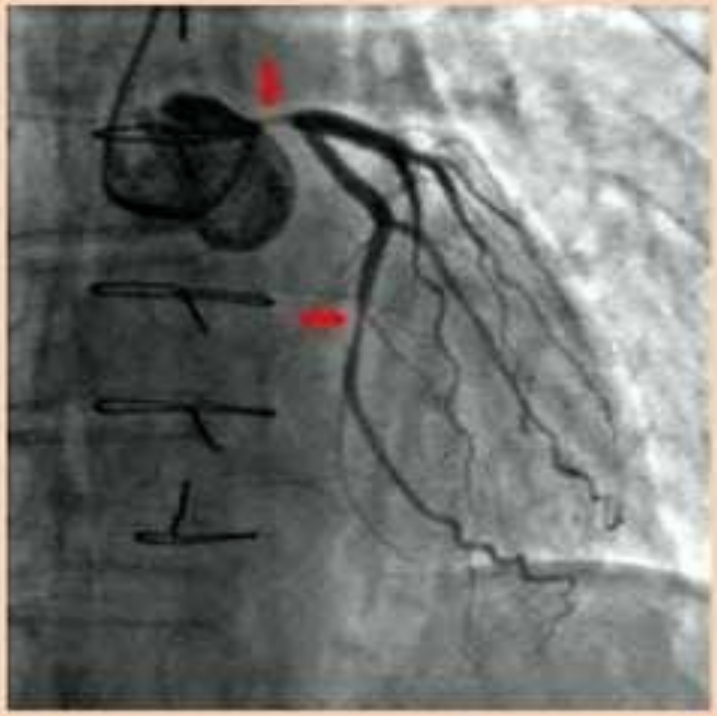
Investigation



- **Resting ECG**
  - may show evidence of previous MI but is often normal, even in patients with severe CAD.
  - Occasionally, there is T-wave flattening or inversion in some leads, providing **non-specific evidence** of **myocardial ischaemia** or damage.
  - The most convincing evidence of myocardial ischaemia - reversible ST segment depression or elevation, with or without T-wave inversion, at the time the patient is experiencing symptoms
- **Exercise ECG**
  - Exercise tolerance test (ETT) - standard treadmill or bicycle while monitoring the patient's ECG, BP and general condition.
  - Planar or down-sloping ST segment depression of ≥ 1mm is indicative of ischaemia (**A, B**)
  - Up-sloping ST depression is less specific and often occurs in normal individuals (**C**)

Investigation

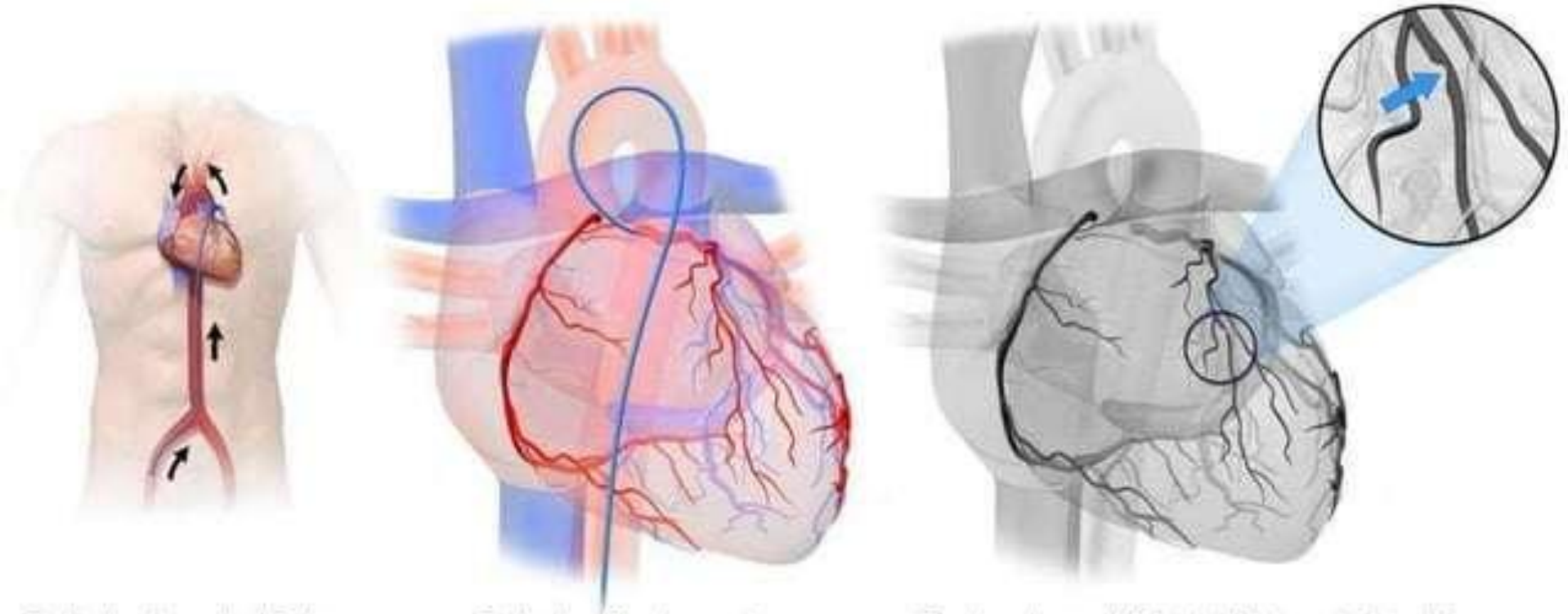
Investigation



- **Other forms of stress testing**
  - *Myocardial perfusion scanning*
  - *Stress echocardiography*
- **Coronary arteriography**
  - detailed anatomical information about the extent and nature of coronary artery disease
  - indicated when non-invasive tests have failed to establish the cause of atypical chest pain
  - under local anaesthesia
  - requires specialised radiological equipment, cardiac monitoring and an experienced operating team

Investigation

Coronary Angiography



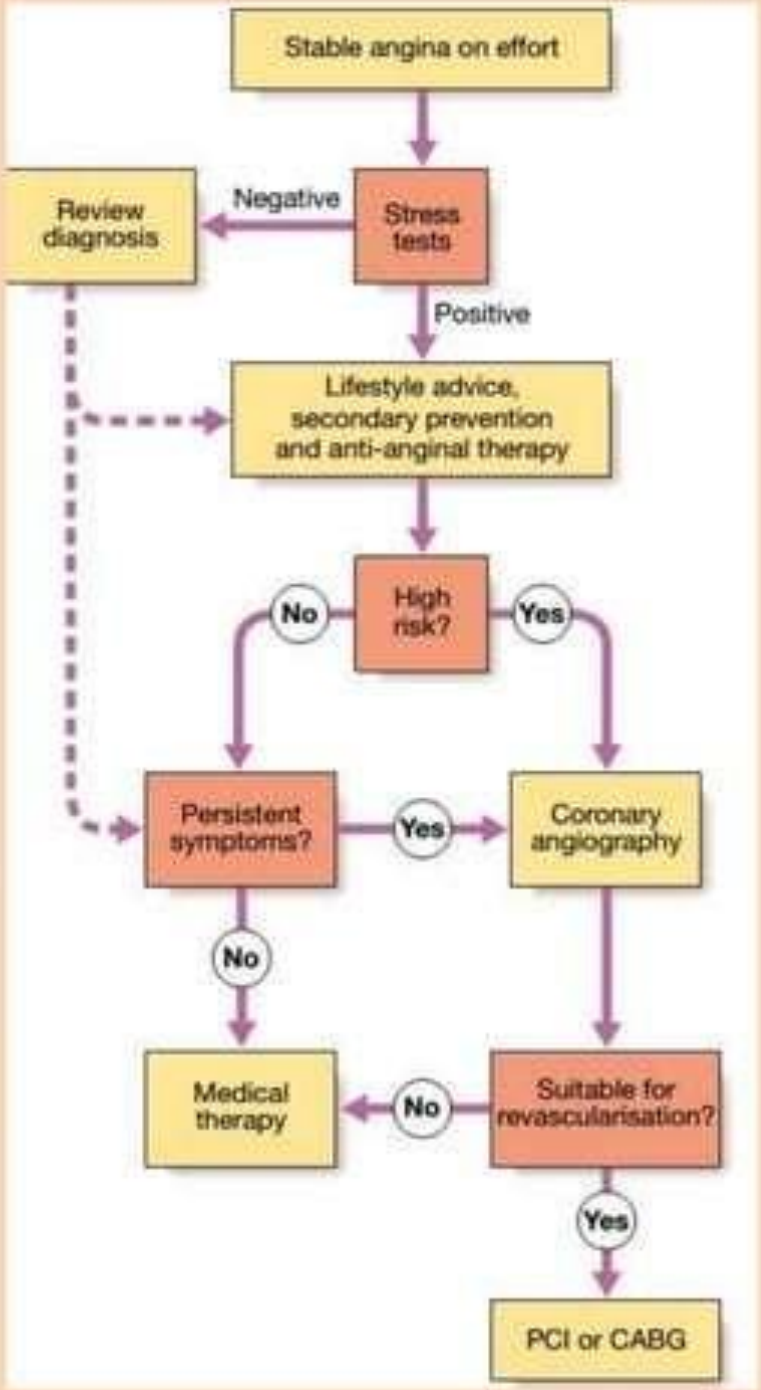
Catheter inserted in leg and guided up the aorta

Catheter tip stops at left coronary artery

Contrast agent injected into arteries. X-ray imaging shows stenosis in left coronary artery

Management

- Management of angina pectoris involves
  - careful **assessment** of the likely **extent** and **severity** of arterial disease
  - identification and control of **risk factors** such as smoking, hypertension and hyperlipidaemia
  - use of measures to **control symptoms**
  - Identification of **high-risk patients** for treatment to improve life expectancy.



Management: Medical

- **Antiplatelet therapy**
  - Low-dose (75 mg) aspirin
    - reduces the risk of adverse events such as MI
    - prescribed for all patients with CAD indefinitely
  - Clopidogrel (75 mg daily)
    - equally effective ALTERNATIVE
    - if aspirin causes dyspepsia or other side-effects
- **Anti-anginal drug treatment**: Five groups of drug
  - Nitrates
  - β-blockers
  - calcium antagonists
  - potassium channel activators
  - I_f channel antagonist

Management: Medical

Preparation	Peak action	Duration of action
Sublingual GTN	4–8 mins	10–30 mins
Buccal GTN	4–10 mins	30–300 mins
Transdermal GTN	1–3 hrs	Up to 24 hrs
Oral isosorbide dinitrate	45–120 mins	2–6 hrs
Oral isosorbide mononitrate	45–120 mins	6–10 hrs

- Nitrates
  - act directly on **vascular smooth muscle** to produce **venous** and **arteriolar dilatation**
  - reduction in myocardial oxygen demand
  - Increase in myocardial oxygen supply
  - prophylactically before taking exercise that is liable to provoke symptoms.
  - Continuous nitrate therapy can cause pharmacological tolerance
    - avoided by a 6–8-hour nitrate-free period
    - **Nocturnal angina:** longacting nitrates can be given at the end of the day

Management: Medical

- **β-blockers**: lower myocardial oxygen demand by reducing heart rate, BP and myocardial contractility
  - provoke bronchospasm in patients with asthma.
- **Calcium antagonists**
  - inhibit the slow inward current
  - caused by the entry of extracellular calcium through the cell membrane of excitable cells,
  - particularly cardiac and arteriolar smooth muscle
  - lower myocardial oxygen demand by reducing BP and myocardial contractility

Drug	Dose	Feature
Nifedipine	5–20 mg 8-hourly*	May cause marked tachycardia
Nicardipine	20–40 mg 8-hourly	May cause less myocardial depression than the other calcium antagonists
Amlodipine	2.5–10 mg daily	Ultra long-acting
Verapamil	40–80 mg 8-hourly*	Commonly causes constipation; useful anti-arrhythmic properties (p. 572)
Diltiazem	60–120 mg 8-hourly*	Similar anti-arrhythmic properties to verapamil

Management: Medical

- **Potassium channel activators**
  - arterial and venous dilating properties
  - but do not exhibit the tolerance seen with nitrates.
  - **Nicorandil (10–30mg 12-hourly orally)** - only drug in this class currently available for clinical use
- **I_f channel antagonist**
  - **Ivabradine** is the first of this class of drug
  - Induces **bradycardia** by modulating ion channels in the **sinus node**
  - Comparatively, does not have other cardiovascular effects
  - Safe to use in patients with heart failure

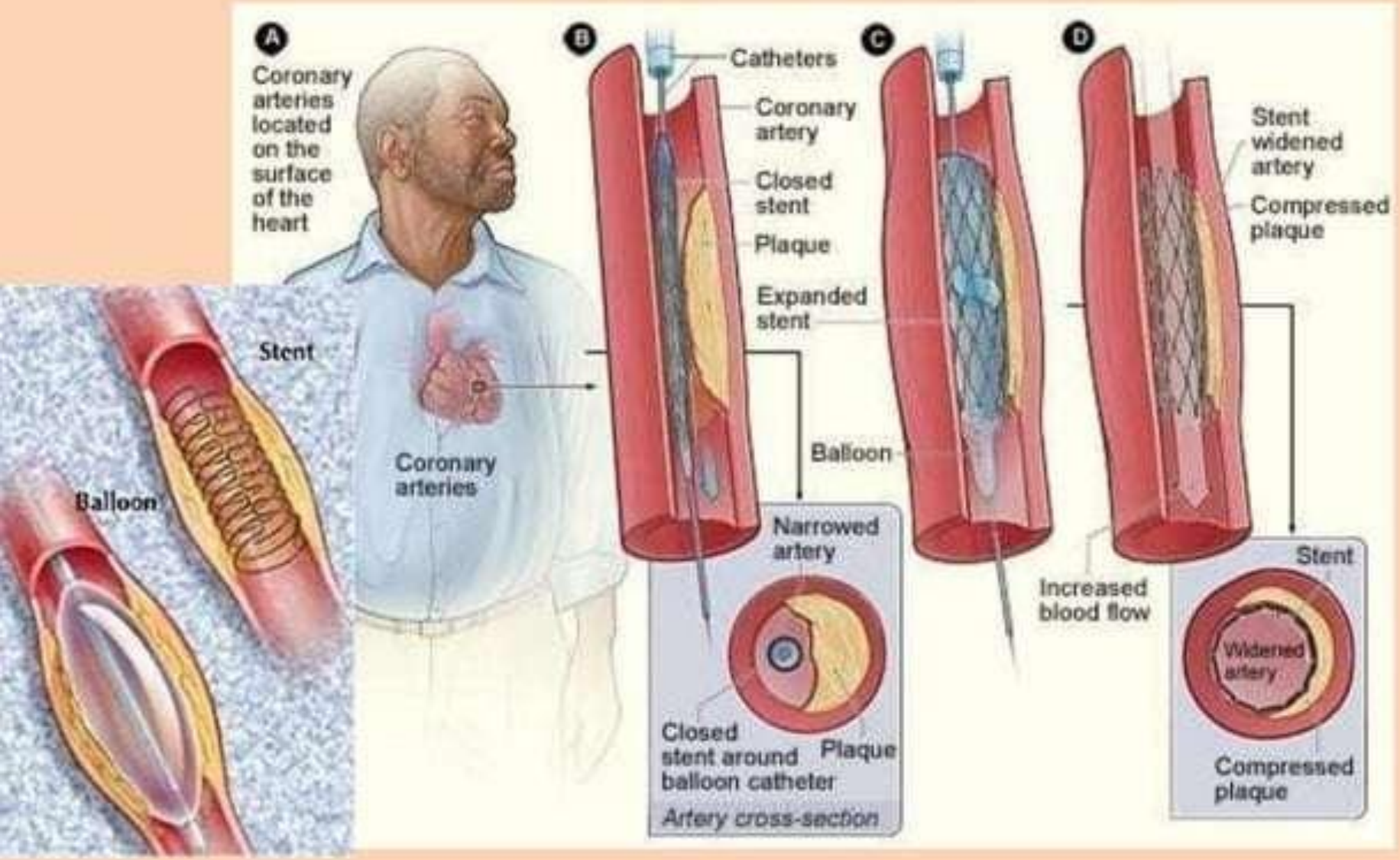
Management: Medical

- It is conventional to start therapy with
  - low-dose aspirin,
  - a statin,
  - sublingual GTN
  - β-blocker,
- And then add a **calcium channel antagonist** or a **long-acting nitrate** later if needed
- goal is the control of angina with minimum side-effects and the simplest possible drug regimen
- little evidence that prescribing multiple anti-anginal drugs is of benefit,
- **Revascularisation** - if an appropriate combination of two or more drugs fails to achieve an acceptable symptomatic response

Percutaneous Coronary Intervention (PCI)

- Passing a fine **guide-wire** across a **coronary stenosis** under radiographic control
- **Ballon** is placed and then inflated to dilate the stenosis
- Then a **coronary stent** is deployed on a balloon
  - maximise and maintain dilatation of a stenosed vessel
  - reduces both acute complications and the incidence of clinically important restenosis
- Mainly used in single or two-vessel disease

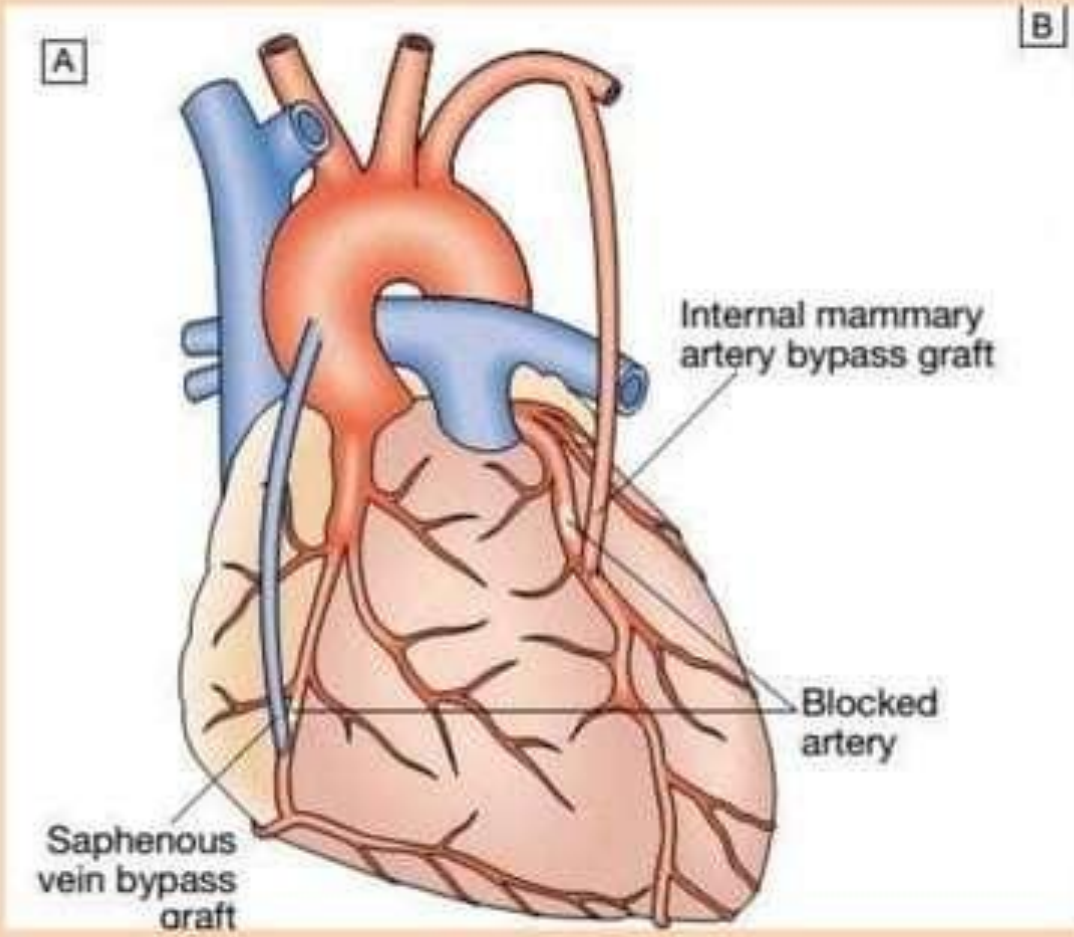
Percutaneous Coronary Intervention (PCI)

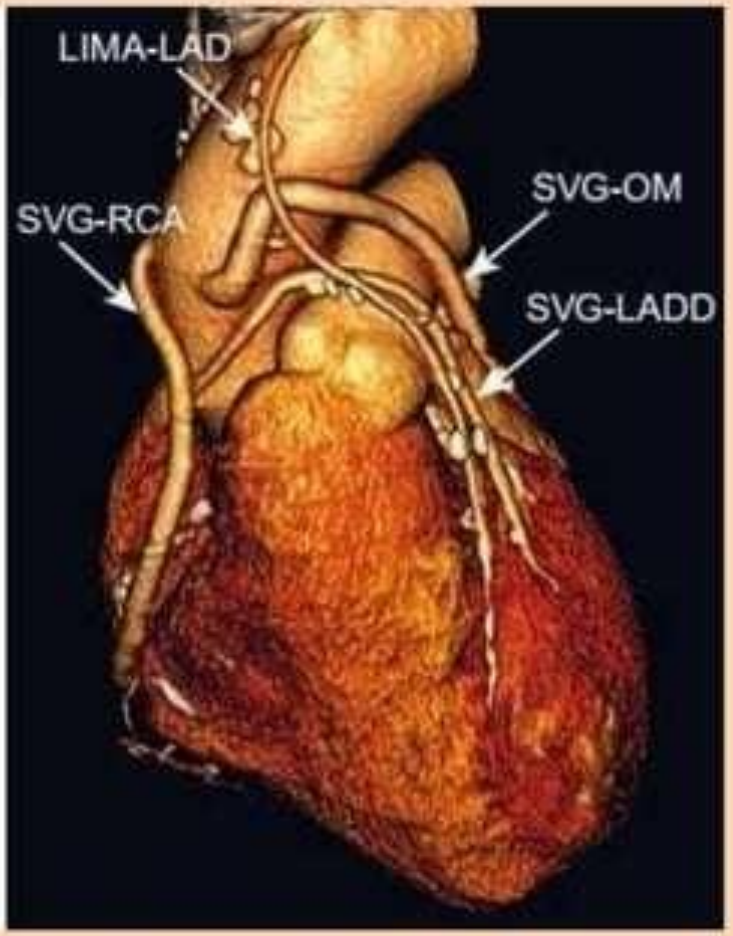


Coronary artery bypass grafting (CABG)

- Stenosed artery is by-passed with
  - **internal mammary arteries**
  - **radial arteries**
  - reversed segments of the patient's own **saphenous vein**
- Major surgery under **cardiopulmonary bypass**,
- But in some cases, grafts can be applied to the beating heart: **'off-pump' surgery**
- Operative mortality is approximately 1.5% but risks are higher
  - elderly patients,
  - with poor left ventricular function
  - those with significant comorbidity, such as renal failure
- 90% of patients are free of angina 1 year after CABG surgery, but fewer than 60% of patients are asymptomatic after 5 or more years.

Coronary artery bypass grafting (CABG)





Acute Coronary Syndrome

- It consist of
  - **Myocardial Infarction: ST-elevation myocardial infarction (STEMI) or Non-ST-elevation myocardial infarction (NSTEMI)**
    - symptoms occur at rest
    - evidence of myocardial necrosis - increased **cardiac troponin** or **Creatine kinase-MB** isoenzyme
  - **Unstable angina (UA).**
    - new-onset or rapidly worsening angina (crescendo angina),
    - angina on minimal exertion
    - or angina at rest in the absence of myocardial damage

Acute Coronary Syndrome

- Present as a new phenomenon or against a background of chronic stable angina.
- Complex **ulcerated or fissured atheromatous plaque** with adherent platelet rich thrombus and local coronary artery spasm.
- **Dynamic process**: degree of obstruction may either increase or regress
- Without treatment, the infarct-related artery remains permanently occluded in 20–30% of patients

Unstable Angina/Unstable Angina Pectoris: *Pathogenesis and clinical findings*

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Secondary causes

- Coronary artery vasospasm-primary or drug induced (Ex: cocaine, triptans)
- Coronary Embolism (Ex: endocarditis, artificial heart valve)
- Increased Blood viscosity (Ex: polycythemia, thrombocytopenia)
- Coagulopathy (Ex: Protein C deficiency)
- Spontaneous coronary artery dissection
- Vasculitic syndromes (Ex: Takayasu arteritis)
- Congenital Anomalies (Ex: myocardial bridge)
- ↑ Myocardial O_2 demand (tachycardia, shock, anemia, exertion, stress)

Atherosclerosis (Primary, most common cause)

Coronary arterial atherosclerotic plaque rupture or erosion

Platelet aggregation and thrombus formation

Partial occlusion of the involved artery

↑ Myocardial O_2 demand

↓ Myocardial blood supply

Myocardial ischemia results from imbalance between blood supply and oxygen demand

Unstable Angina/Unstable Angina Pectoris

Myocardial ischemia causes cells to switch from aerobic to anaerobic metabolism

Note: Unstable angina vs. stable angina, NSTEMIs, and STEMIs: Unstable angina, NSTEMIs and STEMIs are typically progressive in frequency, severity, or duration. They can be new and can occur at rest. Stable angina differs in that the disease does not occur at rest or change over time. Troponins will be increased in NSTEMIs and STEMIs but typically not in unstable angina.

Impaired myocardial relaxation

↑ End diastolic pressure → ↑ pulmonary pressures

Dyspnea

Cardiac sensory fibres mix with somatic sensory fibres and enter the spinal cord via the T1-T4 nerve roots

Retrosternal discomfort: may present as pain, heaviness, pressure, or squeezing

Pain radiation to T1-T4 dermatomes (Left shoulder and arm, lower jaw, neck, abdomen, upper back)

No cardiac myocyte necrosis

Normal serum troponin

Non-transmural or subendocardial ischemia

ECG: ST depression or T wave inversion

Non-inferior wall ischemia: Predominantly ↑ sympathetic nervous system activity

Diaphoresis

Epinephrine / Norepinephrine release

Binds cardiac β1 receptors

Tachycardia

Binds arterial smooth muscle α1 receptors → vasoconstriction

Hypertension

Inferior wall ischemia: Predominantly ↑ parasympathetic nervous system activity (Vagal)

Hypotension

Nausea

Syncope

Bradycardia

Legend: Pathophysiology | Mechanism | Sign/Symptom/Lab Finding | Complications

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Universal definition of Myocardial Infarction (MI)

- Evidence of **myocardial necrosis** in a clinical setting consistent with **myocardial ischaemia**, in which case any one of the following meets the diagnosis for MI:
  - Detection of rise and/or fall of cardiac biomarkers (preferably troponin),
  - ECG changes indicative of new ischaemia (new ST-T changes or new left bundle branch block)
  - Development of pathological Q waves
  - Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality

Clinical features : Symptoms

- Pain is the cardinal symptom
- Prolonged cardiac pain: chest, throat, arms, epigastrium or back
- Anxiety and fear of impending death
- Nausea and vomiting
- Breathlessness
- Collapse/syncope

Clinical features : Sign

- Sympathetic activation: pallor, sweating, tachycardia
- Vagal activation: vomiting, bradycardia
- Signs of impaired myocardial function
- Hypotension, oliguria, cold peripheries
- Narrow pulse pressure
- Raised JVP
- Third heart sound
- Quiet first heart sound
- Diffuse apical impulse
- Lung crepitations
- Tissue damage: fever
- Other complications: e.g. mitral regurgitation, pericarditis

Myocardial Infarction:
Findings on History

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Myocardial infarction (tissue necrosis)

Local myocardial inflammation

Inflammatory cytokines can spread systemically

Cytokines act on hypothalamic T^0 regulator

Mild fever

Inflammatory mediators irritates nerves innervating the heart (the cardiac plexus)

Irritation of T1-T4 sympathetic afferents

Signals enter spinal cord, mixes with T1-T4 dermatomes

Brain perceives nerve irritation as pain coming from T1-T4 dermatomes

Crushing, Diffuse "Pain" or "tightness": Often retrosternal, with radiation to shoulder, neck, and inner aspect of both arms (R > L). (Onset: often at rest; crescendo)

Irritation of cardiac branches of vagus nerve

Activation of reflexive vagal responses (listed below)

Weakness, dizziness, nausea, vomiting

Note: Myocardial ischemic pain may differ between patients, but recurrences usually feel the same in any given patient.

↓ Systolic function *(necrotic myocardium cannot contract as well)*

↓ stroke volume (SV), ↓ cardiac output (CO)

Reflexive ↑ in sympathetic activity (to try to maintain CO)

↑ Sweating (diaphoresis)

Clammy skin

Generalized vasoconstriction

Vasoconstriction of skin arterioles

Cool skin

Blood backs up from the LV, into the left atrium and eventually accumulates in the pulmonary vasculature

High pulmonary venous blood pressure forces fluid out of capillaries, into pulmonary interstitium & alveoli

Soggier lung interstitium ↓ lung compliance

Fluid compresses airways, ↑ resistance to airflow

Respiratory muscles work harder to ventilate lungs

Dyspnea *(Shortness of breath)*

Legend: Pathophysiology | Mechanism | Sign/Symptom/Lab Finding | Complications

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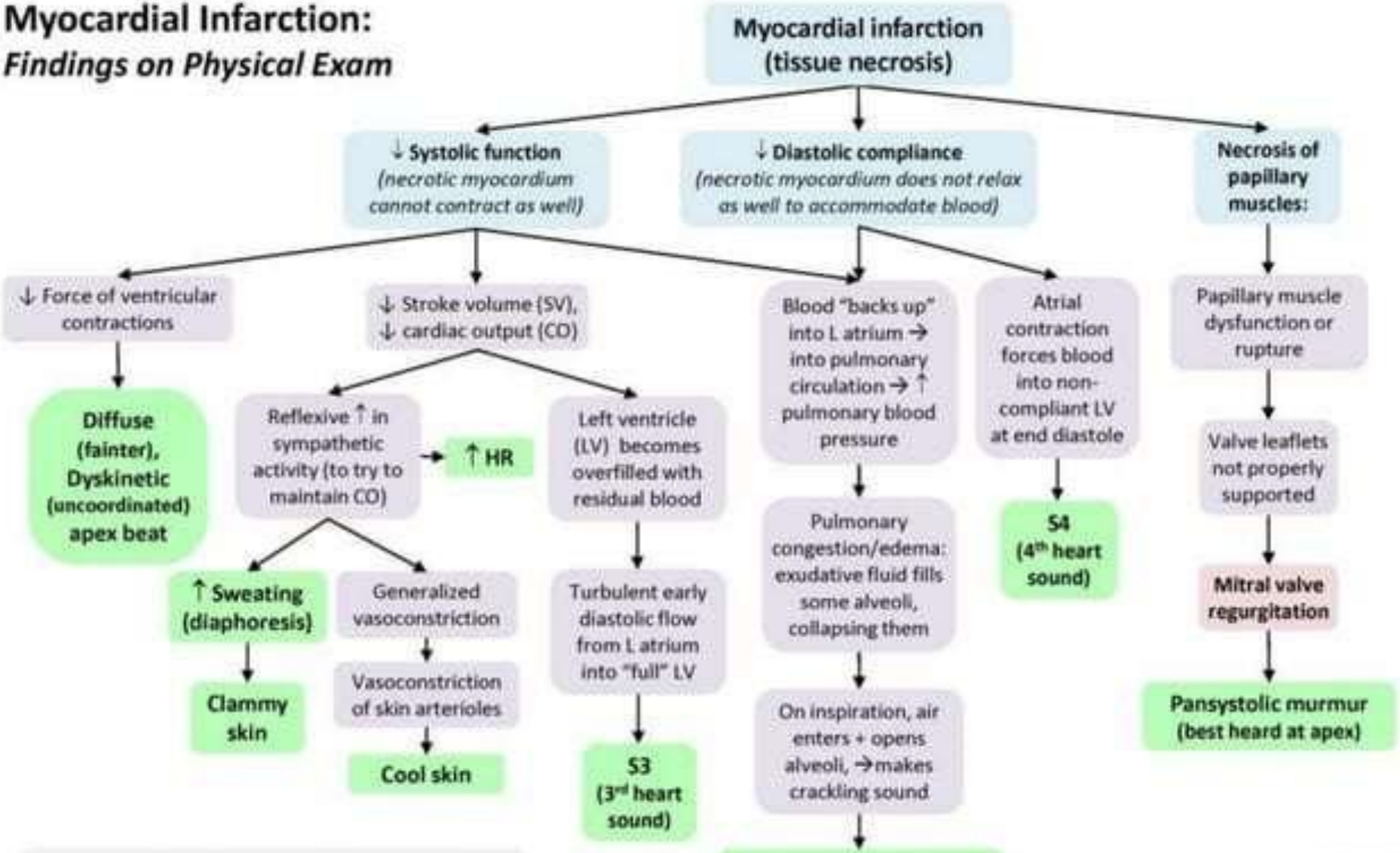
Myocardial Infarction:
Findings on Physical Exam



Note: BP is determined by cardiac output (CO) & systemic vascular resistance (SVR). MI may ↓CO & thus may ↓BP. But generalized vasoconstriction ↑es SVR in attempt to maintain BP. Hence, BP may be normal in MI, and **low BP is NOT a specific sign of MI**.

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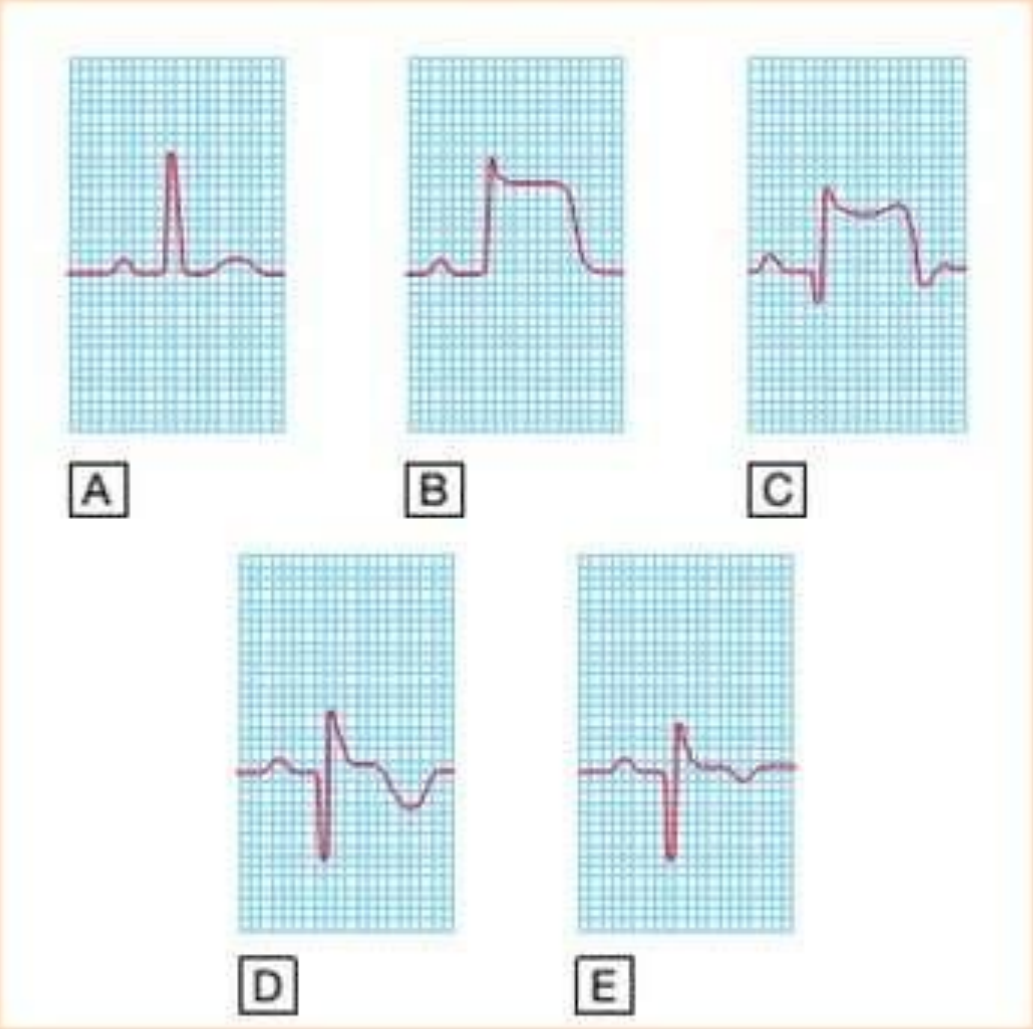
Types of MI

- There are three types of MIs:
- ***Type 1*** **–** spontaneous MI with ischaemia due to a **primary coronary event**, e.g. plaque erosion/rupture, fissuring or dissection
- ***Type 2*** **–** MI secondary to ischaemia due to **increased oxygen demand** or **decreased supply**, such as coronary spasm, coronary embolism, anaemia, arrhythmias, hypertension, or hypotension
- ***Type 3,4,5*** **–** diagnosis of MI in sudden **cardiac death**, after **percutaneous coronary intervention (PCI)** and after **coronary artery bypass graft (CABG),** respectively.

Investigations: Electrocardiography

- Confirmatory diagnosis
- But difficult to interpret if there is bundle branch block or previous MI.
- Repeated ECGs are important: initial ECG may be **normal** or **non-diagnostic** in one-third of cases
- ECG changes are best seen in the leads that 'face' the ischaemic or infarcted area
- **ST-segment deviation**
  - ST-segment elevation
  - T wave inversion - change in ventricular repolarisation
  - persists after the ST segment has returned to normal.
  - reliable for the approximate age of the infarct to be deduced.

Investigations: Electrocardiography

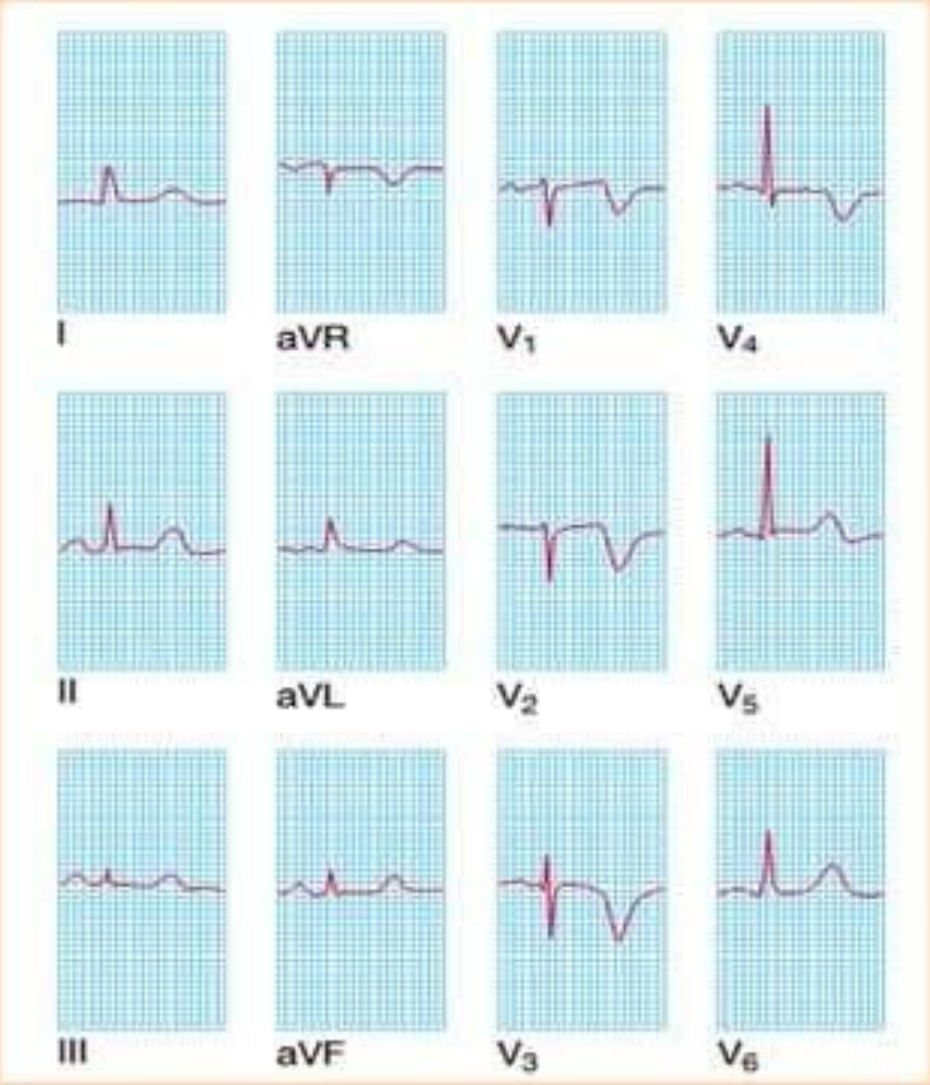


a Normal ECG complex. **B** Acute ST elevation ('the current of injury'). **C** Progressive loss of the R wave, developing Q wave, resolution of the
ST elevation and terminal T wave inversion. **d** Deep Q wave and T-wave
inversion. **E** Old or established infarct pattern

Investigations: Electrocardiography

- **Non-ST segment elevation ACS**
  - **Partial occlusion of a major vessel or complete occlusion of a minor vessel,**
  - **unstable angina or partial thickness (subendocardial) MI.**
    - ST-segment depression and T-wave changes.
  - **Presence of infarction**: loss of R waves in the absence of Q waves

Investigations: Electrocardiography



Recent anterior non-ST elevation (subendocardial) MI.
There is deep symmetrical T-wave inversion together with a reduction in the height of the R wave in leads V1, V2, V3 and V

Coronary anatomy on ECG: *Localizing Ischemia*

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Abbreviations:
CA – Coronary artery
IV – Interventricular
AV – Atrioventricular
MI – Myocardial infarction
SA – Sinoatrial
STEMI – ST-elevation myocardial infarction

Coronary arteries

Two arteries that originate from the root of the aorta behind the cusps (aortic sinus) of the aortic valve. The left posterior aortic sinus gives rise to the left CA, and the anterior aortic sinus gives rise to the right CA. These arteries supply the myocardium

Right vs. left dominant circulation is determined by the artery that gives rise to the posterior descending artery. In 70% of hearts, it is the RCA. 20% of hearts are co-dominant, and 10% are left-dominant.

- **Right coronary artery**
  - **Posterior Descending Artery**
    - Right ventricle, posterior left ventricle
      - Posterior MI: Leads V1-V4. **Since this is posterior, evidence of STEMI will be depression*
  - Right atrium, right ventricle and SA and AV nodes
    - Inferior MI: Leads II, III, aVF

      Can also cause bradycardia and heart blocks (SA and AV node problems)
- **Left coronary artery**
  - **Left Main Artery**
    - **Left Circumflex Artery**
      - Lateral left ventricle and left atrium
        - Anterolateral MI: Leads I, aVL, V3-V6
    - Virtually entire left ventricle including septum +/- some of the right ventricle
      - Difficult to determine. Can have changes in all leads.
    - **Left Anterior Descending Artery**
      - Septum, Anterior left ventricle, Apex of the left ventricle
        - Anteroseptal MI (septal branch occlusion): Leads V1 – V3

ECG changes vary based on the degree of occlusion:

- STEMI – ST segment elevation at least 2 mV (little squares) in precordial leads V1-V6 or 1 mV in the limb leads (all other leads). Indicates total occlusion of the artery supplying the affected area and transmural ischemia. Reciprocal changes in opposite leads present as ST depression
- Non-STEMI – can present as ST segment depression or T wave flattening or inversion. Indicates severe blockage but not complete occlusion of an artery or transmural ischemia

Legend: Main branch | Branch of RCA or LCA | Territory supplied | ECG Changes

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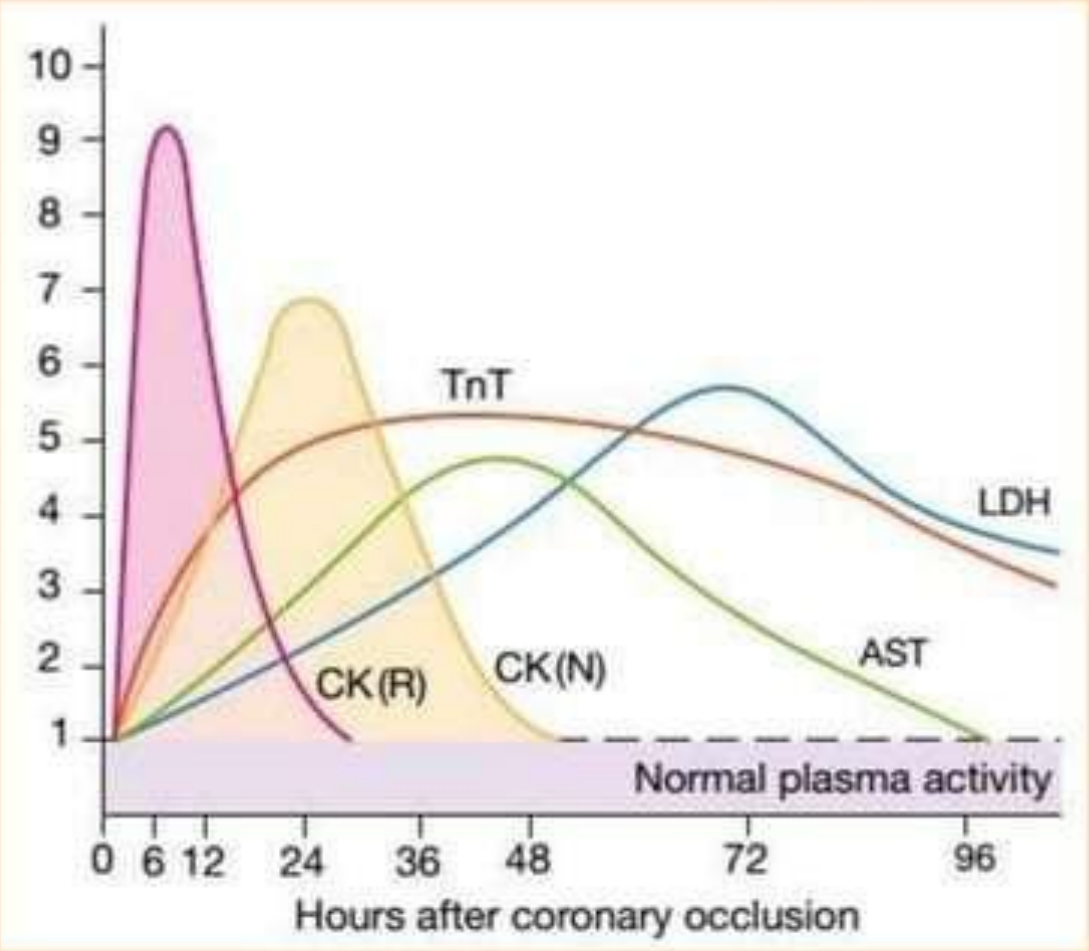
Investigations: Plasma Cardiac Markers

- **Unstable Angina:** no detectable rise in cardiac markers or enzymes
- **Myocardial Infarction:** creatine kinase **(CK)**, a more sensitive and cardiospecific isoform of this enzyme **(CK-MB),** and the **cardiospecific proteins, troponins T and I**
- Also present in skeletal muscle but not CK-MB
  - intramuscular injection,
  - vigorous physical exercise
  - particularly in older people,
  - a fall

Investigations: Plasma Cardiac Markers

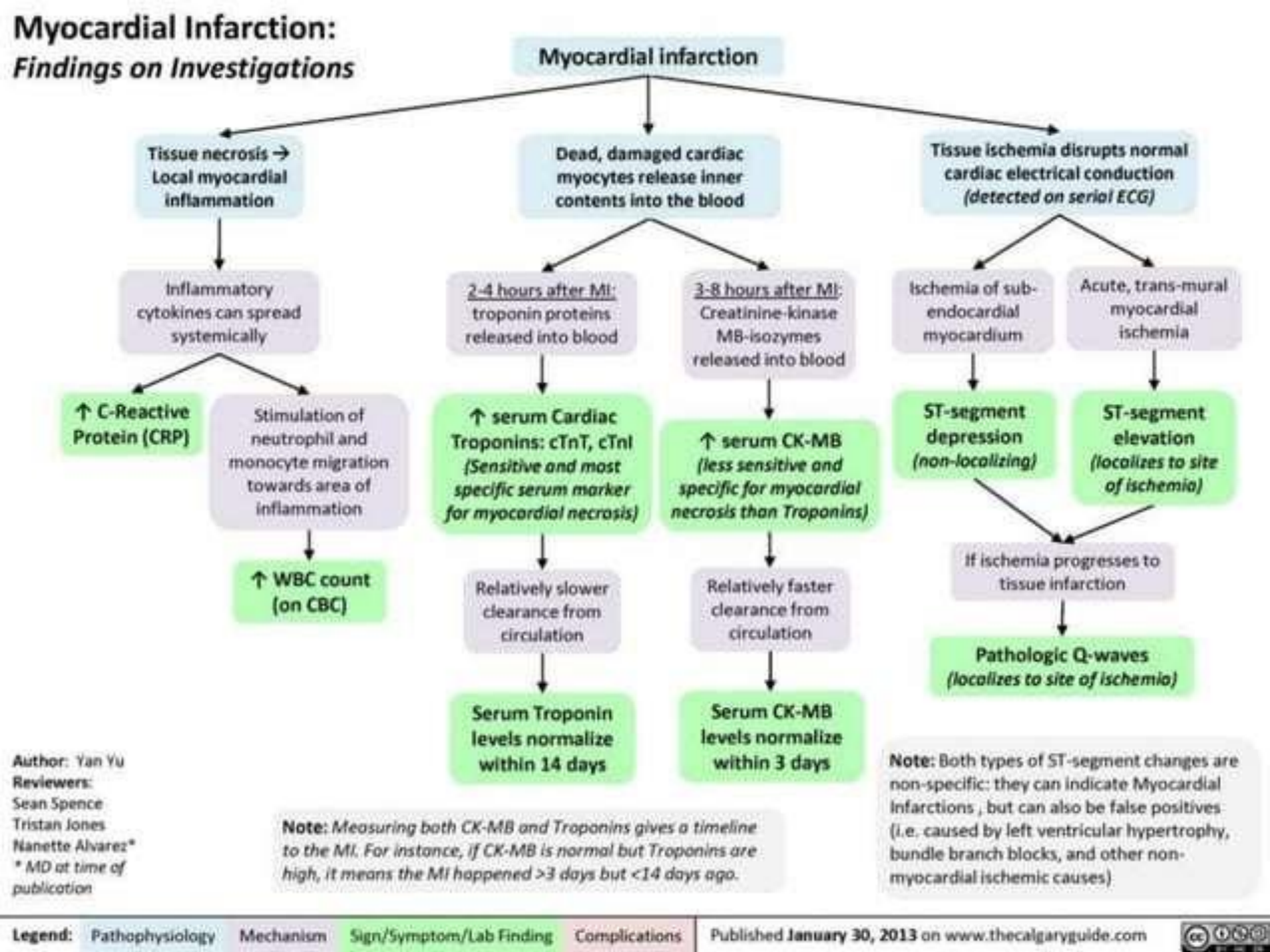


Creatine kinase (CK) and troponin T (TnT) are the first to rise, followed by aspartate aminotransferase (AST) and then lactate (hydroxybutyrate) dehydrogenase (LDH)

Investigations

- **Other blood tests:** erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are also elevated
- **Chest X-ray**
  - pulmonary oedema that is not evident on clinical examination
  - heart size is often normal
  - But there may be cardiomegaly due to pre-existing myocardial damage
- **Echocardiography**
  - assessing left and right ventricular function
  - detecting important complications such as
    - mural thrombus,
    - cardiac rupture,
    - ventricular septal defect,
    - mitral regurgitation and
    - Pericardial effusion.

Myocardial Infarction:
Findings on Investigations



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Note: *Measuring both CK-MB and Troponins gives a timeline to the MI. For instance, if CK-MB is normal but Troponins are high, it means the MI happened >3 days but <14 days ago.*

Note: Both types of ST-segment changes are non-specific: they can indicate Myocardial Infarctions , but can also be false positives (i.e. caused by left ventricular hypertrophy, bundle branch blocks, and other non-myocardial ischemic causes)

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Early Medical Management

- Admitted urgently to hospital because of significant risk of **death** or recurrent **myocardial ischaemia**
- Reduce the incidence by at least 60%
- **Oxygen** – nasal cannula 2–4 L/min if hypoxia is present
- Brief history/risk factors and immediate
  - Intravenous access + blood for markers
  - 12-lead ECG
- Aim of early management
  - **Analgesia**
  - **Antithrombotic therapy**
  - **Anti-anginal therapy**
  - **Reperfusion therapy**

Anti-anginal Therapy

- **Sublingual glyceryl trinitrate (300–500 μg)**: valuable first-aid measure
- **IV nitrates (GTN 0.6–1.2mg/hour or isosorbide dinitrate 1–2mg/hour):** left ventricular failure and the relief of recurrent or persistent ischaemic pain
- **IV β-blockers (Atenolol 5–10mg or Metoprolol 5–15 mg given over 5mins) :** relieve pain, reduce arrhythmias and improve short-term mortality. Contraindicated in
  - Heart failure (pulmonary oedema),
  - Hypotension (systolic BP < 105mmHg)
  - Bradycardia (heart rate < 65/min).
- **Dihydropyridine calcium channel antagonist:** nifedipine or amlodipine can be added to the β-blocker if there is persistent chest discomfort
  - but may cause an unwanted tachycardia if used alone.
  - Because of their rate-limiting action, verapamil and diltiazem are the calcium channel antagonists of choice if a β-blocker is contraindicated.

Analgesia

- Essential not only to relieve distress, but also to lower adrenergic drive
- **IV opiates:** initially morphine sulphate 5–10mg or diamorphine 2.5–5 mg)
- **IV Antiemetics:** initially metoclopramide 10mg
- Intramuscular injections should be avoided
  - Poor skeletal muscle perfusion
  - Painful haematoma

Antithrombotic Therapy

- ***Antiplatelet therapy***
  - **Aspirin:** oral dose of 300mg first tablet within the first 12 hour, followed by 75 mg.
  - **Aspirin + clopidogrel 600 mg**: early (within 12 hours), followed by 150 mg daily for 1 week and 75mg daily thereafter
  - **Ticagrelor** (180 mg followed by 90 mg 12-hourly): more effective than clopidogrel
  - Antiplatelet treatment with i.v. **glycoprotein IIb/IIIa inhibitors** reduces the combined endpoint of death or MI and used in context of PCI

Antithrombotic Therapy

- **Anticoagulants**
  - reduces the risk of **thromboembolic** complication
  - prevents **reinfarction** in the absence of **reperfusion** therapy or after successful thrombolysis
  - **Unfractionated heparin, fractioned** (low molecular weight) **heparin** or a **pentasaccharide**.
  - Continued for 8 days or until discharge from hospital or **coronary revascularisation**

Reperfusion therapy

- Depending on type of MI, outcome of reperfusion therapy varies
  - **NSTEMI:** No demonstrable benefit
  - **STEMI:** restores coronary artery patency and preserves left ventricular function and improves survival
- Medium- to high-risk patients do benefit but this does not need to take place in the first 12 hours.
- **Primary percutaneous coronary intervention (PCI)**

Reperfusion therapy

- **Thrombolysis**
  - reduce hospital mortality by 25–50%
  - this survival advantage is maintained for at least 10 years
  - **Alteplase** (human tissue plasminogen activator)
    - over 90 minutes (bolus dose of 15 mg)
    - Followed by 0.75 mg/kg body weight, but not exceeding 50mg, over 30 mins
    - then 0.5mg/kg body weight, but not exceeding 35mg, over 60mins
    - better survival rates than other thrombolytic agents, such as **streptokinase**,
  - **Analogues of tPA (tenecteplase and reteplase):** longer plasma half-life than alteplase and can be given as an intravenous bolus

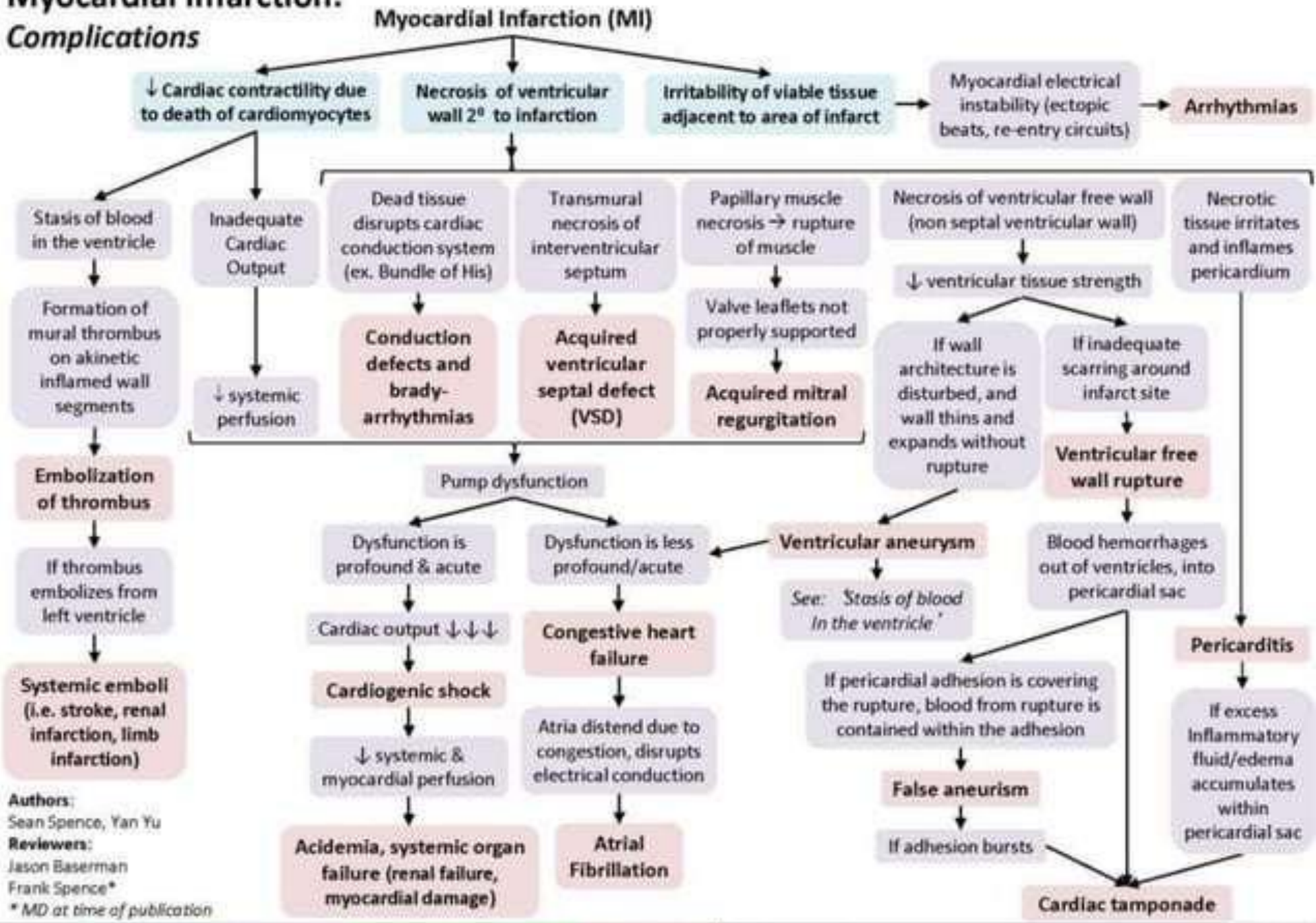
Late Management of MI

- **Risk stratification and further investigation lifestyle modification**
  - Cessation of smoking
  - Regular exercise
  - Diet (weight control, lipid-lowering)
- **Secondary prevention drug therapy**
  - Antiplatelet therapy (aspirin and/or clopidogrel)
  - β-blocker
  - ACE inhibitor
  - Statin
  - Additional therapy for control of diabetes and hypertension
  - Aldosterone receptor antagonis
- **Rehabilitation devices**: Implantable cardiac defibrillator (high-risk patients)

Complications of Acute Coronary Syndrome

- **Arrhythmias**
- **Ischaemia**
- **Acute circulatory failure**
- **Pericarditis**
- **Mechanical complications**
  - Rupture of the papillary muscle
  - Rupture of the interventricular septum
  - Rupture of the ventricle
- **Embolism**
- **Impaired ventricular function, remodelling and ventricular aneurysm**

Myocardial Infarction: *Complications*



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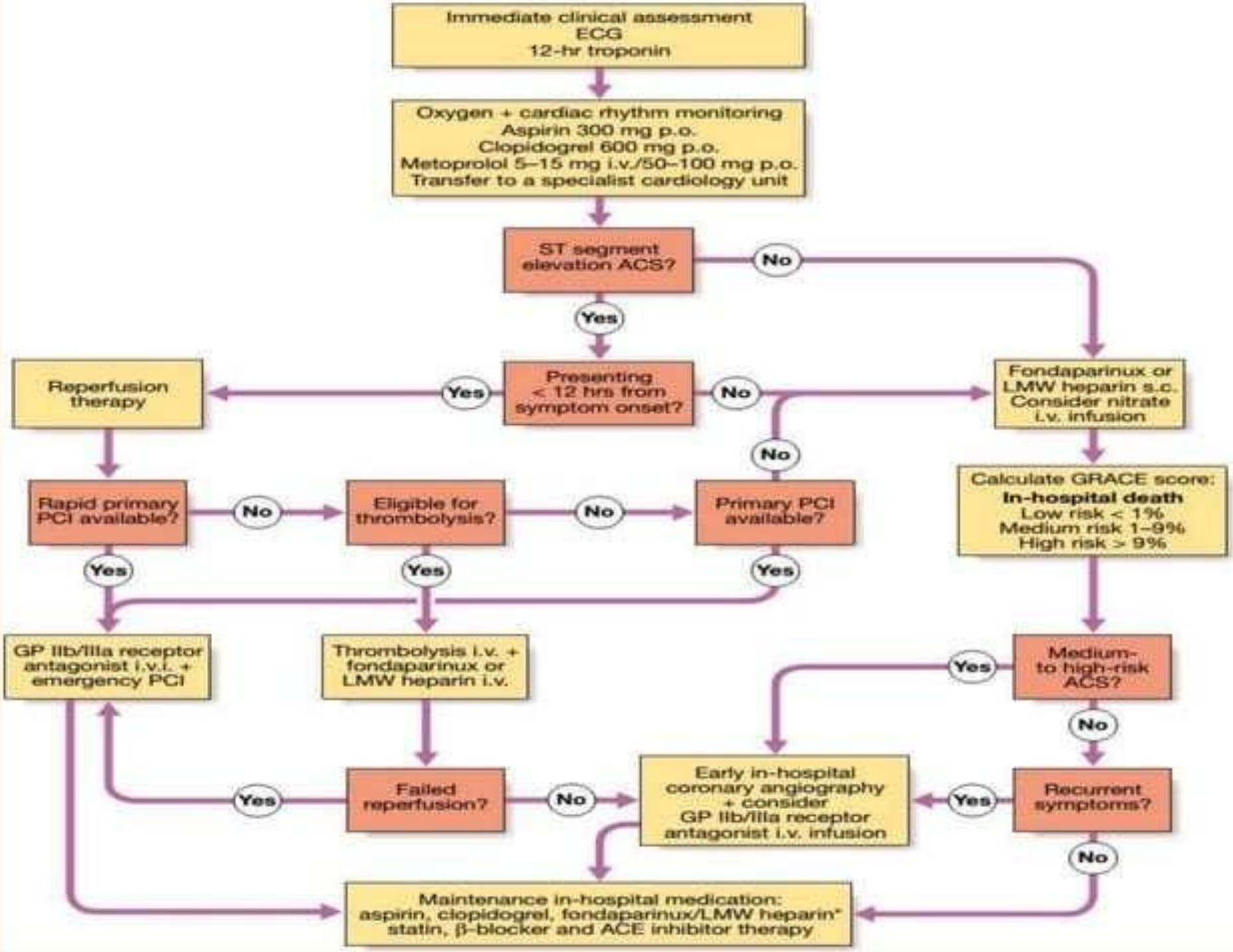
Immediate clinical assessment
ECG
12-hr troponin
Oxygen + cardiac rhythm monitoring
Aspirin 300 mg p.o.
Clopidogrel 600 mg p.o.
Metoprolol 5–15 mg i.v./50–100 mg p.o.
Transfer to a specialist cardiology unit
ST segment elevation ACS?
No
Yes
Reperfusion therapy
Yes
Presenting < 12 hrs from symptom onset?
No
Fondaparinux or LMW heparin s.c.
Consider nitrate i.v. infusion
No
Rapid primary PCI available?
No
Eligible for thrombolysis?
No
Primary PCI available?
Calculate GRACE score:
In-hospital death
Low risk < 1%
Medium risk 1–9%
High risk > 9%
Yes
Yes
Yes
GP IIb/IIIa receptor antagonist i.v.i. + emergency PCI
Thrombolysis i.v. + fondaparinux or LMW heparin i.v.
Yes
Medium- to high-risk ACS?
No
Yes
Failed reperfusion?
No
Early in-hospital coronary angiography + consider GP IIb/IIIa receptor antagonist i.v. infusion
Yes
Recurrent symptoms?
No
Maintenance in-hospital medication:
aspirin, clopidogrel, fondaparinux/LMW heparin*
statin, β-blocker and ACE inhibitor therapy

References

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THANKS.....

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