ATHEROSCLEROSIS

Coronary Artery Disease

- Atherosclerosis is the leading cause of death and disability in the developed and developing world
- Clinical manifestations depend on the particular vascular bed affected:
    - Coronary vasculature: angina, MI, sudden death
    - Cerebral: TIA, stroke
    - Peripheral : claudication, gangrene
    - Renal: hypertension

Disease impact:

In 1997, more than 5mn Americans had CVD
Currently one in five American has some form of CVD

Each year 1mn deaths are due to CVD (42% of all deaths!)
One-sixth of CVD deaths are in persons <65 yrs of age

Annually

- 1.5mn Americans have MI
- 0.5mn die from CHD
- 0.5mn have stroke
- 0.15mn die from stroke

Death rates from CHD has decreased by 40% since 1968

CVD still remains the leading cause of death in developed nations

CHD & stroke are the 2nd and 3rd leading causes of mortality even in the developing regions

Pathophysiology

- CAD is almost always due Atherosclerosis. Occasionally, other such as aortitis, polyarteritis

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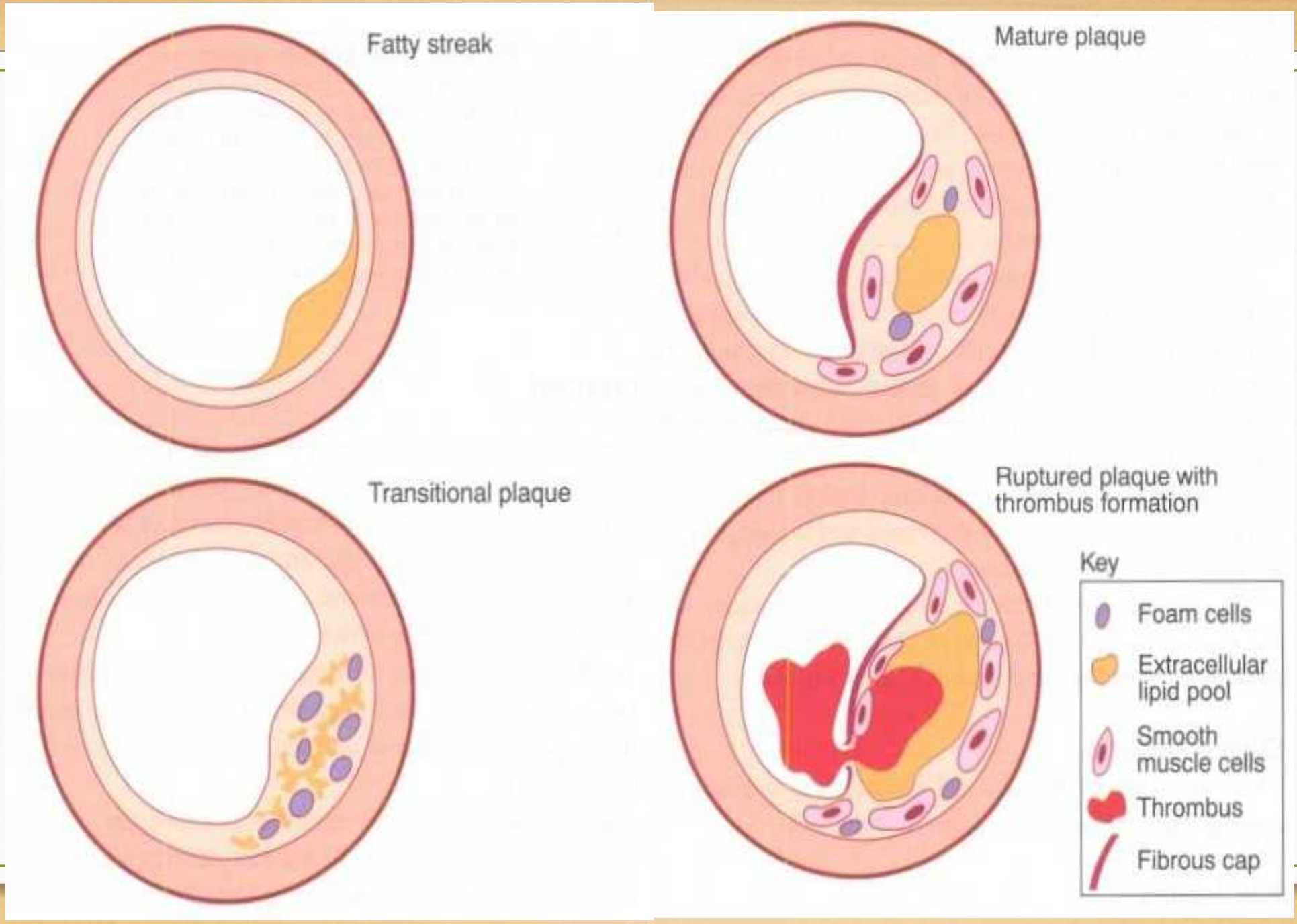
- Atherosclerosis is a progressive inflammatory disorder of the arterial wall that is characterised by focal lipidrich deposits of atheroma.
- Development of lesions, starting in childhood, progress through phases, caused by injury to intima of artery
- Phase I : fatty streaks – do not obstruct flow
- Phase II: fibrous plaque- elevated lesion protruding into lumen obstructs flow to varying degrees
- Phase III: complicated lesions – partially or totally occlude lumen

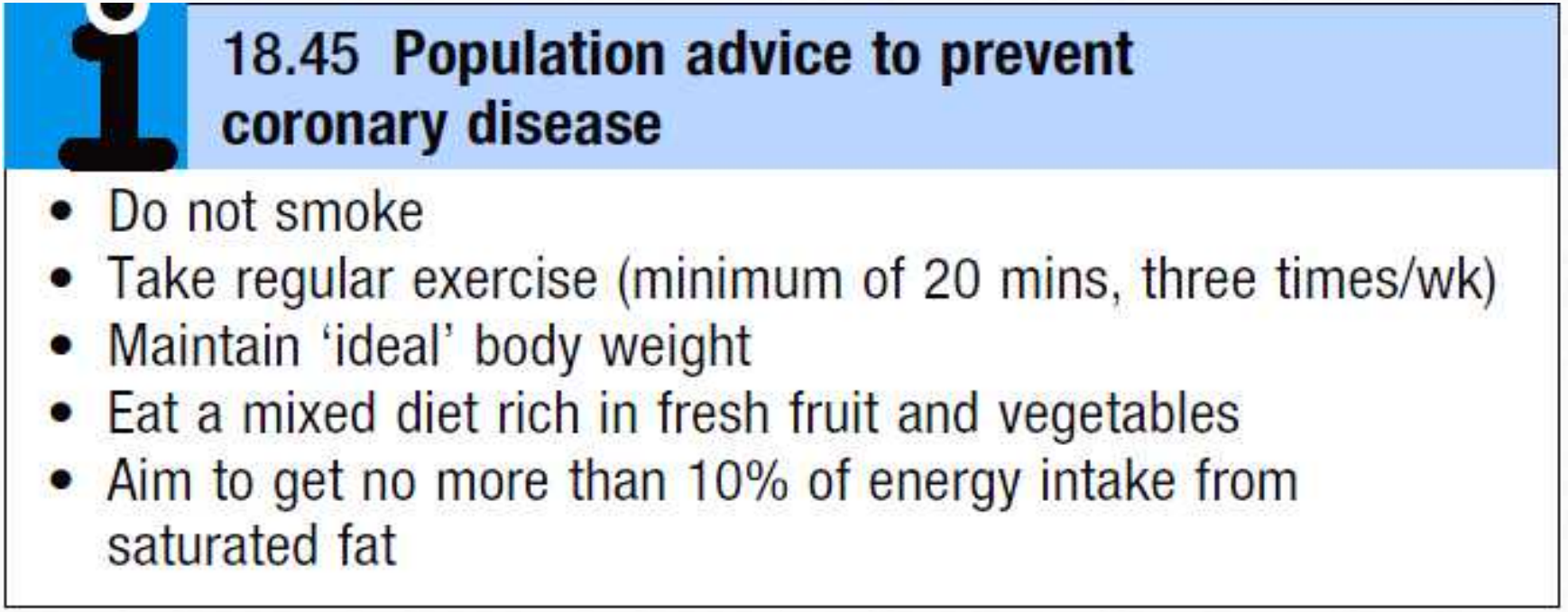

Fatty streak
Mature plaque
Transitional plaque
Ruptured plaque with thrombus formation
Key
Foam cells
Extracellular lipid pool
Smooth muscle cells
Thrombus
Fibrous cap

Risk factors

- Non-modifiable risk factors
  - Age: death from CAD ↑ with age
  - Sex
  - Family history
  - Race: afro-Americans have = 45% > hypertension than Caucasians

- Modifiable Risk Factors
  - Cigarette smoking: 2X increased risk for CAD
  - HTN: damages blood vessels leading to plaque formation and atherosclerosis
  - Hyperlipidemia: ↑CAD and atherosclerosis by causing build up in artery walls
  - Physical Inactivity:↑ risk of CAD 2X
  - Diabetes: ↑ risk 2X in men; 3X in women
  - Obesity
  - Stress : increased catecholamine release; ↑ sympathetic response

Managements of atherosclerosis



18.45 Population advice to prevent coronary disease

- Do not smoke
- Take regular exercise (minimum of 20 mins, three times/wk)
- Maintain 'ideal' body weight
- Eat a mixed diet rich in fresh fruit and vegetables
- Aim to get no more than 10% of energy intake from saturated fat

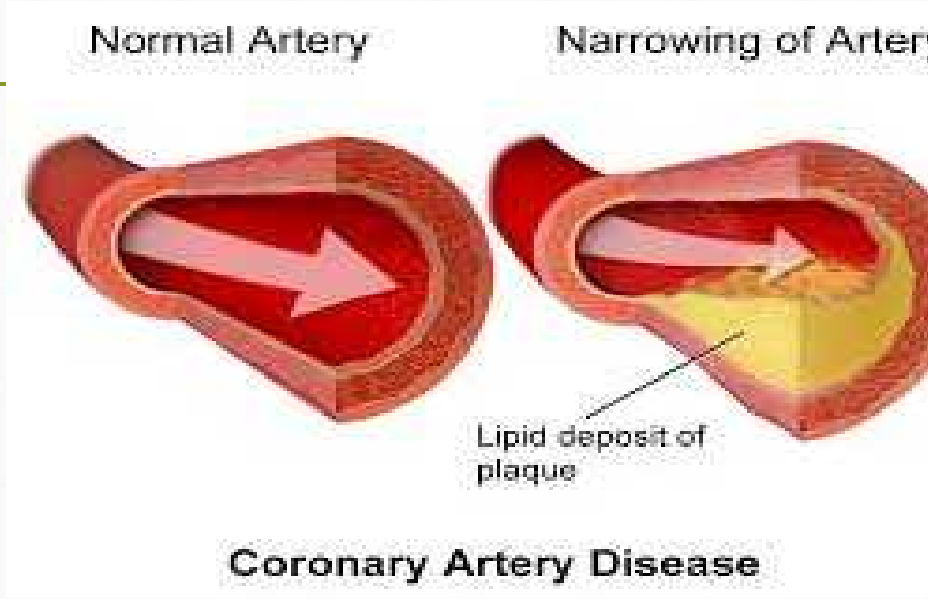
Coronary artery disease

18.49 Coronary artery disease: clinical manifestations and pathology

Clinical problem	Pathology
Stable angina	Ischaemia due to fixed atheromatous stenosis of one or more coronary arteries
Unstable angina	Ischaemia caused by dynamic obstruction of a coronary artery due to plaque rupture or erosion with superimposed thrombosis
Myocardial infarction	Myocardial necrosis caused by acute occlusion of a coronary artery due to plaque rupture or erosion with superimposed thrombosis
Heart failure	Myocardial dysfunction due to infarction or ischaemia
Arrhythmia	Altered conduction due to ischaemia or infarction
Sudden death	Ventricular arrhythmia, asystole or massive myocardial infarction

Chronic stable angina

- Angina pectoris is the clinical syndrome caused by transient myocardial ischaemia. It may occur whenever there is an imbalance between myocardial oxygen supply and demand. Coronary atheroma is by far the most common cause of angina.



Coronary Artery Disease

Clinical features

- Chest discomfort caused by transient myocardial ischemia without cell death
- Usually brought on by ↑ physical or emotional stress and promptly relieved by rest.
- Precipitated by 4 "E's"
  - Extreme emotion
  - Extreme temperature
  - Excessive eating
  - Exercise

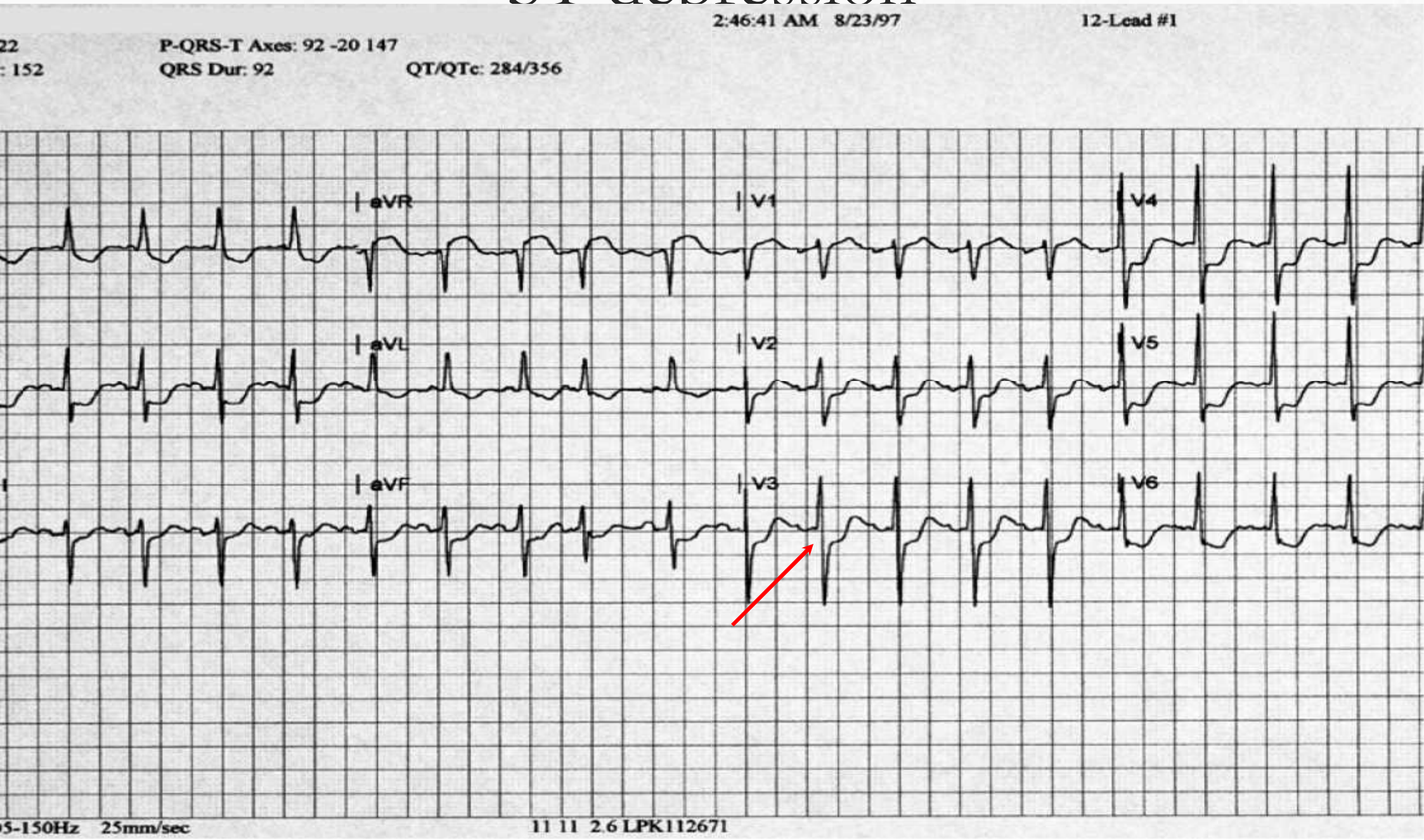
Physical examination is frequently unremarkable.

Investigations

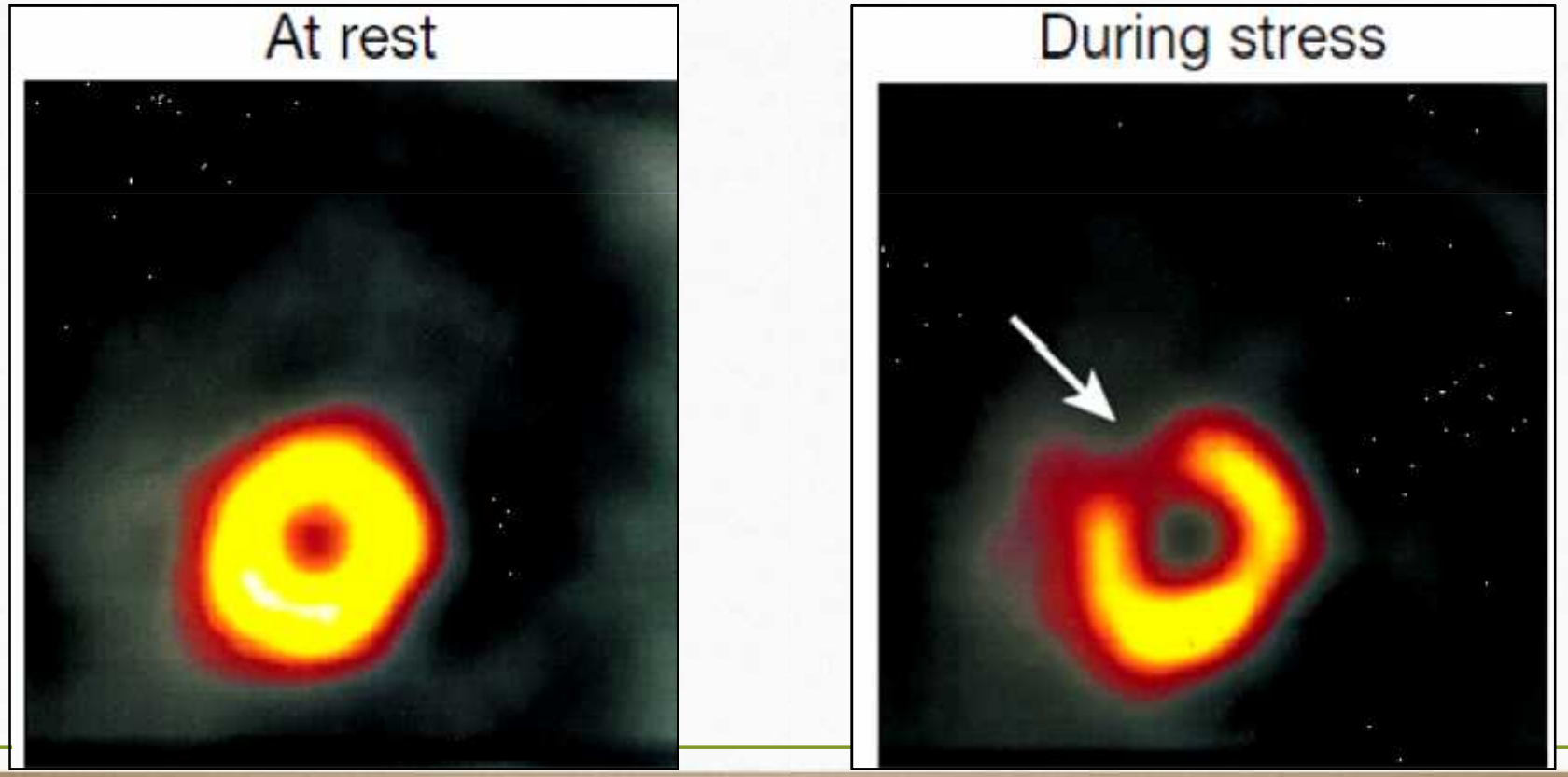
- Resting ECG often normal.
- Exercise ECG.
- Myocardial perfusion scanning.
- Stress echocardiography.
- Coronary arteriography

Exercise (stress) ECG

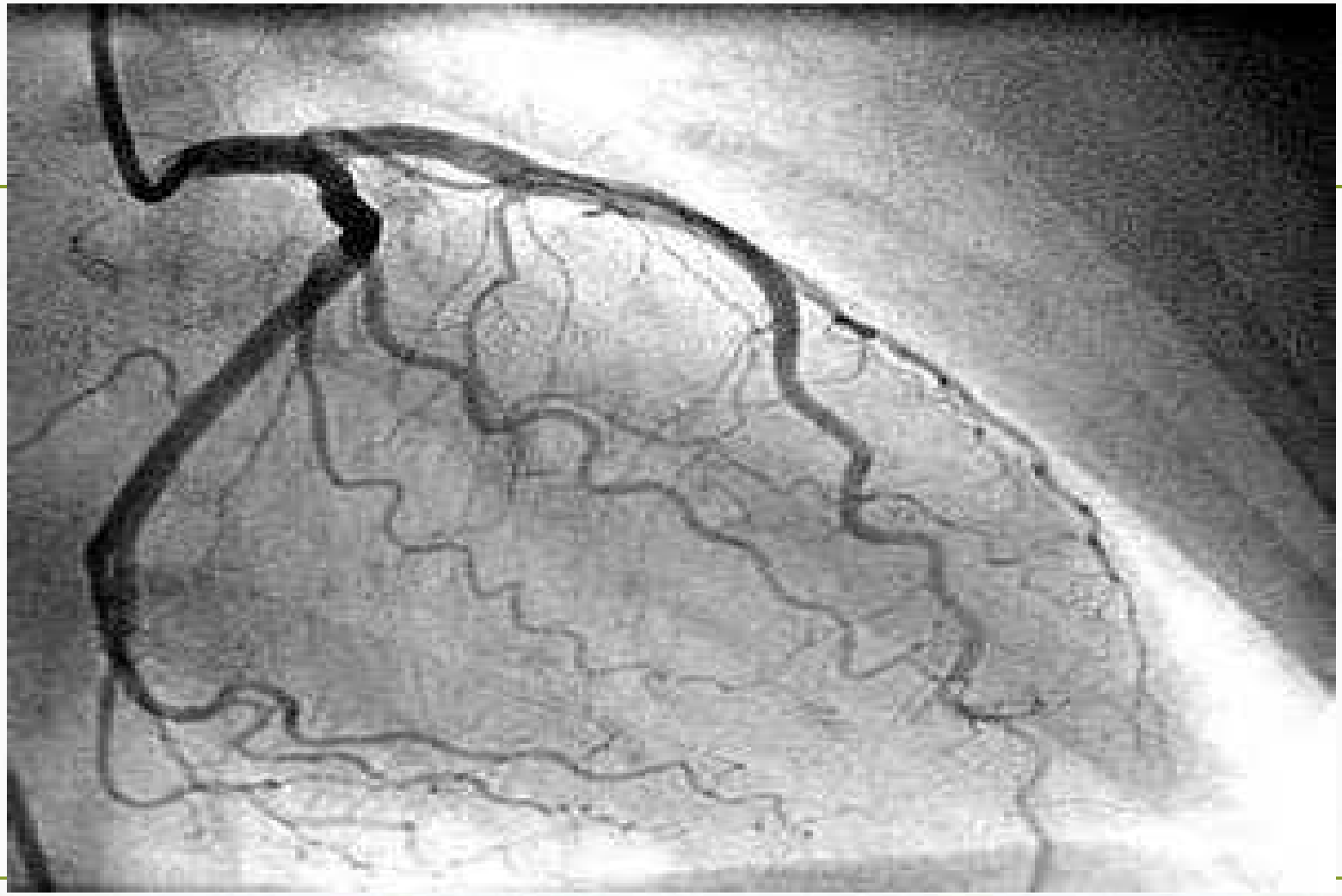
ST depression

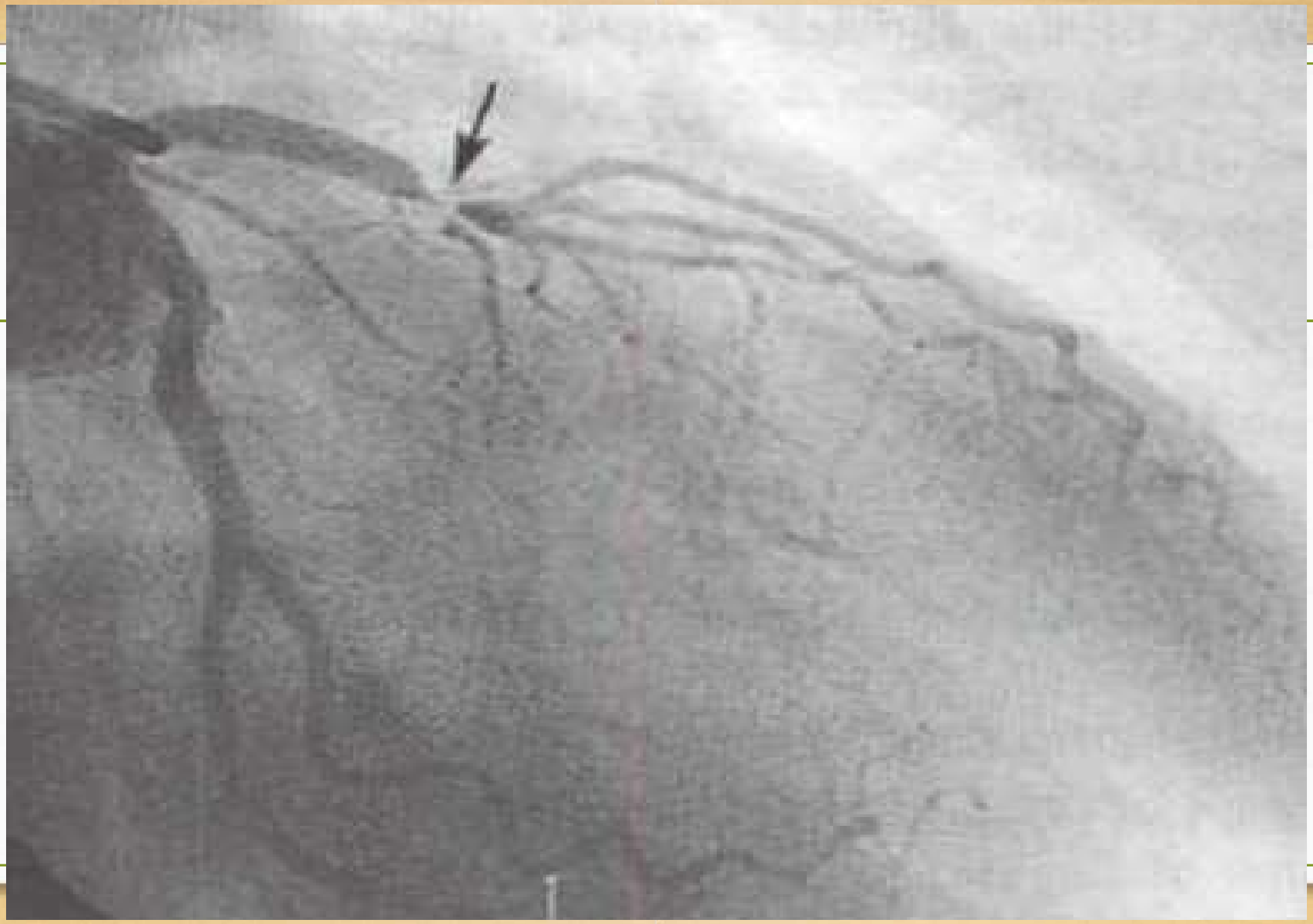


Myocardial perfusion scanning



Coronary Angiography





Management of Stable Angina

18.53 Advice to patients with stable angina

- Do not smoke
- Aim for ideal body weight
- Take regular exercise (exercise up to, but not beyond, the point of chest discomfort is beneficial and may promote collateral vessels)
- Avoid severe unaccustomed exertion, and vigorous exercise after a heavy meal or in very cold weather
- Take sublingual nitrate before undertaking exertion that may induce angina

Management of Stable Angina

- **Drug therapy:**
  - Antiplatelets
  - Antianginal
    - Nitrate
    - B Blockers
    - CCB
    - Potassium channel activators
    - Ivabradine
- ***Invasive therapy:***
  - PTCA
  - CABG

- **Antiplatelet therapy**

Low-dose aspirin reduces the risk of adverse events such as MI and should be prescribed for all patients with coronary artery disease indefinitely .Clopidogrel (75 mg daily) is an equally effective.

- ***Nitrates:***
- These drugs act directly on vascular smooth muscle to produce venous and arteriolar dilatation.
- Their beneficial effects are due to a reduction in myocardial oxygen demand (lower preload and afterload) and an increase in myocardial oxygen supply (coronary vasodilatation).
- It given as Sublingual glyceryl trinitrate (GTN) tab or spray ; however, a variety of alternative nitrate preparations can provide a more prolonged therapeutic effect. GTN can be given transcutaneously as a patch (5–10 mg daily), or as a slow-release buccal tablet (1–5 mg 4 times daily). Other nitrates, such as isosorbide dinitrate (10–20 mg 3 times daily) and isosorbide mononitrate (20–60 mg once or twice daily), can be given by mouth.
- Side-effects include headache, symptomatic hypotension and, rarely, syncope.

- ***Beta-blockers:***

- These lower myocardial oxygen demand by reducing heart rate, BP and myocardial contractility,

- ***Calcium channel antagonists:***
- These drugs 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, and lower myocardial oxygen demand by reducing BP and myocardial contractility.
- verapamil and diltiazem are particularly suitable for patients who are not receiving a β-blocker (e.g. those with airways obstruction) because they slow SA node firing, inhibit conduction through the AV node and tend to cause a bradycardia.
- Calcium channel antagonists reduce myocardial contractility and can aggravate or precipitate heart failure. Other unwanted effects include peripheral oedema, flushing, headache and dizziness.

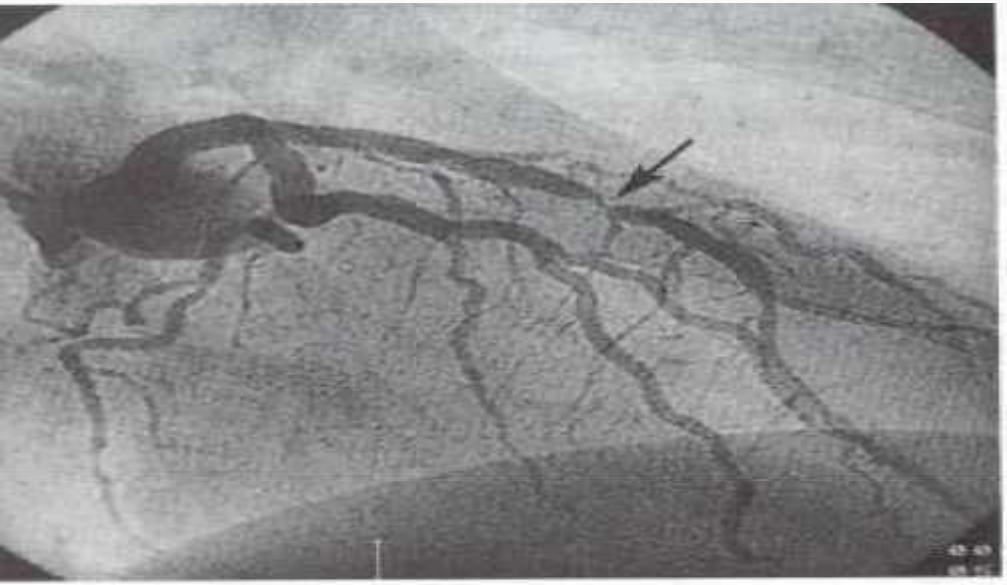
- ***Potassium channel activators:***

- These have arterial and venous dilating properties but do not exhibit the tolerance seen with nitrates. Nicorandil (10–30 mg twice daily orally) is the only drug in this class currently available for clinical use.

- ***If channel antagonist:***

- Ivabradine is the first of this class of drug. It induces bradycardia by modulating ion channels in the sinus node. In contrast to β-blockers and rate-limiting calcium antagonists, it does not have other cardiovascular effects.

Percutaneous Coronary Intervention



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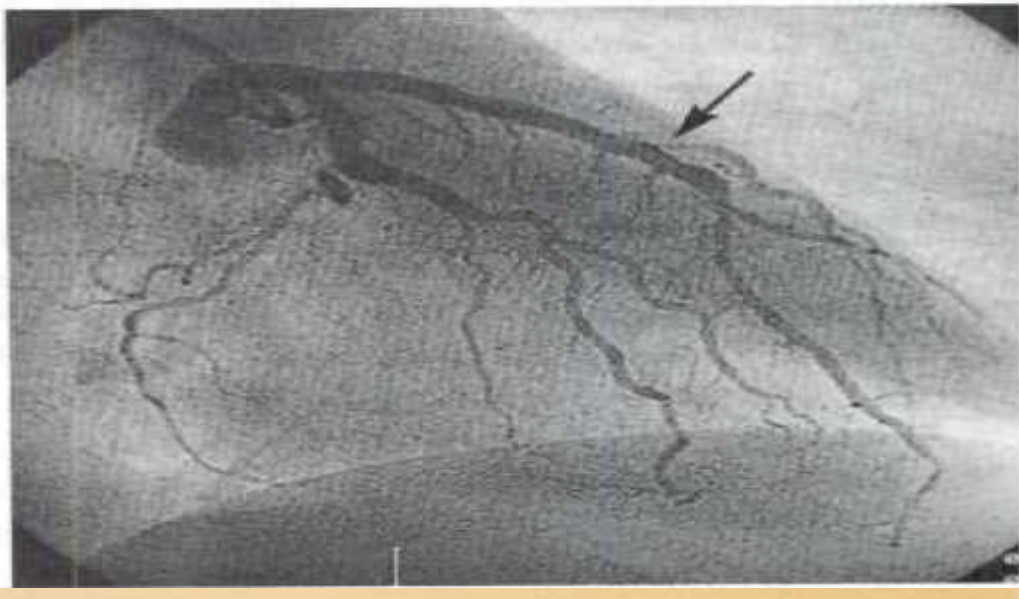
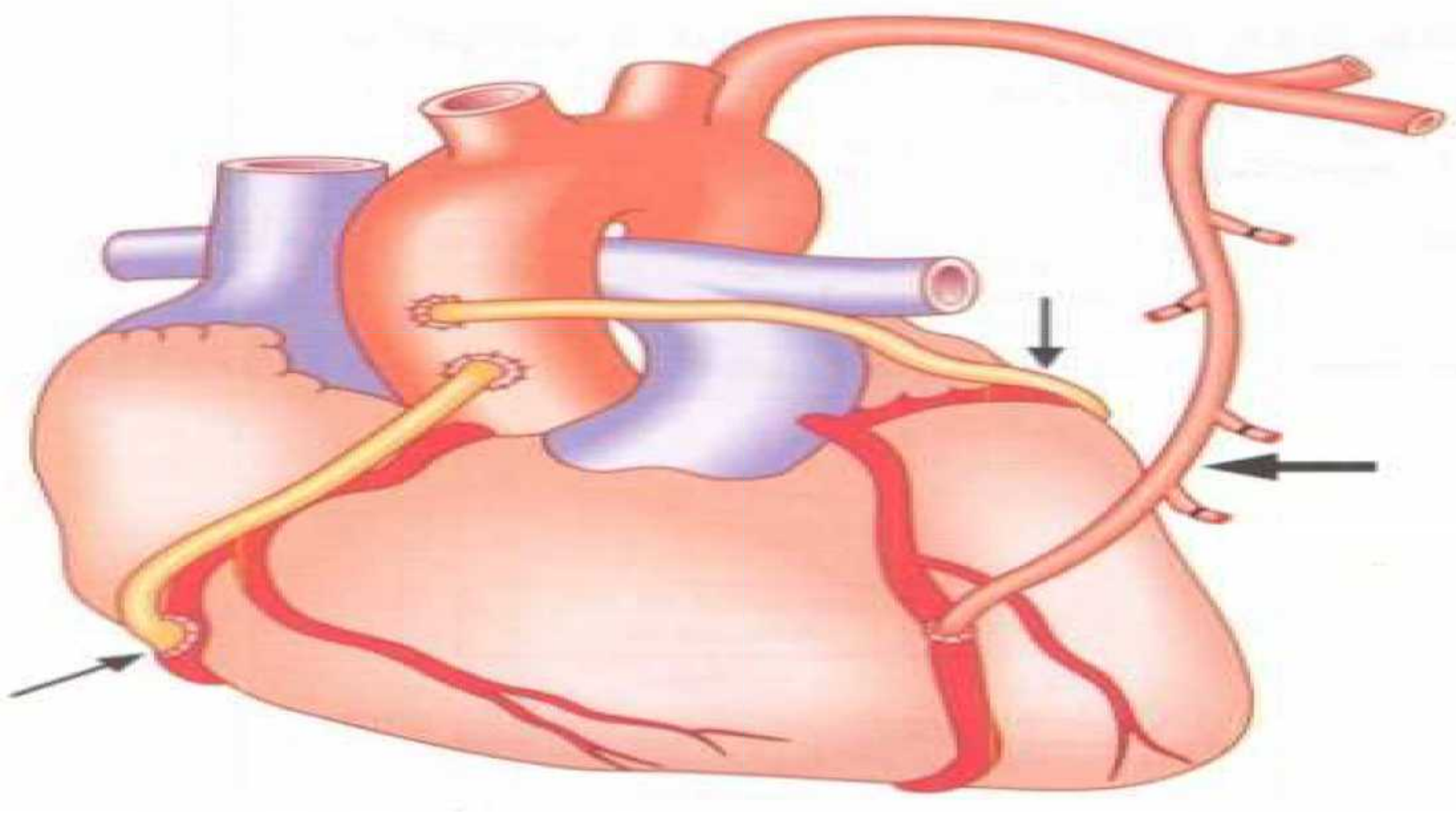


Coronary Artery Bypass Grafting



Prognosis:

- Symptoms are a poor guide to prognosis; nevertheless, the 5-year mortality of patients with severe angina is nearly double that of patients with mild symptoms. In general, the prognosis of coronary artery disease is related to the number of diseased vessels and the degree of left ventricular dysfunction