Myocardial Infarction (Heart Attack)

Death of cardiac muscles resulting from ischemia

Incidence & Risk factors

- In industrialized countries MI accounts for 10-25% of all deaths
- Frequency rises with age
- Risk factors to atherosclerosis:

  - diabetes, hypertension, smoking, hyperlipidemia
- M>F; incidence rises after menopause, HRT not protective

Pathogenesis

1.) Myocardial ischemia

- Diminished coronary blood flow e.g in coronary A dis, shock.
- Increased myocardial demand e.g exercise, emotions
- Hypertrophy of heart without simultaneous increase of coronary blood flow: HT, valvular heart dis

2.) Role of platelets

3.) Acute plaque rupture

4.) Non-atheromatous causes (10%)

- vasospasm
- emboli: vegetative endocarditis, paradoxical emboli
- unexplained: vasculitis, hematologic abnormalities

Myocardial Response

Profound functional, biochemical & morphological changes

1. Cessation of aerobic respiration (within seconds)
   - inadequate production of CPK
   - glycogen depletion
   - ATP loss
   - accumulation of noxious products (lactic acid)
2. Loss of contractility (function): (60 sec -<2min)
   can cause CHF in absence of infarction

3. Changes of reversible injury on EM (upto 10-30 min):
   - glycogen depletion
   - swelling of cell/ mitochondria
   - disruption of sarcolemma
4. Irreversible injury i.e myocardial necrosis: begins after 30 min, complete by 6hrs

First subendocardium then transmural thickness over a period of 3-4 hrs

Morphology

- **Transmural infarct** (95%) : ischemic necrosis involving full thickness or nearly full thickness of the ventricular wall

  - encompasses nearly the entire distribution zone of a single coronary A, >75% occlusion

  - assoc with plaque change

  - assoc with epicarditis

- **Subendocardial infarct**: involves inner 1/3 or upto half of the ventricular wall

  - may extend beyond the perfusion of single coronary A

  - can also result from prolonged and severe reduction in systemic blood flow

Location

- Nearly all transmural infarcts involve a portion of LV, including ventricular septum
- RV involved in 1-3% cases because of less demand and thin wall
- Infarct of LA least common due to supply of O2 blood

- LAD (40-50%): ant wall of LV, circumference of apex, ant portion of vent septum
- RCA (30-40%): inf / post wall of LV, inf / post wall of RV, post portion of vent septum
- LCX (15-20%): lat wall of LV

Size of infarct

Depend on:

1. Severity and rate of development of obstruction
2. Size of vascular bed perfused by the vs
3. Duration of ischemia
4. Myocardial demand (Increase with hypertrophy, tachycardia)
5. Sytemic blood pressure drop can worsen situation
6. Extent of collaterals

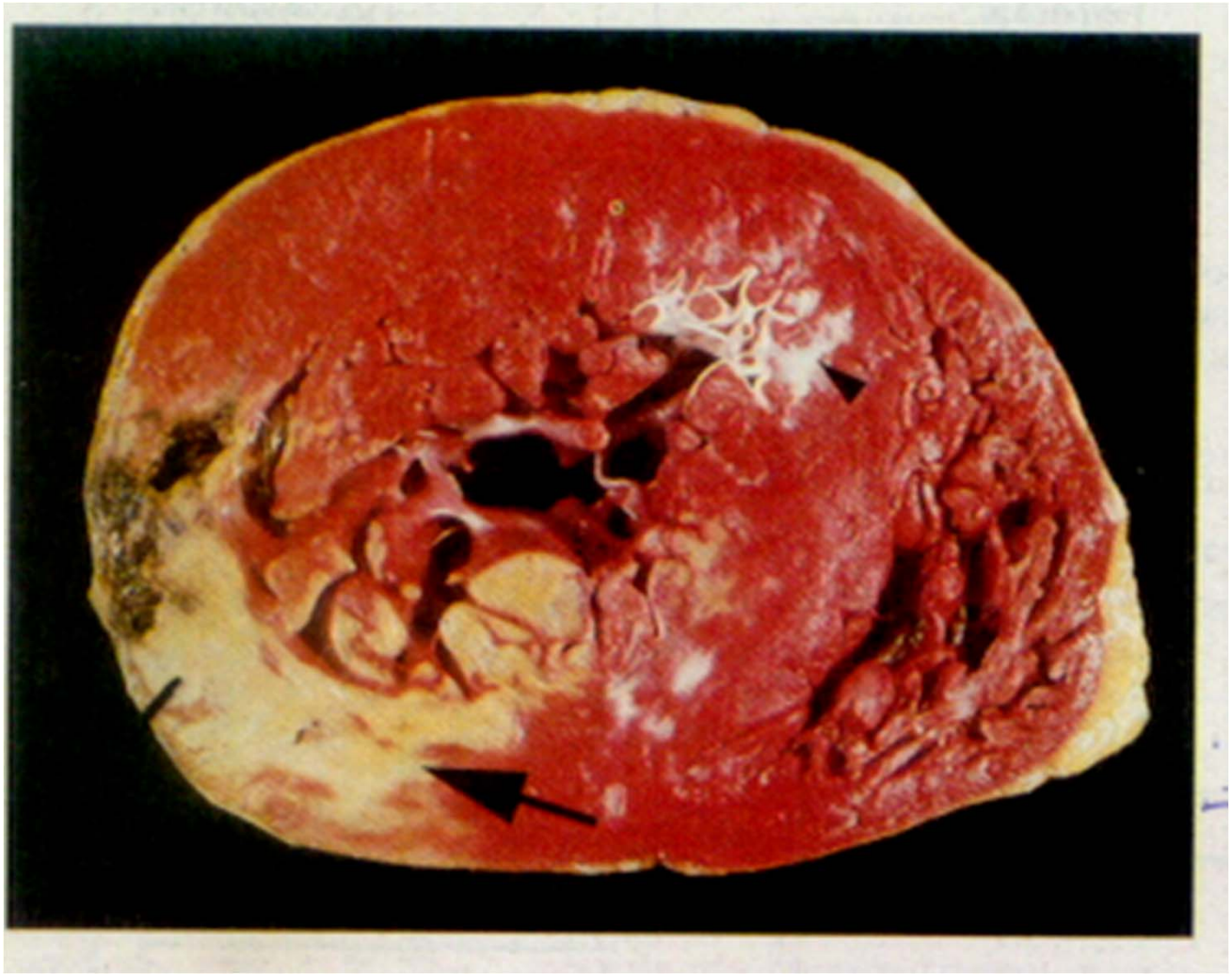
Gross

- Most infarcts single, 4-10 cm size
- <12 hr old: no gross changes, may be difficult to diagnose

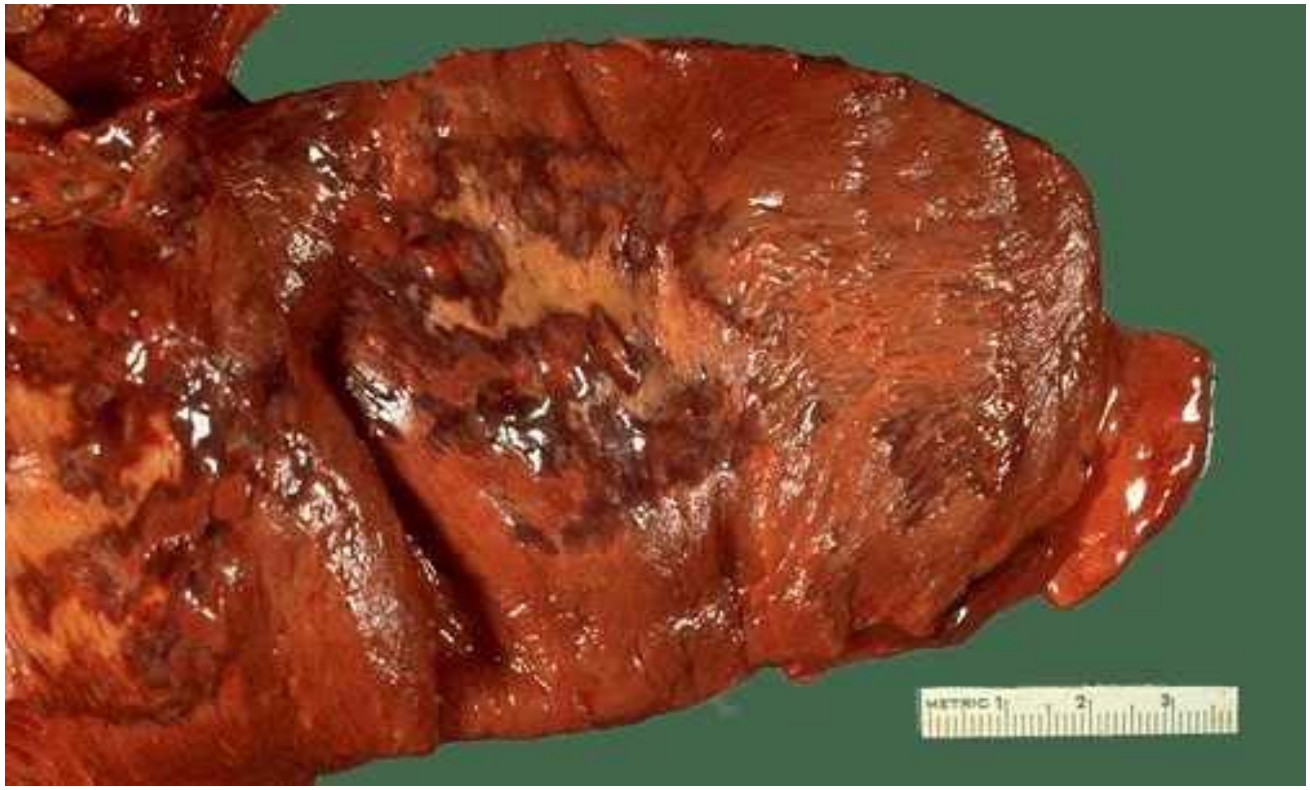
  Triphenyl tetrazolium chloride (TTC) dye on gross imparts a brick red color to the viable myocardium, infarcted area fails to stain as it lacks dehydrogenase enzyme
- 12-24 hrs: appears as red-blue hue due to stagnated trapped blood
- 48-72 hrs: progressively yellow-tan border
- 3-7 days: centre soft with hyperemic borders
- 10-15 days: soft yellow area surrounded by red rim of inflammatory granulation tissue
- > 15 days gradually replaced by a thin, g/w fibrous scar

Microscopic changes

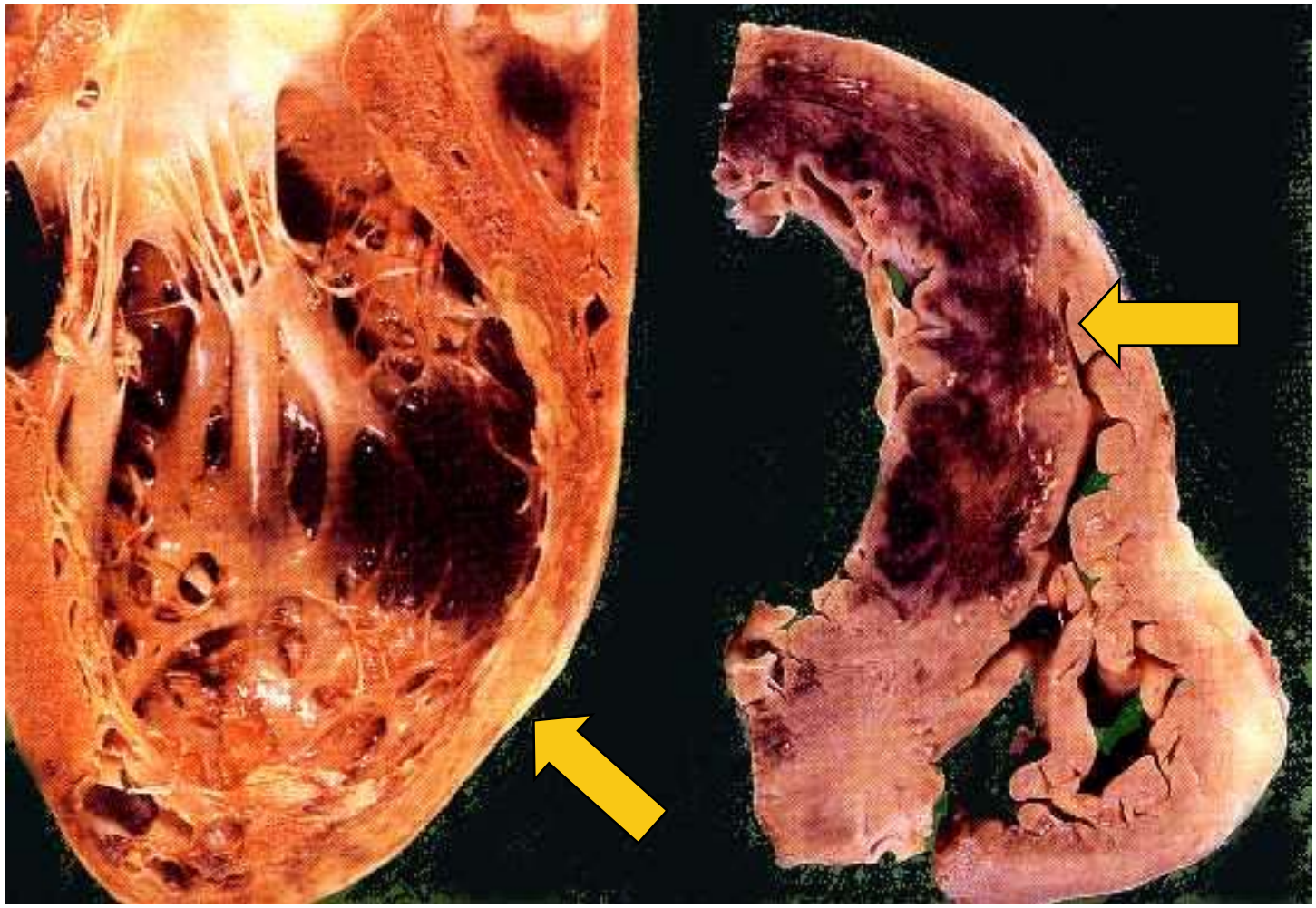
- 0-6 h: no changes, waviness of fibres
- 6-12 h: edema b/w myocardial fibres, myocytolysis of peripheral fibres
- 24 h: coagulative necrosis (loss of striations, eosinophilic hyaline app, nuclear changes), h'ge & edema in interstitium, neutrophils at the margin
- 1-3 d: complete coagulative necrosis, neutrophilic infiltrate
- 3-7d: resorption of necrosed muscle by macrophages, granulation tissue
- 10-14 d: necrosed muscle removed, pigmented macrophages, chronic inflammatory cells
- 4-6 W: less vascularity, few cells, dense fibrosis



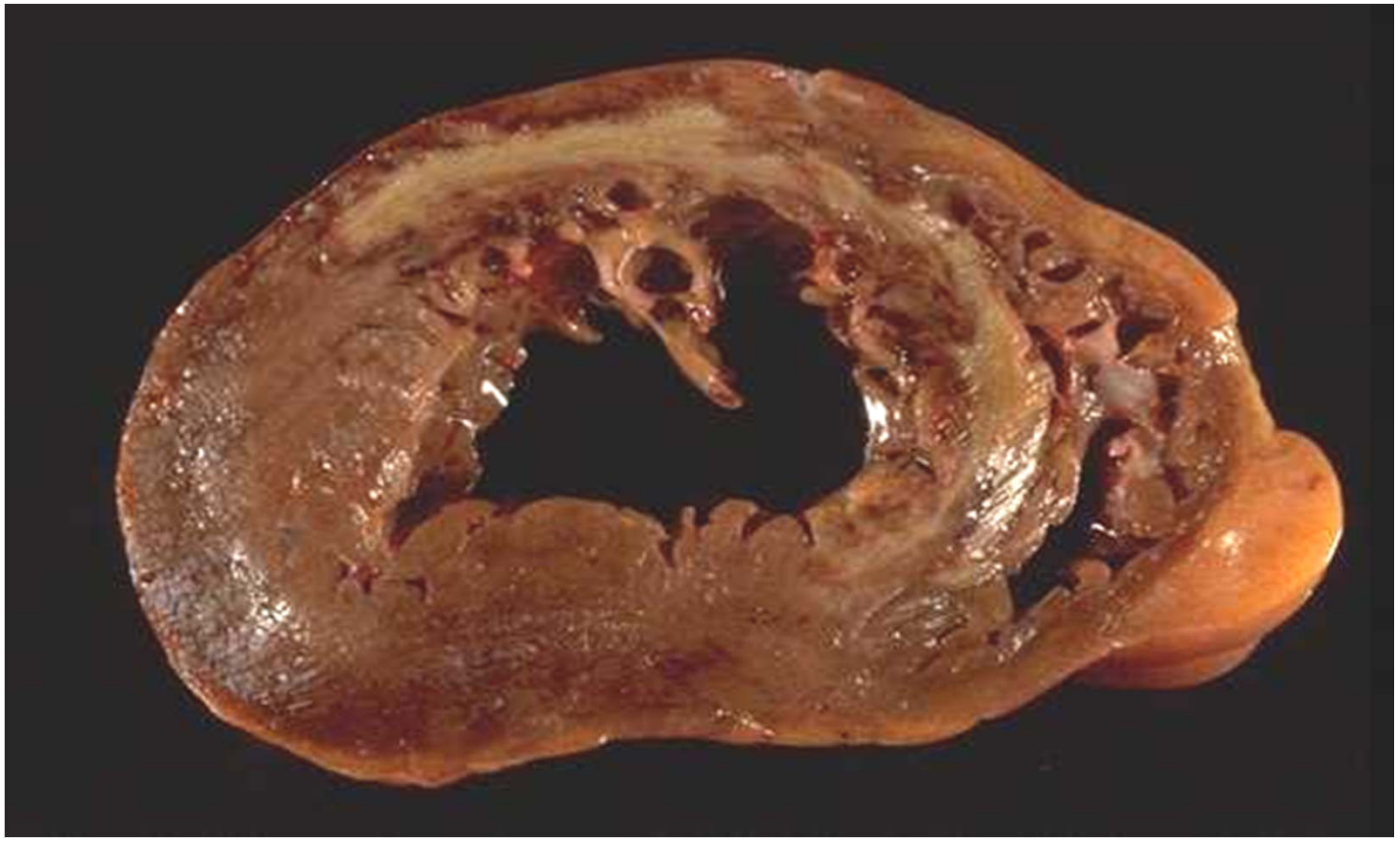
Myocardial Infarction – Gross 3-7D

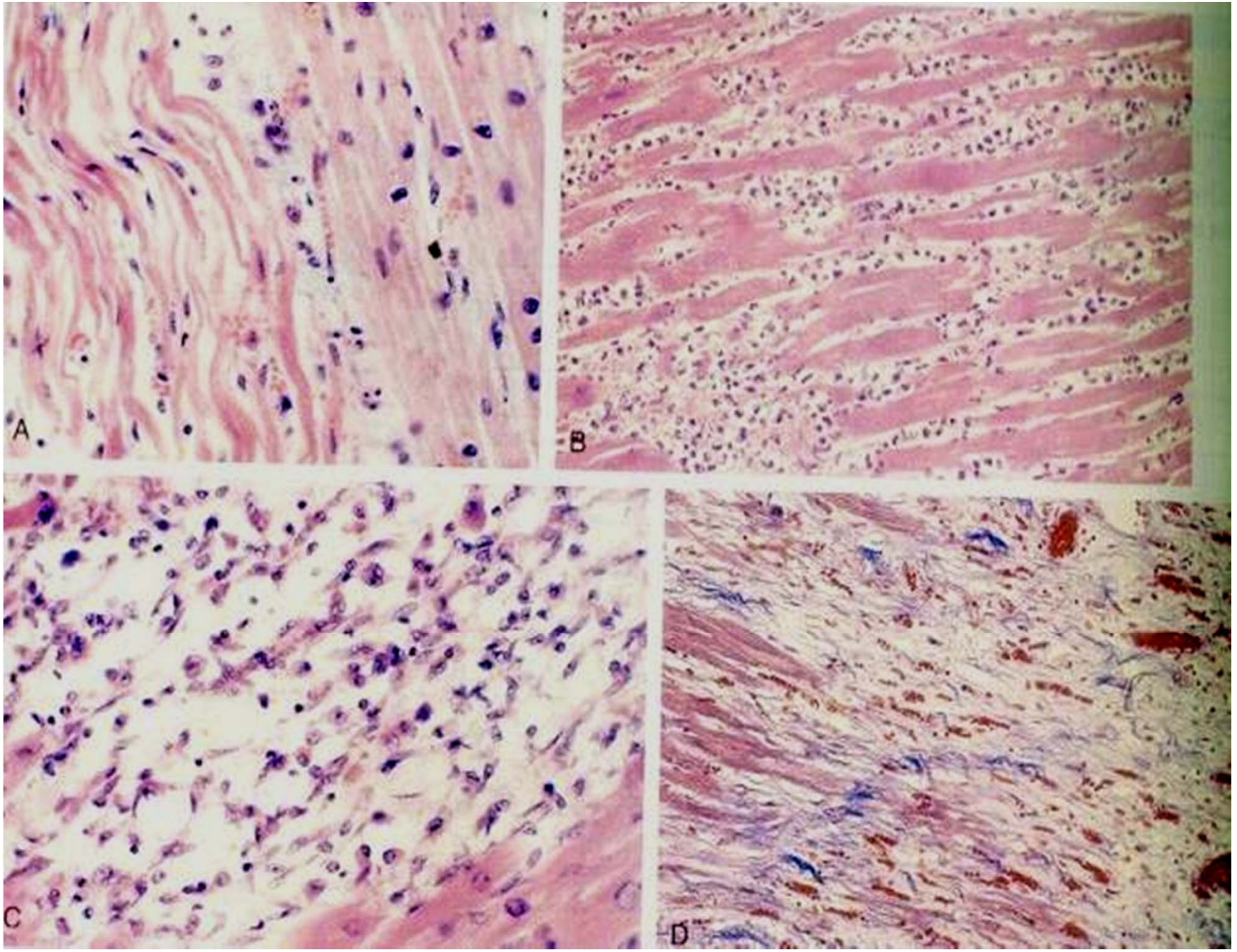


2 wk - Myocardial Infarction - 3d

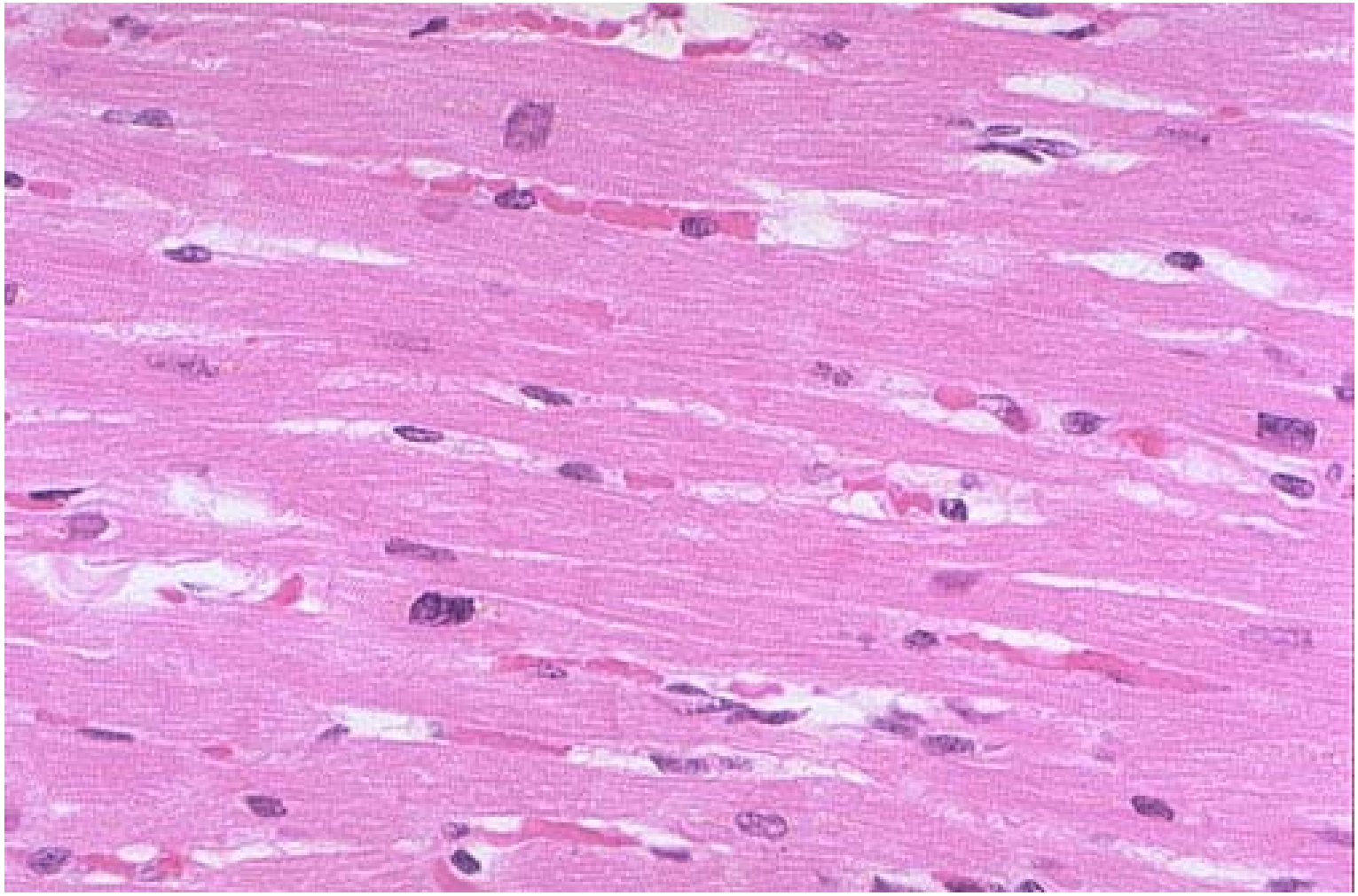


Myocardial Infarction-4w

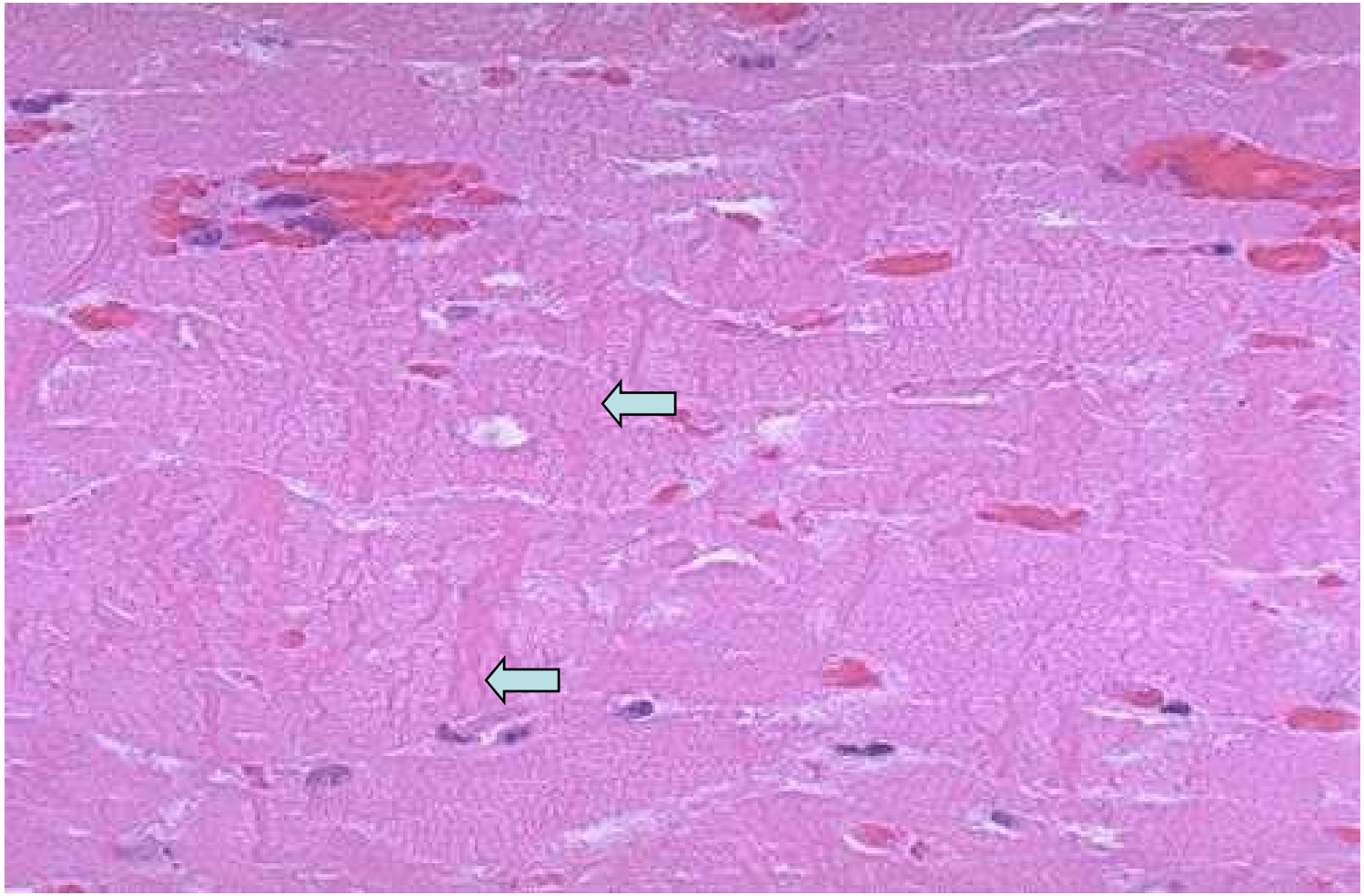



A
B
C
D

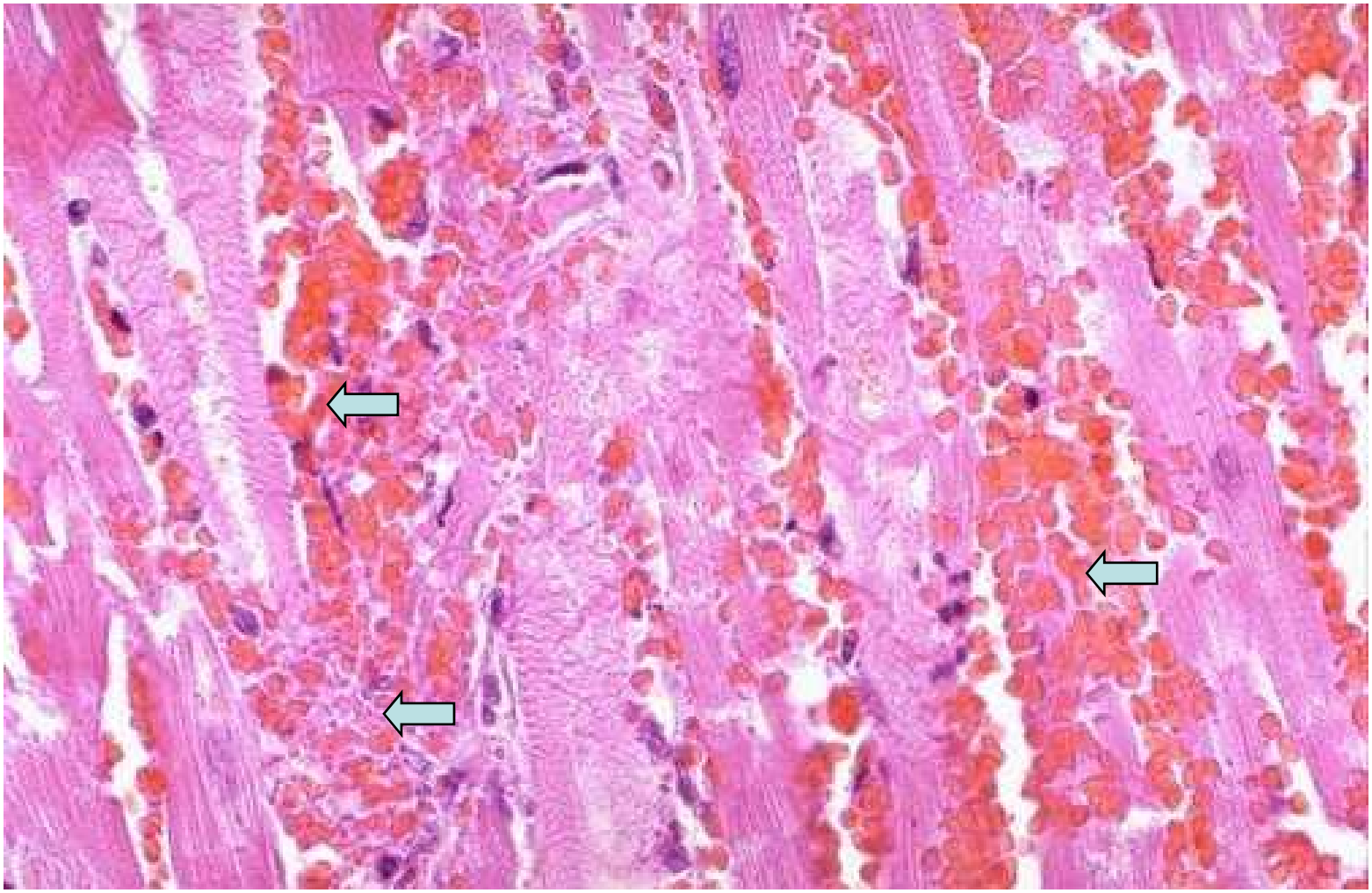
Normal Myocardium:



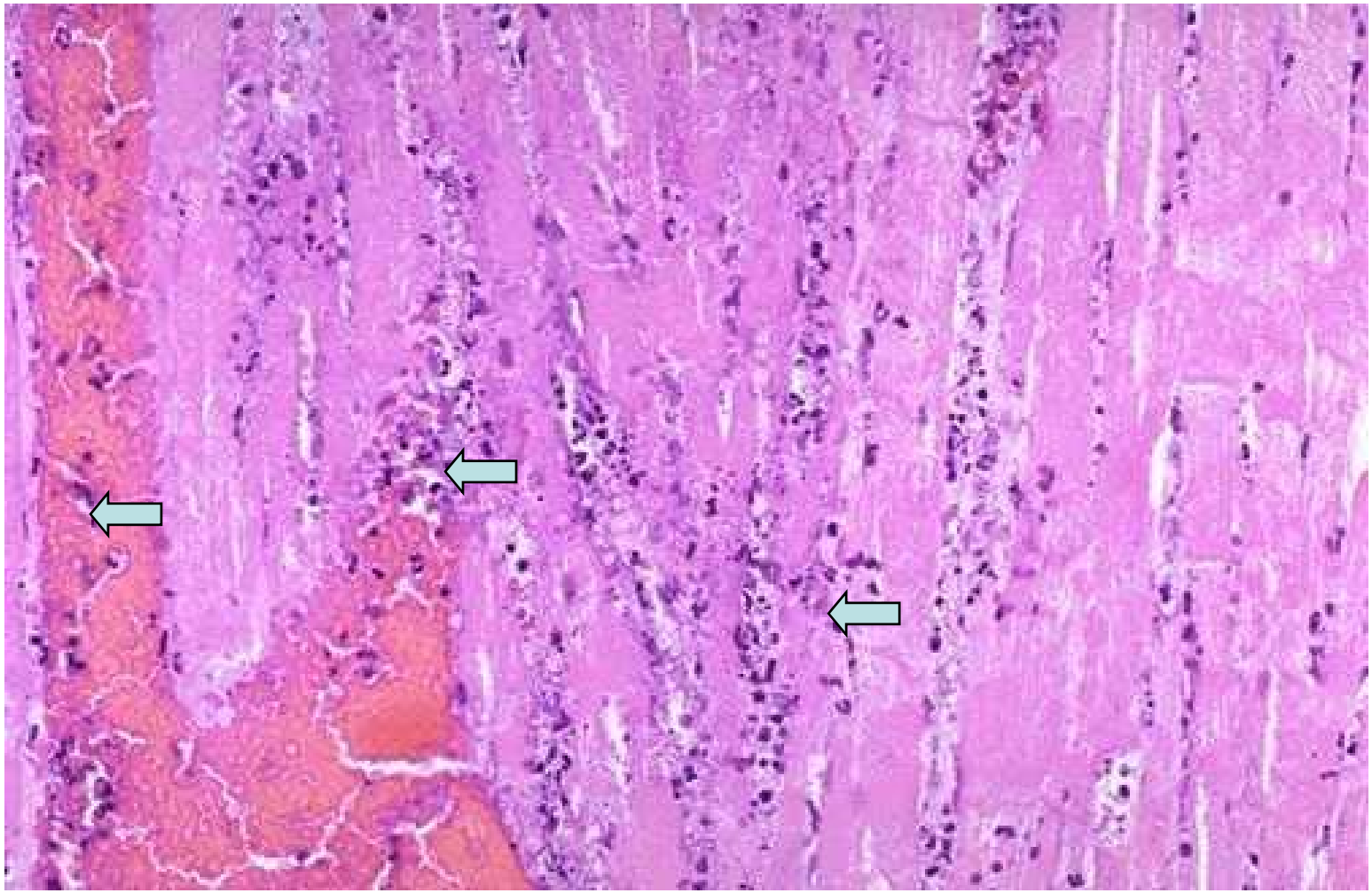
MI 18-24 hr- loss of nucleus, contraction bands, coagulative necrosis



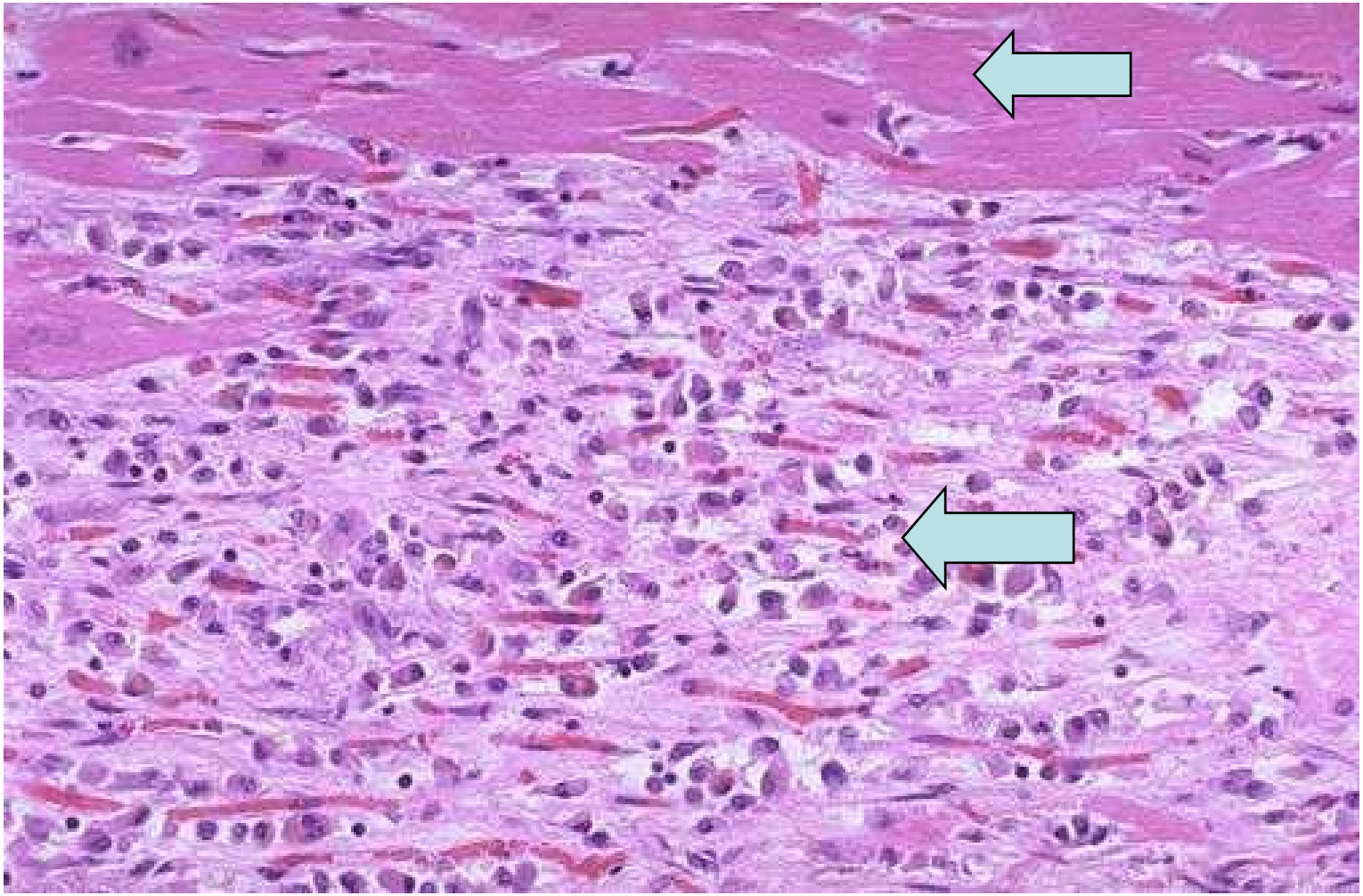
MI 2-4 day – Hemorrhage, inflammation



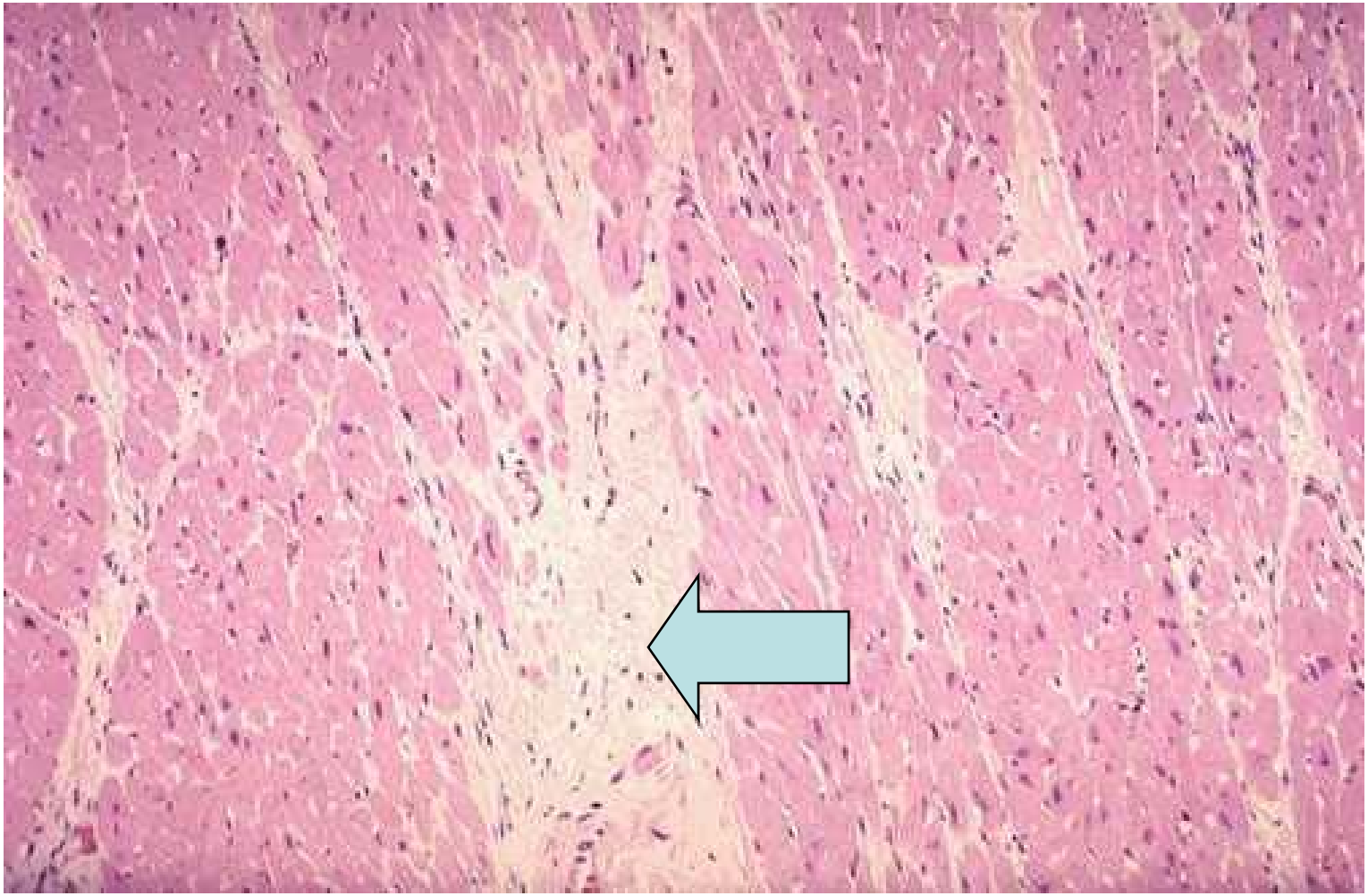
MI: 3-10D



MI 2-4 W - Resorption, fibrosis



MI >4-6 W - Collagen Scar



Infarct modification by reperfusion

- Restoration of coronary flow by balloon angioplasty, thrombolytic therapy within 15 – 20 min may prevent all necrosis; after longer interval may salvage some myocytes
- Reperfused area: hemorrhagic d/t microvascular injury
- Endothelial swelling of reperfused capillaries obstruct the flow: no-reflow, more rapid disintegration of dead myocytes
- Contraction bands in the necrosed myocytes; are eosinophillic bands of hypercontracted sarcomeres d/t Ca influx by restored blood
- Reperfusion injury: oxidative stress→ ↑ apoptosis

Diagnosis

World Health Organization criteron requires ≥ 2 of the following:

1) Prolonged ischemic-type chest discomfort
2) Serial electrocardiogram (ECG) changes
3) Rise and fall of serum cardiac markers

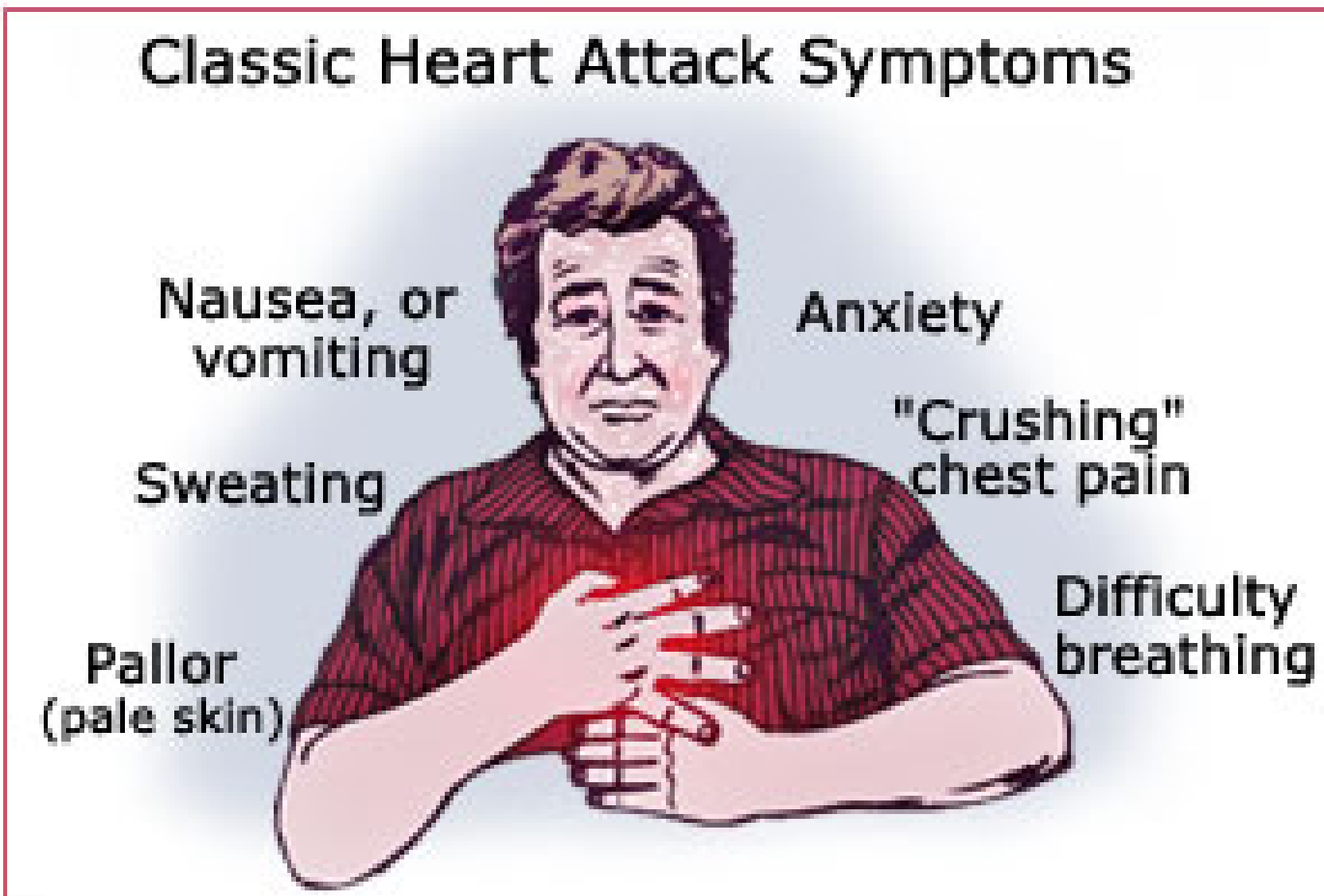
Diagnosis: Clinical

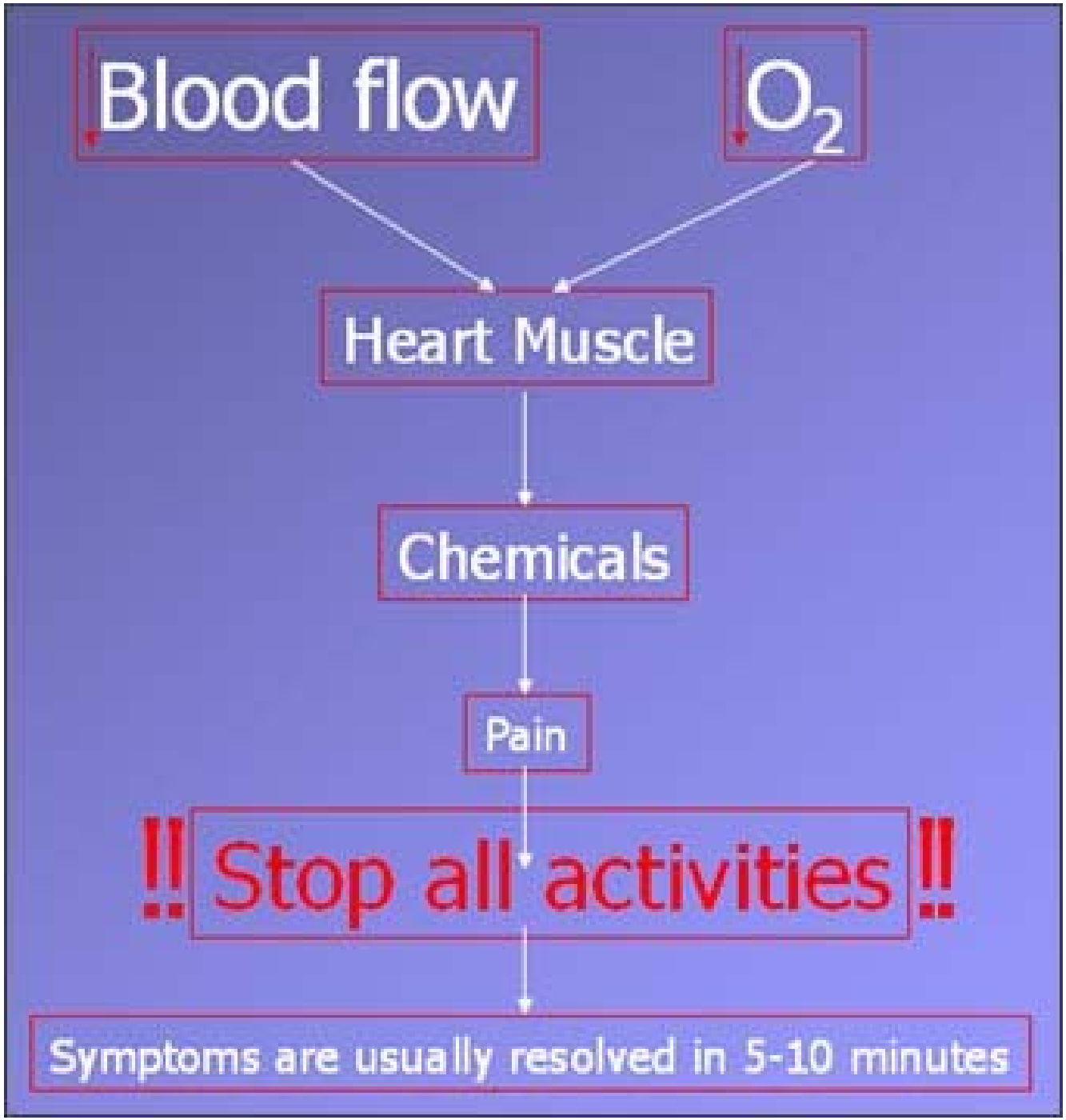
- Ischemic-Type Chest Pain
- Typically prolonged (>30 min) and at rest
- Pattern and accompanying symptoms (including “a sense of doom”)
- 25% of patients admitted to “rule out MI”actually suffer MI
- Can be mimicked by pericarditis, reflux, spontaneous pneumothorax, musculoskeletal disease (costochondritis)
- Clinically, 3 serious causes of severe chest pain – acute MI, aortic dissection, pulmonary embolus

Clinical Features

- Precordial chest pain with radiation to lt midarm, epigastrium
- Diaphoresis
- Indigestion
- Shock: rapid weak pulse, oliguria
- Low grade fever
- Acute pulmonary edema
- 10-15% asymptomatic “**Silent MI**” in elderly and diabetic

Classic Heart Attack Symptoms




Blood flow
O_2
Heart Muscle
Chemicals
Pain
!! Stop all activities !!
Symptoms are usually resolved in 5-10 minutes

ECG

- ST-segment elevation (with compatible history) specificity=91%, sensitivity=46%

  The higher the elevation and the more the leads involved, the larger the infarct and the greater the mortality
- T- wave inversion
- Appearance of wide deep Q-waves

Serum cardiac markers

Intracellular macromolecules that leak out due to infarction; should be sensitive and specific

- Creatine Kinase

  CK- Isoenzymes

  - MM - muscles cardiac & skeletal
  - MB - exclusively in cardiac muscle.
  - BB - brain, bowel & bladder
- Troponins
- LDH
- Myoglobin

Creatine Kinase

- First detectable in 3-4 hours, peaks in 8-24 hours, lasts for 3-4 days
- Not very specific – abnormal in skeletal and smooth muscle injury, severe CNS injury
- Peak value commonly used as a index of MI
- size (e.g. “a 1,400 peak CK infarct”)
- CK- MB

  More specific for cardiac muscle than total CK (though not perfect)

  Rises and falls slightly earlier than total CK

  Should be considered the current standard for diagnosing MI

Troponins

- Contractile muscle proteins present in cardiac & skeletal muscle
- Cardiac troponin (cTnT and cTnI), not found normally in blood
- Very sensitive and specific marker of MI
- Early rise in serum levels as CK-MB (2-4 hours) but stays elevated longer (10-14 days)
- Good marker for patients presenting late after MI
- May be mildly elevated in unstable angina

Lactic Dehydrogenase

- Very nonspecific (liver, lung, kidney, sk muscle, RBCs)
- High LDH1 isoenzyme more specific
- Ratio of LDH1:LDH2 above 1 is helpful in making diagnosis
- Rises late after 24 hours and stays elevated 4-5 days
- Should be replaced by troponin T

Myoglobin

- First marker to be detected in 1-4 hours, peaks in 6 hours, lasts for 24 hours
- Non-specific – also present in skeletal muscle
- Not widely used, but may be useful for early detection of MI

Complications

- 80-90% develop major complications
- Sudden Cardiac Death: 50% deaths occur within 1 hr
- Arrhythmias: occur d/t conduction disturbances or myocardial irritability
  - sinus tachycardia, bradycardia, atrial or vent fibrillation
  - heart block in case of involvement of bundle of His
- CHF- cause of death in 40% cases, Lt or Rt or both
- Cardiogenic shock
- Mural thrombus & thromboembolism:
  - d/t stasis and endothelial injury
  - venous thrombosis in legs due to bed rest
- Ventricular aneurysm: due to weakening of the infarcted area

- Myocardial rupture: due to mechanical weakening of the wall; most frequent after 3-7days when max neutrophillic infiltrate and lysis of connective tx

  - rupture of ventricular free wall: cardiac tamponade, hemopericardium

  - rupture of interventricular septum: L→R shunt

  - rupture of papillary muscle: MR
- Progressive heart failure: Chronic IHD due to ventricular remodelling: change in size, shape and thickness comprising early ventricular thinning
- Pericarditis: fibrinous, 2-3 days post transmural infarct, resolves on its own
- Post myocardial infarction syndrome (Dresslers synd): in 3-4%, after 1-6 weeks of MI, pneumonitis

Prognosis

- Poor prognostic factors: females, advanced age, diabetes, previous MI
- Long term prognosis depends on ventricular function and degree of coronary obstruction
- **C-Reactive Protein**: serum CRP > 3mg/l associated with highest risk of MI/ reinfarction

Chronic Ischemic Heart disease

- Development of progressive cardiac dysfunction leading to heart failure as a consequence of ischemic myocardial damage
- Ischemic cardiomyopathy
- Post infarct cardiac decompensation due to
  - exhaustion of viable myocardial tissue or
  - diffuse myocardial dysfunction d/t chronic ischemia
- Clinically: insidious onset of CHF after recurrent M.I

Morphology

- Enlarged, heavy heart due to L.V hypertrophy/ dilation
- Atherosclerosis of coronary vs
- Grey-white scars of healed infarcts
- Diffuse subendocardial vacuolation (atrophy of cardiac muscle fibres)

Sudden Cardiac Death

- Unexpected death due to cardiac causes within 1 hour of onset of symptoms or even without symptoms
- SCD is a complication and often1st manifestation of IHD
- Sudden plaque rupture→thrombosis/embolism → myocardial ischemia → fatal ventricular arrhythmia
- Victims of SCD most often have marked coronary atherosclerosis, only 10-20% have non- atherosclerotic conditions
- Most often the ultimate cause of death is arrhythmia (asystole/ V tach/ fibrillation)
  - Due to ischemia of the conduction system or
  - Electrical irritability of the ischemic myocardium

Nonatherosclerotic causes:

- Aortic valve stenosis
- Myocarditis
- Hereditary or acquired abnormalities of cardiac conduction system
- Pulmonary hypertension
- Congenital abnormalities
- Isolated hypertension/ hypertrophy

Morphology

- High grade stenosis with plaque disruption
- Features of previous M.I/ chronic ishemia in form of subendocardial vacuolization
- There may no morpholgic abnormality