Pathology team 441

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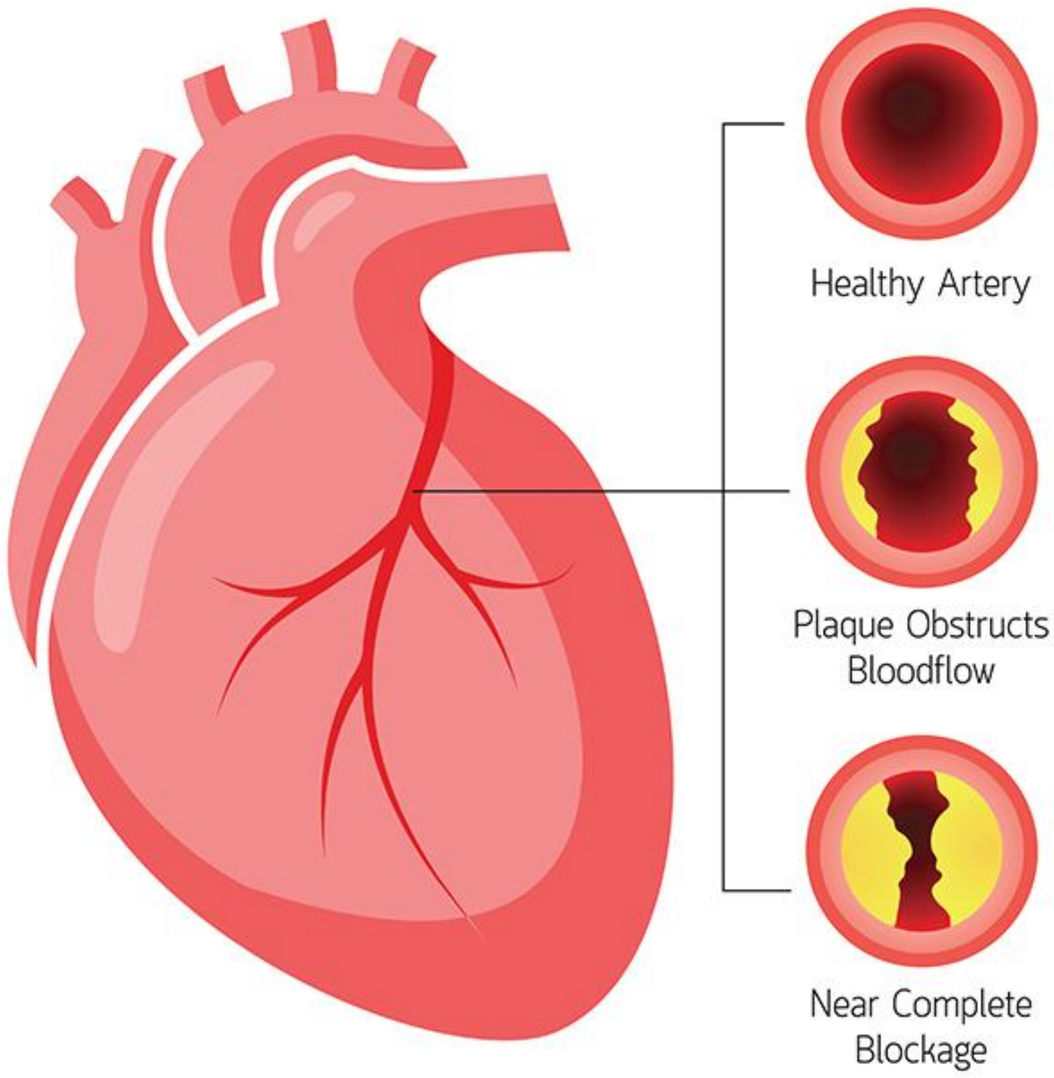
MED441
KING SAUD UNIVERSITY

# Ischemic heart disease




## Editing File

**Color Index:**

- Main text
- **Important**
- Boys slides
- Girls slides
- Dr's notes
- Extra

# Objectives

1. Be able to discuss pathology and complications of ischaemic heart diseases with special emphasis on myocardial infarction.

2. Know how lifestyle modifications can reduce the risk of ischaemic heart disease.

3. Know how lifestyle modifications can reduce the risk of ischemic heart diseases

# Ischemic Heart Disease

-Helpful video

## Definition

IHD = A group of closely related conditions/syndromes caused by an imbalance between the myocardial oxygen demand and blood supply . Usually caused by decreased coronary artery blood flow ("**coronary artery disease**") .
Ischemia: is an insufficient blood supply

The **most common** cause if IHD is coronary artery atherosclerosis , and Less commonly it is due to vasospasm and vasculitis .

## Related conditions \ syndromes

- Acute myocardial infarction (with e.g necrosis)
- Angina pectoris (chest pain) (no necrosis)
- Chronic ischemic heart disease with CHF
- Sudden cardiac death

## Epidemiology of Ischemic Heart syndromes Disease

- Peak incidence: 60y for males and 70y for females.
- Men are more affected than women. (women has estrogen for protection).
- **Contributing factors** are same as that of atherosclerosis e.g.
  - Diabetes mellitus
  - Hypertension
  - Smoking
  - Genetic factors (direct or indirect)
  - High levels of LDL (Cholesterol)
  - Lack of exercise

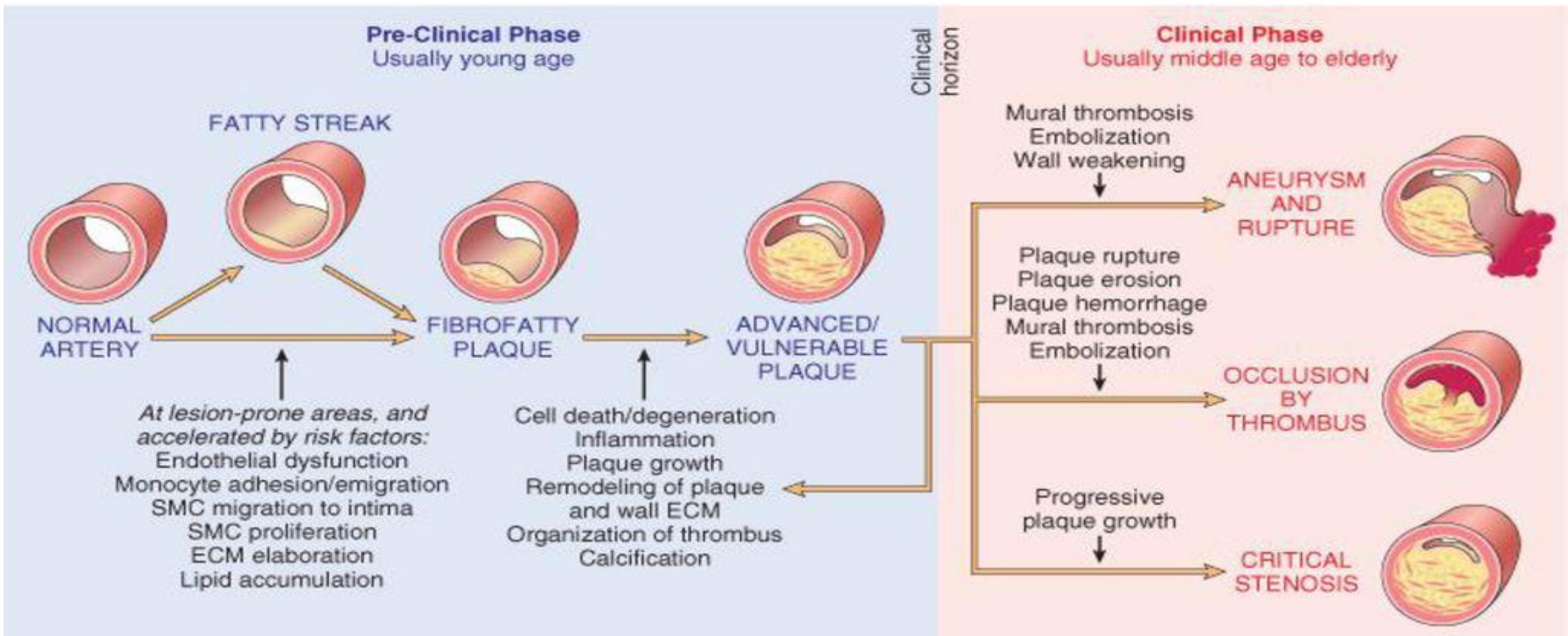
## Pathogenesis of IHD

1. Role of Critical stenosis or obstruction
2. Role of Acute Plaque Change
3. Role of Coronary Thrombus
4. Role of Vasoconstriction
5. Role of Inflammation

# Pathogenesis of IHD

1- Role of Critical stenosis or obstruction, Will lead to

(>=75% of the lumen of one or more) (coronary arteries blocked by atherosclerotic plaque).



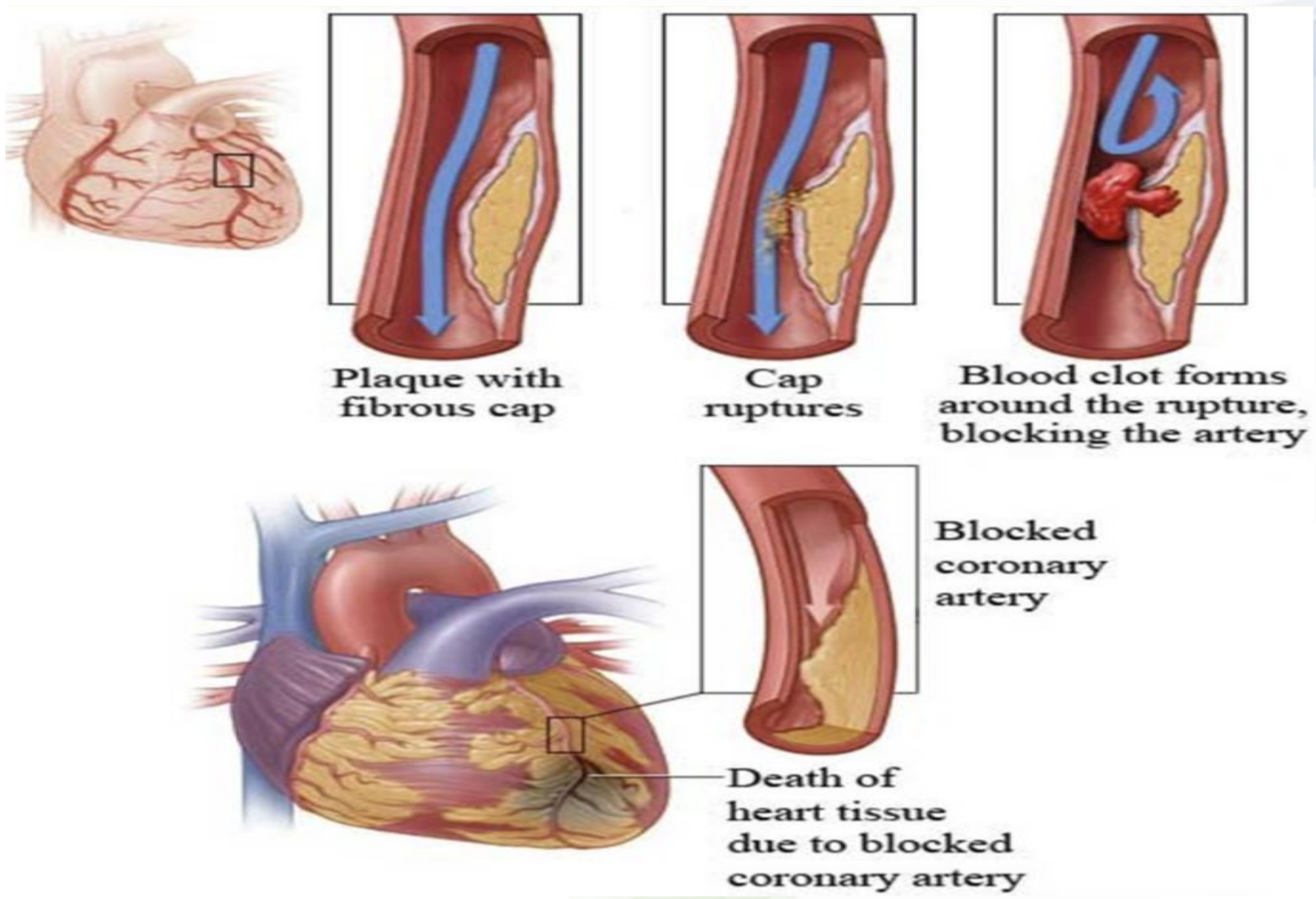

2- Role of Acute Plaque Change

Disruption of a mildly stenosing plaque leading to rupture/ ulceration which can lead to:

1. hemorrhage into the atheroma which will expand in volume
2. exposure of the pro-thrombogenic basement membrane just below the endothelial cells → thrombosis → the formed thrombus will further block the lumen of the blood vessel

So, Acute plaque change can cause myocardial ischemia in the form of:

**a. unstable angina**
**b. acute myocardial infarction**
**c. and sudden cardiac death**



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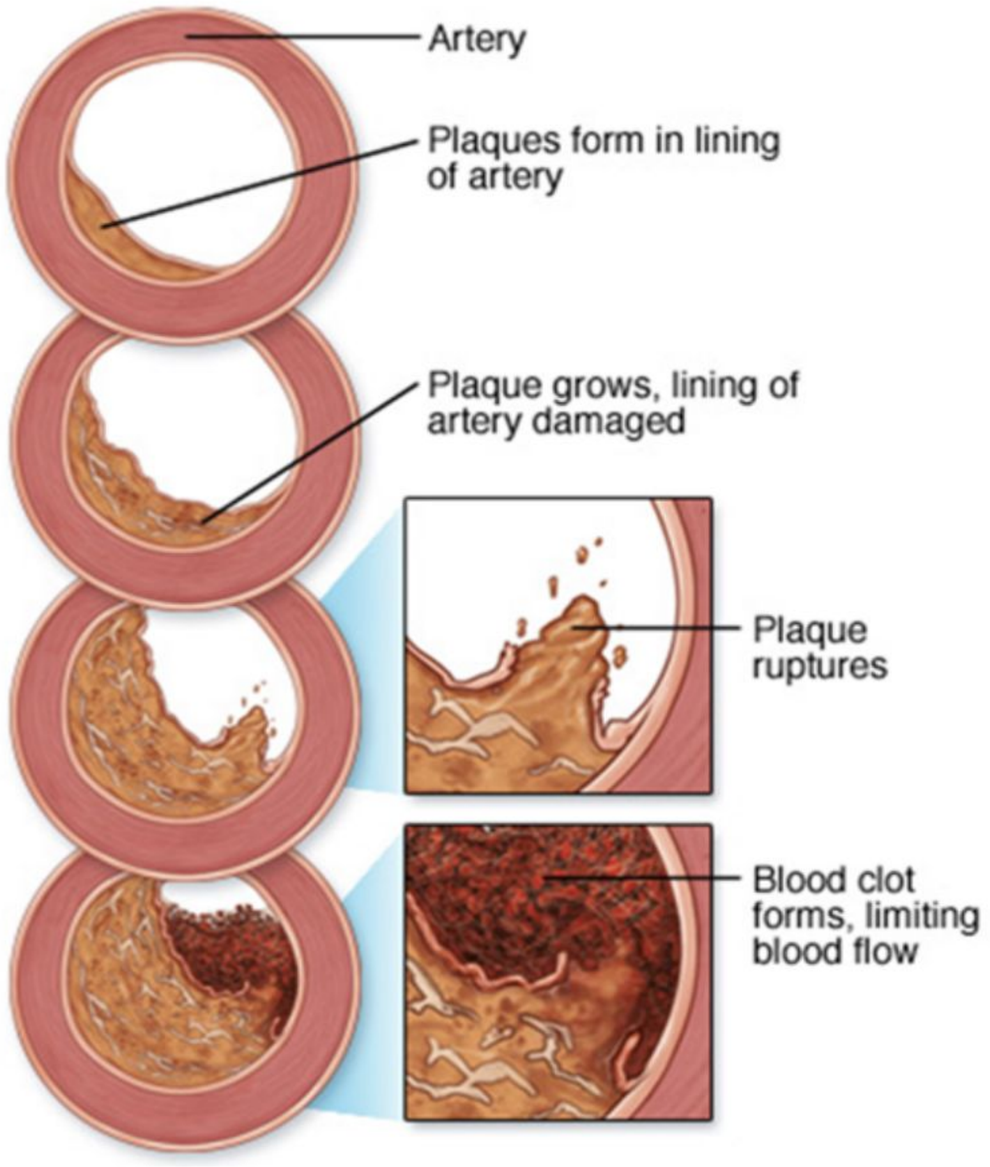
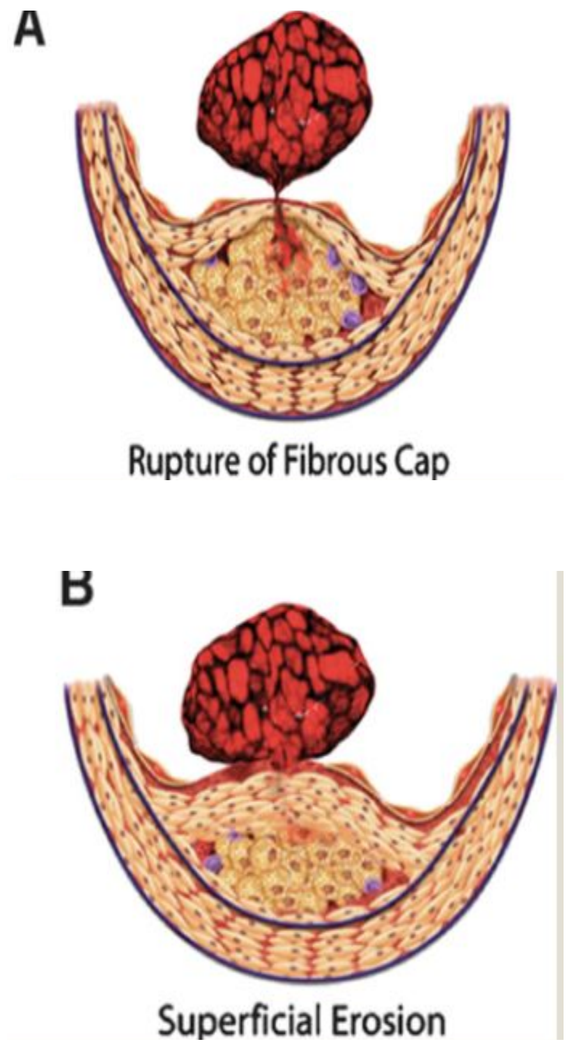



## 3- Role of Coronary Thrombus

Thrombus in coronary artery can also embolize .

Thrombus superimposed on a disrupted partially occluding plaque can convert the plaque to either

1.A total occlusion leading to acute transmural MI or sudden death.

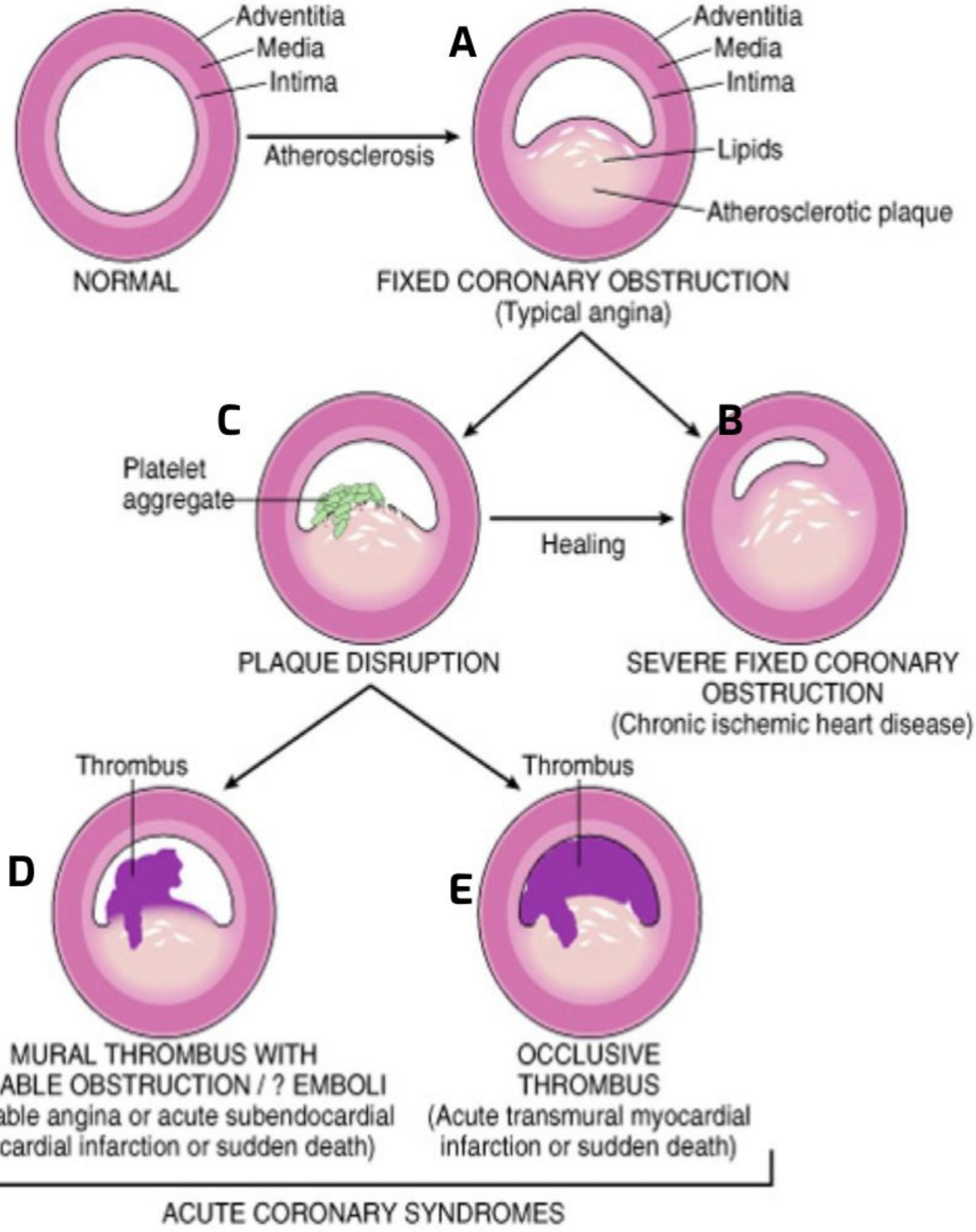
2. Or a partial/incomplete/subtotal occlusion leading to unstable angina, acute subendocardial infarction, or sudden death.

## 4- Role of Vasoconstriction

Vasoconstriction reduces lumen size and can therefore potentiate plaque disruption (lumen become more narrow)

## 5- Role of Inflammation

Inflammatory processes play important roles at all stages of atherosclerosis




**A:** We have fixed coronary obstruction (Typical Angina), Atherosclerotic Plaque in the intima blocks 70% of the vessel.

**B:** Severe Fixed coronary artery, more than 70% is blocked (not important)

**C:** When the Plaque is disrupted it can lead to D AND E .

**D:** Mural thrombus with a Non complete obstruction (causes Unstable angina or acute subendocardial myocardial infarction or sudden death.)

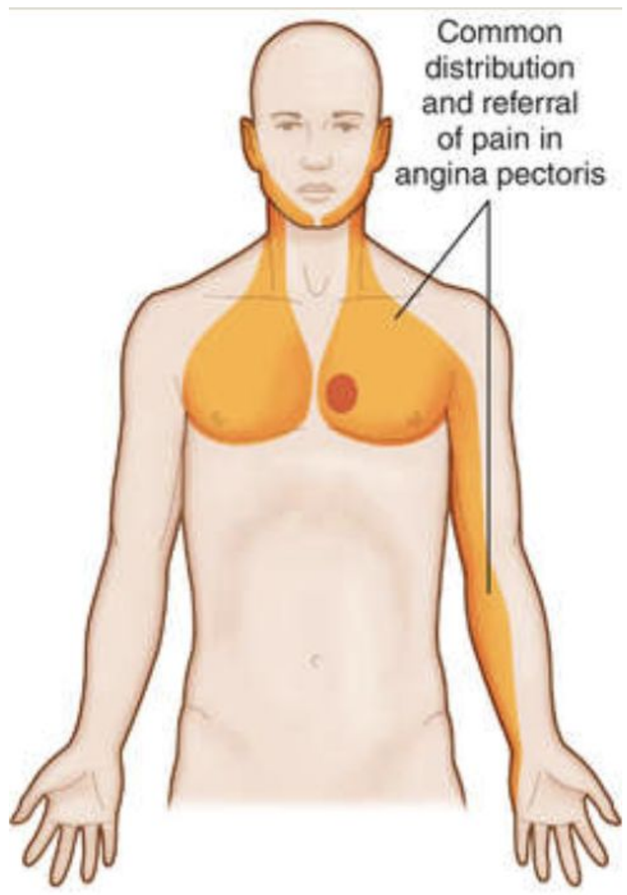
**E:** When a complete obstruction happen it causes  Acute transmural myocardial infarction or sudden death.

# Angina pectoris

## Definition

**Angina pectoris** (Chest pain) ,is a type of IHD characterized by paroxysmal(episodic) and usually recurrent attacks of substernal or precordial chest discomfort.

- described as constricting, crushing, squeezing, choking, or knifelike pain.
- The pain can **radiate** down the left shoulder, left arm, neck or left jaw (called as referred pain).



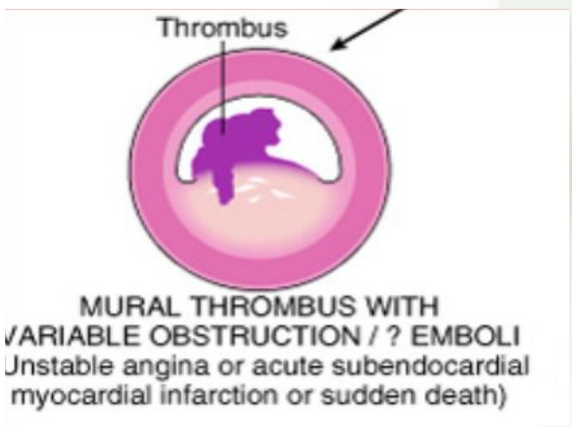

## Cause

Angina pectoris is due to inadequate (lack of) perfusion and is caused by **transient (15 seconds to 15 minutes) myocardial ischemia** that falls short of inducing necrosis i.e. duration and severity is not sufficient to cause infarction(irreversible injury)

## Types of Angina pectoris

- Stable angina
- Unstable angina
- Variant angina

# Types of angina pectoris

| Stable Angina (Typical Angina) | Unstable or crescendo Angina | Variant (prinzmetal) Angina |
|---|---|---|
| • Is the most common form of angina<br>Is due to a fixed stenosis.<br>The chest pain is episodic.<br>• Is caused by atherosclerotic disease with usually ≥70% narrowing of lumen (i.e. fixed stable critical stenosis).<br>• This reduction (due to ≥ 70% stenosis) of blood flow in coronary vessels makes the heart vulnerable, so whenever there is increased demand e.g. physical activity, emotional excitement, or any other cause of increased cardiac workload, there is angina pain.<br>• Relieved by rest (i.e. decreasing demand) or with vasodilators like sublingual nitroglycerin.<br>  <br>SEVERE FIXED CORONARY OBSTRUCTION<br>(Chronic ischemic heart disease) | - It is an unstable and progressive condition.<br>- Pain occurs with progressively increasing frequency, and is precipitated with progressively less exertion or even at rest, and tends to be of more prolonged duration.<br>- It is induced by disruption or rupture of an atheroma plaque (acute plaque change) triggering:<br>• Platelet aggregation<br>• Vasoconstriction<br>• Formation of a mural thrombus that may not be occlusive.<br>- with superimposed thrombosis and partial occlusion of a coronary vessels.<br>Unstable angina is often the precursor of subsequent acute MI. Thus also called as **preinfarction angina**.<br>  <br><br>MURAL THROMBUS WITH VARIABLE OBSTRUCTION / ? EMBOLI<br>(Unstable angina or acute subendocardial myocardial infarction or sudden death) | • uncommon pattern of episodic angina that occurs at rest and is due to coronary artery spasm.<br>• Not related to atherosclerotic disease<br>• The etiology is not clear<br>• Prinzmetal angina generally responds promptly to vasodilators, such as nitroglycerin and calcium channel blockers |

**Angina pectoris summary**

- **intermittent chest pain caused by transient, reversible ischemia**
- **Typical (stable) angina**
  - **pain on exertion**
  - **fixed narrowing of coronary artery**
- **Unstable (pre-infarction) angina**
  - **increasing pain with less exertion**
  - **plaque disruption and thrombosis**
- **Prinzmetal (variant) aIngina**
  - **pain at rest**
  - **coronary artery spasm of unknown etiology**

# Myocardial infarction

-Helpful video

## Definition

The death of cardiac muscle (coagulative necrosis) resulting from ischemia. (the severity or duration of ischemia is enough to cause MI)

## Risk factors

- **Predisposing factors and risk factors** : are the same as those of coronary atherosclerosis.
- Atherosclerosis + age + male gender.
- Females are more affected after menopause due to decreased estrogen production

## Sequence of events usually occur:

1. Long standing atherosclerotic plaque
2. acute plaque change
3. disruption of the plaque
4. thrombus formation
5. ischemia
6. Hypoxia
7. irreversible cell injury
8. Cardiac muscle necrosis

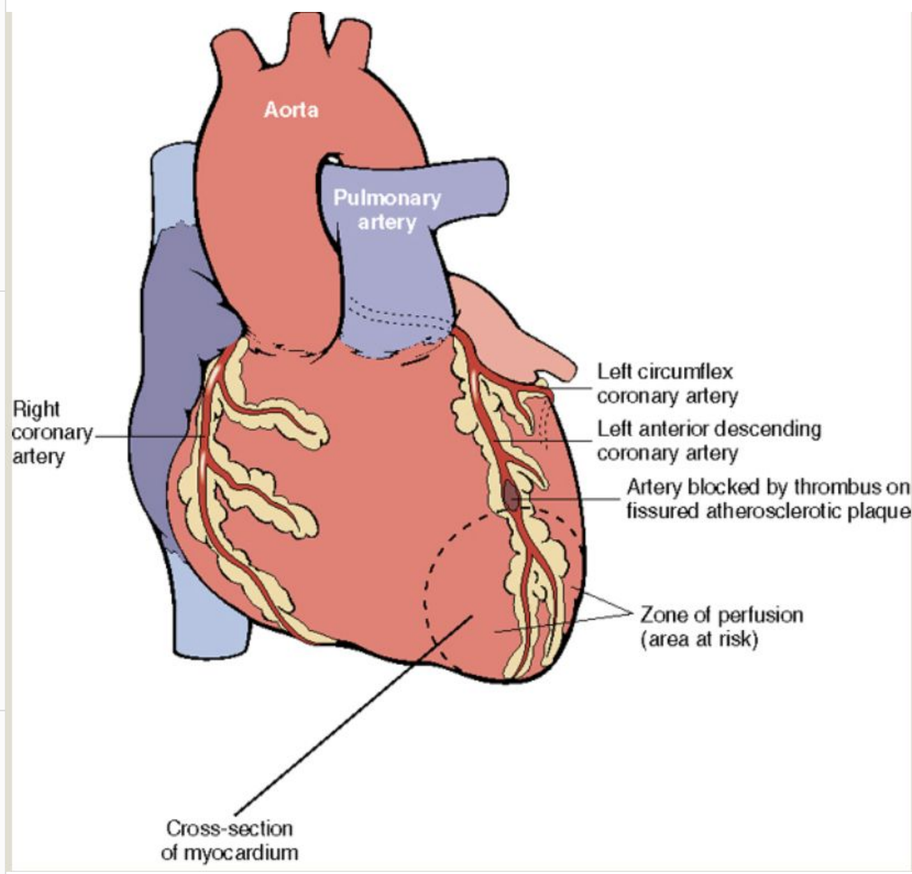
**Note**: the thrombus usually evolves to completely occlude the lumen of the coronary vessel within minutes

# Cont..

## MI common locations

**In persons with right dominant coronary artery heart (90% of population) the commonly affected blood vessels are:**

| | |
|---|---|
| **Left anterior descending artery** | **40-50%**<br>- Anterior left ventricle<br>- Anterior septum<br>- Apex |
| **Left circumflex** | **Up to 20%**<br>Infarct involves lateral left Ventricle except the apex |
| **Right coronary artery** | **30-40%**<br>Posterior left ventricle<br>Posterior septum<br>Right ventricular free wall,sometime |




**Types**

- transmural
  - Full thickness(>50% of the wall)
- subendocardial
  - Inner 1/3 of myocardium
  - Two mechanisms
    - 1-Fixed atherosclerosis but with increased demand,vasospasm or hypotension
    - 2-Evolving transmural with relieve of the obstruction (often multifocal)

# Pathogenesis of MI

Most common cause is **thrombosis** on a preexisting disrupted atherosclerotic plaque. In the typical case of MI, the following sequence of events usually occur:

1. **Acute plaque change** (sudden change in the structure of an atheromatous plaque e.g. disruption, ulceration, rupture or intraplaque hemorrhage).
2. Exposure of the thrombogenic subendothelial basement membrane resulting in **thrombus formation.**
3. **Frequently within minutes**, the **thrombus** evolves to completely **occlude** the lumen of the coronary vessel.

## Severity of ischemia

Severe ischemia lasting at least 20 to 40 minutes causes **irreversible injury** and **myocardial necrosis** on the ultrastructural level (on electron microscopy)

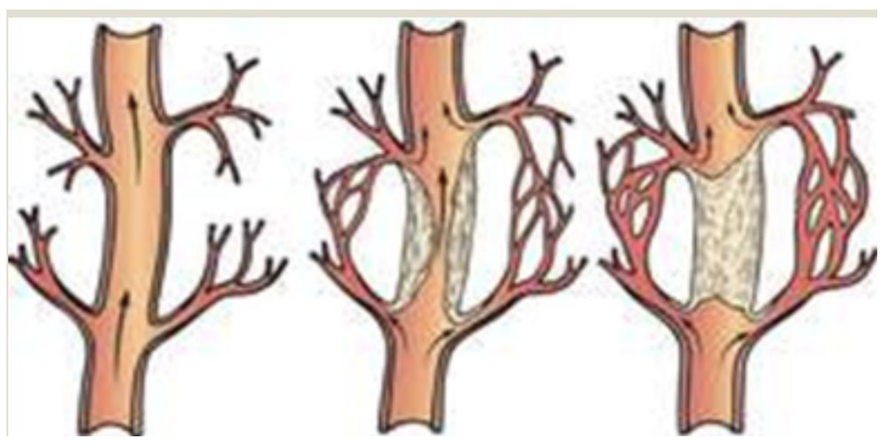
Myocardial necrosis mostly starts in the **sub-endocardial region** (because it is less perfused and has high intramural pressure).

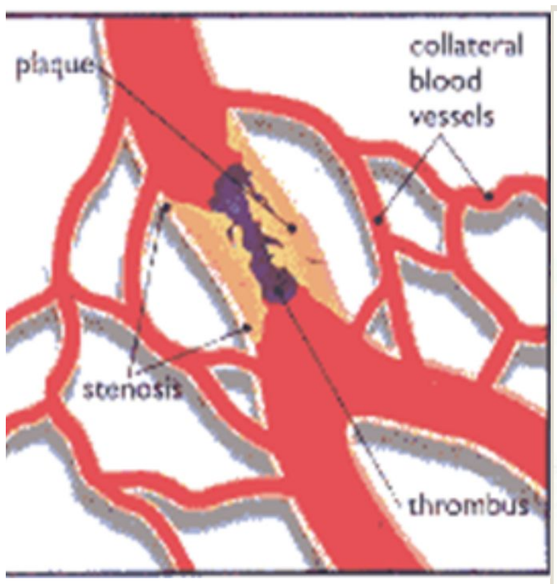
The full size of the infarct is usually determined within **3-6 hours** of the onset of severe myocardial ischemia. During this period,**lysis** of the **thrombus** by treatment with streptokinase or tissue plasminogen activator, may **limit** the size of the infarct. So any intervention in this time frame can potentially limit the final extent of necrosis.

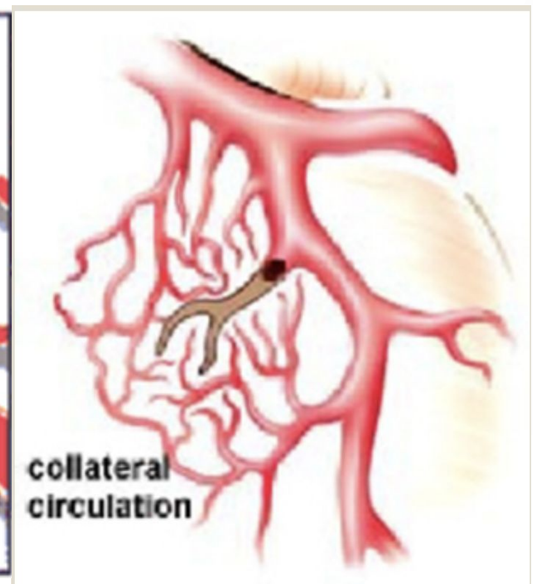
# Con..

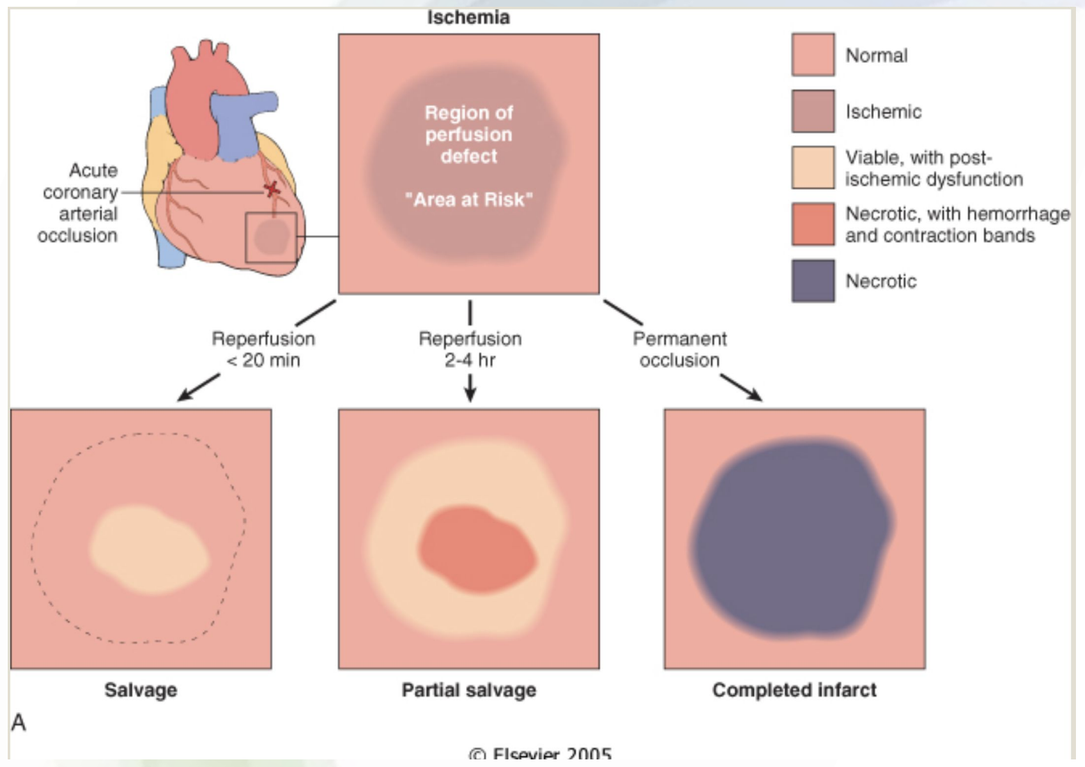
**The precise location, size, and specific morphologic features of an acute myocardial infarct depend on:**

1. The location, severity, and rate of development of coronary atherosclerotic obstructions
2. The size of the area supplied by the obstructed vessels
3. The duration of the occlusion
4. The oxygen needs of the myocardium at risk
5. The extent of collateral blood vessels
6. Other factors, such as blood vessel spasm, alterations in blood pressure, heart rate, and cardiac rhythm.
7. In addition reperfusion may limit the size of the infarct.





# Morphologic changes in MI

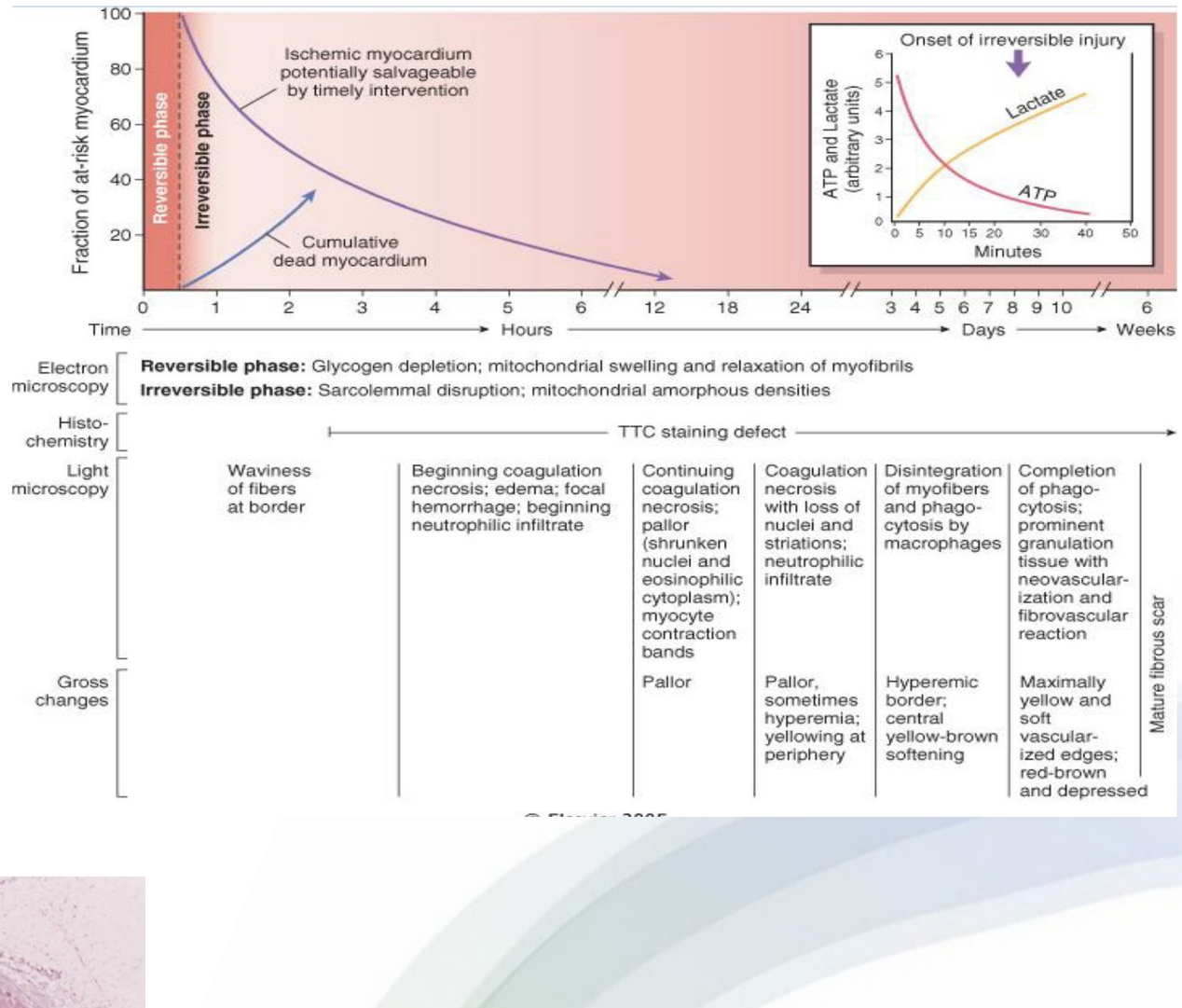
- Begins with coagulative necrosis and inflammation (**initially** neutrophils and **later** macrophages)
- Followed by formation of **granulation tissue**
- Heals by formation of **fibrous scar**

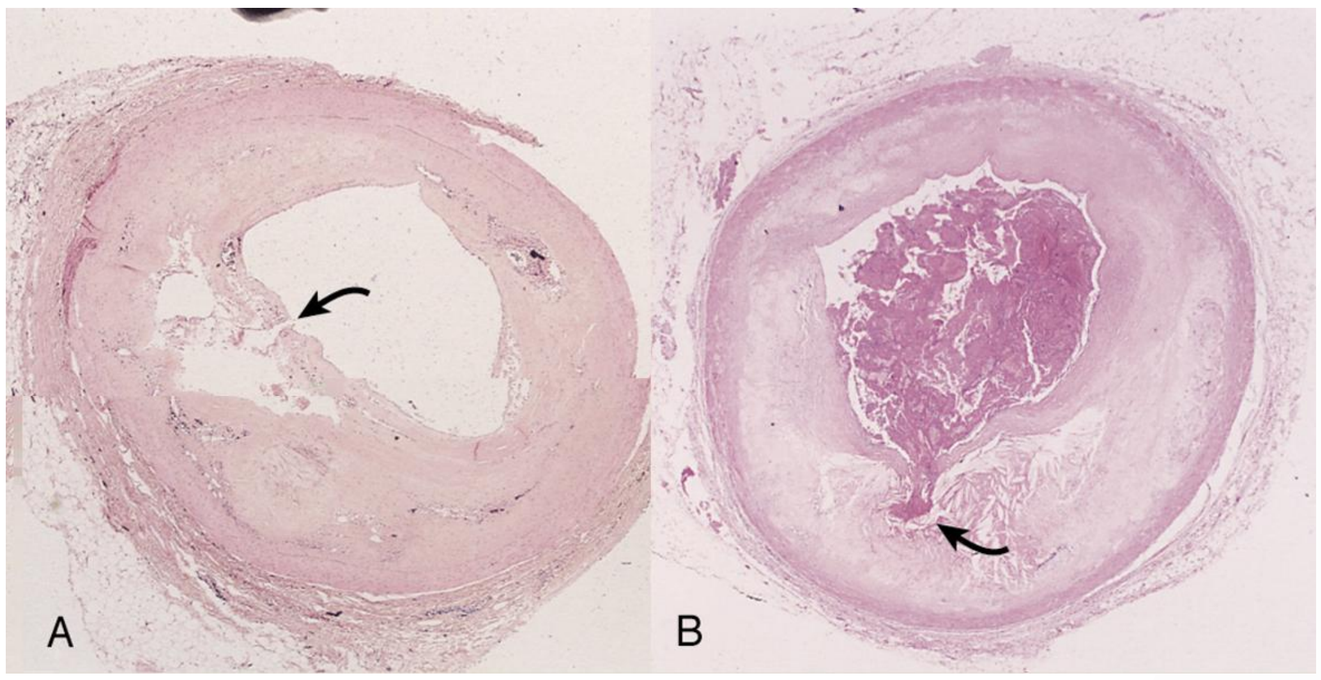
| | Gross changes | Microscopic changes |
|---|---|---|
| **0-4h** | None | None |
| **4-12h** | Mottling | **Coagulation necrosis** |
| **12-24h** | Mottling | Coagulation necrosis , **neutrophils** come in |
| **1-7d** | Yellow infarct center | Neutrophils die, **macrophages** come to eat dead cells |
| **1-2w** | Yellow centar, red borders | **Granulation tissue** |
| **2-8 w** | Scar | **Collagen** |

Additional information (girls Dr)

| Time | Gross Features | Light Microscope | Electron Microscope |
|---|---|---|---|
| **REVERSIBLE INJURY** | | | |
| 0–½ hr | None | None | Ralaxation of myofibrils; glycogen loss; mitochondrial swelling |
| **IRREVERSIBLE INJURY** | | | |
| ½–4 hr | None | Usually none; variable waviness of fibers at border | Sarcolemmal disruption; mitochondrial amorphous densities |
| 4–12 hr | Dark mottling (occasional) | Early coagulation necrosis; edema; hemorrhage | |
| 12–24 hr | Dark mottling | Ongoing coagulation necrosis; pyknosis of nuclei; myocyte hypereosinophilia; marginal contraction band necrosis; early neutrophilic infiltrate | |
| 1–3 days | Mottling with yellow-tan infarct center | Coagulation necrosis, with loss of nuclei and striations; brisk interstitial infiltrate of neutrophils | |
| 3–7 days | Hyperemic border; central yellow-tan softening | Beginning disintegration of dead myofibers, with dying neutrophils; early phagocytosis of dead cells by macrophages at infarct border | |
| 7–10 days | Maximally yellow-tan and soft, with depressed red-tan margins | Well-developed phagocytosis of dead cells; early formation of fibrovascular granulation tissue at margins | |
| 10–14 days | Red-gray depressed infarct borders | Well-established granulation tissue with new blood vessels and collagen deposition | |
| 2–8 wk | Gray-white scar, progressive from border toward core of infarct | Increased collagen deposition, with decreased cellularity | |
| >2 mo | Scarring complete | Dense collagenous scar | |

From Boys slide

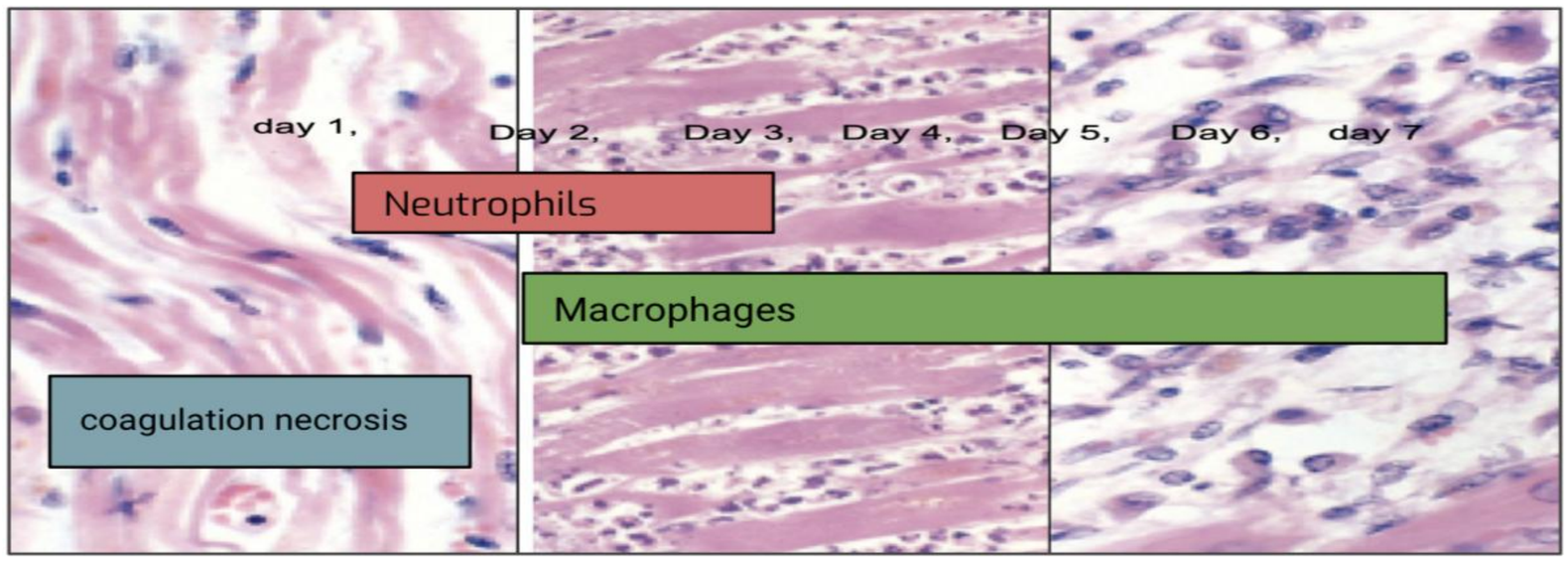


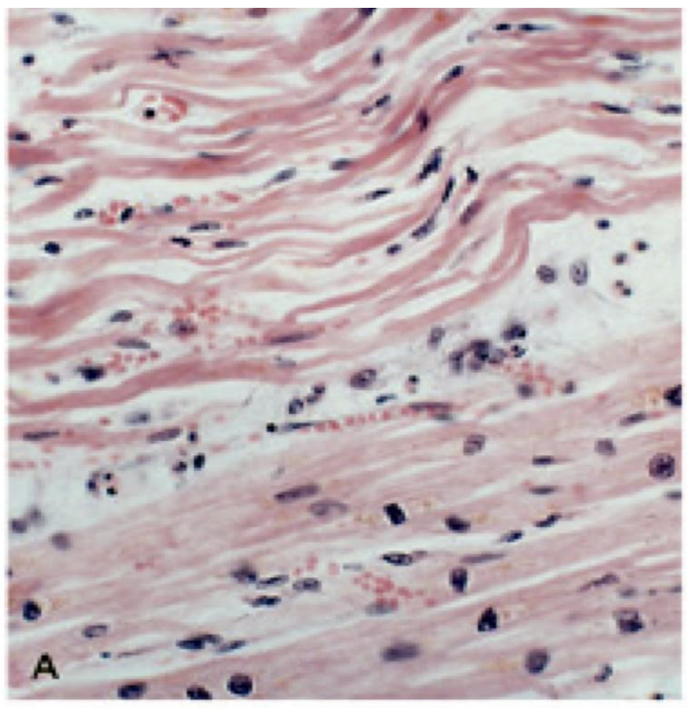




A. plaque rupture without superimposed thrombus in patient who died suddenly

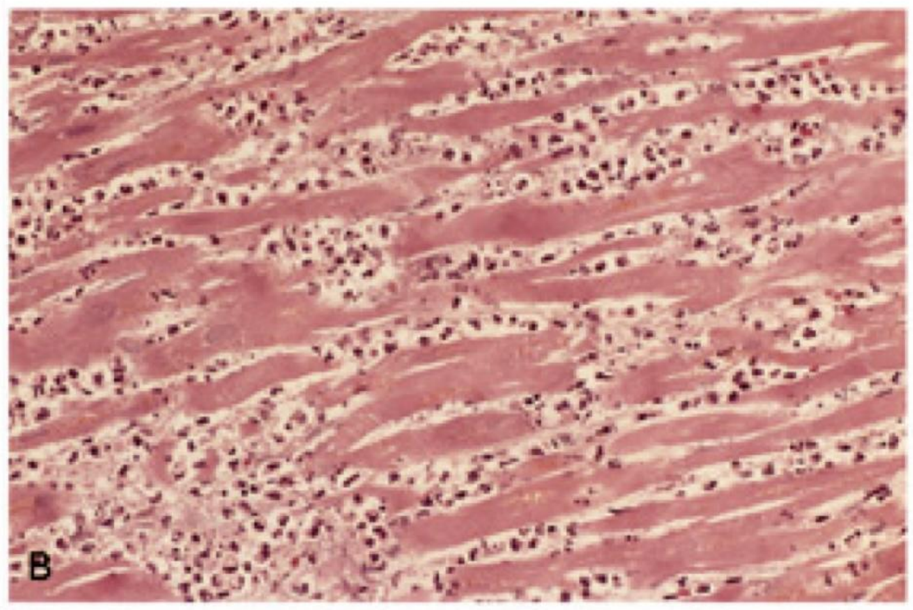
B. Acute coronary thrombosis superimposed on an atherosclerotic plaque with focal disruption of the fibrous cap, triggering fatal myocardial infarction

# Cont.

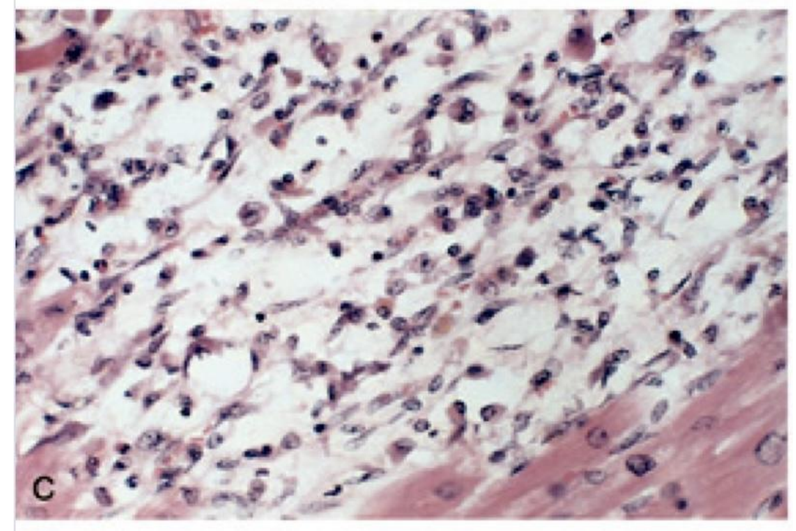


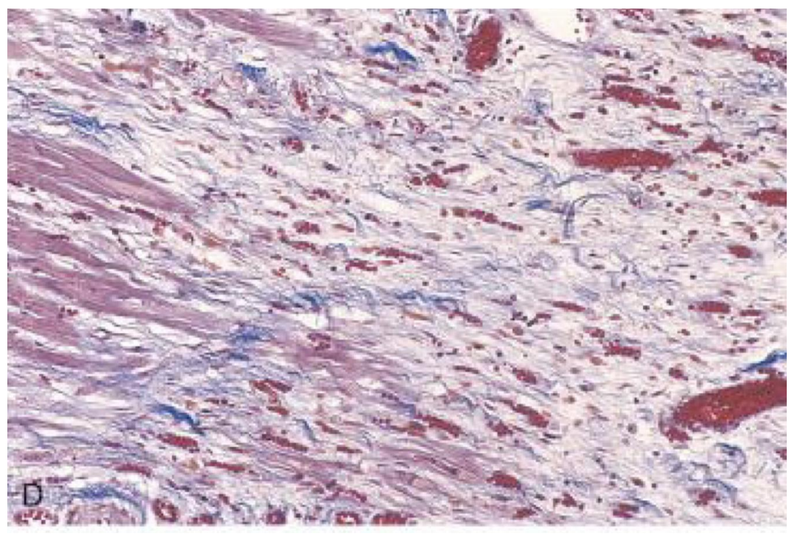

A. One-day-old infarct showing coagulative necrosis with few neutrophils, wavy fibers with elongation, and narrowing, compared with adjacent normal fibers (lower right).



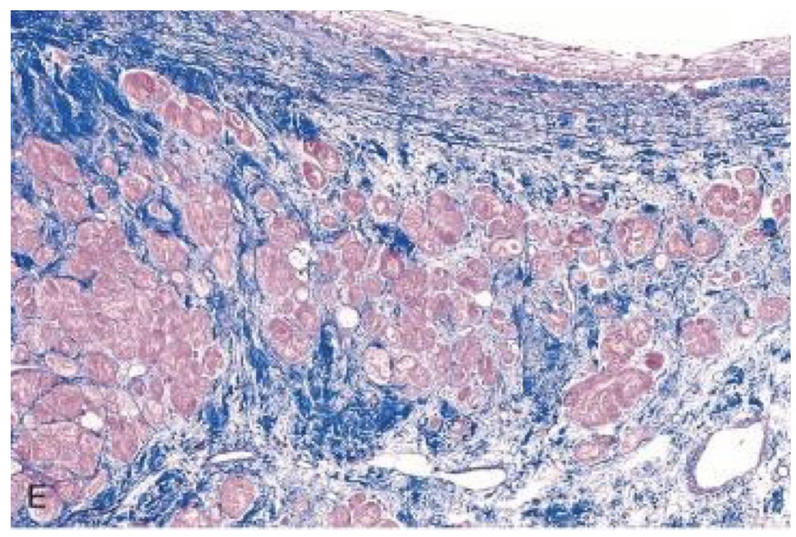

B. Dense neutrophilic infiltrate in an area of acute myocardial infarction of 3 to 4 days' duration.




C. Nearly complete removal of necrotic myocytes by phagocytosis (approximately 7 to 10 days).




Granulation tissue approximately 3 weeks post MI




Healed MI with replacement of the necrotic fibers by dense collagenous scar. Residual cardiac muscle cells are present

# Laboratory evaluation

1

**Troponins**: best marker, TnT, TnI (more specific).

- TnI and TnT are not normally detectable in the circulation
- After acute MI both troponins become detectable after 2 to 4 hours, peaks at 48 hours. Their levels remain elevated for 7 to 10 days

2

**CK-MB** is the second best marker: (for detecting reinfarction)
It begins to rise within 2 to 4 hours of MI, peaks at 24 hours and returns to normal within approximately 72 hours

3

**Lactate dehydrogenase (LD)**:
Rise 24 hrs, peaks 72 hrs, gradually disappears in 5 to 14 days.

4

**Myoglobins**

# Clinical features of MI

**Diaphoresis** (sweating)

rapid and weak **pulse**

**dyspnea**

**Symptoms**

**cardiogenic shock**
can be seen in massive MI (>40% of it. ventricle)

**ECG** shows typical findings of ischemia

changes :
- Q waves ( indicating transmural infarct )
- ST-segment abnormalities
- T-wave inversion

Extra:

Non-ST-segment elevation MI (**NSTEMI**)→ST depression →subendocardial infarct

ST-segment elevation MI (**STEMI**)→ST elevation →transmural infarct

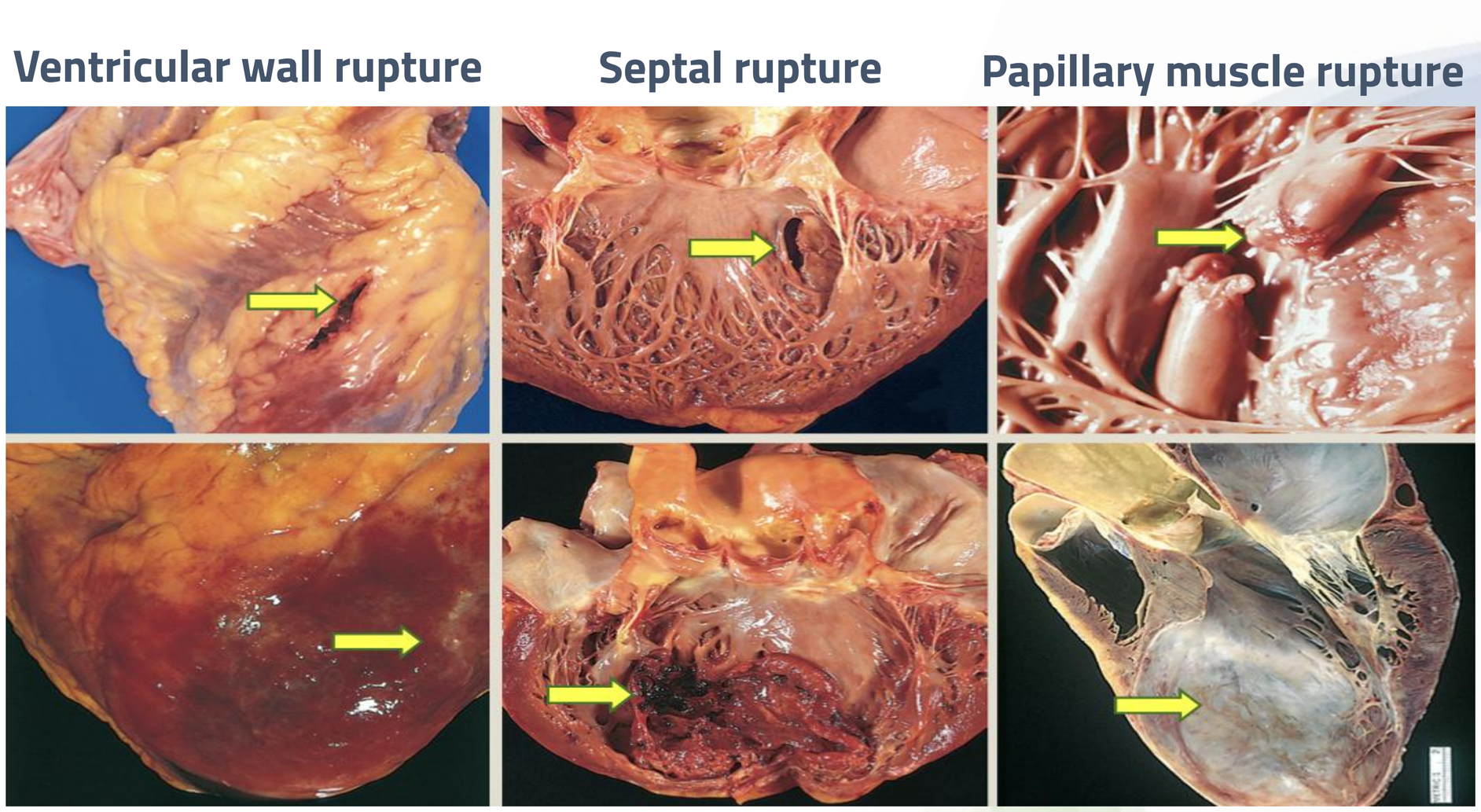
**Pain**:
(the ischemia → release of adenosine, bradykinin → pain)

- Severe crushing sub-sternal chest pain, which may radiate to the neck, jaw, epigastrium, shoulder or left arm.
- Pain lasts for hours to days and is not relieved by nitroglycerin.
- No pain (silent) in 20-30% of patients (diabetics, hypertensive, elderly).

# Complications of MI

- No complications in 10-20%.
- 80-90% experience one or more of the **following complications:**

1. Myocardial infarction lead to sudden death in some cases, even before reaching the hospital.
2. Cardiac arrhythmia (75-90%): patients have conduction disturbances → sudden death esp. in ventricular arrhythmia.
3. Left ventricular failure with pulmonary edema (60%).
4. Cardiogenic shock (10%).
5. Myocardial rupture: rupture of free wall, septum, papillary muscle.
6. Thromboembolism (15-49%): the combination of myocardial abnormality in contractility (causing stasis) and endocardial damage (due to exposure of underlying thrombogenic basement membrane) can lead to cardiac thrombosis and embolism.
7. Pericarditis
8. Infarct extension and expansion
9. External rupture of the infarct with associated bleeding into the pericardial space (hemopericardium).
10. Ventricular aneurysm (ventricle is dilated and the wall is thinned out).
11. Progressive late heart failure in the form of chronic IHD.



قال تعالى: {وَمَن يَتَوَكَّلْ عَلَى اللَّهِ فَهُوَ حَسْبُهُ}

قال ابن القيم : لو أن أحدكم هَمّ بإزالة جبل وهو واثق بالله لأزاله

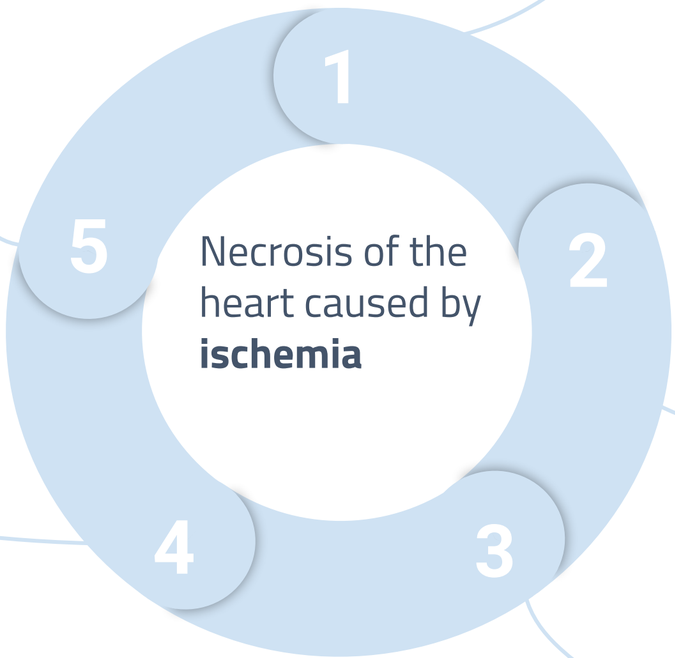
# Cont.

## Laboratory evaluation

- **Troponins** increase within 2-4 hours, remain elevated for a week.
- **CK-MB** increases within 2-4 hours, returns to normal within 72 hours

# Summary of MI

Girls slide




## due to acute coronary artery thrombosis

- sudden plaque disruption
- platelets adhere
- coagulation cascade activated
- thrombus occludes lumen within minutes
- irreversible injury/cell death in 20-40 minutes

## Clinical features

- Severe, crushing chest pain ± radiation
- Not relieved by nitroglycerin, rest
- Sweating, nausea, dyspnea
- Sometimes no symptoms

## complication

- contractile dysfunction
- arrhythmias
- rupture
- chronic progressive heart failure

## Prognosis

- depends on remaining function and perfusion
- Prompt reperfusion can salvage myocardium

# Chronic ischemic heart disease

Girls Dr For your level just this

Progressive heart failure due to ischemic injury, either from:

- prior infarction(s) (most common)
- or chronic low-grade ischemia

# sudden cardiac death

**Definition**: Unexpected death from cardiac causes either without symptoms or within 1 to 24 hours of symptom onset

→ Results from a fatal arrhythmia, most commonly in patients with severe coronary artery disease

# Acute coronary syndrome (boys slide)

- is applied to three catastrophic manifestations of IHD:

- Unstable angina
- Acute MI
- Sudden cardiac death

MED441
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