

Pathology

teamwork

Lecture (3):

Ischemic heart disease, angina, and MI.

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Revised by

Editing File

Color Index :-

- VERY IMPORTANT**
- Extra explanation
- Examples**
- Diseases names: Underlined**
- Definitions**

*وإنَّ الطَّبَّ مَهْنَةٌ كُلُّ حُرٍّ، رَأَى أَنْ يَبْدَلَ الْجَهْدَ اجْتِهَادًا

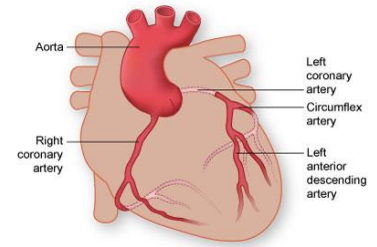
Objectives :

- Understand the pathogenesis and clinical consequences of atherosclerosis.
- Be able to discuss pathology and complications of ischemic heart diseases with special emphasis on myocardial infarction.
- Know how lifestyle modifications can reduce the risk of ischemic heart diseases.

Key principles to be discussed:

- Risk factors of atherosclerosis.
- Pathogenesis of the fibro lipid atherosclerotic plaque.
- Clinical complications of atherosclerosis.
- Commonest sites for the clinically significant coronary atherosclerosis.
- Macroscopic and microscopic changes in myocardial infarction.
- Biochemical markers of myocardial infarction.
- Complications of myocardial infarction: immediate and late.

Ischemic Heart Disease/IHD (Coronary Heart Disease)



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”)

Four syndromes:

Angina pectoris
(Chest Pain)

Acute
Myocardial
Infarction

Sudden Cardiac
Death

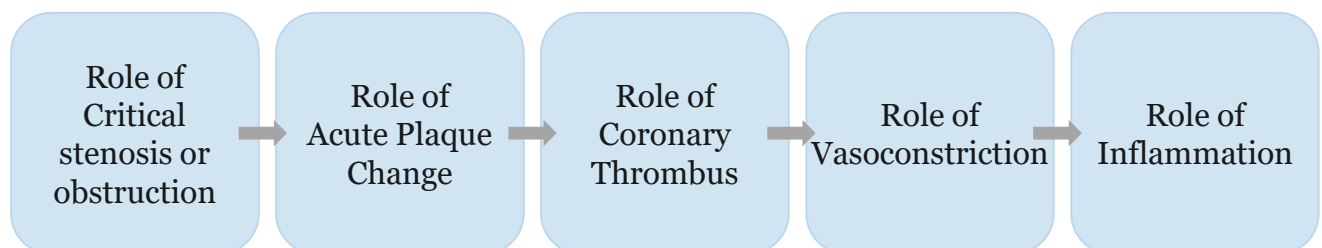
Chronic ischemic
heart disease with
congestive heart
failure

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

Epidemiology

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

Pathogenesis



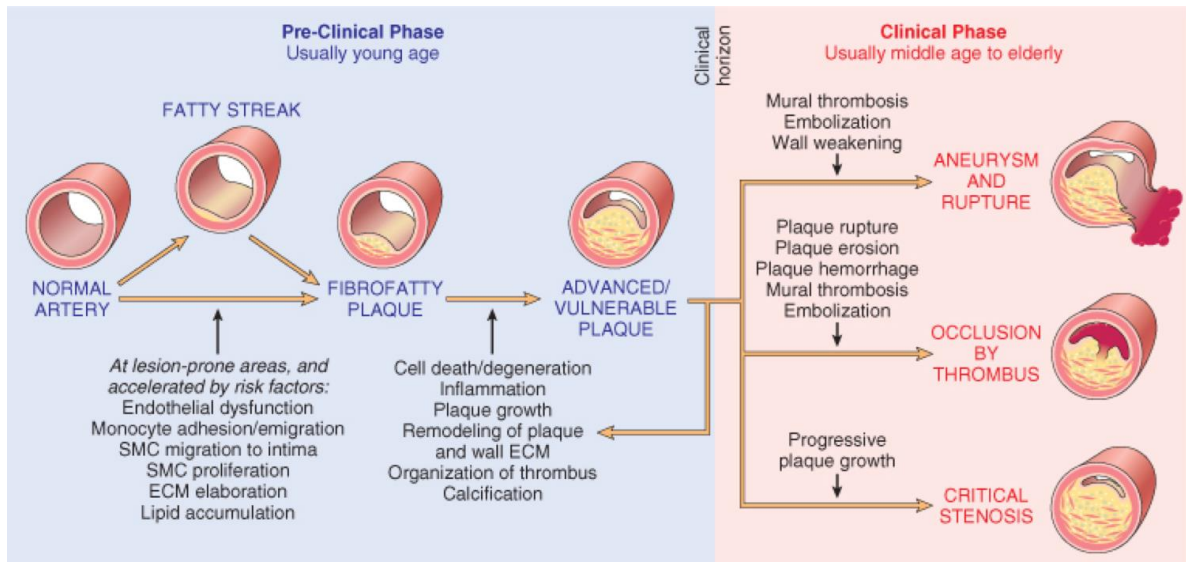
-Ischemic heart disease is caused by atherosclerosis, which means insufficient blood supply to the myocardium.

-Myocardial infarction → full obstruction → no blood supply

Pathogenesis of Ischemic Heart Disease

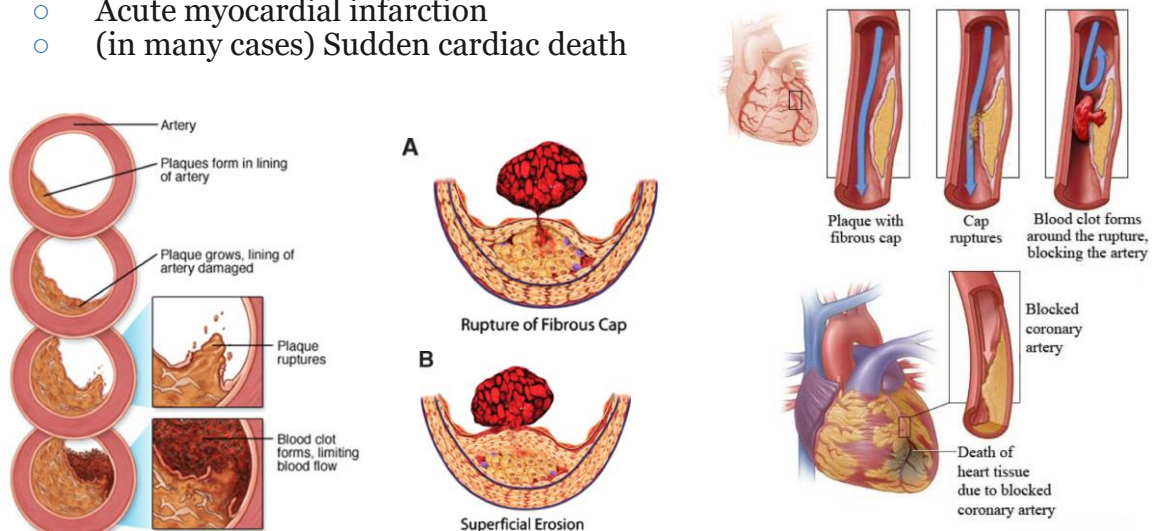
1. Role of Critical stenosis or obstruction:

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



2. Role of Acute Plaque Change:

- Disruption of a mildly stenosing plaque leading to rupture/ ulceration. This can lead to:
 - Hemorrhage into the atheroma which will expand in volume.
 - Exposure of the thrombogenic basement membrane just below the endothelial lining followed by thrombosis
- Acute plaque change can cause myocardial ischemia in the form of:
 - Unstable angina
 - Acute myocardial infarction
 - (in many cases) Sudden cardiac death



Acute plaque change → rupture/ulceration → thrombus formation → total blockage → myocardial infarction → hypoxia → cell injury (reversible or irreversible)
(if irreversible → coagulation necrosis) as in MI

3. Role of Coronary Thrombus:

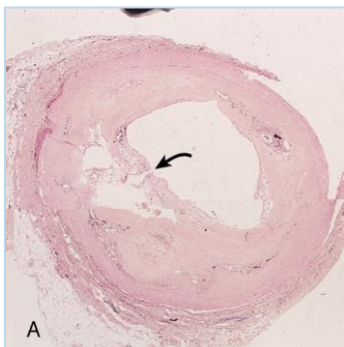
- Thrombus superimposed on a disrupted partially occluding plaque can convert the plaque to either
 - A total occlusion leading to acute transmural MI. (full thickness of the muscle)
 - Or a partial/incomplete/subtotal occlusion leading to unstable angina, acute subendocardial infarction, or sudden cardiac death.
- Thrombus in coronary artery can also embolize.

4. Role of Vasoconstriction:

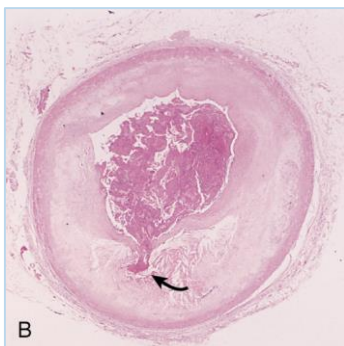
Vasoconstriction reduces lumen size and can therefore potentiate plaque disruption.

5. Role of Inflammation:

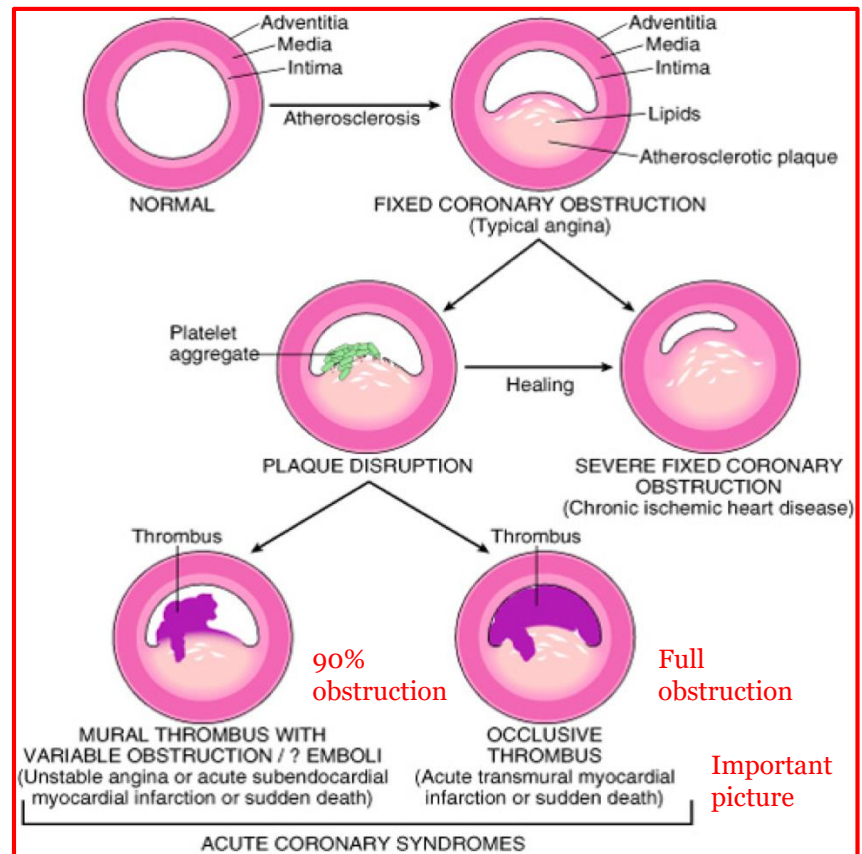
Inflammatory processes play important roles at all stages of atherosclerosis.



A
Plaque rupture without superimposed thrombus in a patient who died suddenly.



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



Ischemic Heart Disease

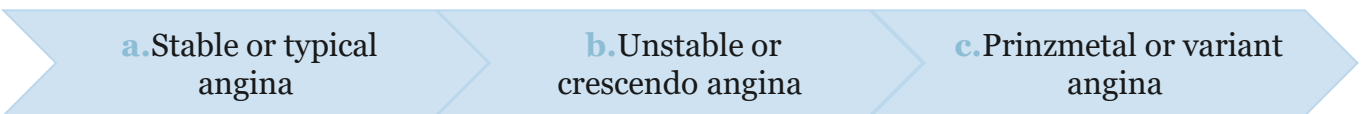
Four closely related conditions/syndromes that come under IHD are:



*both angina pectoris and MI has ischemia and hypoxia but the difference between them is that the ischemia in angina pectoris is not enough to cause necrosis while in MI the ischemia will cause necrosis.

Angina pectoris

- Angina pectoris is a type of IHD characterized by **paroxysmal** (episodes) and usually recurrent attacks of **substernal** or **precordial chest discomfort**, described as constricting, crushing, squeezing, choking, or **knifelike pain**. The **pain may radiate down the left arm or to the left jaw** *(called as **referred pain**(pain felt in a part of the body other than its actual source)).**
- Angina pectoris is due to **inadequate perfusion** and is caused by **transient** (not continuous)(**15 seconds to 15 minutes**) myocardial ischemia that **falls short of inducing the cellular necrosis** that defines infarction i.e. **duration and severity is not sufficient for infarction*****
- There are three types of angina pectoris:



*Why the left side? because the heart is lying on the left side

The patient will complain of episodic substernal pain described as knifelike pain which radiate to the **left arm, neck or jaw

***there will be a non continuous ischemia lasts for 15 sec to 15 min which is not enough to cause necrosis "**there is no necrosis in angina pectoris**"

a. Stable/ typical angina pectoris:*

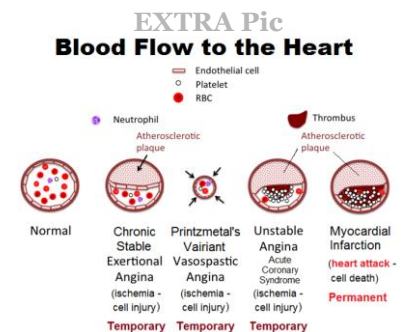
- is the **most common** form of angina.
- It is caused by **atherosclerotic disease** with usually $\geq 70\%$ to 75% narrowing of lumen i.e. (**critical stenosis** or **fixed chronic stable stenosis**).
- This reduction (70 to 75% stenosis) of coronary vessels makes the heart vulnerable (exposed to the possibility of being attacked or harmed, either physically or emotionally), so **whenever there is increased demand**, e.g. **physical activity, emotional excitement, or any other cause of increased cardiac workload, there is angina pain.**
- The chest pain is **episodic** and **associated with exertion or some other form of stress.**
- Is usually **relieved by rest** (thereby decreasing demand) or with a **strong vasodilator** like **nitroglycerin.**

b. Unstable or crescendo (increasing) angina:

- It is an unstable and **progressive condition.**
- Pain occurs with **progressively increasing frequency****, and is precipitated with progressively **less exertion, even at rest**, and tends to be of **more prolonged duration.**
- It is induced by disruption or rupture of an atheroma plaque with **superimposed partial thrombosis.**
- Unstable angina is often the **precursor of subsequent acute MI.** Thus also called as **preinfarction angina** (“morning sign of heart attack” that’s why we can’t send the patient home)

c. Prinzmetal variant angina

- is an uncommon pattern of episodic angina that occurs at rest and is **due to coronary artery spasm.**
- Prinzmetal angina generally **responds promptly to vasodilators**, such as **nitroglycerin and calcium channel blockers.**
- **Not related to atherosclerotic disease**
- The etiology is not clear.



*The patient will have an episodic attack of pain after any exertion or some other form of stress and will be relieved by rest and nitroglycerin

**The patient before, has the pain during climbing stairs

But then, the pain comes during walking then during standing and then it start even at rest

IMPORTANT:

-A lesion obstructing 70%-75% or more of a vessel lumen so called critical stenosis, generally causes symptomatic ischemia (angina) only in the setting of increased demand

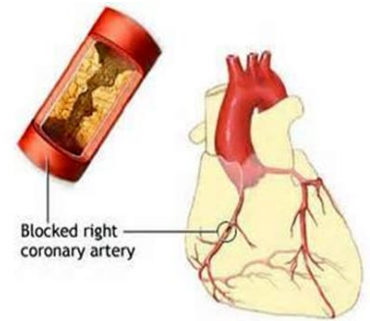
-A fixed 90% stenosis can lead to inadequate coronary blood flow even at rest

In most patients, unstable angina, infarction occur because of abrupt plaque change “rupture, fissuring or ulceration” followed by thrombosis

Myocardial Infarction (MI)

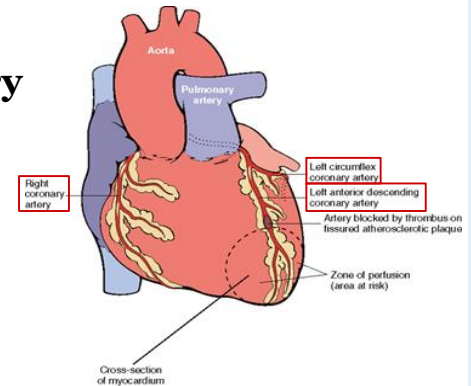
Definition: MI, also known as "heart attack," is the death of cardiac muscle (coagulative necrosis) resulting from ischemia.

Risks are the same as those of coronary atherosclerosis.



The commonly affected coronary vessel in MI in persons with right dominant coronary artery heart (90% of population) are:

- ❖ Left anterior descending artery (40-50%)
- ❖ Right coronary artery (30-40%)
- ❖ Left circumflex artery (about 20%)



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:**

Acute plaque change (sudden **change in the structure of an atheromatous plaque** e.g. disruption, ulceration, rupture or intraplaque hemorrhage).

Exposure of the thrombogenic subendothelial basement membrane resulting in **thrombus formation**.

Frequently within minutes, the thrombus evolves to **completely occlude the lumen** of the coronary vessel.

- ❖ **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). **It's begins within 20-30 minutes**.
- ❖ **The full size of the infarct** is usually determined **within 3-6 hours (mainly 4 hours)** of the onset of severe myocardial ischemia. During this period, lysis of the thrombus by 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. **Treatment up to 6 hours may help. After 6 hours, no response.**

*streptokinase used to break down clots.

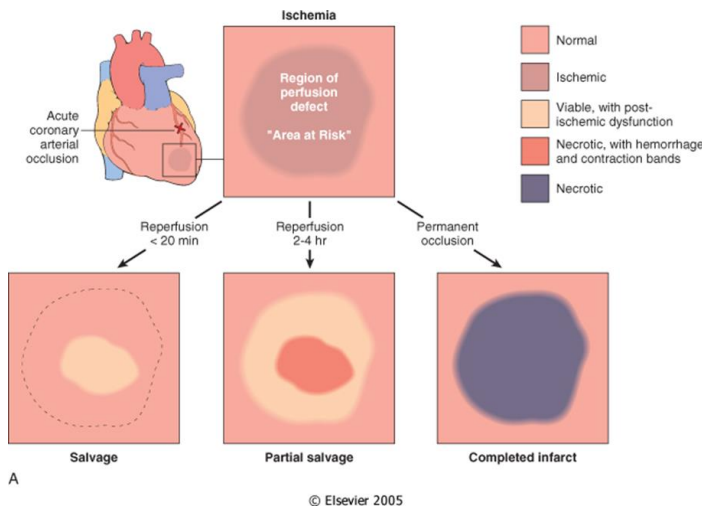
** Plasminogen is the precursor of plasmin, which lyses fibrin clots to fibrin.

-MI is a complete obstruction due to atherosclerosis that lead to thrombosis.

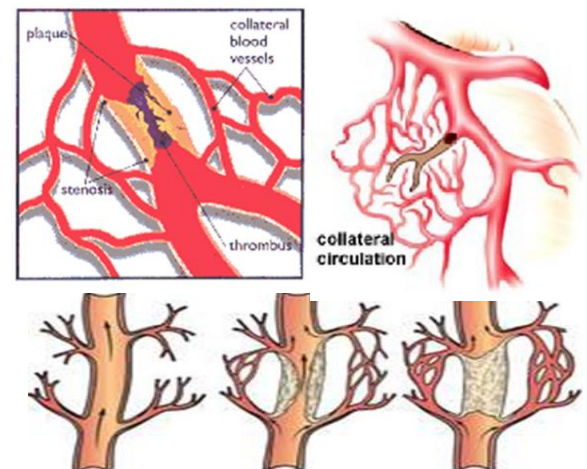
Pathogenesis of MI

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.



Collateral circulation



MI types and morphology

❖ TYPES:

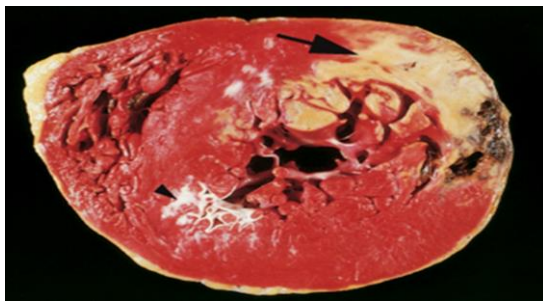
1. **Transmural:** Full thickness (>50% of the wall).
2. **Subendocardial:** Inner 1/3 of myocardium.

❖ MORPHOLOGY:

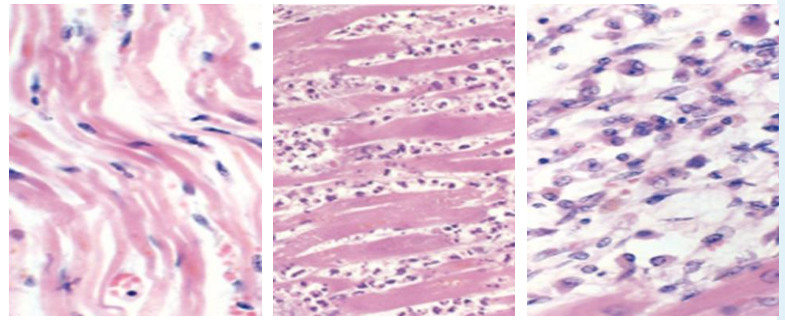
- Begins with **coagulative necrosis** and inflammation (initially mainly neutrophils and later macrophages).
- Followed by formation of granulation tissue.
- Heals by formation of a fibrous scar.

Morphologic Changes in Myocardial Infarction

Time	Gross changes	Microscopic changes
0 - 4h	None	None, by electron microscope you see necrosis (not seen in LM)
4 - 12h	Mottling تبقع	Coagulation necrosis
12- 24h	Mottling	More coagulation necrosis; neutrophils come in
2 - 7d	Yellow infarct center	Neutrophils die, macrophages come to eat dead cells
1 - 2w	Yellow center, red borders	Granulation tissue
2 - 8w	Scar	collagen (fibrosis)



Acute Myocardial Infarction



MI: day 1, day 3, day 7

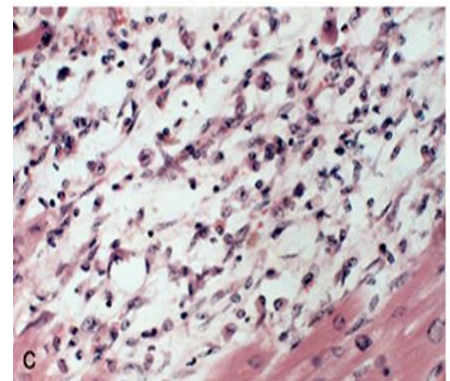
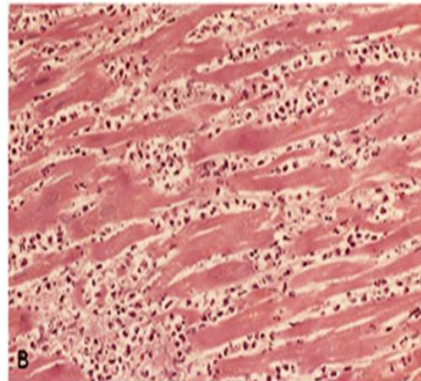
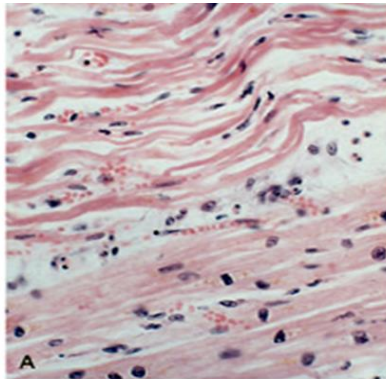
Microscopic features of myocardial infarction

- 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).

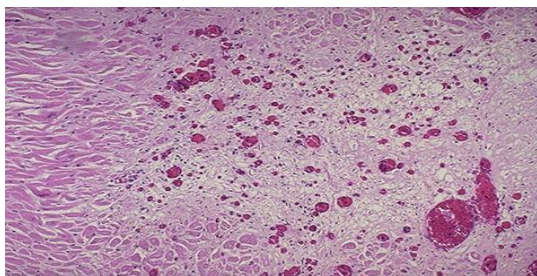
(A)

(B)

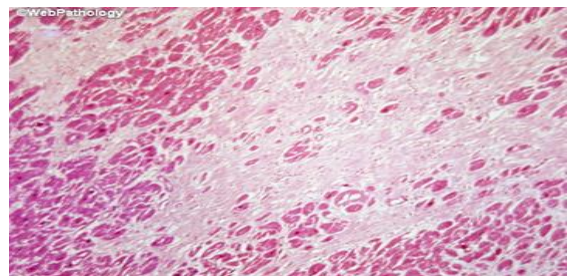
(C)



**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**



Myocardial Infarction: Clinical Features

- ❑ **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**. Sublingual to minimize pain.
 - No pain in 20-30% of patients (**diabetics, hypertensive, elderly**).
- ❑ **Pulse is rapid and weak.**
- ❑ **Diaphoresis (sweating) , Dyspnea.**
- ❑ **Cardiogenic shock can be seen in massive MI (>40% of Lt. ventricle).**
- ❑ **ECG shows typical findings of ischemia.**

Ischemic Heart Disease Laboratory evaluation

Time is important

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**:

- ❖ It begins to rise within **2 to 4 hours** of MI, **peaks at 24 to 48 hours** and returns to **normal within approximately 72 hours**. So at day 3, if you find normal CK-MB; it doesn't mean that your patient doesn't have MI.

3- Lactate dehydrogenase (LD)... LD1.

- ❖ Rise 24 hrs, peaks 72 hrs, persists 72 hrs.

Myocardial Infarction: Outcomes or complications

- ❑ **No complications in 10-20%.**
- ❑ **80-90% experience one or more of the following complications:**
 - Cardiac **arrhythmia*** (75-90%). Patients have conduction disturbances and myocardial irritability which **can lead to sudden death** especially in ventricular arrhythmia.
 - **Left ventricular failure** with mild to severe pulmonary edema (60%).
 - **Myocardial rupture**** : Rupture of free wall, septum, rupture of papillary muscle (leading to papillary muscle and associated valve incompetence/dysfunction)
 - **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
 - Pericarditis , Progressive **late heart failure** in the form of chronic IHD.
 - Infarct **extension and expansion**, **Cardiogenic shock** (10%).
 - Ventricular aneurysm in which the ventricle is dilated and the wall is thinned out.
 - External **rupture** of the infarct with associated bleeding into the pericardial space (hemopericardium).

-MI may be asymptomatic. For example, diabetics having MI most likely won't develop chest pain.

*Most common cause of sudden death.

** Leading to hemorrhage & could cause death.

Chronic ischemic heart disease & Sudden cardiac death

Chronic ischemic heart disease

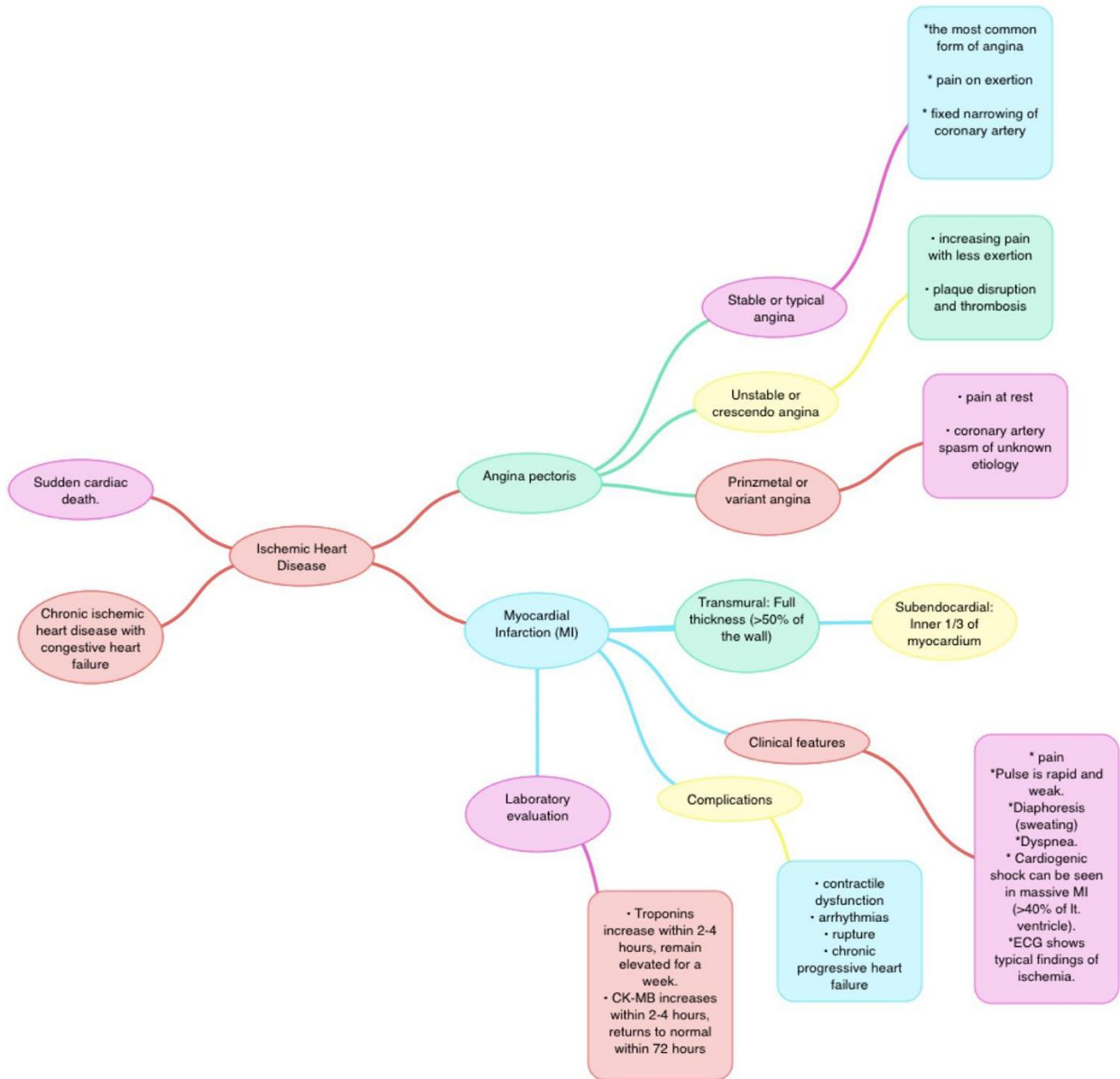
Progressive heart failure due to ischemic injury, either from:

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

Sudden cardiac death

- 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

Summary



Questions

IMPORTANT

1- A 50-year-old man who had an experience of episodes of severe substernal chest pain every time he performs a task that requires moderate exercise. What is the diagnosis?

- Typical angina pectoris

2- What is the finding in the coronary artery ?

- Atherosclerosis narrowing exceeds 75%.

3- What are the risk factors of this disease ?

- Diabetes mellitus, hypertension, hyperlipidemia, smoking, Age, male, genetics familial

4- What is the pathogenesis for this?

- Endothelial cell injury

5- What are possible complications for this disease?

- Cerebral infarction, myocardial infarction , aortic aneurysm, gangreneetc

6- After a period of time , The previous patient had chest pain even at rest?

- Unstable (preinfarction) angina

7- What are the expected findings in the coronary artery?

- plaque disruption and thrombosis

8- Now the patient suffer from Severe crushing substernal chest pain, which radiate to the left shoulder and arm. ECG showed findings of myocardial infarction. What blood test support this diagnosis?

- Troponin and CK-MB

9- After 4 days, which one of these blood tests is positive and which one is negative?

- Troponin will be +ve and CK-MB will be -ve

10- What are the possible complications of myocardial infarction?

- Arrhythmia, Left ventricular failure , Cardiogenic shock , Thromboembolism ...etc

11- What are the microscopic findings in the first 30 minutes of myocardial infarction?

- No microscopic findings

12- Coagulation necrosis starts after which period of time of MI?

- 4 hours

Females:

-Leader : فاطمة بالشرف

ريناد الغريبي
منيرة المسعد
شوق القحطاني
رزان الزهراني
الرحيمي بتول
فاطمة الديحان
الجوهرة الشنفي
نورة القاضي
غادة الحيدري
مها العمري
غرام الجليدان
آلاء الصويغ
ال فهدة السليم
شيرين حمادي
رناد الفرم
نورة الحربي
ميعاد النفيعي

Males:

-Leader : منصور العبرة

خالد العقيلي
عبدالجبار اليماني
بندر الجماز
محمد المحيميد
راكان الغنيم
سليمان الزميع
طارق العلوان
أحمد الصبي
أنس السيف
تركي آل بنهار
خالد المطيري
سعد الفوزان
سعود الأحمرري
سيف المشاري
عبدالعزیز العبدالکريم
عبدالله العبيدان
عبدالله السرجاني
فهد الفايز
محمد الأصقه
محمد بن معيوف

اقربنا الى ربنا الذي خلقنا

Kindly contact us if you have any questions/comments and suggestions:

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* **TWITTER :** [@pathology437](https://twitter.com/pathology437)

GOOD LUCK ! 😊

***references:**

- Robbins Basic Pathology
- Slides