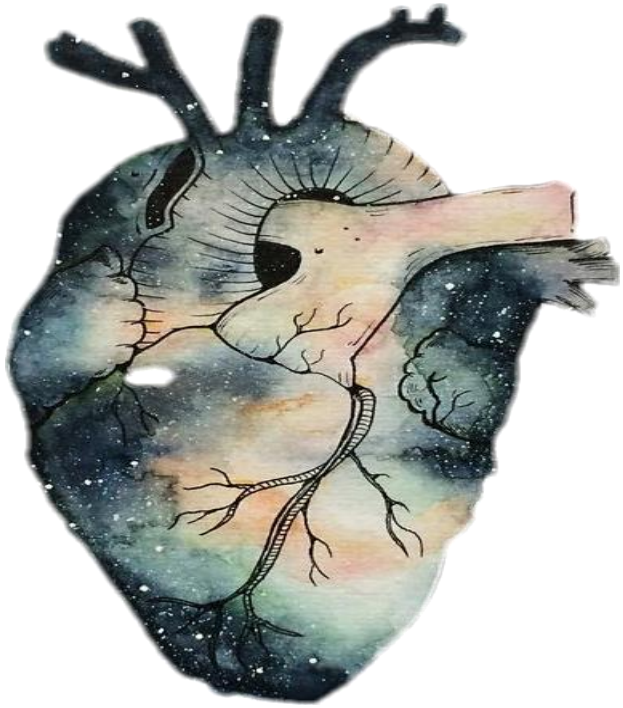
PATHOLOGY TEAM 436

MEDICINE
KING SAUD UNIVERSITY

Pathology & pathogenesis of ischemic heart diseases



Revised by
شوق الأحمري & طراد الوكيل

Objectives:

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

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

Key principles to be discussed:

1- Macroscopic and microscopic changes in myocardial infarction.

2- Biochemical markers of myocardial infarction.

3- Complications of myocardial infarction: immediate and late.

Black: Doctor's slides.

Red: important!

Green: Doctor's notes.

Grey: Extra.

Purple: Female's slides.

Blue: Male's slides.

Ischemic Heart[1] Disease/IHD (Coronary Heart Disease):

IHD: is a group of closely related conditions/syndromes **caused by an imbalance between the myocardial oxygen demand[2] and blood supply.** Usually caused by decreased coronary artery blood flow so it's called also ("coronary artery disease")

- Cardiac function is strictly dependent upon the continuous flow of oxygenated blood through the coronary arteries.
- 90% of cases, IHD is a consequence of reduced coronary blood flow secondary to obstructive atherosclerosis.

Four syndromes:	✓-Angina pectoris (chest pain).
	✓-Acute myocardial infarction.
	✓-Sudden cardiac death.
	✓-Chronic ischemic heart disease with congestive heart failure.

Causes:

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

IHD Epidemiology (coronary atherosclerosis):

- 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

[1] Insufficient blood supply to the myocardium *muscular tissue of the heart* mainly caused by atherosclerosis
[2] الحاجة / الطلب

Pathogenesis of Ischemic Heart Disease:

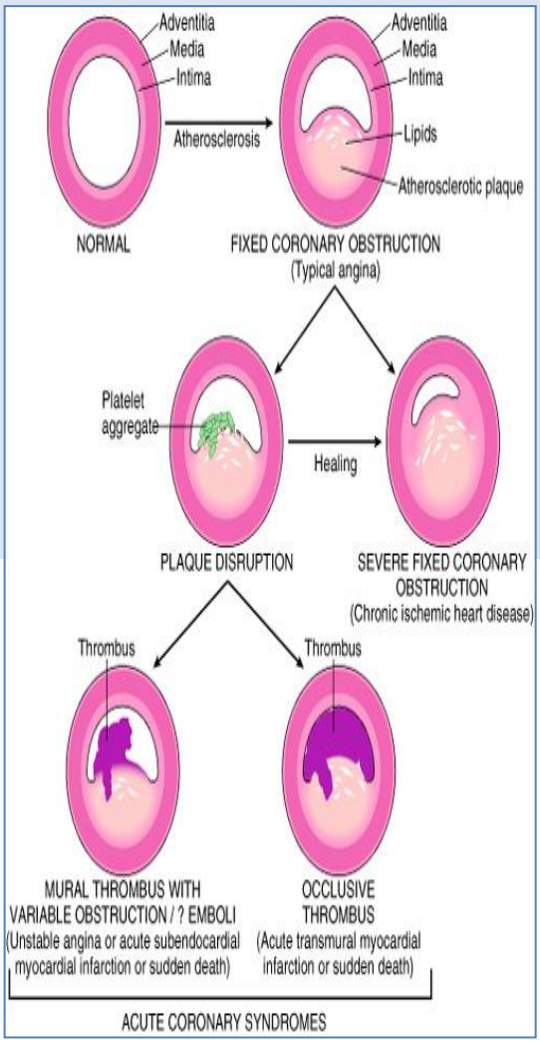
Because of the huge **different** between Dr.Sufia & Dr.Ahmed in the way the explained the pathogenesis. We wrote the two ways starting with Dr.Ahmed way because it is shorter.

Fixed obstruction that occludes **less than 70%** of coronary vessel lumen typically are **asymptomatic**.

In comparison lesions that occlude[3] **more than 70%** of a vessel lumen –so- called critical stenosis-generally causes symptomatic ischemia (angina) only in the setting of increased demand. مثل لما يصعد الدرج تزيد الحاجة للأكسجين فيكون فيه ألم

A fixed stenosis that **occludes 90% or more** can lead to inadequate coronary blood flow with symptoms even at **rest** (one of the forms of unstable angina).

In most patients, unstable angina, infarction, occur because of abrupt[4] plaque change[5] followed by thrombosis.

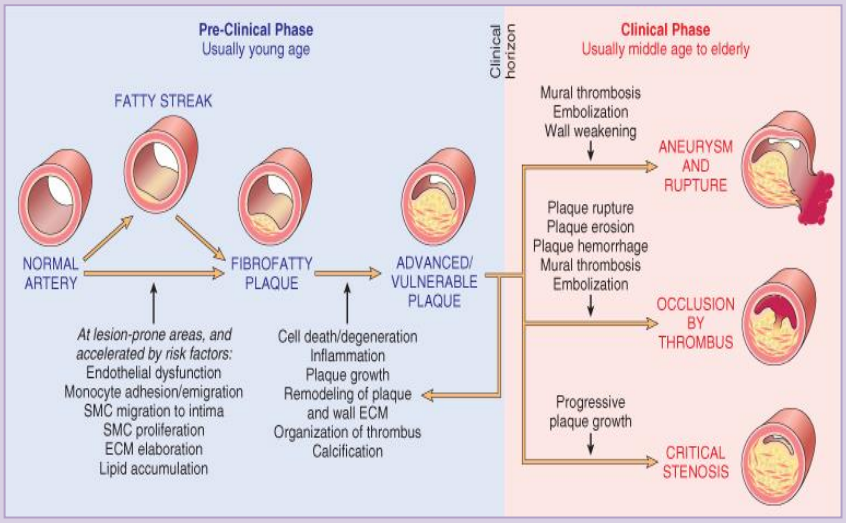


Role of Critical stenosis or obstruction*.

1. Role of Acute Plaque Change.
2. Role of Coronary Thrombus.
3. Role of Vasoconstriction.
4. Role of Inflammation.

1. Role of Critical stenosis[6] or obstruction

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



*Dr. Sufia said that the important thing is to know the **first 3**. The last two just know the names.

[3] Obstruct
[4] sudden
[5] *Rupture, fissuring, or ulceration*

[6] Abnormal narrowing or constriction of passage in the body.

Role of Acute Plaque Change[7]

- Disruption of a mildly stenosing plaque leading

to rupture / ulceration. This can lead to:

1. Hemorrhage into the atheroma which will expand

in volume.

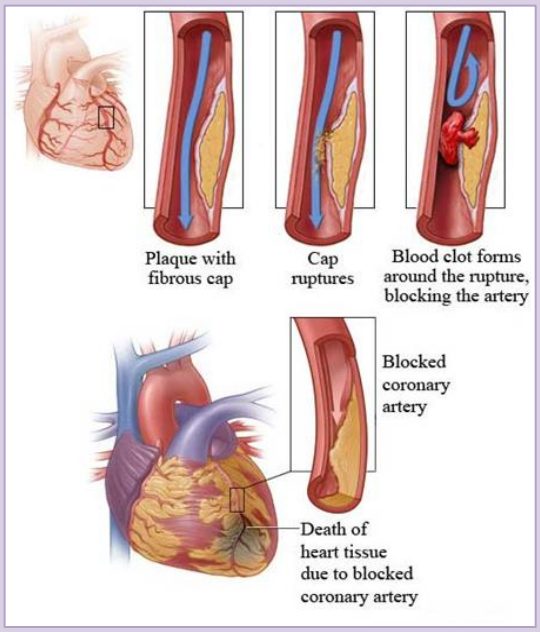
2. Exposure of the thrombogenic basement membrane

just below the endothelial lining followed by

thrombosis.

- Acute plaque change can cause myocardial

ischemia in the form of unstable angina, acute myocardial infarction and (in many cases) sudden cardiac death.



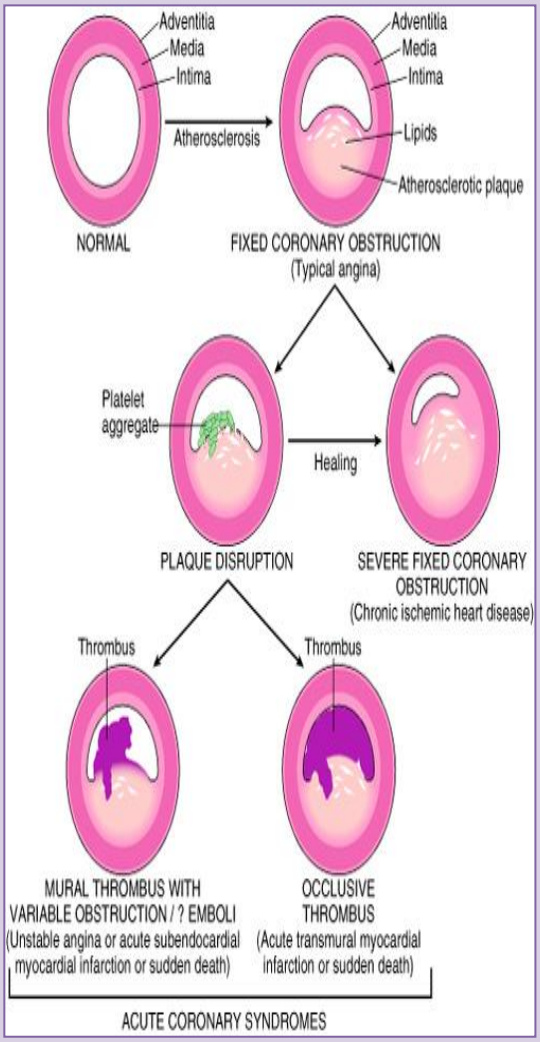
3. Role of Coronary Thrombus

- Thrombus superimposed[8] on a disrupted but previously only partially stenotic plaque converts it to either:

1. A total occlusion leading to acute transmural MI.

2. Or an 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.

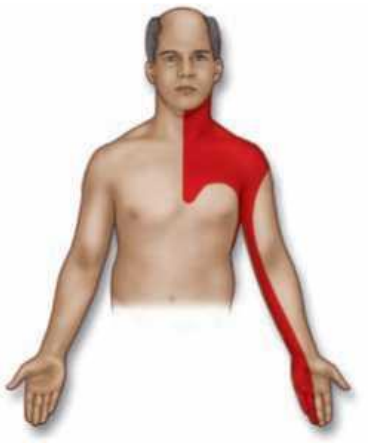
5. Role of Inflammation

Inflammation processes play important roles at all stages of atherosclerosis.

So normal blood vessel> AS "which is obstruction of blood vessel by atherosclerotic plaque + lipid"> plaque undergo disruption "rupture"> Thrombosis> **If** it occlusive thrombus= acute transmural MI. **If** the thrombus partially occlude = unstable angina.

[7] Sudden change in Atheroma like: Rupture, fissuring, or ulceration
[8] To place or lay over something متداخل/ متراكب

Angina pectoris (AP)



Angina pectoris is a type of IHD characterized by paroxysmal[9] and usually recurrent attacks of substernal or precordial chest discomfort, described as constricting, crushing, squeezing, choking, or knifelike pain. May radiate down the left arm or to the left jaw (called as **referred pain**).

Angina pectoris is an intermittent chest pain caused by transient, reversible myocardial ischemia.

Angina pectoris is due to inadequate perfusion and is caused by transient (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.

Every word in **black** it is important and mentioned in Dr. Sufia & Dr.Ahmed slides.

There are three types of angina pectoris:

1-Stable angina / typical angina pectoris:

- The most common form of angina.
- It is caused by atherosclerotic disease with usually ≥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[10], 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**[11] or some other form of stress.
- Is usually relieved by rest (thereby decreasing demand) or with a strong vasodilator like nitroglycerin. Take it sublingually. Send it home.

2-Unstable or crescendo 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[12] **plaque** with superimposed partial **thrombosis**. Not complete rupture. If it complete=MI.
- Unstable angina is often the precursor of subsequent acute MI. Thus also called as preinfarction angina.

3-Prinzmetal variant angina: ذبحة صدرية مخالفة للمعتاد

- It's 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.
- **Pain at rest.**
- **The etiology is not clear.**

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[9] A severe attack or a sudden increase in intensity of a disease, usually recurring periodically.
[10] مُعرّض للخطر
[11] مجهود
[12] Degeneration of the walls of the arteries caused by accumulated fatty deposits and scar tissue, and leading to restriction of the circulation and a risk of thrombosis.

Myocardial Infarction (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.

متى يصير؟ لما يكون فيه

Disruption of an atherosclerotic plaque results in the formation of thrombus.

يعني نقدر نقول:
ال atherosclerosis كان مسكر 75% بعدين تكونت ال thrombus وسكرت الجزء المتبقي100%

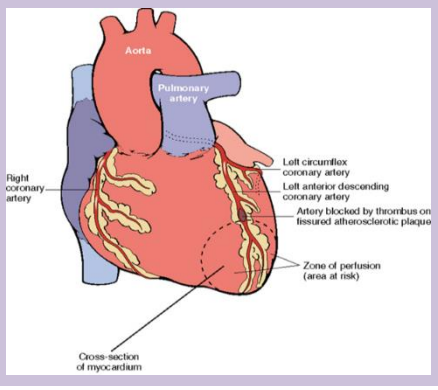
MI: commonly affected coronary vessel in persons with right dominant coronary artery heart (90% of population)

1- **Left anterior descending artery** (40-50%)

2- **Right coronary artery** (30-40%)

3- **Left circumflex artery** (about 20%)

Dr. Sufia: know the names with arranging them "most common to least".



Pathogenesis of MI:

Because of the huge **different** between Dr.Sufia & Dr.Ahmed in the way the explained the pathogenesis. We wrote the two ways starting with Dr.Ahmed way because it is shorter.

- Myocardial necrosis begins within 20-30 minutes, mostly starting at the subendocardial region (less perfused, high intramural pressure).
- Infarct reaches its full size within 3-6 hrs. During this period, lysis of the thrombus by streptokinase or tissue plasminogen activator, may limit the size of the infarct.
- Irreversible cell injury: 20-40 min

Most common cause is Thrombosis on a pre-existing disrupted atherosclerotic plaque.

In the typical case of MI, the following sequence of events can be proposed:

1- Acute plaque change: A sudden change in the structure of an atheromatous plaque, like; disruption, ulceration, rupture and intra-plaque hemorrhage.
2- Exposure of the thrombogenic subendothelial basement membrane and necrotic plaque resulting in thrombus formation.
3- Frequently within minutes, the thrombus evolves[13] to completely occlude the lumen of the coronary vessel.

[13] يتطور

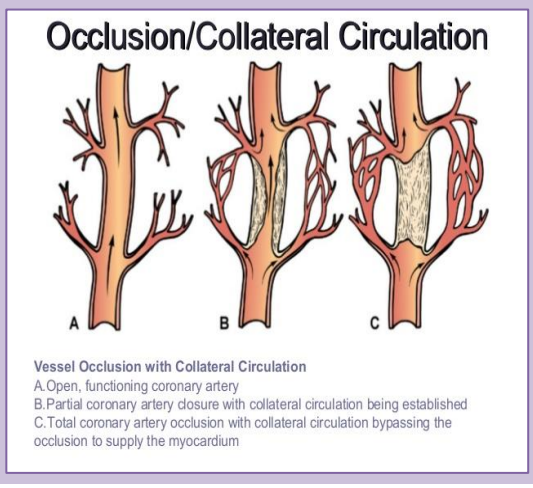
*If we treat the patient before this period, it may save the heart of this patient

Myocardial response to 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). It is the last area receives blood delivered by epicardial vessels and also exposed to high intramural pressure which acts to impede[14] the inflow of blood.
- **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 streptokinase[15] or tissue plasminogen activator[16] may limit the size of the infarct "Main aim".
- So any intervention[17] in this time frame can potentially limit the final extent of necrosis.

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[18].
4. The oxygen needs of the myocardium at risk.
5. The extent of collateral blood vessels[19].
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.



Types of MI:

1- **Transmural**[20]: Full thickness (>50% of the wall).

2- **Subendocardial**: Inner 1/3 of myocardium. As previously mentioned; the subendocardial region is most vulnerable to hypoperfusion and hypoxia.

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[14] إعاقة
[15] A medication it is used to break down clots in some cases of myocardial infarction
[16] Is a protein involved in the breakdown of blood clots
[17] تدخلات
[18] انسداد
[19] When your body produce new blood vessels "angiogenesis" and it depends on the person's health. مثل لما يكون الطريق زحمة فنروح مع طرق ثانية بكذا الشريايان جتى لو انسد ما يؤثر فينا لأن الدم سوا له طرق جديدة ينتقل فيها.
[20] Existing or occurring across the entire wall of an organ or blood vessel.

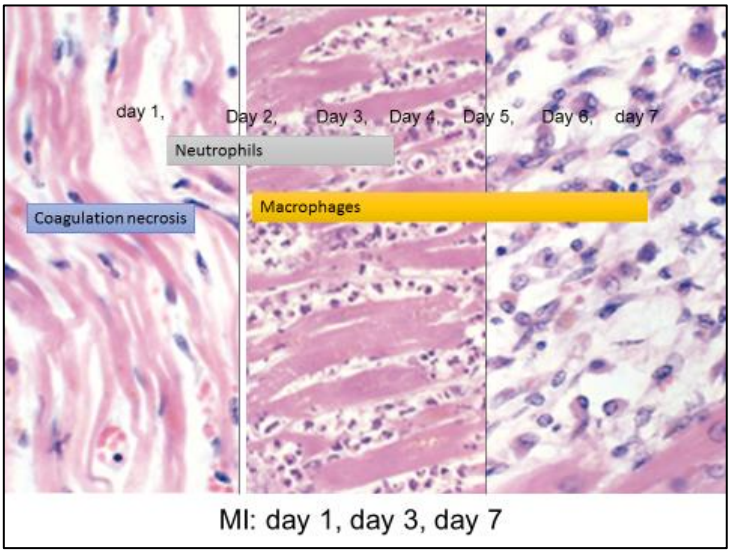
Morphology:

Begins with coagulative necrosis[21] and Inflammation (Initially mainly neutrophils and later macrophages) > Followed by formation of granulation tissue > Heals by formation of fibrous scar.

لما نشوف سكار بالقلب بالأوتوبسي هذا يعطينا هِنت أو علامة إن هذا الشخص قد صارله Heart attack

Skip or Give it a quick look if you want عن الذمّة☹;)

Time Frame	Gross Features	Light Microscopic Findings	Electron Microscopic Findings
Reversible Injury			
0–1½ hours	None	None	Relaxation of myofibrils; glycogen loss; mitochondrial swelling
Irreversible Injury			
½–4 hours	None	Usually none; variable waviness of fibers at border	Sarcolemmal disruption; mitochondrial amorphous densities
4–12 hours	Occasionally dark mottling	Beginning coagulation necrosis; edema; hemorrhage	
12–24 hours	Dark mottling	Ongoing coagulation necrosis; pyknosis of nuclei; hypereosinophilic appearance of myocytes; marginal contraction band necrosis; beginning neutrophilic infiltrate	
1–3 days	Mottling with yellow-tan infarct center	Coagulation necrosis with loss of nuclei and striations; 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 weeks	Gray-white scar, progressive from border toward core of infarct	Increased collagen deposition, with decreased cellularity	
>2 months	Scarring complete	Dense collagenous scar	



MI: day 1, day 3, day 7

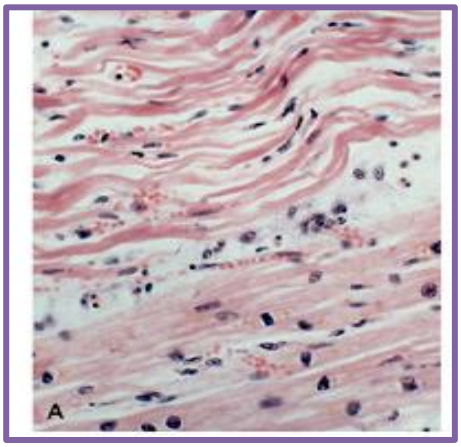
Morphologic changes: هنا نتكلم عن مسل الهارت نفسها مو الفيسيلز.

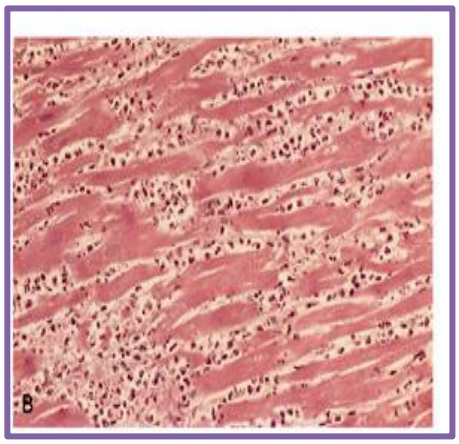
Time	Gross changes	Microscopic changes مهم
0-4h	None	None
4-12h	Mottling تبقع	Coagulation necrosis
12-24h	Mottling	More coagulation necrosis; neutrophils come in
1-7 d	Yellow infarct center	Neutrophils die, macrophages come to eat dead cells
1-2 w	Yellow center, red borders	Granulation tissue
2-8 w	Scar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

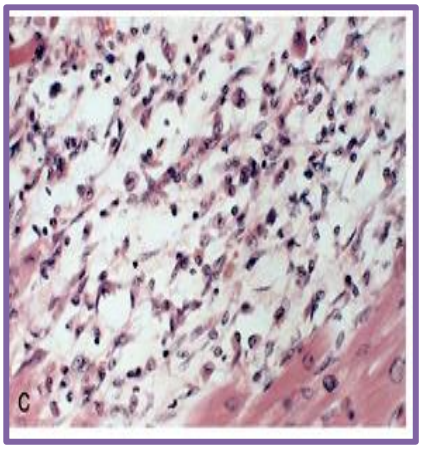
Morphology: Electron microscopy finding will start after 20-30 min of MI but light microscopy finding we can see it after 2-3 hrs or 4 hrs

[21] Is a type of accidental cell death typically caused by ischemia or infarction. the architecture of dead tissue is preserved for at least a couple of days.

You can skip this page if you want





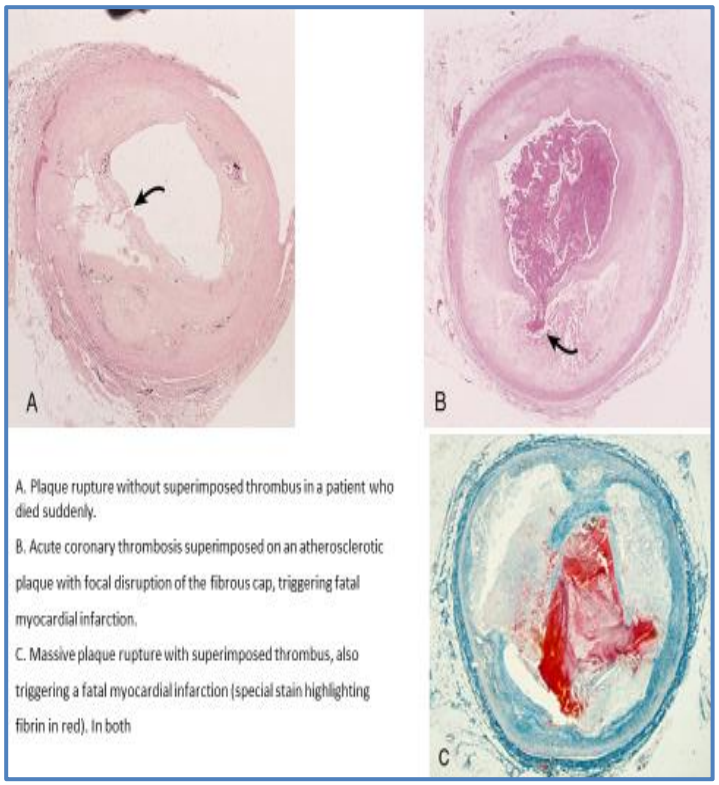


Microscopic features of myocardial infarction: **skip it ;)**

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



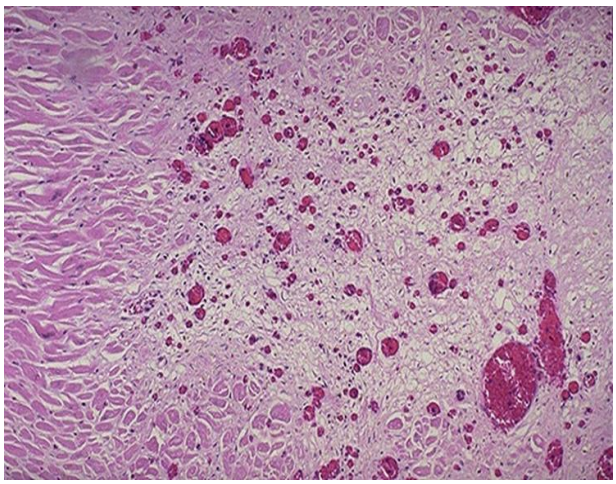
A. Plaque rupture without superimposed thrombus in a patient who died suddenly.

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

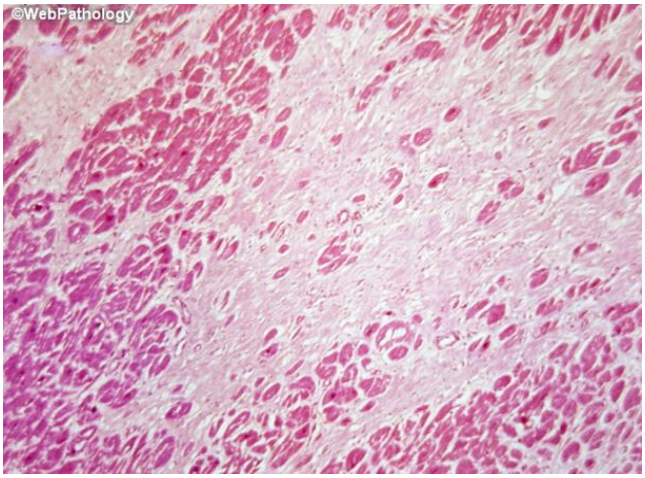
C. Massive plaque rupture with superimposed thrombus, also triggering a fatal myocardial infarction (special stain highlighting fibrin in red). In both

Granulation tissue: repair process consists of newly form fibroblast and some blood vessels

- **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

Myocardial Infarction's clinical Features:
1- pain: • **Severe crushing sub-sternal chest pain, which may radiate to the neck, jaw, epigastrium[22], shoulder or left arm.** • **Pain lasts for hours to days and is <u>not relieved by nitroglycerin.</u>** لما يجينا مريض كذا يكون عندنا إحتمالين يا MI or unstable AP • **No pain in 20-30% of patients (diabetics, hypertensive, elderly).** Neuropathy nerve's don't feel this pain.
2- Pulse is rapid and weak.
3- Diaphoresis (sweating)
4- Dyspnea
5- Cardiogenic shock[23] (>40%of lt. ventricle)
6- ECG shows typical findings of ischemia

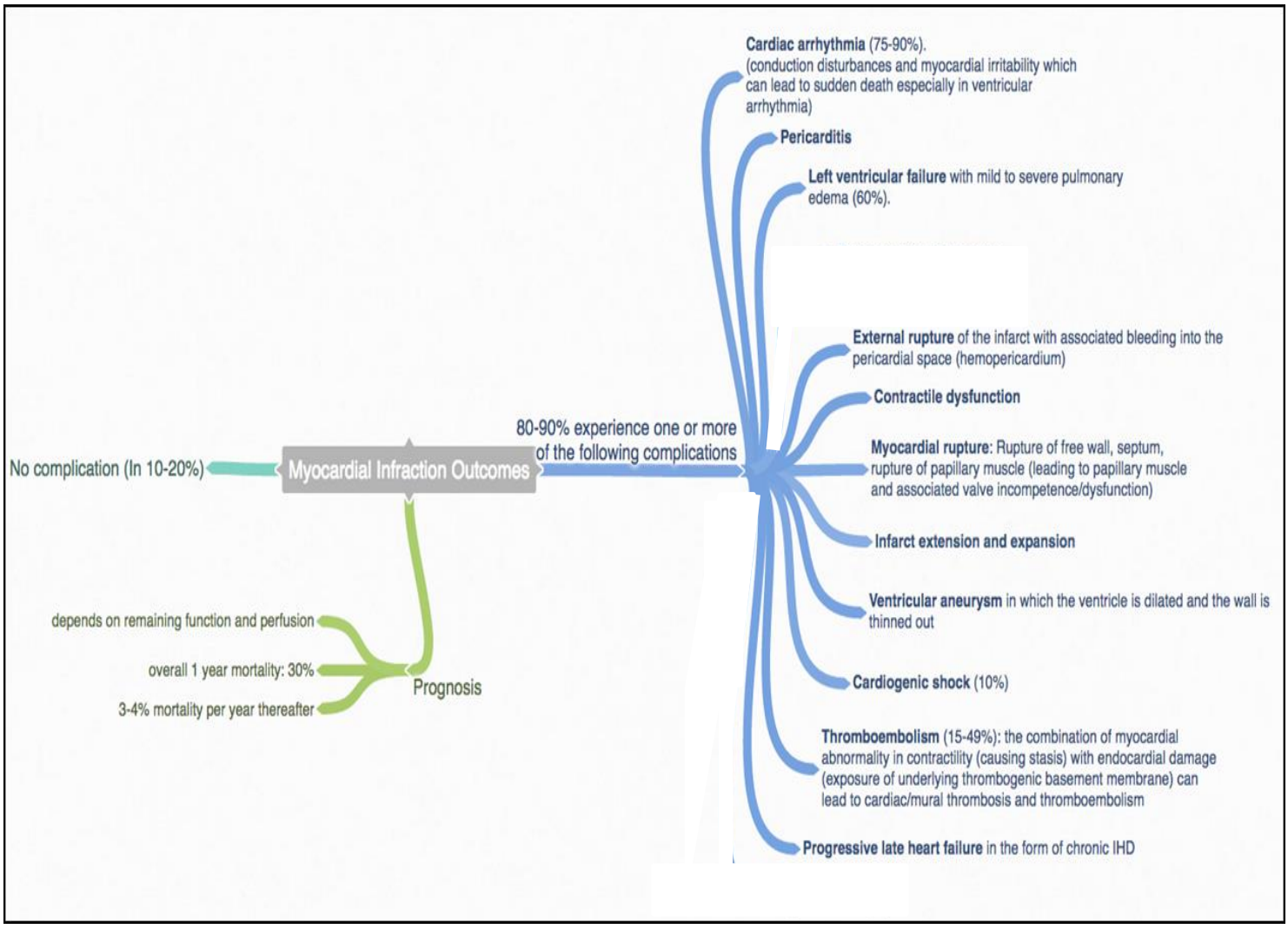
Ischemic Heart Disease Laboratory evaluation

Myocardial Infarction's Laboratory Evaluation:	
Troponin "Tn" (best marker)	• Two types: TnT and **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
Creatine kinase MB "CK-MB" (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
Lactate dehydrogenase (LD)	• LD1 • Rise 24 hrs, peaks 72 hrs, persists 72 hrs.

[22] upper abdomen (over the stomach

[23] is a condition in which your heart suddenly can't pump enough blood to meet your body's needs. The condition is fatal if not treated immediately

Myocardial Infarction: Outcomes or complications



Chronic ischemic heart disease: مو مرة مهم

Progressive heart failure due to ischemic injury, either from:

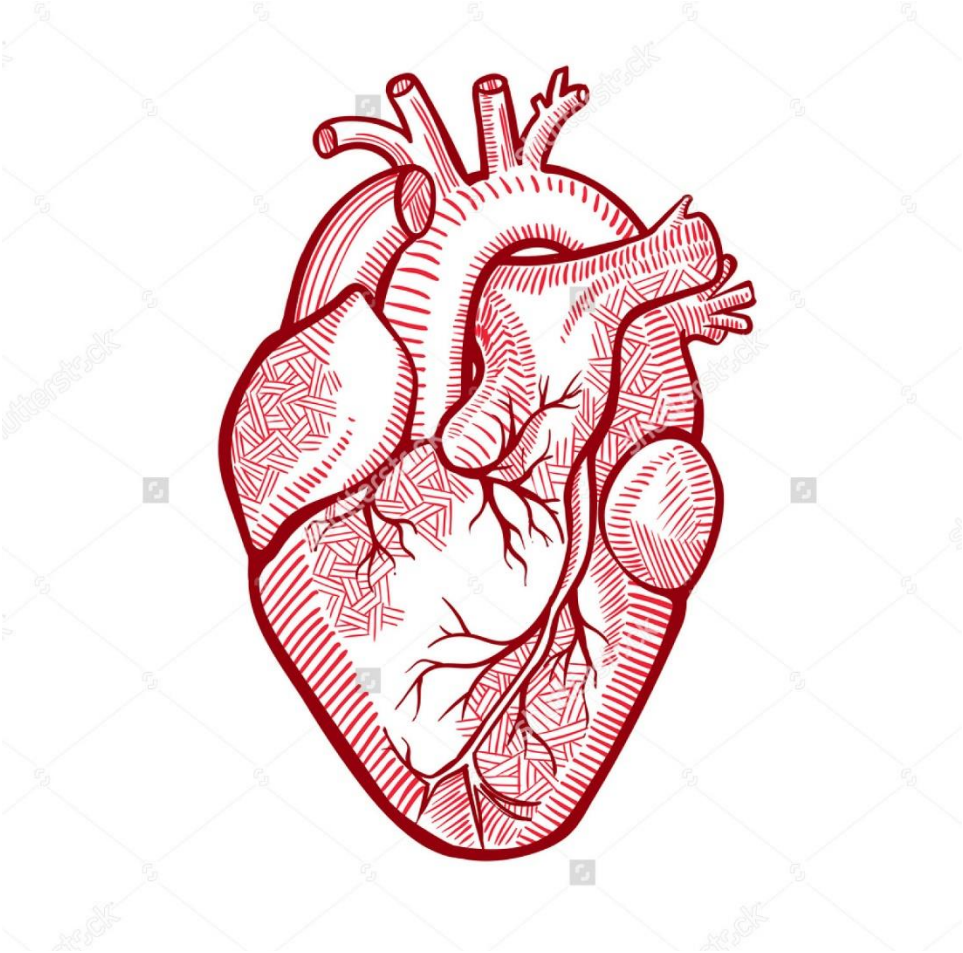
- prior infarction(s) (most common) or chronic low-grade ischemia

Sudden cardiac death: مو مرة مهم

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.

"اللهم لا سهل إلا ما جعلته سهلًا و أنت تجعل الحزن إذا شئت سهلًا"



MCQs

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القادة

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الأعضاء

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روان الوادعي **ريما الشايع**

لمى التميمي **لمى الفوزان**