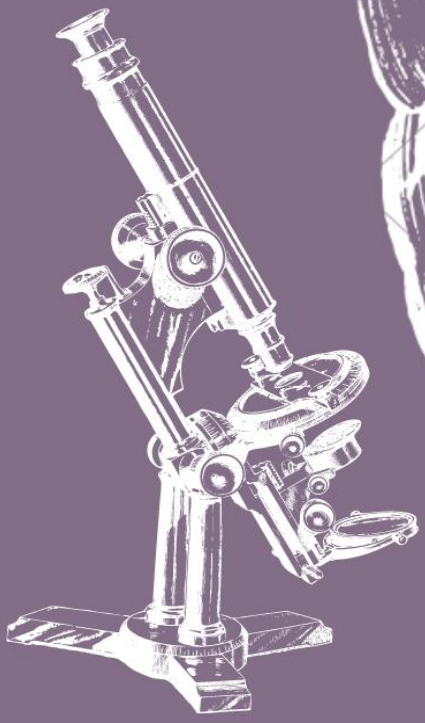
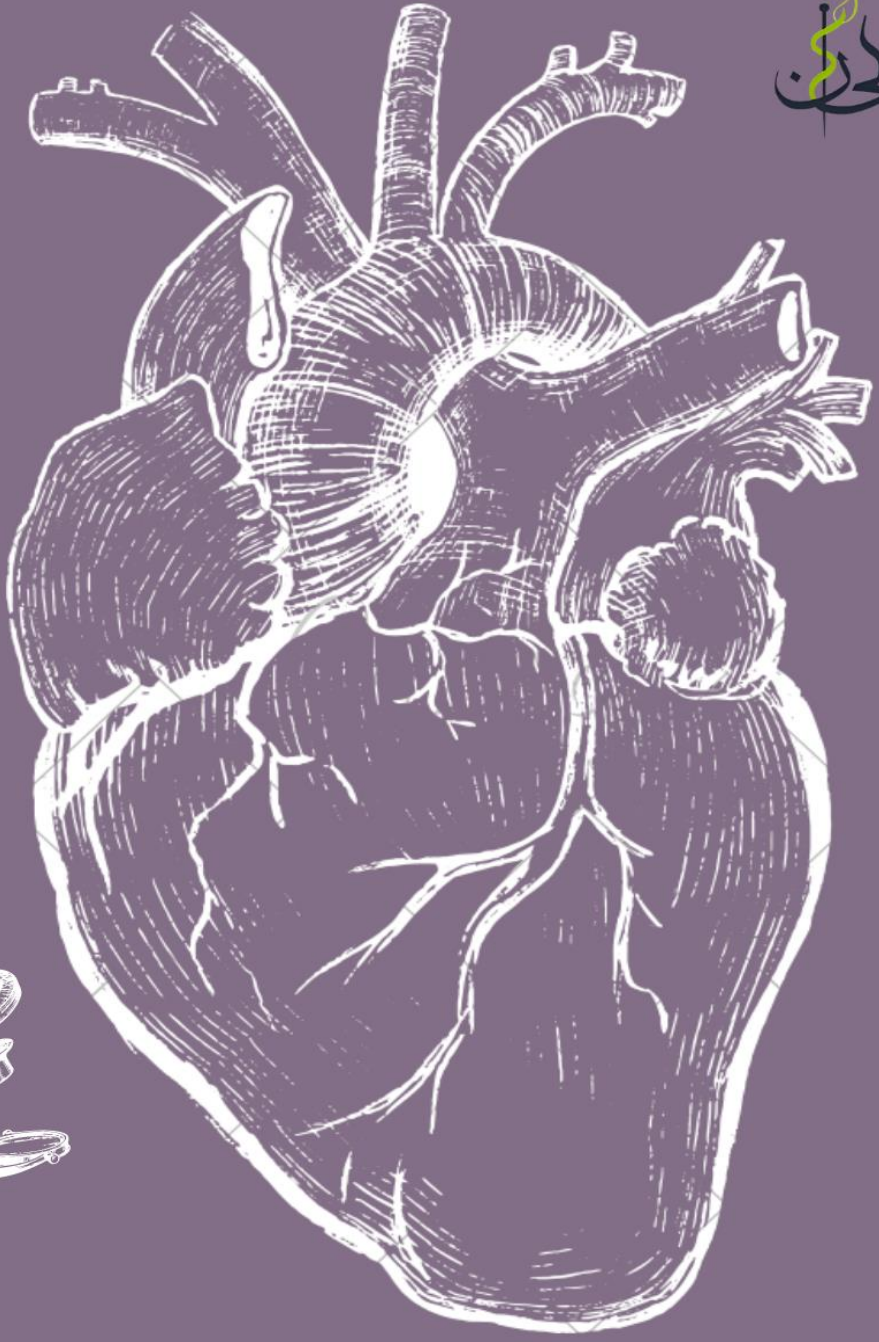
PATHOLOGY





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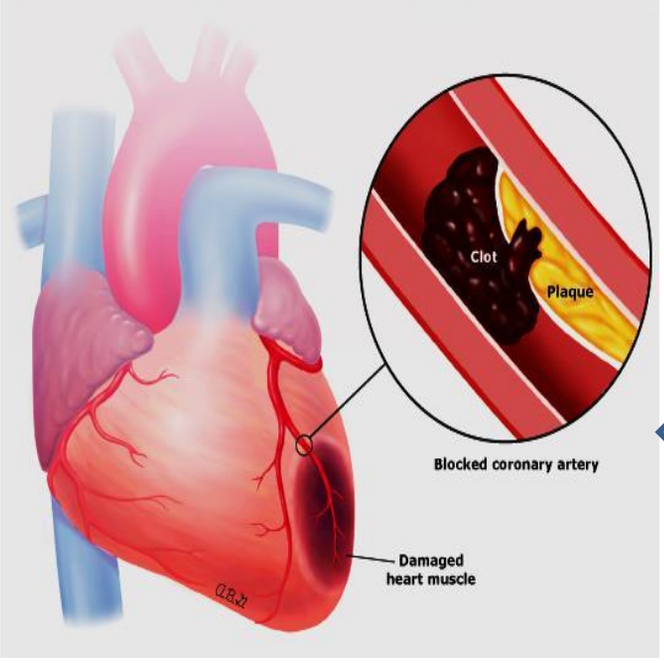
Sheet no. : 8

Ischemic Heart Disease

Acute Myocardial Infarction

Acute myocardial infarction is also known as ***"Heart Attack"***: it is **necrosis** of the heart muscle due to ischemia.

*It is considered a significant cause of death worldwide.



As you can see from the pic. , there is an atherosclerotic plaque inside one of the coronary arteries and this atherosclerotic plaque is complicated by a superimposed blood clot (thrombus), this acute occlusion of the coronary artery will lead to ischemia of the downstream tissues that are supplied by that particular coronary vessel , so there will be necrosis in the heart muscle that is supplied by that coronary artery . AND this is the definition of **acute myocardial infarction.**

Clinical features of acute MI, they encompass certain classical signs and symptoms:

1) The most significant and distinguishing one is having the ischemic cardiac pain which is usually described by patients as: Severe, crushing, substernal chest pain that radiates to the neck, jaw, epigastrium or left arm.

similar to the pain of angina pectoris,
but the duration of pain in MI is longer and less responsive to medications like nitroglycerin and rest.

Other common symptoms are:

2)Dizziness, sweating.

3) Rapid and weak pulse.

related to sympathatic stimulation

4) Dyspnea (means shortness of breath): is common **when** there is pulmonary congestion and edema.

5) Nausea: happens especially in cases of posterior MI; because of activation of the vagus nerve.

6) Cardiogenic shock: occurs when there is **massive** MI ; (Massive means that a large portion or volume of the heart is affected, so when there **is >40% of the left ventricle affected by MI, there will be loss of the pumping action of the heart leading to cardiogenic shock).**

7) SOMETIMES in a variable percentage of patients, there will be no (classical/typical) symptoms, we call this condition **"Silent Infarct"**.

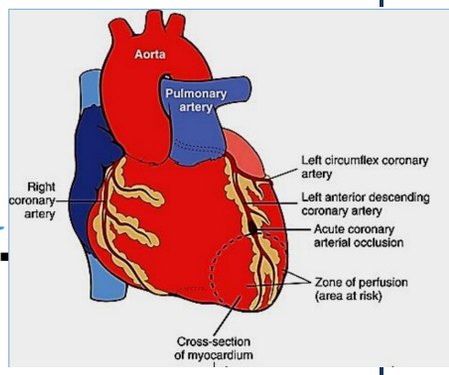
SO, silent infarct describes a patient that is having acute MI without the classical symptoms of acute cardiac ischemia; so, this type of MI can only be examined and confirmed by **ECG** and **lab workup**.

Patients who are particularly prone to develop silent infarct:

1)Diabetic patients (peripheral neuropathies). 3- unconsious people

2) Elderly.

* Coronary Arteries supplies the heart



MI-Causes:

The main cause of MI is acute occlusion of the coronary arteries, it was found that acute occlusion of the left anterior descending (LAD) artery is the cause of 40% to 50% of all MI cases.

proximal

MI-Evolution

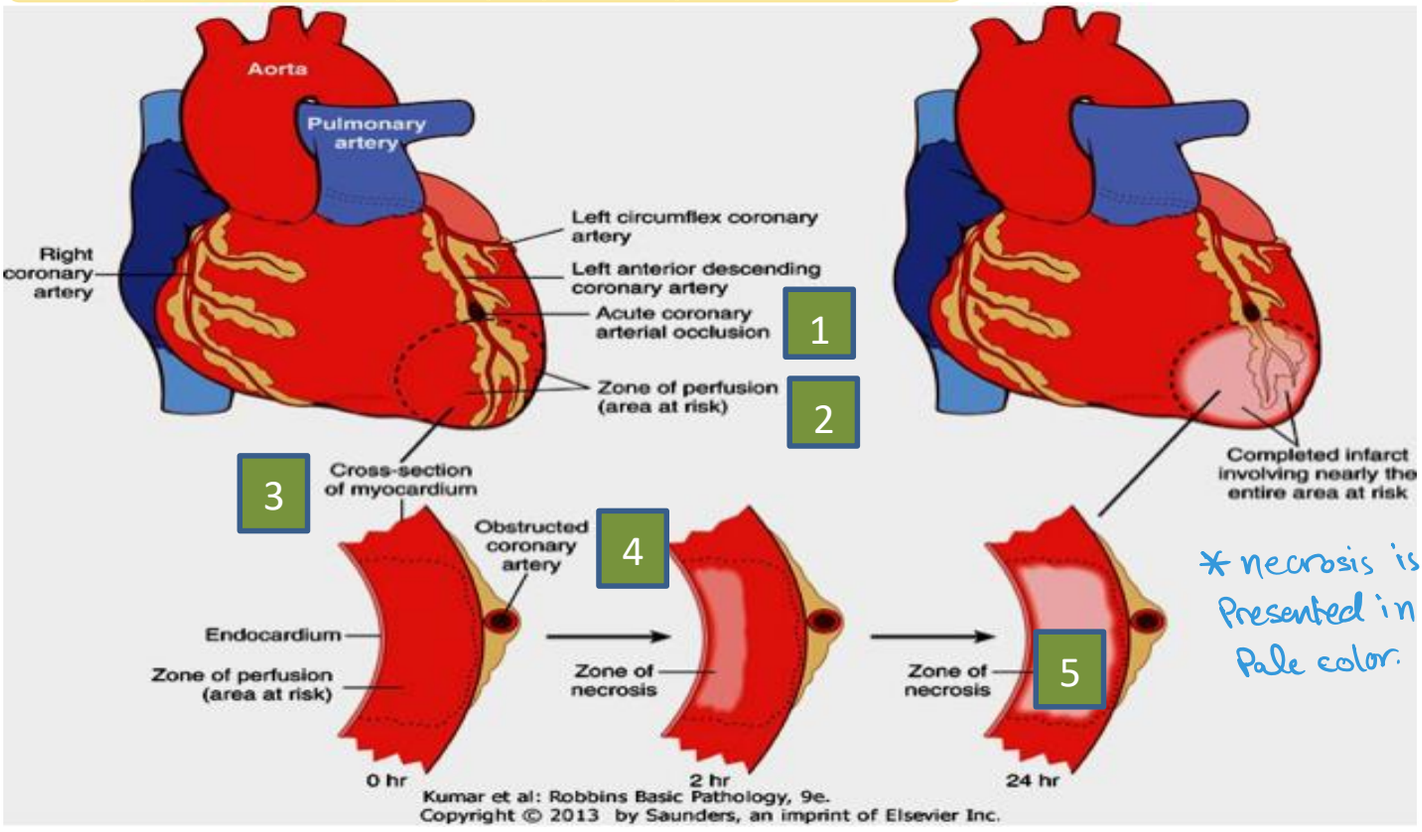
This diagram (below) shows how myocardial infarction evolutes , for example if you look at the left side you will see an acute coronary arterial occlusion in the left anterior descending artery (marked by number 1), the part of the cardiac tissue that is directly supplied by that artery, is now at risk of ischemia and this area is called **"zone of perfusion"** (marked by number 2)**.** If you take a cross section from the myocardium of this area (marked by number 3) you will see that the occluded coronary artery is located just beneath the pericardium overlying the myocardium (marked by number 4), so, endocardium is the furthest part of the cardiac tissue from the blood supply, all this area is called zone of perfusion (again) or area at risk of ischemia. After more than 30 minutes, necrosis starts to develop, and the **"zone of necrosis"** describes the area of necrotic cardiac tissue (marked by 5). Note that necrosis begins just beneath the endocardium, so the first part of cardiac tissue to show necrosis is the furthest part from the coronary artery blood supply and these are called the subendocardial areas of the myocardium.

ATTENTION: Endocardium will be spared from the necrosis because it can get the blood supply through diffusion from cardiac chambers. so it can resist the ischemia

it take 20-30 min to develop necrosis, before necrosis there are no morphological changes
there may be ultrastructural changes

- 2 hours following the infarct, the zone of necrosis would be the subendocardial myocardial muscle.

IF this area of ischemia (zone of perfusion) is not treated, zone of necrosis will expand until it covers all the (area at risk/zone of perfusion) 24 hours after of the onset of occlusion. (zone of perfusion is completely replaced by zone of necrosis).



Evaluation of MI

MI is the main cause of morbidity and mortality worldwide, so management is important.

Evaluation can be done by:

1) clinical signs and symptoms (already discussed).

2) electrocardiographic (ECG) test: detecting any abnormalities in the ECG could indicate MI. (usually done in emergency department).

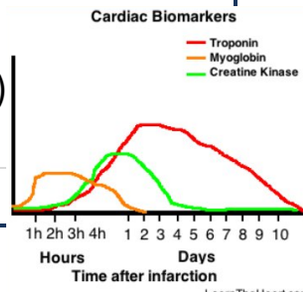
3) Laboratory evaluation: blood levels of intracellular macromolecules that leak out of injured myocardial cells through damaged cell membranes.

macromolecules normally inside myocardial cells ,after damage to these cells, macromolecules leak out to the circulation

Those intracellular cardiac molecules that leak into the circulation following cardiac damage are called "**Cardiac enzymes**" OR "**Cardiac markers of MI**", these include:

↳ released from necrotic cardiac muscle

1- Myoglobin.
2- Cardiac Troponins T and I (TnT, TnI).
3- Creatine kinase (CK), specifically the myocardial-specific isoform (CK-MB)
4- Lactate dehydrogenase. non specific for heart



The best marker for acute MI is Cardiac troponins T and I; because they are very specific for cardiac muscle and stay elevated for a long period following acute MI.

The second-best marker after cardiac – specific troponins is Creatinine kinase CK-MB isoform because it is also specific to cardiac muscles.

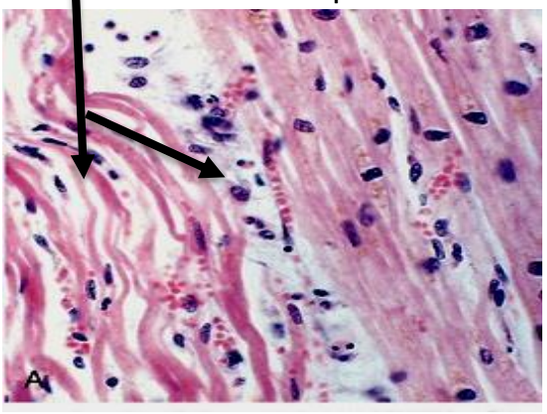
white infract:
1-solid organ
2-arterial occlusion

Microscopic features of acute myocardial infarction and its repair:

It is not a part of the diagnostic process of myocardial infarction, you should understand that this is just an autopsy confirmation, so whenever someone dies due to cardiac causes and there is a suspicion or confirmation of acute MI; the following findings can be seen under the microscope, and they describe the chronological pattern and evolution of MI over time.

cell Injury -> inflammation -> repair

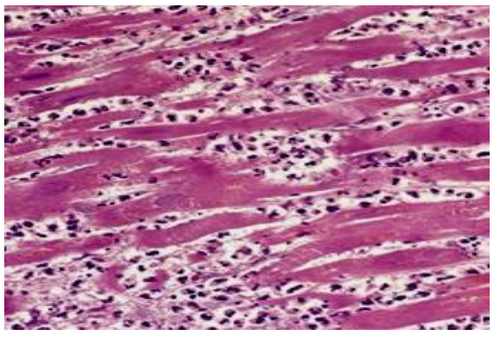
1) microscopic feature that occurs within the first 24 hours following the onset of coronary occlusion **(<24 hrs)** is **coagulative necrosis** of myocardial muscles; this necrosis will lead to **wavy fibers** (which are necrotic and wavy cardiac muscle), also necrosis will be associated with **edema** which separates necrotic cells from each other.



Stain: conventional Hematoxylin & Eosin (H&E), which uses the pink and blue colors.

2) second phase of MI evolution (occurs during the **2-3 days** following the onset of the infarct): **dense neutrophil infiltrate** will replace the edema and necrotic tissue , because necrosis is always associated with inflammation, this inflammation would be acute inflammation and neutrophils would be recruited.

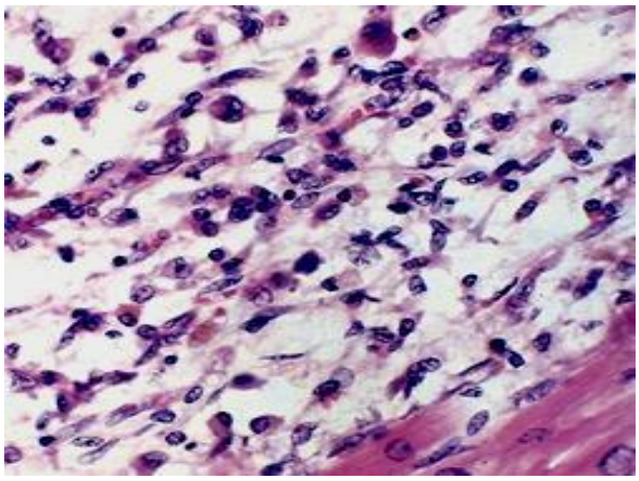
* Neutrophils have short life span, so after 1-2 days another type of cells will appear which is the Macrophage.



Stain: conventional Hematoxylin & Eosin (H&E), which uses the pink and blue colors.

3) **During 7 to 10 days** following the onset of MI , other inflammatory cells called **macrophages** will appear, and in this phase there will be **complete removal of necrotic myocytes** by those macrophages, so this is a different phase of inflammation that happens following tissue necrosis.

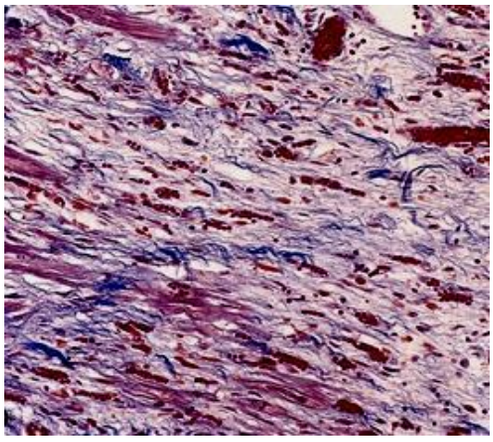
↳ responsible for chronic phases of inflammation and responsible for phagocytosis, which is needed to remove the necrotic tissue.



Stain: conventional Hematoxylin & Eosin (H&E), which uses the pink and blue colors.

weak

4)Within the first 14 days following MI (**up to 14 days**) and actually at day 14, there will be **Granulation tissue formation** (granulation tissue formation will peak 2 weeks after MI). Granulation tissue is **[loose connective tissue (blue) and abundant capillaries (red)]**. this is the repair phase.



The stain used here is **Masson Trichrome (MT),** which uses blue and red colors.

The blue color: is for the connective tissue or collagen fibers

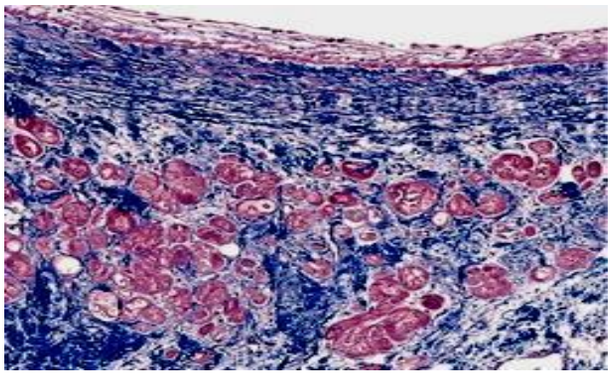
The red color: shows a lot of blood vessels.

This tissue is weak and does not have the same strength as original myocardium.

Conclusion: We started with cell damage or necrosis →then two phases of inflammation →then the third important phase which is tissue repair.

- **Tissue repair of acute MI would always end with a scar or connective tissue fibrosis**

5) The last phase: there is development of **dense collagenous scar**, **this occurs several weeks after MI**. At least 6 weeks are needed to develop a strong, dense scar that replaces the non-viable myocardium. (although this tissue is strong, but it is not strong as the original myocardial muscles, it doesn't have the same contractile ability as the myocardial muscles, so it will always be abnormal).



Stain : Masson Trichrome (MT) .

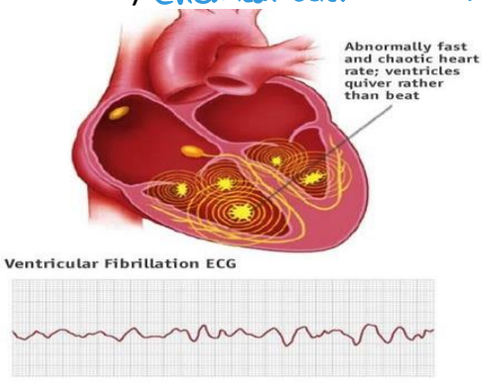
Blue color: is the scar that has developed inside the necrotic area of myocardium.

The red color: the remaining viable myocardial cells.

Consequences & Complications of MI

1)The most important and feared consequence is **Death:** 50% of deaths due to MI occurs before reaching hospital (within 1 hour of symptom onset as a result of lethal arrhythmias and this is called **(Sudden Cardiac Death)**).

- Arrhythmias are caused by electrical abnormalities that involves the ischemic myocardium and the conduction system itself.
- With current medical care, patient outcome is better (in-hospital death rate has declined). Chemical disturbances, infarction site ⇒ also affect the myocardial cells and conduction system.



This is an example of lethal arrythmias that usually lead to death or acute MI, and it is called "ventricular fibrillation".

So, there is abnormally fast and chaotic heart rate and ventricles quiver rather than beat appropriately.

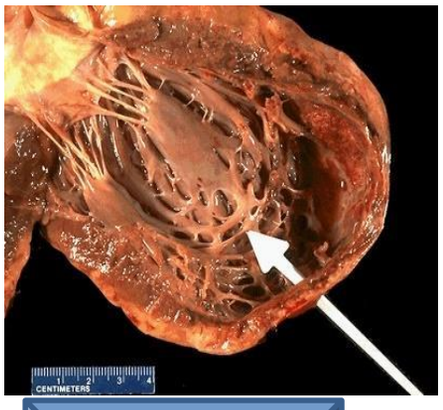
2) **Cardiogenic shock.**
- occurs in 15% of large infarcts (involve >40% of Left ventricle and result in pump failure of the heart).
- it is significant and dangerous due to 70% mortality rate and it is an important cause of in-hospital deaths.

3)**Myocardial rupture**: depends on the location of rupture, so it is divided into:

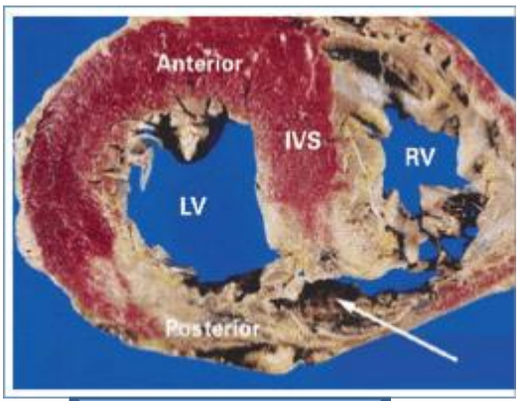
A-Rupture of the ventricular free wall which leads to hemopericardium and cardiac tamponade (usually fatal). hematoma that compress the heart
↳ False aneurysm

B-Rupture of the interventricular septum which leads to ventricular septal defect (VSD) and left-to-right shunt .

C-Rupture of Papillary muscles that surround the valves, which leads to valve abnormalities like severe mitral regurgitation.



A



B

C

4)**Pericarditis**: inflammation
irritation to the pericardiam,
if the patient survive the MI usually the pericarditis will resolve

- immunologic condition that develops 2 to 3 days after a transmural MI.
↳ The whole thickness of the wall is affected.

-spontaneously resolves (immunologic mechanism).

5)**Infarct expansion**:

- disproportionate stretching, thinning, and dilation of the infarct region (especially with anteroseptal infarcts).

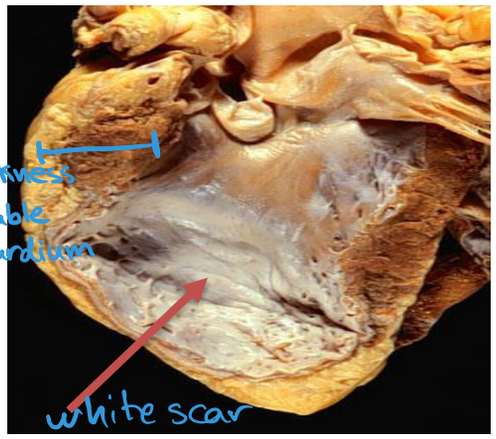
6)**Mural thrombus**:

-loss of contractility inside the damaged chamber (causing stasis; one of the factors in Virchow triad) and endocardial damage (associated with ischemia) will together lead to thromboembolism.

7)**Ventricular aneurysm**:

- A late complication; needs several weeks to happen because it needs to have scar tissue to develop.

- most commonly results from a large transmural anteroseptal infarct that heals with the formation of thin scar tissue.



As you can see, the tissue with red arrow is very thin scar tissue in comparison with the remaining viable myocardium in the upper part of the picture

this thin scar is very weak and cannot have the same contractile capacity of the viable myocardium, so this area is prone to develop aneurysm.

True Aneurysm: abnormal, prominent dilatation especially during cardiac contraction (systole).

scar tissue -> collagen fibers

Potential complications of ventricular aneurysms include:

1-Development of mural thrombus inside the affected chamber. Stasis

2-Development of arrhythmias, because this scar has abnormal conduction process inside it.

3-Heart failure. because we negatively affect the cardiac output.

4- Risk of rupture (because of aneurysm), this rupture may cause cardiac tamponade
↳ if happened it will be False aneurysm.

8)**Progressive late heart failure**.

Long-term prognosis after MI

ejection fraction

- depends on many factors like the remaining left ventricular function and the severity of atherosclerosis in the remaining viable myocardium, etc .

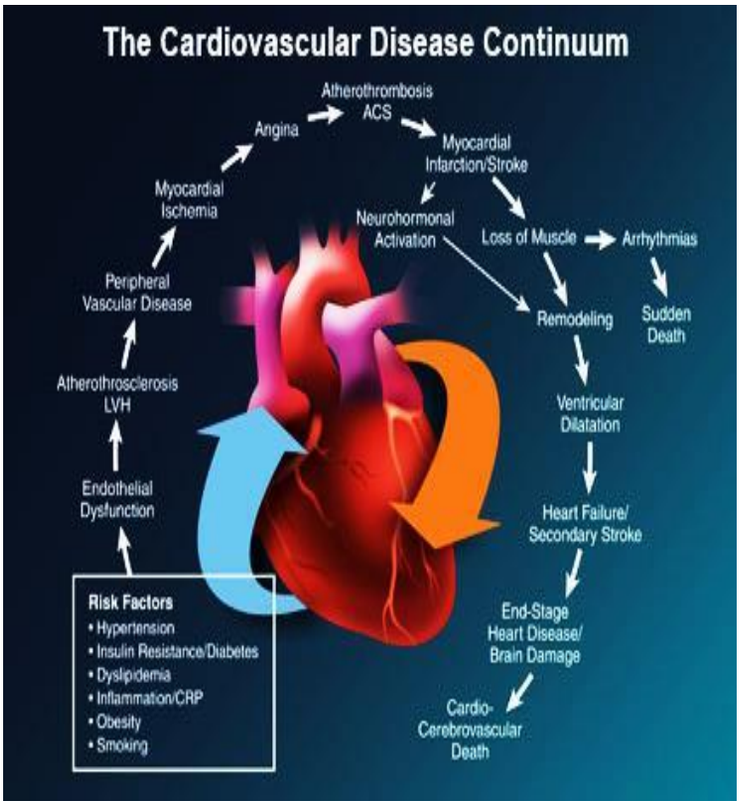
not necrotic

-The **highest mortality rate** following acute MI is during the first year **(1st year) =30%**

Thereafter, the annual mortality rate is always constant and much less than before =3%

NOW, moving to the THIRD clinical syndrome of ischemic heart disease which is:

Chronic Ischemic Heart Disease



As you can see here, cardiovascular disease has a continuum, it starts with endothelial dysfunction, atherosclerosis, hypertension or peripheral vascular disease, all of these can lead to myocardial ischemia.

Remember :the first clinical syndrome of myocardial ischemia is ANGINA, and with more and more ischemia there will be MYOCARDIAL INFARCTION ,then following acute MI , in a patient who survives there will be some kind of remodeling and ventricular dilatation that will lead to progressive heart failure that is called “Chronic Ischemic Heart Disease”.

Chronic ischemic heart disease:

- Results from post-infarction cardiac decompensation that follows exhaustion of hypertrophic viable myocardium.
- It is a progressive heart failure that is sometimes punctuated by episodes of angina or MI .
- Arrhythmias of less significance can also develop and are common in this condition.

* Cardiac muscle tries to compensate the loss of function by hypertrophy → ↑ Function , ↑ Energy expenditure, ↑ Oxygen demand and the need for nutrients and if these conditions are not available, the cardiac muscle will became exhausted causing decompensation (heart failure).

THE FOURTH and the last clinical syndrome of ischemic heart disease is:

Sudden Cardiac Death (SCD)

EXTRA 020: The background is usually atherosclerosis, but the recent cause of SCD is the lethal arrhythmias.

- **Defined as: Unexpected death from cardiac causes either without symptoms or within a short period after symptoms onset (< 24 hours of symptoms onset).**
- CAD (atherosclerosis) is the most common underlying cause.
- Lethal arrythmias (v. fibrillation) is the **most** common direct mechanism of death.
- With **younger** victims -and victims with SCD **without a significant atherosclerotic** disease- other **non-atherosclerotic causes** are more common:

- Congenital coronary arterial abnormalities
- Aortic valve stenosis
- Mitral valve prolapse
- Myocarditis
- Dilated/ hypertrophic cardiomyopathy
- Pulmonary hypertension
- Hereditary/ acquired abnormalities of cardiac conduction system
- unknown causes....

These can be seen in young patients, athletes or people who have certain hereditary or acquired abnormalities in cardiac conduction system or cardiac muscle.