PATHOLOGY TEAM
439

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Ischemic Heart Disease

Objectives:

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

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

Click here for Pathoma's video lecture

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Ischemic Heart Disease

Definition

Ischemia: is an insufficient blood supply

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")

The major cause is **atherosclerosis**
Less commonly it is due to vasospasm and vasculitis

Related conditions/ syndromes

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

Epidemiology oF Ischemic Heart 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.

◦ Hypertension.
◦ Diabetes mellitus.
◦ Smoking.
◦ High levels of LDL.
◦ Genetic factors (direct or indirect).
◦ 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

(Discussed later)

Only in boy's

A lesion obstructing 70% to 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.

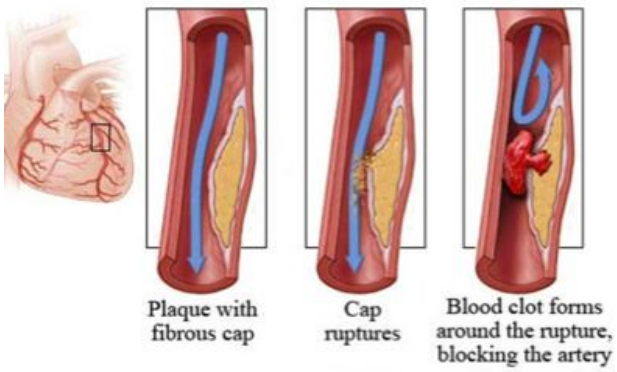
In most patients, unstable angina, infarction, occur because of abrupt plaque change (Rupture, fissuring, or ulceration) followed by thrombosis.

***Will be explained in the next slide**

1 Ischemic Heart Disease

The pathogenesis

(Will be explained in general)



Critical stenosis or obstruction

Will lead to

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

1-Fatty streaks take place
2-atherosclerosis plaque develops and grow progressively (go to AS lecturer)

Role of Acute Plaque Change:

Disruption of a mildly stenosing plaque leading to :

Sudden change on the plaque either hemorrhage or thrombosis

Rupture, Fissuring or Ulceration → hemorrhage into the atheroma which will expand in volume. (Blood strat to collect in the atheroma = blocked Blood vessel) → 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.

Acute plaque change can cause myocardial ischemia in the form of:
a-unstable angina.
b-acute myocardial infarction.
c- sudden cardiac death.

Role of Coronary Thrombus:

Thrombus in coronary artery can also embolize.

Thrombus formation on the top of the atheroma after sudden change will lead to the most serious effect = death or MI (if we didn't treat him at this step will die or develop more complications)

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

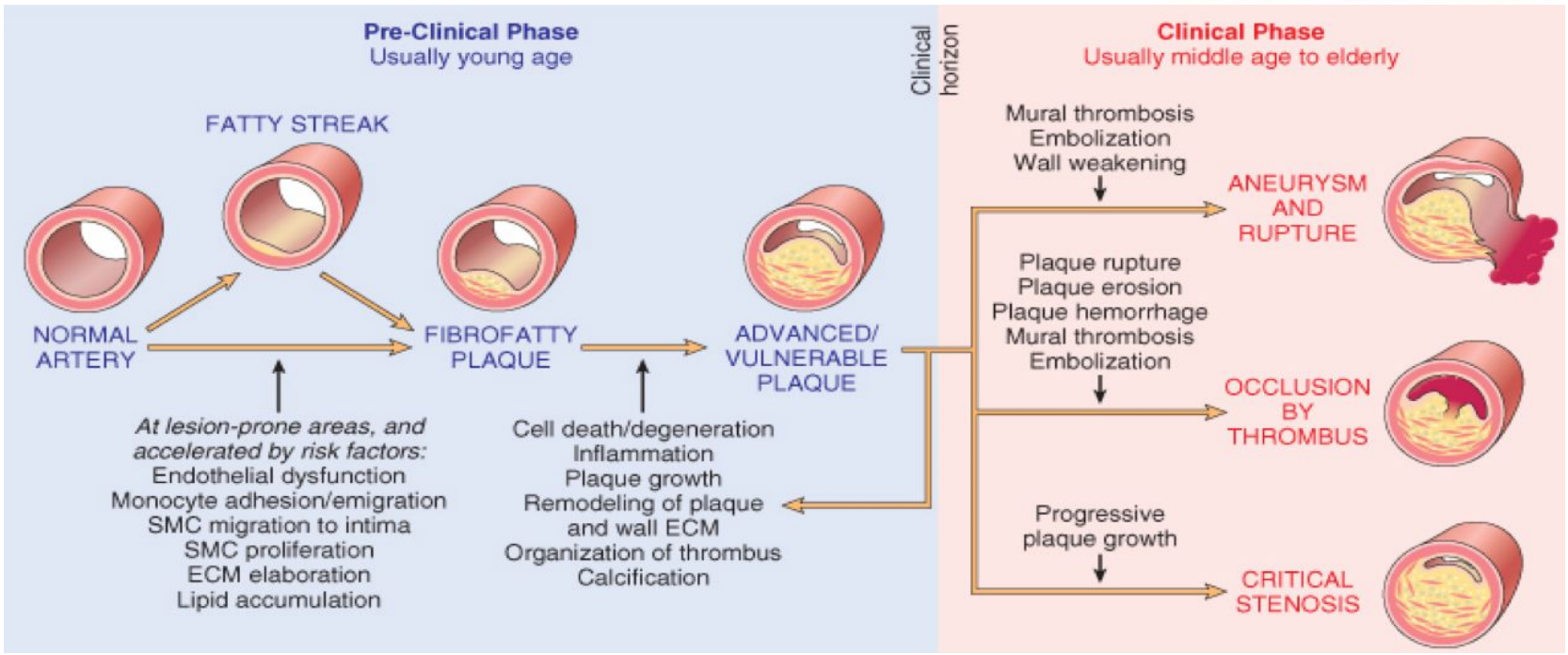
The role of inflammation and the vasoconstriction

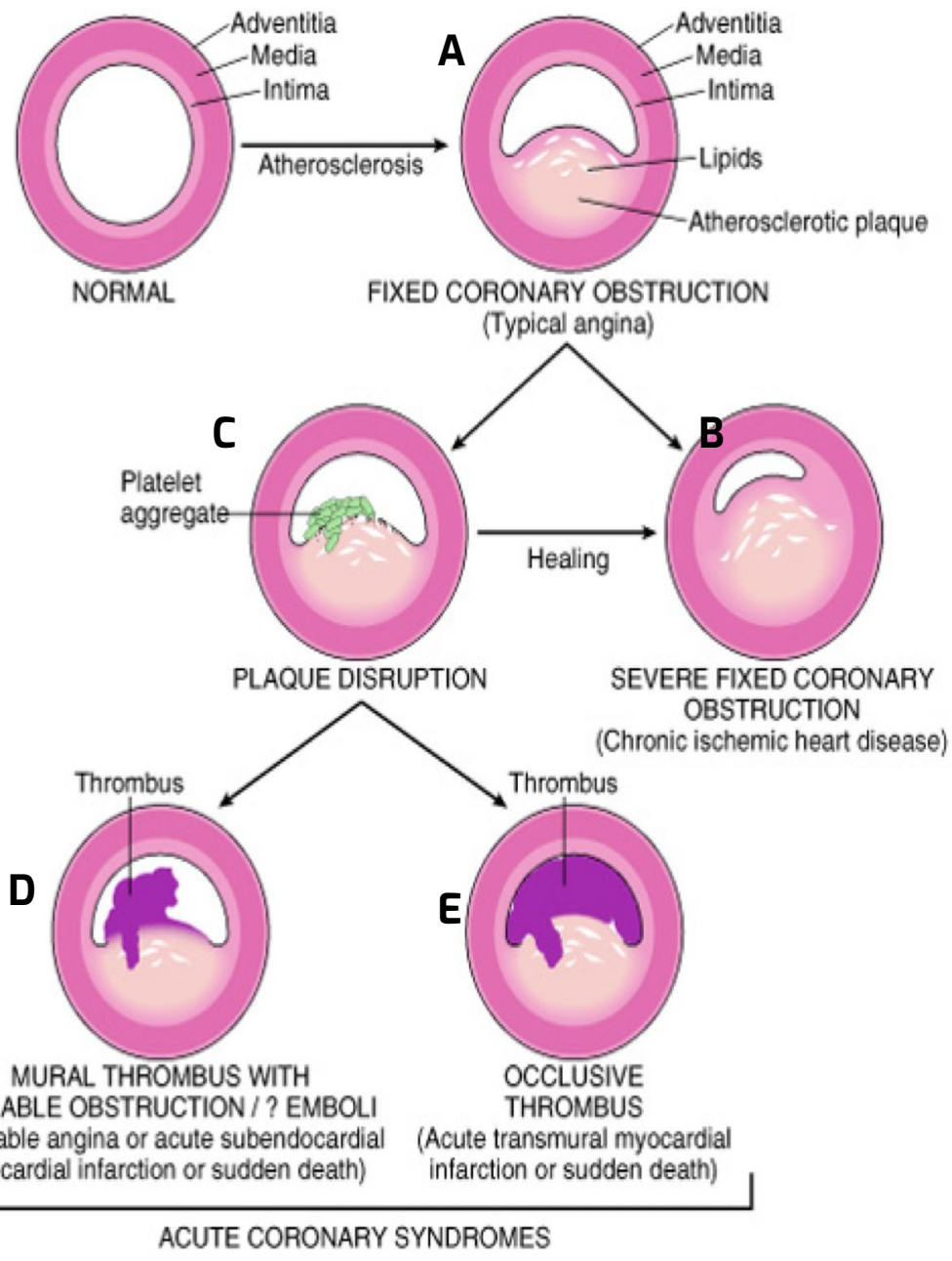
If the vessel already with Atheroma the contraction will make the vessel narrower.

Role of Inflammation: Inflammatory processes play important roles at all stages of atherosclerosis.

Role of Vasoconstriction: Vasoconstriction reduces lumen size and can therefore potentiate plaque disruption.

next slide contain helpful images to understand this slide





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** (Unstable angina or acute subendocardial myocardial infarction or sudden death.

E: When a complete obstruction happen we call it Acute transmural myocardial infarction or sudden death

Angina pectoris

(Blood supply is not enough)

Definition

- Angina pectoris is a type of IHD characterized by **paroxysmal(episodic**)and usually recurrent attacks of substernal chest discomfort (variously described as constricting, crushing, squeezing, choking, or knifelike). **May radiate** down the left arm or to the left jaw (referred pain).
- It's an intermittent chest pain caused by transient, reversible ischemia.

(basically the pain will occur in the left side because as we learned in anatomy the heart is located in the left side of the chest) .

- 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 **pathogenesis** : blood supply is not enough → hypoxia→but not enough to cause necrosis→ it means it's **reversible** injury (we took previously that necrosis happens when the patient comes with **irreversible** injury)

Types

1- Typical (stable) angina
· pain on exertion
· fixed narrowing of coronary artery
2- Unstable (pre-infarction) angina
· increasing pain with less exertion
· plaque disruption and thrombosis
3- Prinzmetal (variant) angina (ذبحة صدرية مخالفة للمعتاد)
· pain at rest
· coronary artery spasm of unknown etiology
it is the only type of angina that is NOT related to(caused by) atherosclerotic disease

Types of angina In more details

Stable angina/ typical angina

- **Is the most common form of angina**
- Is due to a fixed stenosis.
- The chest pain is episodic.

Is **caused by atherosclerotic disease** with usually ≥70% narrowing of lumen (**fixed stable critical stenosis**).
This reduction (due to ≥ 70% stenosis) of blood flow in coronary vessels makes the heart vulnerable, so whenever there is **increased demand**
(Ex:physical activity, emotional excitement,or any other cause of increased cardiac workload) there is **angina pain.**

- Management :

Relieved by rest (ex:decreasing demand) or with vasodilators like sublingual nitroglycerin (sublingual drugs have the fastest absorption, we use it here in order to give immediate response) name of the drug: nitroglycerin (the patient must carry this drug with him so he can use it wherever he have angina attack)

Unstable or crescendo angina

- **It is an unstable and progressive condition**.
- Pain occurs with progressively increasing frequency, and is precipitated with :

1- progressively less exertion,(even at rest).
2- tends to be of more prolonged duration.
3- more pain.

- It is induced by disruption or rupture of an atheroma plaque (acute plaque change)with superimposed thrombosis and partial occlusion of a coronary vessels.
- **Unstable angina is often the precursor of subsequent acute MI. Thus also called as pre-infarction angina.**
- (الفرق بينها وبين اللي قبلها إن هذي خطرة وهي مرحلة تسبق السكتة القلبية فما أقدر أعطي المريض دواء وأقوله أرتاح و خليه في جيبك إذا احتجته، نحتاج تدخل سريع)
- Pre-infarction → immediate investigation → correct the block within hours

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 (most important feature)**
- The etiology is not clear.

Myocardial Infarction(heart attack)

Definition

Is the death of cardiac muscle (coagulative necrosis) resulting from ischemia.

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

1. Left anterior descending artery.(40-50%) .
2. Right coronary artery (30-40%)
3. Left circumflex artery (about 20%)

- Note :(there are two main factors that determine how risky is the heart attack that the patient is having (1- the size of the infarct 2- the location of the infarct)
- ex: if the infarct is at the beginning of the artery → more necrosis→ more damage →higher chances of death → higher chance of complications(if lived)

Risk factors

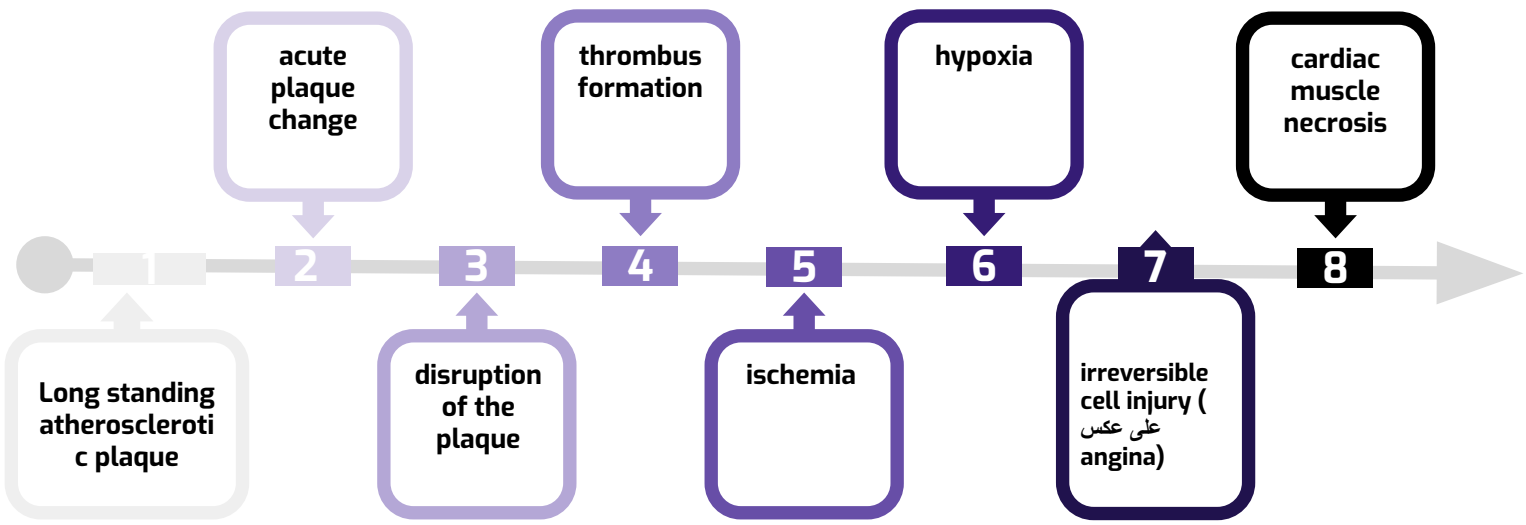
Are the same as those of coronary atherosclerosis.

- Atherosclerosis + age + male gender.
- Females are more affected after menopause due to decreased estrogen production.

(إحتمالية إصابة النساء تتساوى مع الرجال فقط بعد إنقطاع الطمث قبل ذلك إحتمالية إصابتهم أقل)

sequence of events

The following sequence of events usually occur within minutes :



This sequence above will lead to ---> MI
(type of necrosis : coagulative necrosis)
(note: the thrombus usually evolves to completely occlude the lumen of the coronary vessel within minutes).
(Explained later)

Types

1. Transmural: Full thickness (>50% of the wall)

2. Subendocardial: Inner 1/3 of myocardium

Myocardial Infarction(heart attack)

The pathogenesis

(Will be explained in general)

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).

This Will lead to

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.

How much ischemia is bad ?

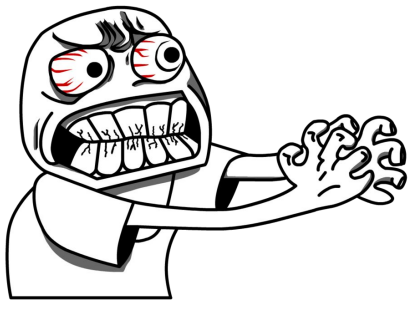
Severe ischemia lasting at least 20 to 40 minutes(15 minutes still angina) causes irreversible injury and myocardial necrosis on the ultrastructural (On Electron microscopy) level.

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

"you don't see the necrosis right away if you opened the heart. At the beginning The necrosis will only be identified on EM As time pass by the necrosis start to be more visible (even to the naked eye & light microscope) depending on how many post-infarct hours "

The full size of the infarct is usually determined within **3-6 hours** (it means within these hours we will decide how good and bad the infarction is) 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).

Note: At this stage the patient already had a heart attack , so all what we want is to limit the area of the infarction (make it smaller not bigger)within the first 3-6 hours because these hours decide the size of the infarction
والهدف من كل هذا الحفاظ على حياة المريض وتجنب تفاقم المشكلة



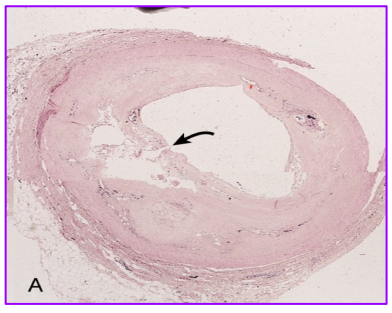
Say you understand it now , otherwise path's team will give you the green folder

Quick cover :
First ; there's atheroma (AS plaque) (in this step if there is a (15s-15 min) ischemia = typical angina
Second : there's a disruption on the Atheroma which will lead to step 3
Third : thrombosis = formed thrombus either blocked the lumen partially so we call it pre-infraction angina or complete occlusion causing severe ischemia leading to MI = coagulative necrosis

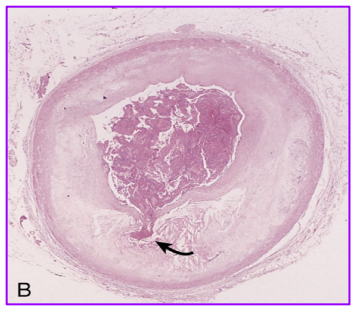
Morphologic Changes in Myocardial Infarction

MCQS can come from this table

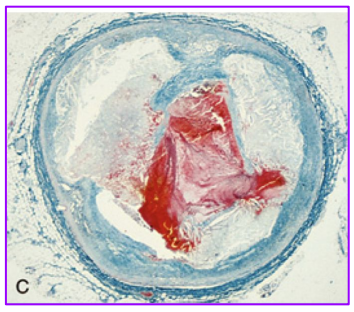
Time	Gross changes	Microscopic changes
0-4h	None	None
4-12h	Mottling	Coagulation necrosis (👻ghost outlines due to Disappearance of nuclei + injured mitochondria)
12-24h	Mottling	More coagulation necrosis; neutrophils come in
1-7 d	Yellow infarct center	Neutrophils die, macrophages come to eat dead cells النيتروتفلز تمثل السوسة اللي تقط نفسها بكل شيء من اختصاصها ولا لا عشان كذا بالنهاية م قدرت تتحمل وماتت
1-2 w	Yellow center, red borders	Granulation tissue
2-8 w	Scar	Collagen



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

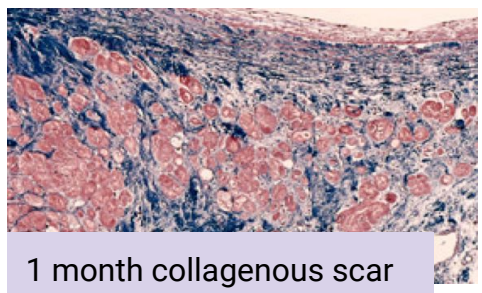


B. Acute coronary thrombosis superimposed on an atherosclerotic plaque with focal disruption of the fibrous cap, triggering fatal myocardial infarction.

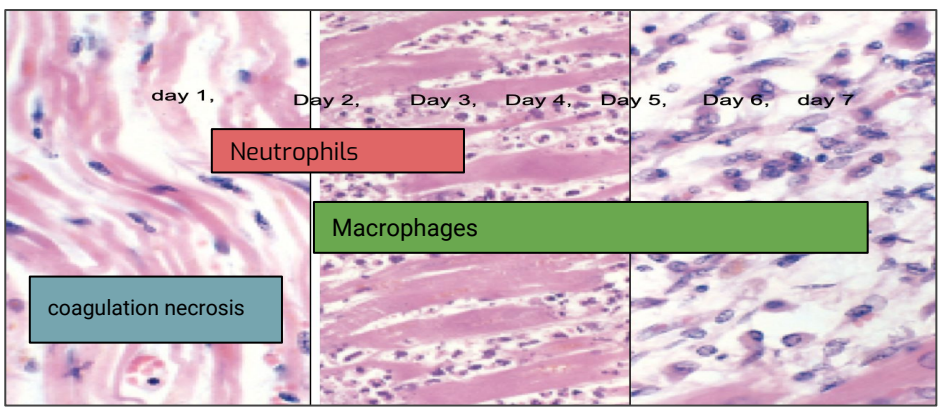


C. Massive plaque rupture with superimposed thrombus, also triggering a fatal myocardial infarction (special stain highlighting fibrin in red). In both

2 week granulation tissue



1 month collagenous scar



Coagulation necrosis: Can be seen after the first 4 hours till the end.
Neutrophils: Can be seen after the first 12 hour till the 3rd day
Macrophages: can be seen after the second day till the 7th day.

Clinical features of Myocardial Infarction

What the mind doesn't know , the eyes don't see . Diseases don't read books , your patient won't show symptoms like what the book wrote exactly, be smart !

MI clinical features

01 **Dyspnea**

02 **ECG shows typical findings of ischemia** (Like inverted U wave)

03 **Rapid and weak pulse**

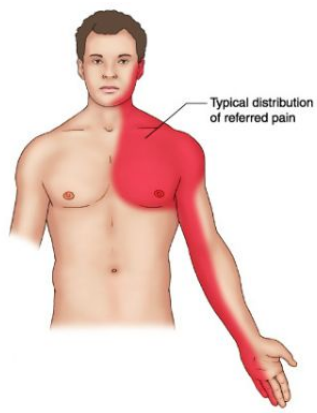
04 **Cardiogenic shock**

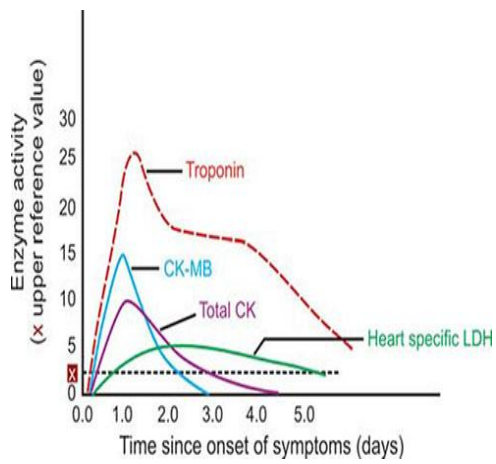
in massive MI, when more than 40% of left ventricle is affected

05 **Pain**

Pain can be :
- Severe crushing substernal 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 (nitroglycerin works on angina, so, you can differentiate between the two by the patient's response to the drug)
-no pain 20% of patients (diabetics, hypertensive, elderly) (So, they can have myocardial infarction without knowing)

06 **Diaphoresis** (sweating)





Laboratory elevations :

1- Troponins: best marker TnT, TnI (most specific)

(Troponins are regulatory proteins that are integral to muscle contraction)

- TnI and TnT are not normally detectable in the circulation
- After acute MI: Both troponins become Detectable after 2 to 4 hours
- Peaksat 48 hours. Their levels
- Remain elevated for 7 to 10 days

2- CK-MB is the second best marker

Creatine kinase is an enzyme expressed by various tissues and cell types 3 isoypes CK-MM, CK-BB and CK-MB. (M: musle B brain)

After acute MI:
- It begins to rise within 2 to 4 hours of MI
- Peaks at 24 to 48 hours
- Returns to normal within approximately 72 hours

3- Lactate dehydrogenase (LD)

A lactate dehydrogenase is an enzyme found in nearly all living cells

After acute MI:
- Rises in 24 hrs,
- Peaks in 72 hrs,

4- Myoglobins (found in girls' slides)

Outcomes\complications of myocardial infarction

- 10 to 20% of patients will experience to complication following MI
- 80 to 90% will experience one or more of the following complications

1-Cardiac arrhythmia **Occurs in 75-90% of patients**	-Many patients have conduction disturbances and myocardial irritability following MI, which can cause sudden death -Sudden death results from fatal ventricular arrhythmia, usually in patients with severe coronary artery disease -Sudden death can be asymptomatic, or within 1 to 24 hours of symptom onset
2- Left ventricular failure **Occurs in 60% of patients**	Associated with mild to severe pulmonary edema
3- Cardiogenic shock **Occurs in 10 % patients**	condition in which your heart suddenly can't pump enough blood to meet your body's needs
4- Myocardial rupture	This causes blood in chest wall
5- Thromboembolism **Occurs in 15-49% of patients**	Combination of contractility abnormality (which'll cause stasis), and endocardial damage (causing thrombogenic surface). This can cause mural thrombosis (thrombosis attaches to the heart chamber wall), and potentially, thromboembolism
6-Pericarditis	Inflammation of the pericardium
7-Ventricular aneurysm	In which the ventricle is dilated and the wall is thinned out
8- External infarct rupture	Associated with hemopericardium (bleeding into the pericardial space)
9-Chronic ischemic heart failure	Caused by: - Prior infarction(s) (most common) - Chronic low-grade ischemia

Males' Doctor Summary

Usually caused by acute coronary artery thrombosis

irreversible injury/cell death occurs within 20-40 minutes

Myocardial infarction

Necrosis of heart muscle is caused by ischemia

Prompt reperfusion can salvage myocardium

In other words, rapid reoxygenation of the myocardium can save it

01

Clinical features

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

02

Laboratory evaluations

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

03

Complications

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

04

Prognosis

- depends on remaining function and perfusion:
- overall 1 year mortality: 30%
- 3-4% mortality per year thereafter

Quiz

1- A 55 year old male comes to the clinic complaining of chest pain that arises when even while resting, there is no previous history of lung diseases and testing for atherosclerosis was negative which of the following could be the diagnosis:			
a- Stable angina	b- Prinzmetal angina	c- Myocardial infarction	d- Thrombosis
2- A 48-year-old man complains of chest pain upon exertion. He had been well until 4 months previously, when he first developed a chest discomfort while jogging. His symptoms have progressed to the point that he now develops chest pain after climbing a single flight of stairs. He has a history of diabetes controlled by diet and of 25 pack-years of cigarette smoking. His father and maternal grandfather both died of heart disease before the age of 60. On the 5th hospital day, the patient develops chest pain during periods of mild activity, which is minimally responsive to sublingual nitroglycerin. Results of laboratory studies include WBC of 8,100/µL, CK-MB of 4.5 ng/mL, and troponin-I of 0.5 ng/mL. Which of the following is the most likely diagnosis?			
a- Myocardial infarction	b- typical angina	c- unstable angina	d- variant angina
3- A 44-year-old man presents to the emergency room with acute chest pain. The ECG is normal. Analysis of which pair of serum markers given below would be most helpful in excluding a diagnosis of acute myocardial infarction in this patient?			
a- Cardiac troponin-I and myoglobin	b- CK-BB and myoglobin	c- CK-MB and cardiac troponin-I	d- CK-MM and lactate dehydrogenase (LDH)-1
4-: ---------- are more prone to be affected by myocardial infarction:			
a- Pre-puberty boys	b- Young adults	c- children	d- Postmenopausal women
5- A 49 year old female came in to the emergency room with difficulty breathing, after doing an ECG on her we see an inverted U wave, what could be the most likely diagnosis?			
a- myocardial infarction	b- stable angina	c- crescendo angina	d- prinzmetal angina
6- Which one of the following conditions isn't a common complication of MI			
a- Pericarditis	b- Thromboembolism	C- Ventricular aneurysm	d- Right ventricular failure

1-b
2-c
3-c
4-d
5-a
6-d

Summary

This summary was taken from
Dr. Ahmed Alhumidi's slides

Understand the pathology, pathogenesis and clinical consequences of atherosclerosis.

pathology Cells, Extracellular matrix:, Lipid, fibrous cap

Pathogenesis endothelial cell injury....dysfunction....smooth muscle immigration .....macrophages and smooth muscle engulf fat ..... smooth muscle proliferation and collagen deposition

Complications

Arterial obstruction.....ischemia

Embolization of plaque material..... ischemia

Weakening with rupture of the arterial wall .....aneurism and rupture of vessel

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

Pathology

MI

0-4 h No pathological findings
4-12h coagulation necrosis
12-1day neutrophils
1 day – 7 days less neutrophils and more macrophages
1 week-2 weeks granulation tissue
2 weeks – 8 weeks fibrosis

1. Typical Angina
2. Unstable angina
3. Prinzmetal angina

Complications

MI

Arrhythmia
Left ventricular failure
Cardiogenic shock
Myocardial rupture
Thromboembolism

Serum Troponins and CK MB

ECG finding

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