Cardiovascular system

Lectures two and three

Summary and MCQs

Risk factors and pathogenesis of atherosclerosis, Ischemic heart diseases: angina and myocardial infarction

Important Notes:

Arteriosclerosis:

Is divided into three types which are:

1- Atherosclerosis.
2- Calcific sclerosis (old age only)
3- Arteriolosclerosis

Atherosclerosis:

Definition:

Presence of Atheroma (Intimal thickening by lipid accumulation and other things)

What's its problem?

Obstruction of vascular lumen + weakening of the underlying media (smooth muscles) maybe aneurysm or rupture

Histology of Blood vessels:

Intima: Endothelial cells

Media: muscle and elastic tissue

Adventitia: Fibrous tissue

Pathology:

Atheroma:

1- Cells (smooth muscle cells migrating from the media +inflammatory calls + foam (facules containing) macrophages engulfing the fat).
2- Extra cellular matrix (collagen + elastic tissue)
3- Lipids

Two phases of Atherosclerosis are:

Pre-clinical:

Patient has Atherosclerosis but no symptoms, little thickening in the intima but nothing else. (little bit of obstruction)

When does it cause a problem and becomes clinical?

When there are complications:

1- Thrombosis – blood has turbulence → atheroma → thrombus formation (what closes up the valve).

See now it was halfway closed but with the thrombus formed it will be closed completely.

2- Rupture (Weaken the underlying media).

3- Aneurysm (dilatation of the artery).

4- Increased atheroma till it causes critical stenosis.

Now we understand that before the complications we don't have symptoms, we only have thickening.

What are the complications?

1- Myocardial infarction (ischemic heart disease)

2- Cerebral infarction. (arteries to the brain may lead to that)

3- Abdominal aortic aneurism

How does it start?

We have fatty streaks caused by foam macrophages (only seen after death) on the inside of the artery. (We see yellow lines).

Before the age of 45 we don't see any signs or symptoms. After 45 we begin to see them.

Risk factors:

Major (imp):

Not modifiable

1- Sex
2- Age
3- Family history and genetics, some people have susceptibility for atherosclerosis.

Modifiable:

1- Diabetes
2- Hypertension
3- Smoking
4- Hyperlipidemia

Minor: not as important

Lipoproteins:

Some are good and some are bad,

Bad lipoproteins (if they were elevated in our blood they will cause atherosclerosis:

- LDLs
- VLDLs
- Chylomicrons

HDL is a good lipoprotein if it was elevated in our blood it will prevent atherosclerosis

Pathogenesis:

What did the risk factor do to actually lead to atherosclerosis?

From the risk factor to the pathology there has to be pathogenesis leading up to it.

1- Endothelial cell injury (most imp).

2- Endothelial cell dysfunction

3- Increase permeability (leukocytes and macrophages will enter inside causing the atheroma: leukocytes and macrophages and lymphocytes)

4- Then smooth muscles from the media will migrate to intima

Ischemic heart disease:

- Consequence of atherosclerosis.
- Ischemic means insufficient blood supply
- Most of the time because of atherosclerosis.

Narrowing Percentage of the coronary artery	What Happens?
60% narrowing	There won't be any symptoms
75% narrowing	We can see symptoms, specially after effort
90% narrowing	Inadequate blood supply even at rest.

Only when it reaches 75% we can see symptoms, how?

1- Angina – chest pain (e.g. after climbing the stairs) why? Because the heart will then try to get more blood and fails because of insufficient blood supply)

2- 90% narrowing there will be inadequate blood supply even at rest.

3- When there is complication like thrombus (closing the valve completely) there will be myocardial infarction. – Death of part of myocardium.

Angina has three types (before MI)

1- **Typical:**
   - 75% narrowing
   - When exercise

2- **Unstable:**
   - 90% narrowing
   - Even at rest
   - Very important to watch because they are at risk of mi
   - Because they have thrombosis but it is not closed completely yet
   - Pain is tolerable compared with MI

3- **Prinzmetal:**
   - Has no relation to atherosclerosis or thrombus formation
   - Spasm of coronary artery of unknown etiology. (Very rare)

Myocardial Infarction:

- Death of myocardium
- Happens when there is disruption of the atherosclerotic plaque.

Pathogenesis:

1- Begins in the sub-endocardial region (بطانة القلب) (ischemia begins here)
2- More severe: it grows bigger in 3-6 hrs.
3- After 5 hours we will see full thickness necrosis

Clinical feature:

Severe crushing sub sternal pain (most important)

If there was a patient in ER and you thought he might have MI, you do ECG and serum blood test (might indicate there is MI):

1- **Troponin:**
   - Best marker and has types (C, T and I) what happens in the heart in T & I
   - We don't usually see it in the circulation, when do we see it?
     After 2-4 hours of infarction and it stays in the circulation for a week. So we find it raised.
   - Let's say a patient came after 3 days of MI, we will see troponin levels elevated in the blood

2- **Creatine kinase MB:**

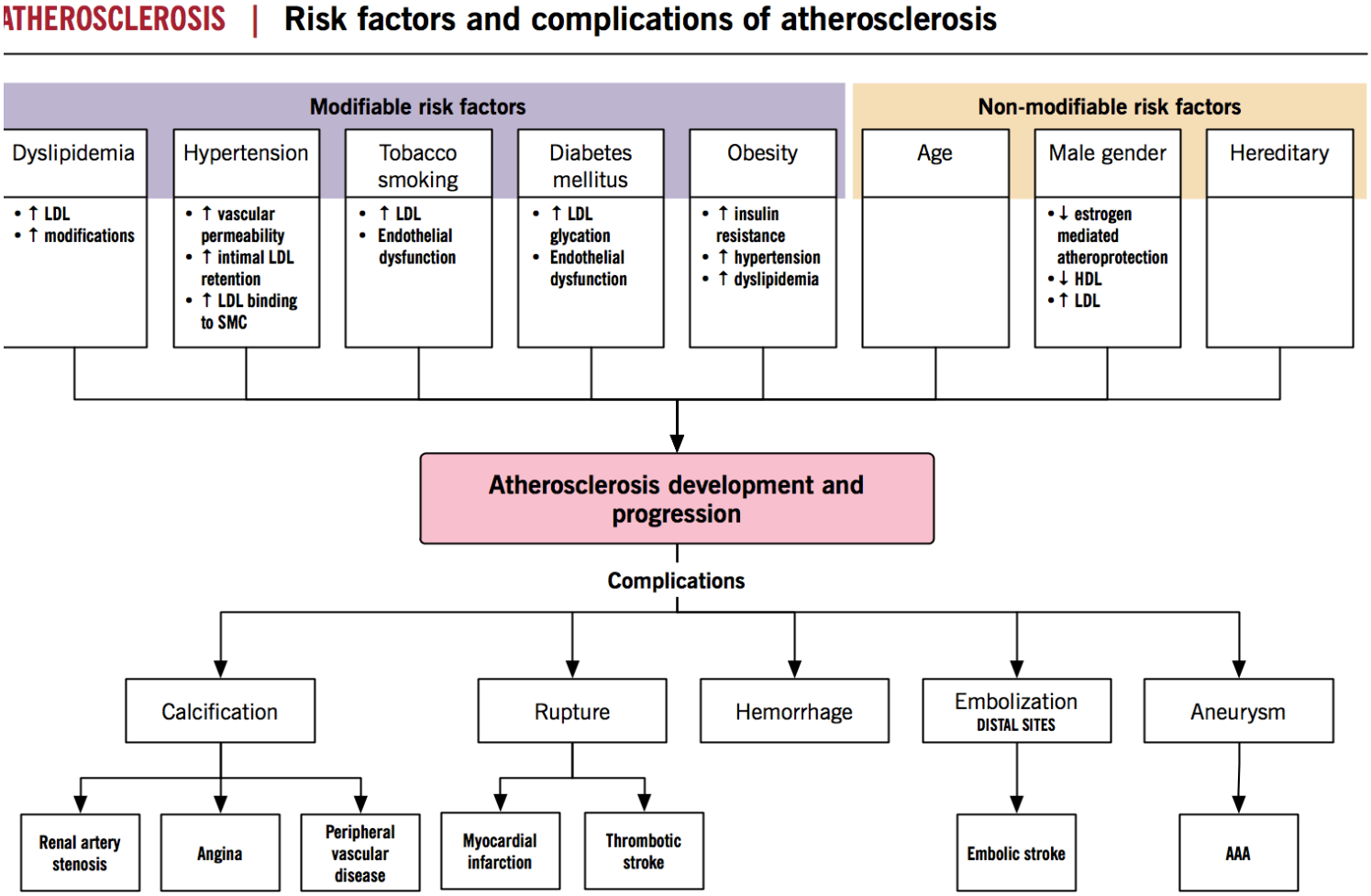
If a patient with mi came after 3 days we will find its levels normal because it returns to normal after 2-3 days.

Complication:

Most common is arrhythmia (may lead to death)

Summary:

Atherosclerosis:



Pathology

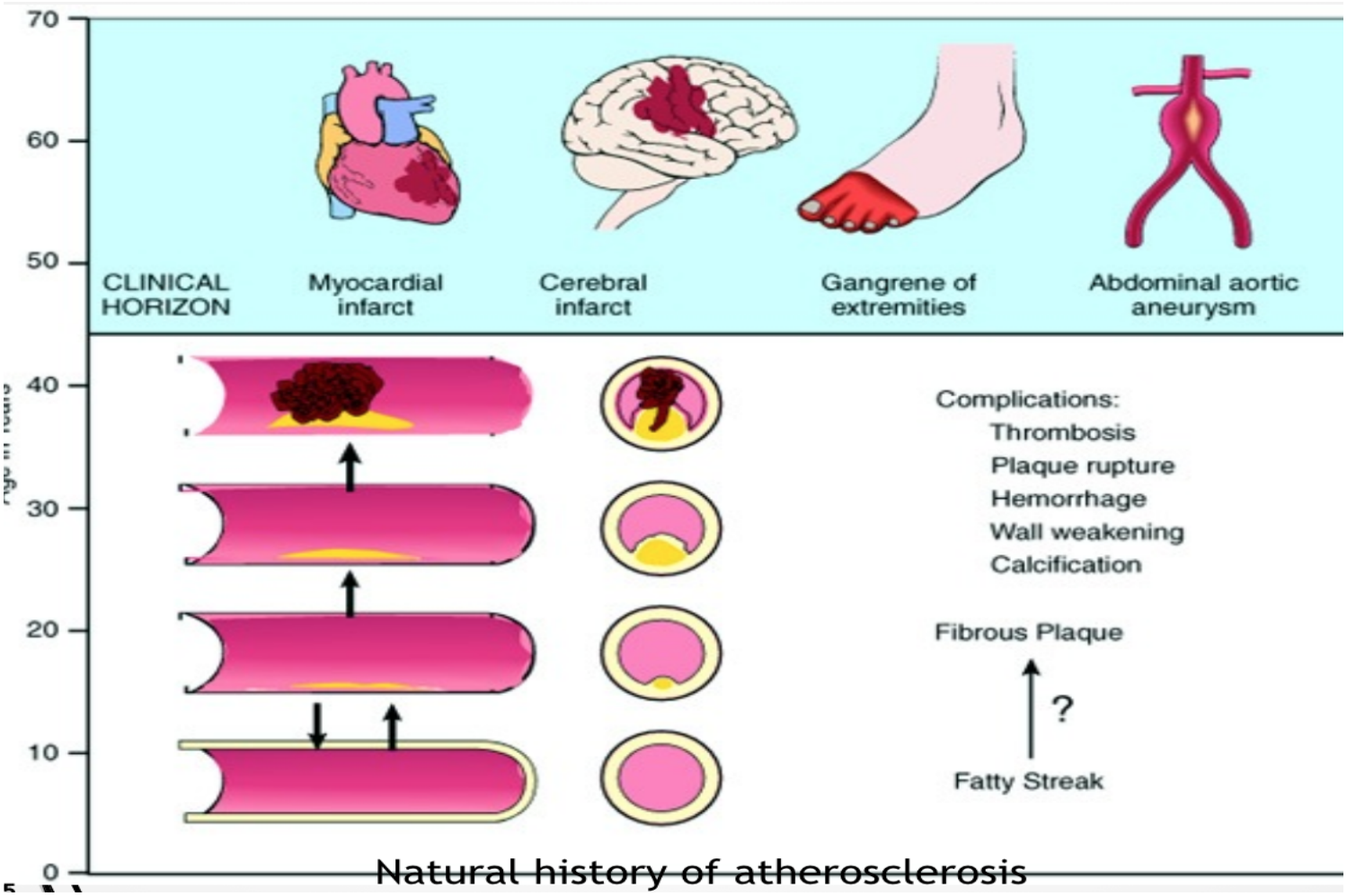
Cells, Extracellular matrix, Lipid, fibrous cap.

Pathogenesis

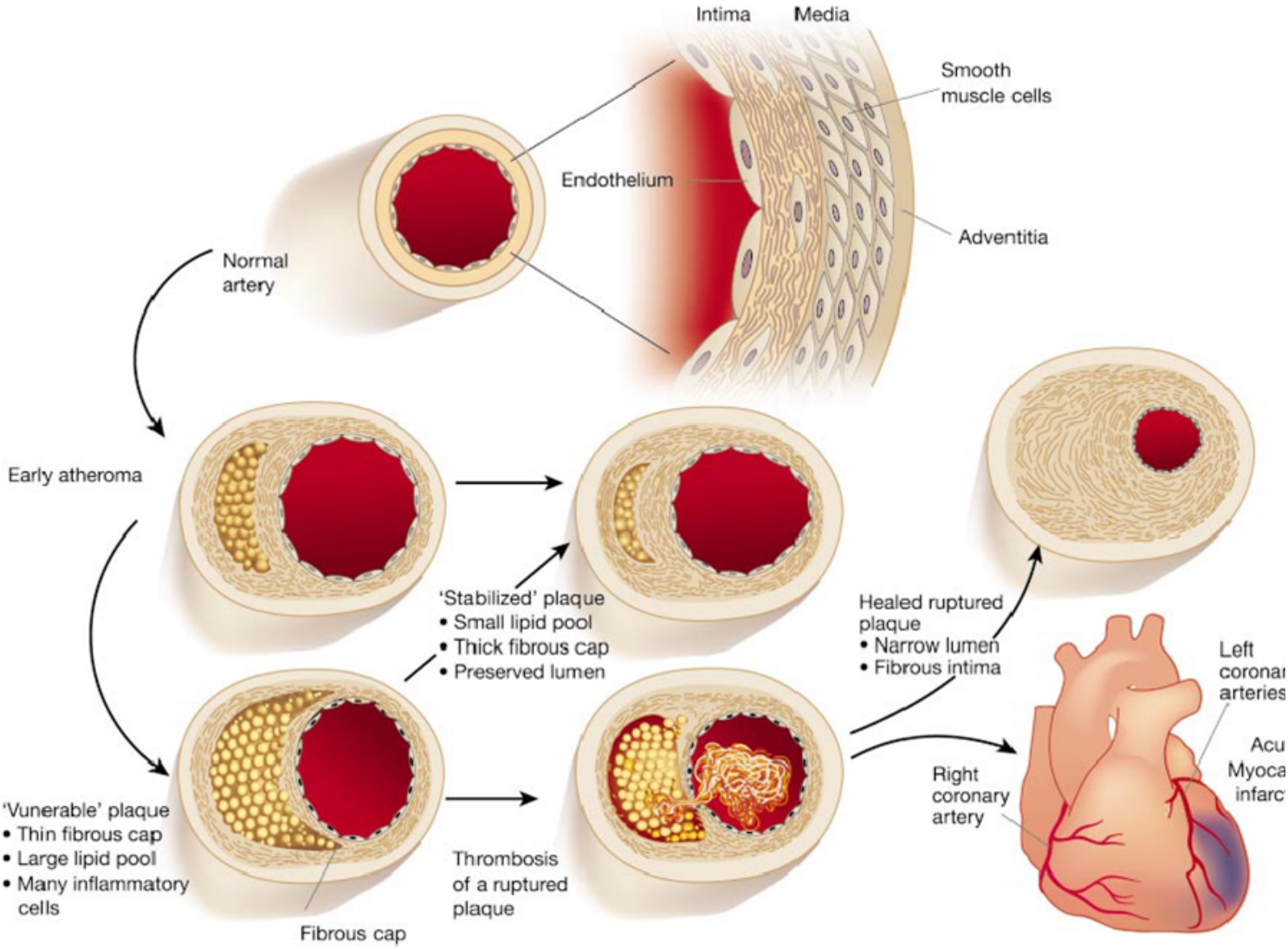
Endothelial cell injury → dysfunction→ smooth muscle immigration → macrophages and smooth muscle engulf fat → smooth muscle proliferation and collagen deposition.

Complications

1. Arterial obstruction→ ischemia
2. Embolization of plaque material → ischemia
3. Weakening with rupture of the arterial wall→ aneurism and rupture of vessel



Plaques usually develop slowly and insidiously over many years, beginning in childhood or shortly thereafter. As described in the text, they may progress from a fatty streak to a fibrous plaque and then to a complicated plaque that is likely to lead to clinical effects.



MI:

- Necrosis of heart muscle caused by ischemia.
- Most due to acute coronary artery thrombosis.
- Irreversible injury/cell death in 20-40 minutes
- Sudden plaque disruption
- Platelets adhere
- Coagulation cascade activated
- Thrombus occludes lumen within minutes
- Prompt reperfusion can salvage myocardium

Clinical features

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

Pathology:

→ 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

Laboratory evaluation:

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

Complications

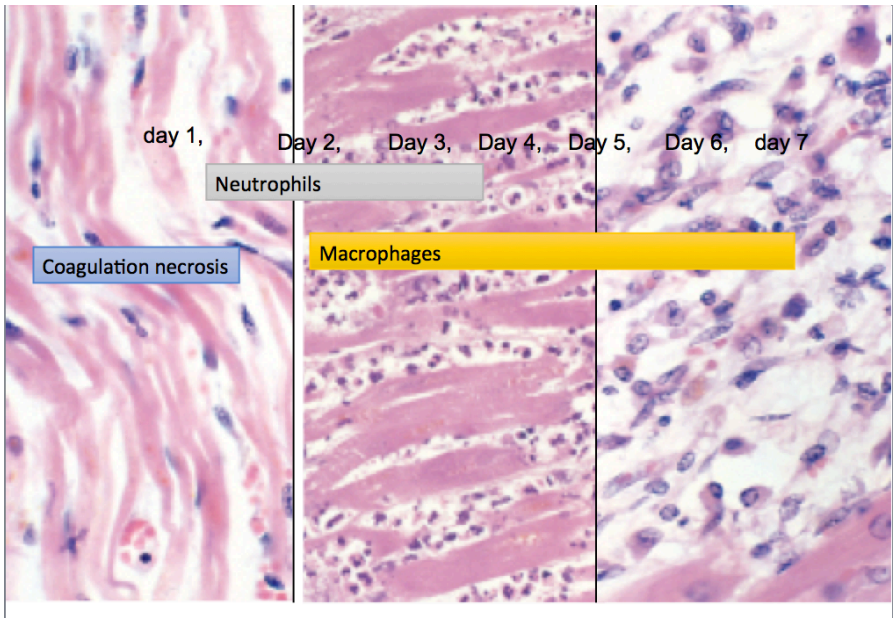
- Contractile dysfunction
- Arrhythmias
- Rupture
- Chronic progressive heart failure
- Arrhythmia
- Left ventricular failure
- Cardiogenic shock
- Myocardial rupture
- Thromboembolism

Prognosis:

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

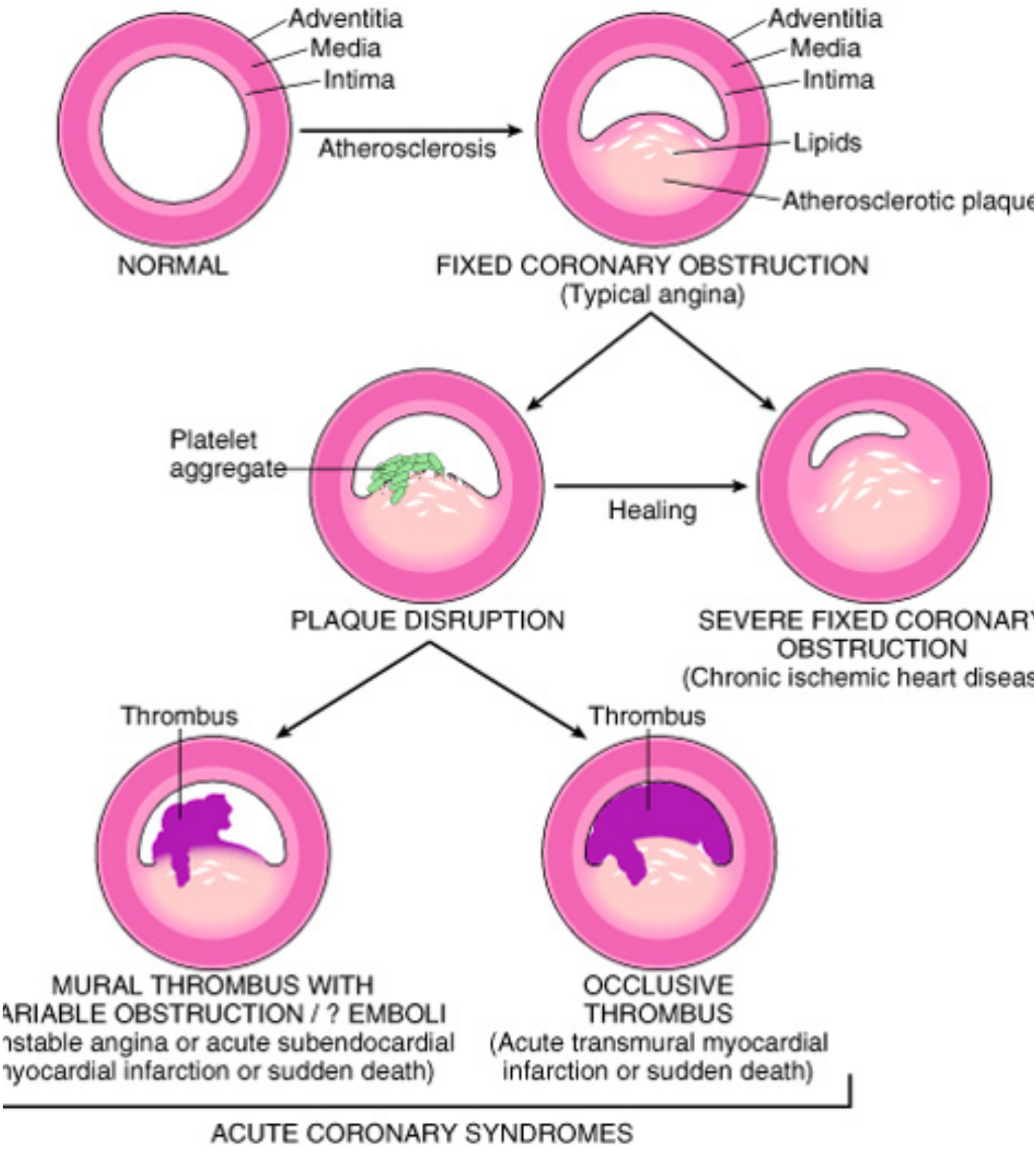
Morphology:

- 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.



MI: day 1, day 3, day 7

IHD:


Adventitia
Media
Intima
Atherosclerosis
Adventitia
Media
Intima
Lipids
Atherosclerotic plaque
NORMAL
FIXED CORONARY OBSTRUCTION
(Typical angina)
Platelet
aggregate
Healing
PLAQUE DISRUPTION
SEVERE FIXED CORONARY
OBSTRUCTION
(Chronic ischemic heart disease
Thrombus
Thrombus
MURAL THROMBUS WITH
ARIABLE OBSTRUCTION / ? EMBOLI
nstable angina or acute subendocardial
nyocardial infarction or sudden death)
OCCLUSIVE
THROMBUS
(Acute transmural myocardial
infarction or sudden death)
ACUTE CORONARY SYNDROMES

الملخص على شكل حالة تمر فيها بأغلب المعلومات اللي في المحاضرتين

1. **A 50-year-old man experiences 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 for 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, gangrene ……etc.

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

   Unstable (pre-infarction) angina

7. **What do you expect the findings in the coronary artery?**

   Plaque disruption and thrombosis

8. **Now the patient suffer from Severe crushing sub-sternal 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 …ect

11. **What is the expected microscopic finding in the first 30 minutes of myocardial infarction?**

    No microscopic findings

12. **Coagulation necrosis starts after which period of time of MI?**

    4 hours

Check your understanding with MCQs.

Q1 A 65-year-old Caucasian male presents to the emergency room with chest pain. Coronary angiography reveals significant stenosis of the left anterior descending (LAD) artery. Which of the following characteristics of the atheroma is the most important physiologically plausible predictor of myocardial necrosis in this patient?

A. Cholesterol crystal presence
B. Rate of formation
C. Calcium content
D. Presence of cytokines
E. Amount of foam cells

Q2 A 50-year-old Caucasian male notices substernal chest pain while walking his dog uphill in Central Park on a sunny Saturday morning. The pain disappears after 5 minutes of rest, and he continues to enjoy his weekend. As he smokes a cigarette later in the day, he wonders: which of the following pathologies were most likely responsible for his chest pain that morning?

A. A fixed atherosclerotic plaque obstructing 80% of one of his coronary arteries
B. A fixed atherosclerotic plaque obstructing 50% of one of his coronary arteries
C. An ulcerated fibrous plaque in one of his coronary arteries
D. A pulmonary embolism
E. A ruptured atherosclerotic plaque in one of his coronary arteries

Q3 A 65-year-old man presents to the Emergency Department complaining of substernal chest pain. An acute coronary event is suspected and a coronary catheterization procedure reveals an atherosclerotic plaque in the patient's left anterior descending artery. In the formation of an atherosclerotic plaque, which of the following pairings is correct?

A. Fibroblasts -- Foam Cells
B. Smooth Muscle Cells -- ECM deposition
C. Endothelial Cells -- Down regulation of VCAM-1
D. Smooth Muscle Cells -- Migration from intima to media
E. LDL chemical reduction -- Endothelial dysfunction

Q4 A 60-year-old male painter with severe chest pain is found to have atherosclerosis of his coronary arteries. What type of cells were most likely injured in the initial stage of his disease?

A. Myocytes
B. Fibroblasts
C. Neutrophils
D. Endothelial cells
E. Smooth muscle cells

Q5. A 14-year-old Caucasian female commits suicide by drug overdose. Her family decides to donate her organs, and her heart is removed for donation. After removing the heart, the cardiothoracic surgeon notices flat yellow spots on the inside of her aorta. Which of the following cell types initially predominate in these yellow spots?

A. Fibroblasts
B. Macrophages
C. Endothelium
D. T-cells
E. Neutrophils

Q6 A 66-year-old woman has sudden paralysis of the left side of her body. She has been smoking a pack of cigarettes daily for the past 45 years. Vital signs: temp: 37.1 C. heart rate 80/minute, respiratory rate 16/minute, and BP 160/100 mm Hg. A cerebral angiogram reveals occlusion of a branch of her middle cerebral artery. Laboratory findings include a hemoglobin A1C of 9%. - Which of the following components of blood lipids is most important in contributing to her disease?

A. Chylomicrons
B. HDL cholesterol
C. Oxidized LDL
D. VLDL

Q7 An autopsy study reveals that atheromas can begin forming during childhood. The gross appearances of the aorta are recorded and compared with microscopic findings of atheroma formation. - Which of the following is most likely to be the first visible gross evidence for the formation of an atheroma?

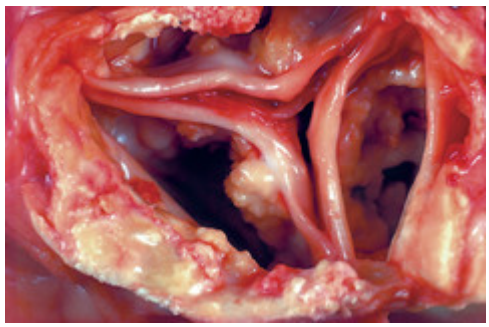
A. Thrombus
B. Fatty streak
C. Calcification
D. Hemorrhage

Q8 A 49-year-old woman with atherosclerosis came to the clinic. She complained of experiencing marked pain in her lower extremities on ambulation (moving) for more than 300 meters for the past 5 months. On physical examination, her lower extremities are cool and pale, without swelling or erythema. No dorsalis pedis or posterior tibial pulses are palpable. Her body mass index is 32 and she is a smoker. - Which type of atherosclerosis complication is most likely responsible for these symptoms?

A. MI
B. Peripheral vascular disease
C. Aortic aneurysms
D. Cerebral stroke

Q9 A 72-year-old man died suddenly from congestive heart failure. At autopsy, the heart weighed 580 g and showed marked left ventricular hypertrophy and minimal coronary arterial atherosclerosis. A serum chemistry panel ordered before death showed no abnormalities. Which of the following pathologic processes best accounts for the appearance of the aortic valve seen in the figure?

A. Amyloidosis
B. Dystrophic calcification
C. Lipofuscin deposition
D. Fatty change



Q10 A 56-year-old man reports reduced exercise tolerance over the past 5 years. Occasionally, he has been having chest pain after ascending a flight of stairs over the past year. He smokes 2 packs of cigarettes per day. He is found to have a blood pressure of 155/95 mm Hg. His body mass index is 30. Laboratory findings include a total serum cholesterol of 245 mg/dL with an HDL cholesterol that is 22 mg/dL. Which of the following vascular abnormalities is most likely his underlying pathology?

A. Hyperplastic arteriolosclerosis
B. Deep venous thrombosis
C. Medial calcific sclerosis
D. Atherosclerosis

Q11 A 63-year-old man has had insulin dependent diabetes mellitus for over two decades. The degree of control of his disease is characterized by the laboratory finding of a hemoglobin A1C of 10.1%. He has noted episodes of abdominal pain following meals. These episodes have worsened over the past year. On physical examination, there are no masses and no organomegaly of the abdomen, and he has no tenderness to palpation. - Which of the following pathologic findings is most likely to be present in this man?

A. Ruptured aortic aneurysm
B. Chronic renal failure
C. Mesenteric artery occlusion
D. Acute pancreatitis

Lecture questions

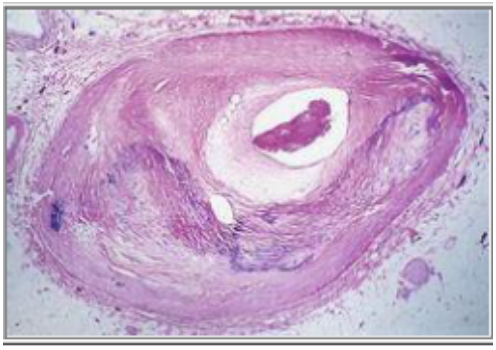
Q12 A 68-year-old obese woman (BMI = 32 kg/m2) presents with substernal chest pain. Results of laboratory studies include an elevated WBC count (13,000/μL), CK-MB of 6.6 ng/mL, and troponin-I of 2.5 ng/mL. ECG confirms a myocardial infarction of the left ventricular wall. Which of the following mechanisms is most likely responsible for the myocardial infarction in this patient?

A. Coronary artery thrombosis
B. Coronary artery vasospasm
C. Decreased collateral blood flow
D. Deep venous thrombosis
E. Paradoxical embolism

Q13 A study of atheroma formation leading to atherosclerotic complications evaluates potential risk factors for relevance in a population. Three factors are found to play a significant role in the causation of atherosclerosis: smoking, hypertension, and hypercholesterolemia. These factors are analyzed for their relationship to experimental models for atherogenesis. Which of the following events is the most important direct biologic consequence of these factors?

A. Endothelial injury and its sequelae
B. Conversion of smooth muscle cells to foam cells
C. Alterations of hepatic lipoprotein receptors
D. Inhibition of LDL oxidation
E. Alterations of endogenous factors regulating vasomotor tone

Q14 A 59-year-old man has experienced chest pain at rest for the past year. On physical examination, his pulse is 80/min and irregular. The figure shows the microscopic appearance representative of the patient's left anterior descending artery. Which of the following laboratory findings is most likely to have a causal relationship to the process illustrated?



A. Low Lp(a)
B. Positive VDRL
C. Low HDL cholesterol
D. Elevated platelet count
E. Low plasma homocysteine

Q15 A 60-year-old man has experienced angina on exertion for the past 6 years. A coronary angiogram performed 2 years ago showed 75% stenosis of the left anterior descending coronary artery and 50% stenosis of the right coronary artery. For the past 3 weeks, the frequency and severity of the anginal attacks have increased, and pain sometimes occurs even when he is lying in bed. Which of the following is most likely to explain these findings?

A. Hypertrophy of ischemic myocardium with increased oxygen demands
B. Increasing stenosis of right coronary artery
C. Fissuring of plaque in left coronary artery with superimposed mural (partial) thrombosis
D. Sudden complete thrombotic occlusion of right and left coronary arteries
E. Reduction in oxygen-carrying capacity owing to pulmonary congestion

Answers:

Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	Q15
B	A	B	D	B	C	B	B	B	D	C	A	A	C	C

Explanations:

Q1 Answer: B
A slow-forming atheroma allows for formation of collateral circulation, thereby lowering the chance of myocardial infarction (MI) and necrosis.

The most important factor as to whether or not a coronary artery plaque will cause an ischemic MI, is the rate in which the artery is occluded. If occluded slowly, there is time for the development of new arterial collaterals which are protective from myocardial ischemia. These collateral vessels provide blood flow to hypoperfused area of cardiac tissue distal to the point of occlusion. Conversely, with rapid coronary occlusion, there is not enough time for collateral development and thus myocardial ischemia is inevitable.
Incorrect Answers:
Answers A, C, D, E: None of these are important predictors of myocardial necrosis.

Q2 Answer: A
The patient displays stable angina pectoris with an underlying risk factor for atherosclerosis (smoking). Fixed atherosclerotic plaques obstructing >75% of coronary arteries are associated with stable angina.

Chronic (stable) angina pectoris is characterized by 3 distinct features: deep, poorly localized chest or arm pain, reproducible with physical exertion, and relieved with 5 minutes of rest or use of sub-lingual nitroglycerin. Hypertension, cigarette smoking, and hyperlipidemia are three major risk factors for atherosclerosis.

Incorrect Answers:
Answer B: Plaques obstructing <75% are usually asymptomatic.
Answer C: Ulcerated fibrous plaques are associated with unstable angina.
Answer D: PE's usually do not typically present like the vignette above describes.
Answer E: Ruptured plaques with a fully obstructive thrombus are associated with a transmural MI.

Q3 Answer: B
In the formation of an atherosclerotic plaque, smooth muscle cells (SMCs) are responsible for the deposition of extracellular matrix (ECM) in the intima. SMC proliferation and SMC-mediated ECM deposition are major processes leading to intimal thickening.

There are several mechanisms leading to endothelial dysfunction, including dyslipidemia and inflammation. This dysfunction allows for the deposition of LDL in the intima and the recruitment of monocytes. Factors released by injured endothelial cells and monocytes contribute to SMC migration and proliferation. Combined, these processes lead to the formation of an atheroma (atherosclerotic plaque).

Incorrect Answers:
Answer A: Macrophages become foam cells following phagocytosis of lipid particles.
Answer C: Endothelial cells upregulate vascular cell-adhesion molecules, such as VCAM-1, which allow for leukocyte adhesion to the injured vascular wall, ultimately facilitating diapedesis.
Answer D: Smooth muscle cells migrate from the media to the intima.
Answer E: Oxidized LDL contributes to endothelial dysfunction.

Q4 Answer: D
Endothelial cell injury (e.g. from hypertension, diabetes, smoking, etc.) results in increased permeability of the endothelium and exposure of subendothelial collagen. Monocytes, lymphocytes, and LDL cholesterol migrate into the intima, and exposure of subendothelial collagen promotes platelet aggregation. A chronic inflammatory state in the intima perpetuates the formation of an atheroma.
Incorrect Answers:
Answers A, B, C, E: While these cells are involved in atherosclersosis, none are the site of initial injury.

Q5 Answer: B

Incorrect Answers:
Answers A, C, D, E: These cell types are not the predominant cells in a fatty streak.
The "yellow spots" are actually fatty streaks that are seen in all persons over 10 years of age. Fatty streaks are mainly made up of macrophages.

In the pathogenesis of atherosclerosis, macrophages engulf LDL cholesterol within the intima, forming foam cells. These foam cells form the yellow fatty streaks described in the vignette above. Fatty streaks are considered a precursor lesion of atheromas which, with time, may evolve to plaques. Not all fatty streaks progress to atherosclerosis.
Incorrect Answers:
Answers A, C, D, E : These cell types are not the predominant cells in a

Q6 Answer: C) CORRECT. She has had a 'stroke' which is most often a consequence of cerebral atherosclerosis or embolic disease from the heart as a consequence of ischemic heart disease from atherosclerosis. LDL brings cholesterol to arterial walls, and when increased LDL is present or when there is hypertension, smoking, or diabetes, there is more degradation of LDL to oxidized LDL which is taken up into arterial walls via scavenger receptors in macrophages to help form atheromas.

Q7 Answer: (B) CORRECT. This is the first sign. It is benign and reversible, but it may be the precursor to more severe plaques.

Q8 Answer (B)

Q9 Answer (B) The idea from this question is aortic calcification narrows the aortic valve & the LV must generate more pressure leading to LV hypertrophy.

Q10 Answer (D)

Q11 (C) CORRECT. He has 'abdominal angina' from diminished blood flow to the bowel as a consequence of severe atherosclerosis. Persons with diabetes mellitus may have this, because all branches of major arteries to the bowel are affected by atherosclerosis

Q12 The answer is A: Coronary artery thrombosis. Coronary artery thrombosis is the most common cause of acute myocardial infarction and is often secondary to rupture of an atherosclerotic plaque.
Diagnosis: Myocardial infarction

Q13 (A) Atherosclerosis is thought to result from a form of endothelial injury and the subsequent chronic inflammation and repair of the intima. All risk factors, including smoking, hyperlipidemia, and hypertension, cause biochemical or mechanical injury to the endothelium. Formation of foam cells occurs after the initial endothelial injury. Although lipoprotein receptor alterations can occur in some inherited conditions, these account for only a fraction of cases of atherosclerosis, and other lifestyle conditions do not affect their action. Inhibition of LDL oxidation should diminish atheroma formation. Vasomotor tone does not play a major role in atherogenesis.

Q14 (C) The figure shows an arterial lumen that is markedly narrowed by atheromatous plaque complicated by calcification. Hypercholesterolemia with elevated LDL and decreased HDL levels is a key risk factor for atherogenesis. Levels of Lp(a) and homocysteine, if elevated, increase the risk of atherosclerosis. Syphilis (positive VDRL test result) produces endarteritis obliterans of the aortic vasa vasorum, which weakens the wall and predisposes to aneurysms. Although platelets participate in forming atheromatous plaques, their number is not of major importance. Thrombocytosis can result in thrombosis or hemorrhage.

Q15 (C) This patient has 75% stenosis of the left anterior descending branch of the coronary artery. This degree of stenosis prevents adequate perfusion of the heart when myocardial demand is increased, **which occurs during exertion. The patient had angina on exertion. The patient has recently developed** unstable angina, which is manifested by increased frequency and severity of the attacks and angina at rest. In most patients, unstable angina is induced by disruption of an atherosclerotic plaque followed by a mural thrombus and possibly distal embolization, vasospasm, or both.
Hypertrophy of the heart is unlikely in this case because there is neither hypertension nor a valvular lesion.
The remaining choices theoretically can give rise to a similar picture, but plaque disruption with mural thrombosis is the most common anatomic finding when the patient develops unstable angina.
It is important to recognize this because unstable angina is a harbinger of myocardial infarction

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قال صلى الله عليه وسلم: من سلك طريقًا يلتمس فيه علمًا سهّل الله له به طريقًا إلى الجنة

دعواتنَا لكم بالتوفيق.