Pathology team

Lecture 2:

ATHEROSCLEROSIS

https://www.youtube.com/watch?v=fLonh7ZesKs
good video of pathogenesis

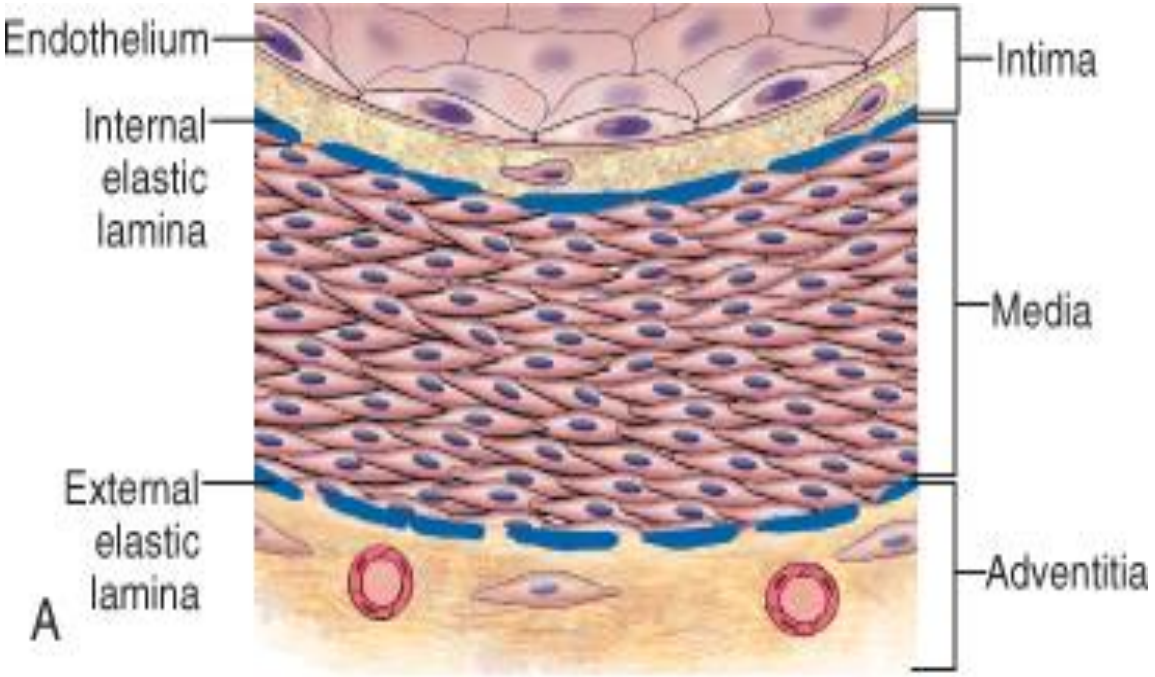
OBJECTIVES

- At the end of these two lectures, the student should:

1. Risk factors of atherosclerosis.
2. Understand the pathogenesis and clinical consequences of atherosclerosis.
3. Pathogenesis of the fibrolipid atherosclerotic plaque.
4. Clinical complications of atherosclerosis.
5. Commonest sites for the clinically significant coronary atherosclerosis.

Vessel wall structure

Any damage of the endothelium can cause many reactions.



WHAT'S Atherosclerosis (AS)?

- A type of arteriosclerosis
- Effects large elastic arteries and medium muscular arteries.
- Chronic inflammatory response in the wall of arteries.
- Slowly progressive.
- A build-up of fat (cholesterol) within the artery wall.
- Characterized by intimal lesions called: atheromas, atheromatous or fibrofatty plaques.

Common sites

*Abdominal aorta.
*Coronary arteries.
*Popliteal artery.
*The internal carotid arteries.
*The vessels of the circle of Willis.
*renal artery

Atherosclerosis Risk factors

major	Lesser, uncertain or non quantitated
Non modifiable	Obesity
Increasing age	Physical inactivity
*Male gender	Stress(type A personality)
Family history	Postmenopausal women
Genetic abnormalities	High carbohydrate intake
Potentially controllable	Alcohol
Dyslipidemia (↑LDL and ↓HDL)	Lipoprotein Lp(a)
Hypertension	Hardened (trans) unsaturated fat intake
Cigarette smoking	Chlamydia pneumonia infection
Diabetes	

*Female have estrogen and the estrogen fight against lipids

LDL Vs HDL :

Low-density lipoproteins (LDLs):	High-density lipoproteins (HDLs):
bad cholesterol	**Good cholesterol**
deliver cholesterol to peripheral tissues	mobilizes cholesterol from developing and existing atheromas and transports it to the liver for excretion in the bile.

***Consequently, higher levels of HDL correlate with reduced risk VLDL.**

Atherosclerosis Pathogenesis

1- Endothelial injury : which do not understood the cause yet. this can lead to **endothelial dysfunction** (increase permeability of leukocyte and monocyte adhesion) by:

A- Hemodynamic disturbances (blood flow, under the action of external forces)

B- Hypercholesterolemia

C- inflammation is an important contributor.

-Adhesion of blood monocytes (and other leukocytes) to the endothelium, followed by their migration into the intima and their transformation into "**Foam cells**" (Macrophages full of lipids)

2- Smooth muscle cell proliferation

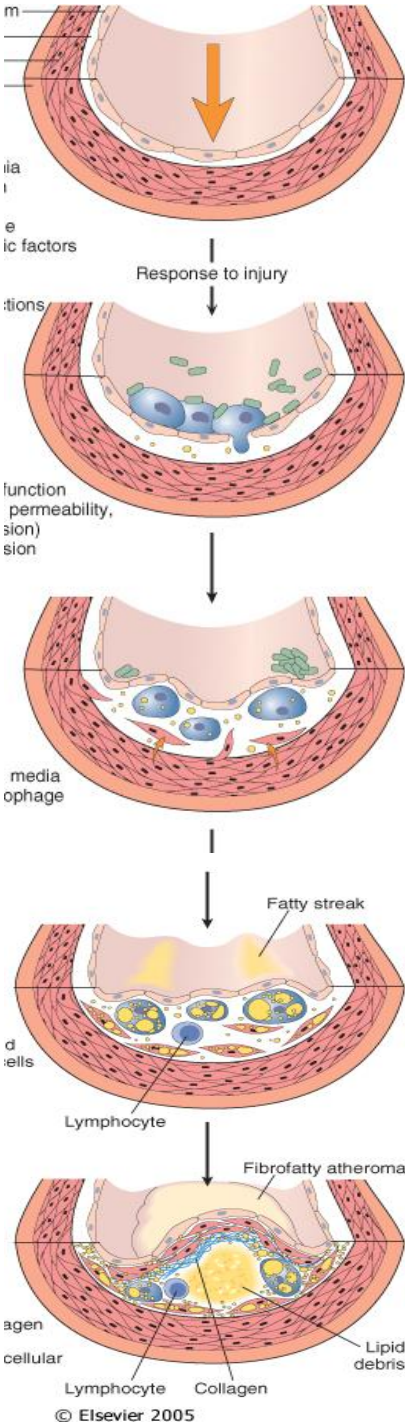
Vascular injury/dysfunction stimulates SMCs. The SMCs:

1.migrate from the media to the intima.

2.In the intima they lose the capacity to contract and gain the capacity to divide. So they multiply/proliferate as intimal SMCs.

3.They synthesize collagen, elastin etc and deposit extracellular matrix (ECM).

(macrophage and smooth muscle engulf the lipid then proliferate)

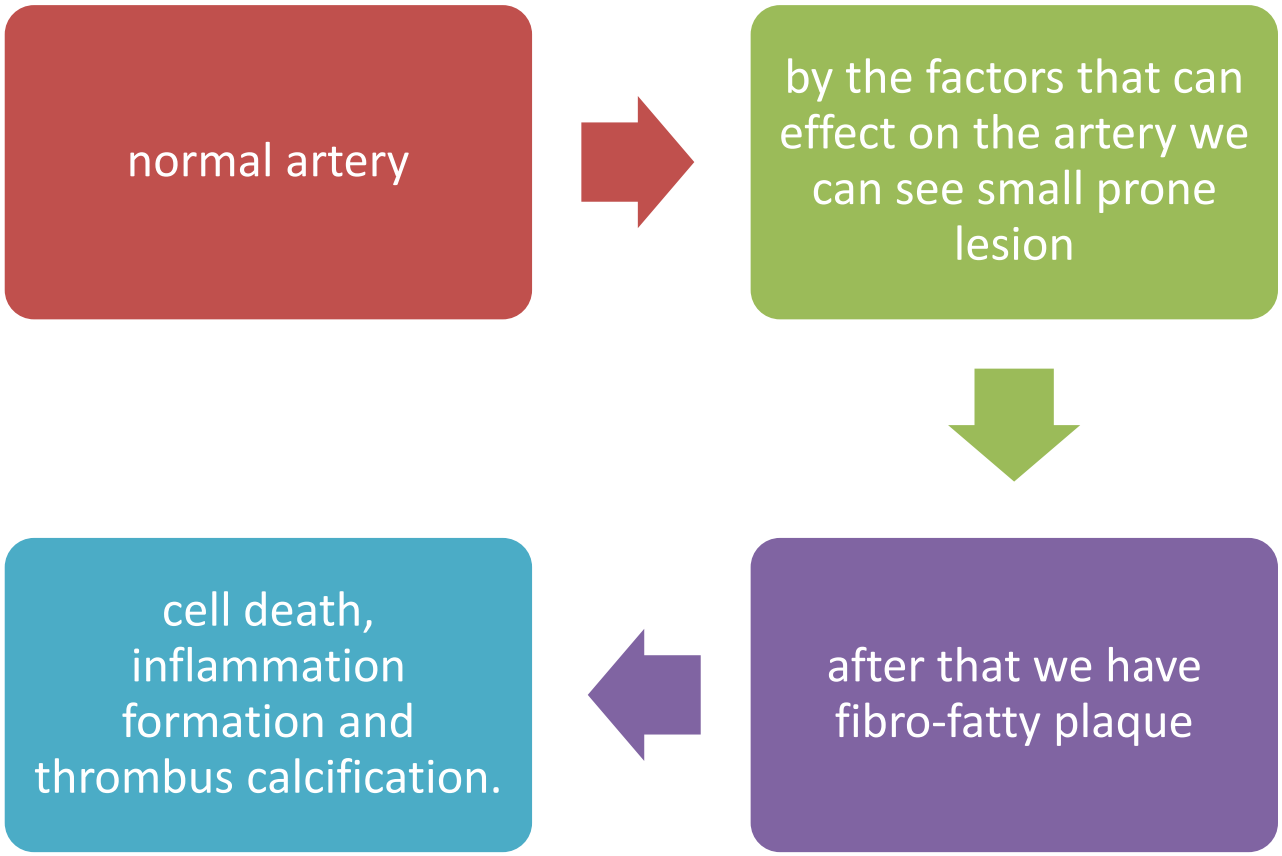


Atherosclerosis

Consequences

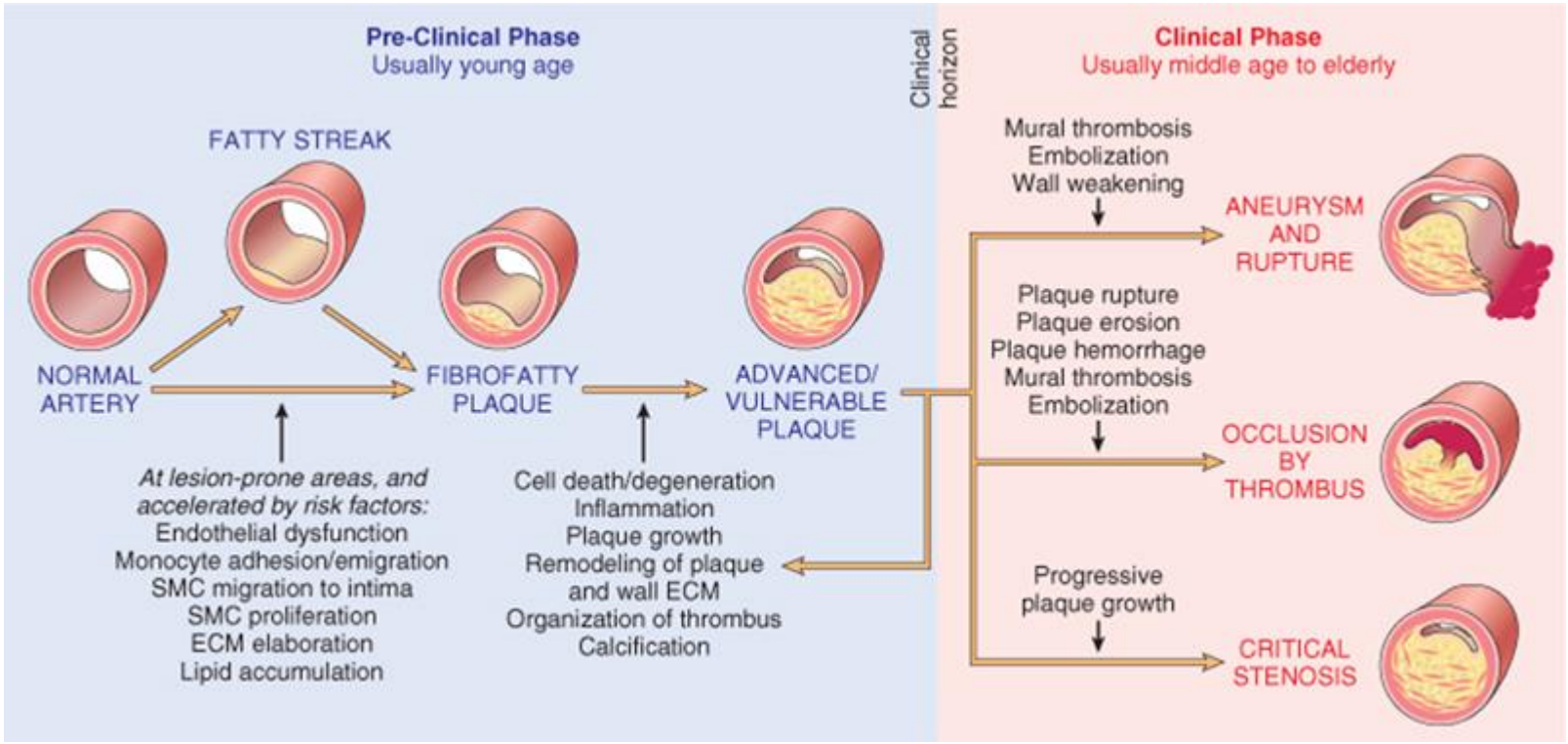
Two categories

1-stable (asymptomatic, are rich in **extracellular matrix** and **smooth muscle cell)**
2-unstable (unstable plaques are rich in **macrophage** and **foam cells** and the extracellular matrix and known as **fibrous cap**)



One of these will happen:

A- Critical stenosis	•(progressive plaque growth).
B- Acute plaque changes	•(plaque rupture > plaque hemorrhage > occlusion by thrombus , & thrombus embolization)
C- Aneurysm and rupture	•(wall weakening & erosion causing hemorrhage)



Formation of Atherosclerosis plaques

The main components of a fibrofatty plaques:

- **Lipids.**
- **Extracellular matrix.**
- **Cells, Proliferating smooth muscle cell.**

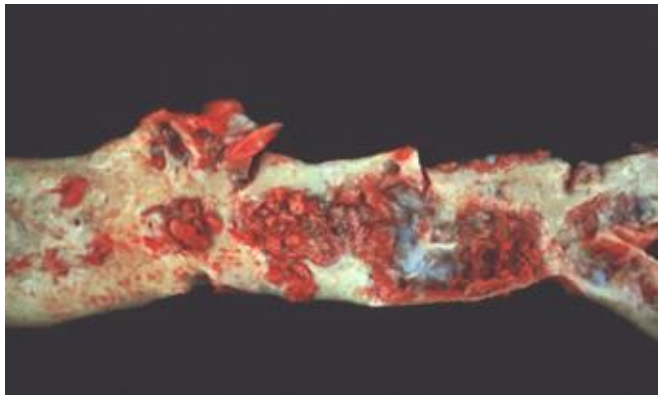
Gross morphology:

atheromatous plaques are patchy and variable along the vessel length

- **how is it start??**
- **Fatty streaks** are the earliest lesion of atherosclerosis they are a collection of lipid laden **foam cells in the intima.**

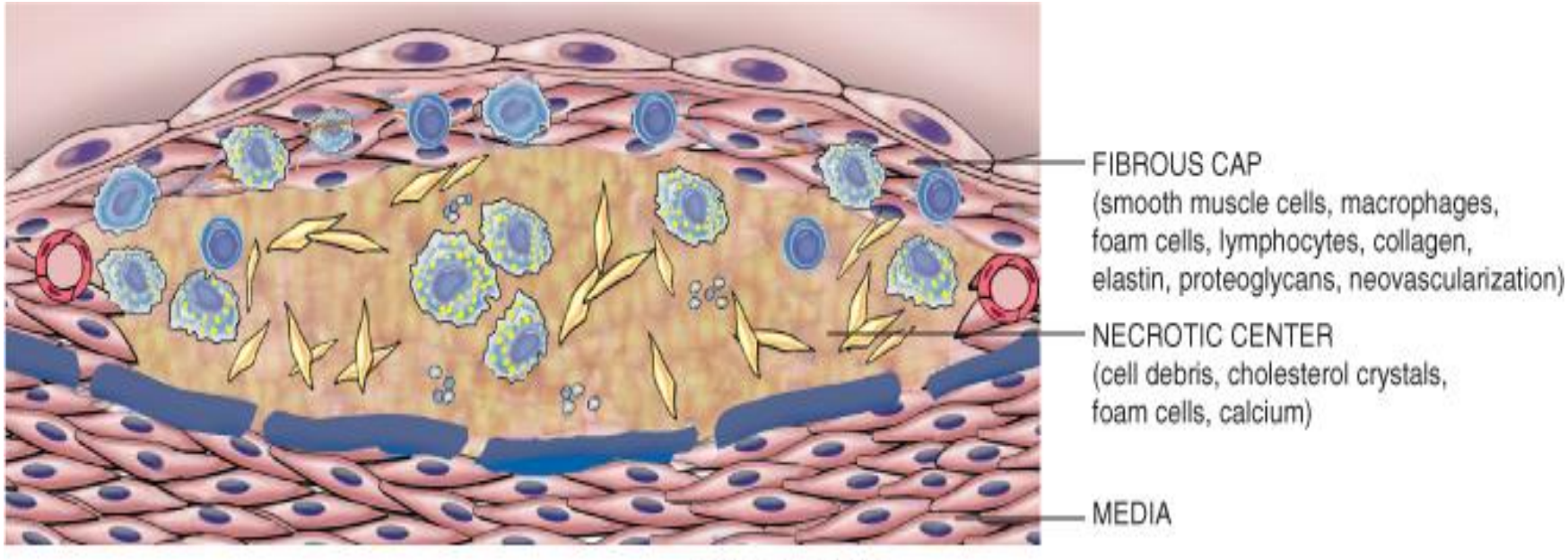
- They **do not** cause any disturbance

in blood flow, But it's the point of the origin



Microscopic Morphology

- the superficial **fibrous cap** is composed of SMCs and dense ECM. Beneath and to the side of the cap (the **"shoulder")** is a cellular area consisting of macrophages, SMCs, and T lymphocytes.
- Deep to the fibrous cap is **a necrotic core**, containing a disorganized **mass of lipid** (primarily cholesterol and cholesterol esters), **cholesterol clefts, debris from dead cells**, **foam cells, fibrin and perhaps calcium.**



Morphological changes in atherosclerosis

1-Thrombosis
2-Neovascularization
3-Medial thinning
4-Cholesterol microemboli
5-Aneurysmal dilatation
6-Calcification
7-Hemorrhage
8-Fissure
9-Ulcer

Atherosclerosis Clinical Complications:

What can happen if the block in:

1- Coronary artery: it will cause **Myocardial infarction** .

2- In brain :cerebra infarct **flush stroke**

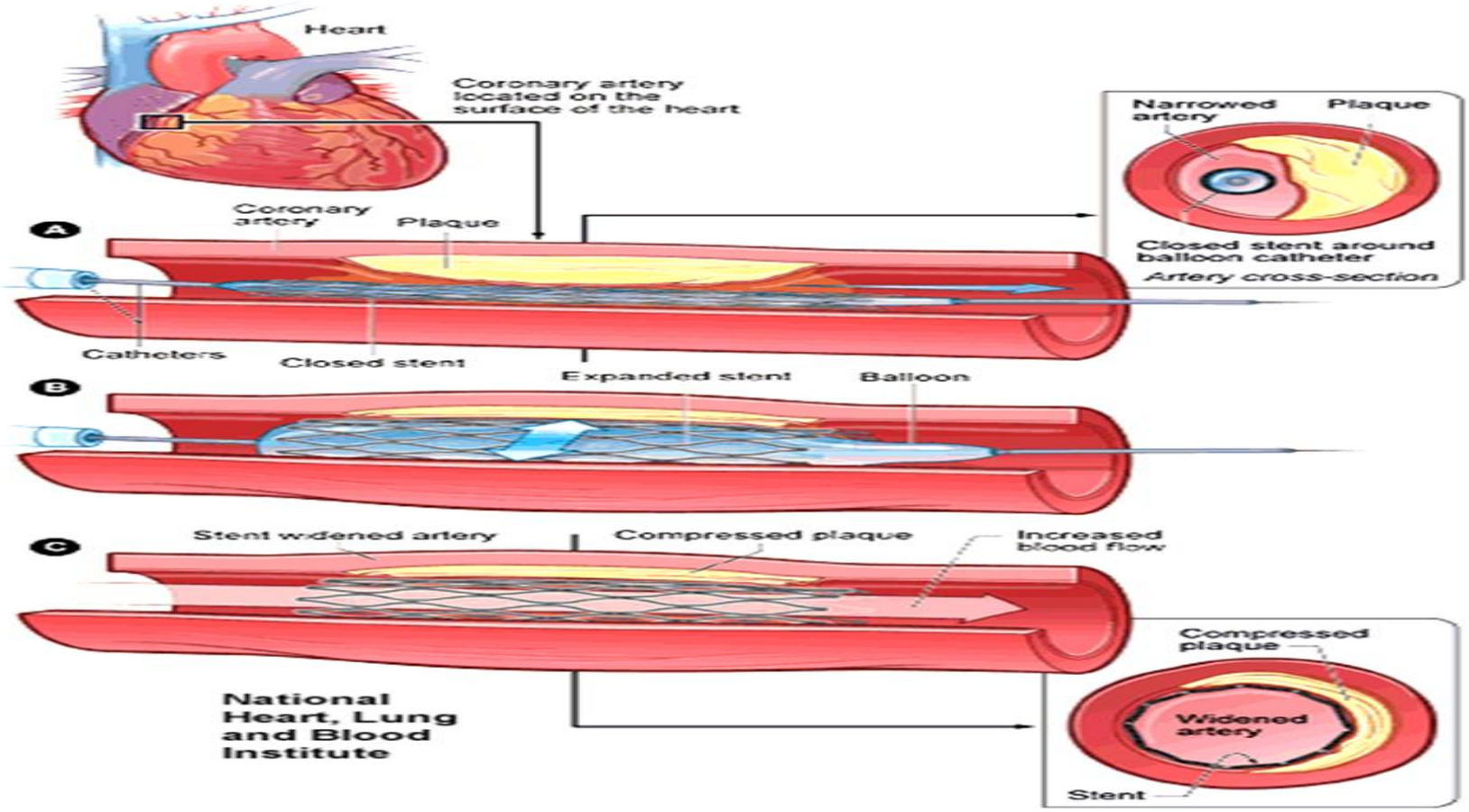
3- In foot (peripheral vascular disease):**gangrene**

4- in the abdominal aorta **: aneurysm** *

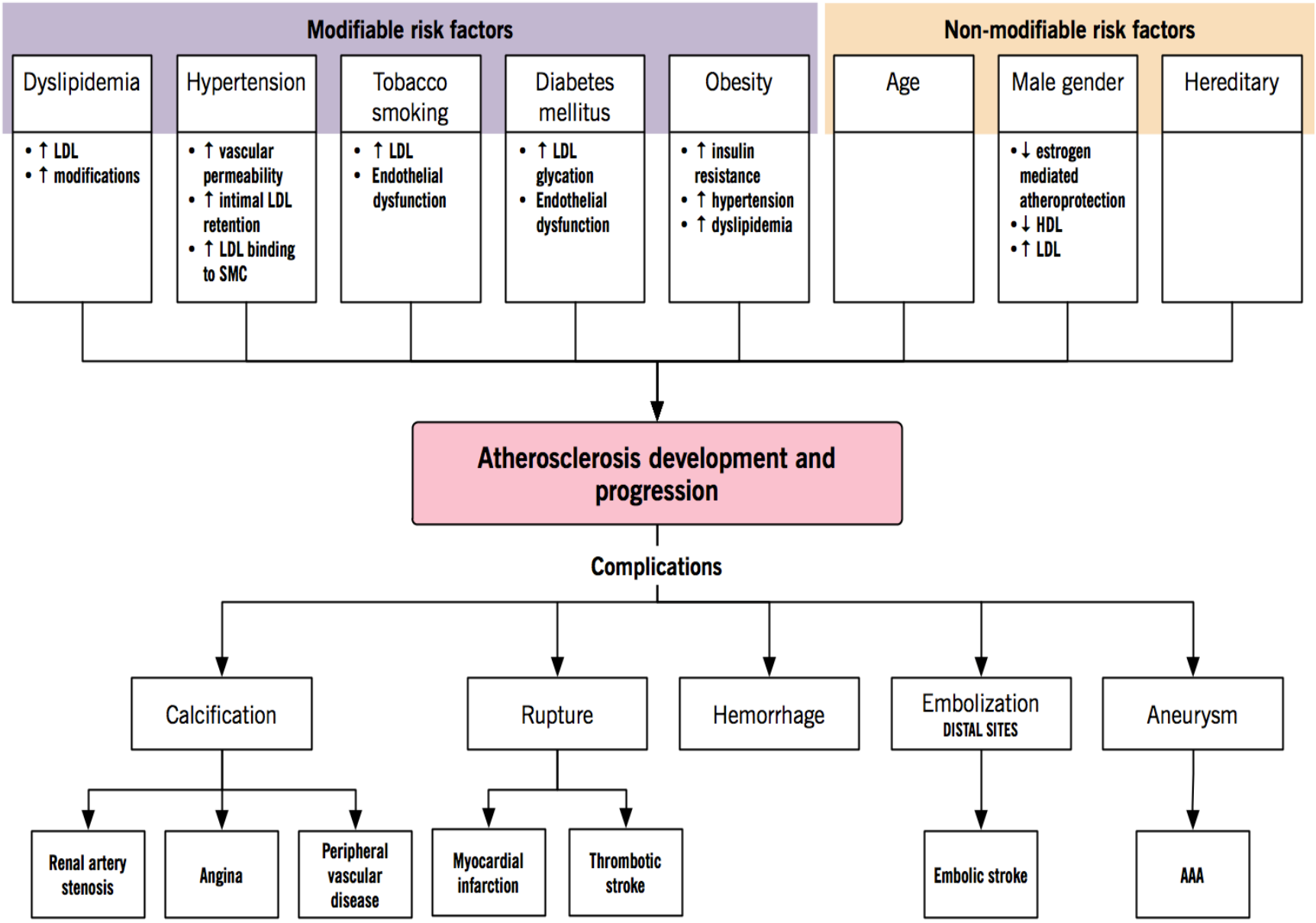
*(localized, blood-filled balloon-like bulge in the wall of a blood vessel), (the wall become week and bulging out >it's horrible disease , because if you have aneurysm in abdominal aorta most of the time the patient has no idea about it)

What's the management

Angioplasty



-SUMMARY:


Modifiable risk factors
Non-modifiable risk factors
Dyslipidemia
• ↑ LDL
• ↑ modifications
Hypertension
• ↑ vascular permeability
• ↑ intimal LDL retention
• ↑ LDL binding to SMC
Tobacco smoking
• ↑ LDL
• Endothelial dysfunction
Diabetes mellitus
• ↑ LDL glycation
• Endothelial dysfunction
Obesity
• ↑ insulin resistance
• ↑ hypertension
• ↑ dyslipidemia
Age
Male gender
• ↓ estrogen mediated atheroprotection
• ↓ HDL
• ↑ LDL
Hereditary
Atherosclerosis development and progression
Complications
Calcification
Rupture
Hemorrhage
Embolization
DISTAL SITES
Aneurysm
Renal artery stenosis
Angina
Peripheral vascular disease
Myocardial infarction
Thrombotic stroke
Embolic stroke
AAA

MCQs

1/ LDL cholesterol deliver cholesterol to?

a- peripheral tissues

b-heart

c-liver

2/ Higher levels of HDL correlate with?

a- increase risk VLDL

b- reduced risk VLDL

c-non above

3/ Which of the following is a major, Nonmodifiable Risk factors?

a-Hyperlipidemia

b-Cigarette smoking

c-Increasing age

d- diabetes

4/ Which of the following is a major, Potentially controllable Risk factors?

a- Male gender

b- Family history

c- Genetic abnormalities

d- Hypertension

5/ Which one of the following is not a complication of atherosclerosis?

A- Myocardial infarction

B- Aortic aneurysms

C- Heart failure

D- Stroke

Answers:
1-A
2-B
3-C
4-D
5-C

MCQs

6 / Which of the following statement is true ?

A) Atherosclerosis is a type of arteriosclerosis
B) Arteriosclerosis is a type of atherosclerosis
C) Arteriosclerosis is the same atherosclerosis
D) No link between atherosclerosis and arteriosclerosis

Answers:
6-A
7-D
8-B

7/ A 56-year-old has not received any medical care nor seen a physician for years. He reports reduced exercise tolerance over the past 5 years. On occasion in the past year he has noted chest pain after ascending a flight of stairs. 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 to be his most serious health risk?

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

8 / 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

Questions

1/ What is the common sites of Atherosclerosis?

*Abdominal aorta.

*Coronary arteries.

*Popliteal artery.

*The internal carotid arteries.

*The vessels of the circle of Willis.

2/ What do HDL "good cholesterol" do?

mobilizes cholesterol from developing and existing atheromas

and transports it to the liver for excretion in the bile.

3/ What atherosclerosis characterized by ?

intimal lesions called atheromas/ atheromatous/ fibrofatty plaques,

4/ The most heavily involved vessels are :

the abdominal aorta then coronary arteries

5/ What is The key processes in AS ?

intimal thickening and lipid accumulation.

Questions

6/ What are three principal components Atherosclerotic plaques have?

1- Cells: SMCs, macrophages, lymphocytes and foam cell (lipid-laden macrophages)

2- Extracellular matrix: including collagen, elastic fibers, and proteoglycans

3- Lipid: Typical atheromas contain relatively abundant lipid both intracellular and extracellular lipid .

7/ What is the categories of atherosclerosis ?

1-stable(asymptomatic, are rich in extracellular matrix and smooth muscle cell)

2-unstable(unstable plaques are rich in macrophage and foam cells and the extracellular matrix and known as fibrous cap)

8/ What happened to SMCs when stimulated by an injury (dysfunction) ?

- migration from media to intima
- lose the capacity to contract and gain the capacity to proliferate
- synthesise ECM

Questions

9/ How does atherosclerosis start?

it starts as a fatty steak that compose of lipid filled foam cells (its harmless with no symptom)

10/ If LDL increases what does that mean ?

high risk of atherosclerosis

11/ What gander have a major risk of atherosclerosis?

Before menopause, men are more risk than women. After menopause, however, the incidence of atherosclerosis increase and, in old age, even exceeds that in men.

12/ What are the complications of AS?

- It depends upon the effected artery :
- Myocardial infarction (heart attack)
- Cerebral infarction (stroke)
- Aortic aneurysms because of the wall weakening and its may rupture
- Mesenteric occlusion
- Peripheral vascular disease (gangrene of the legs) intermitted claudication (cramp)

Team's members:

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