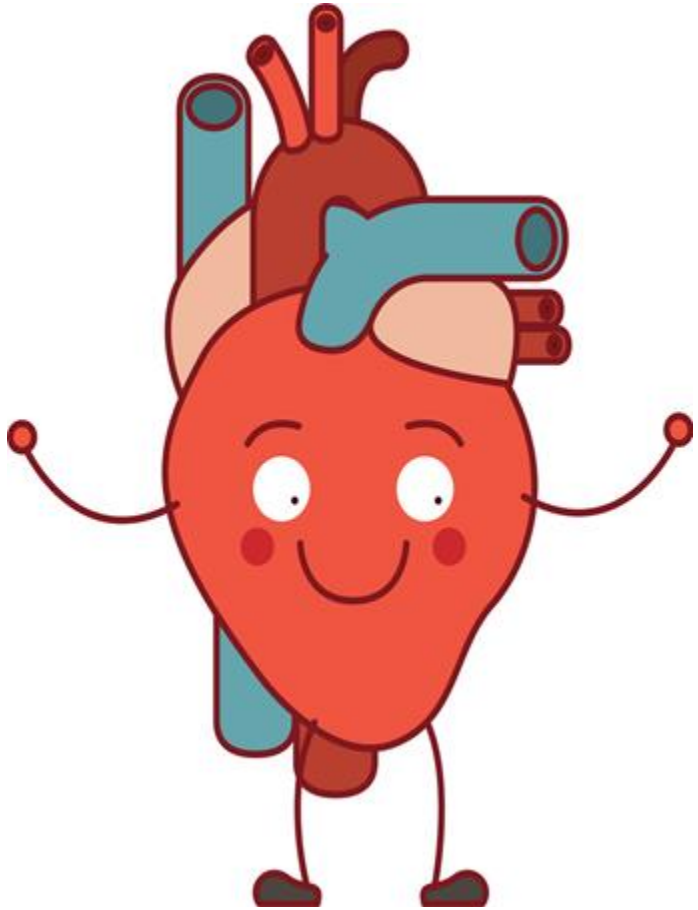

Arteriosclerosis
Cardiovascular Module 2024

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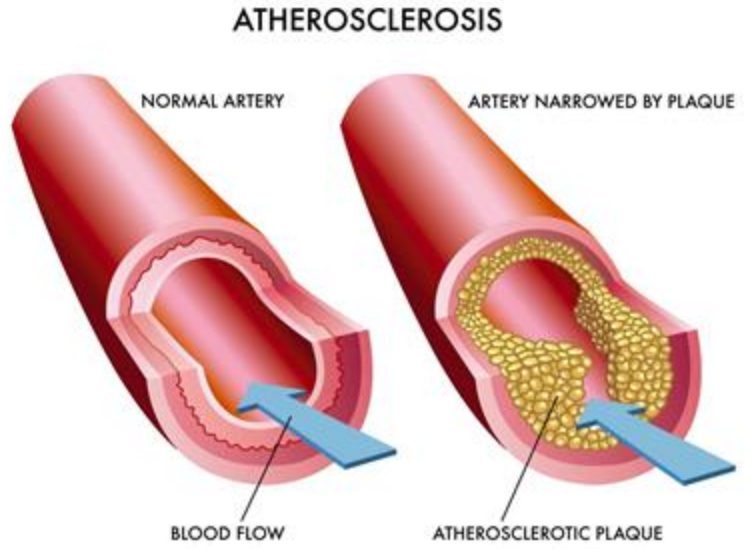
2024

Arteriosclerosis

Arteriosclerosis **is <u>hardening</u> and <u>narrowing</u> of the arterial wall, leading to <u>poor circulation</u> throughout the body**

Three patterns:

1. Atherosclerosis
2. Arteriolosclerosis
3. Monckeberg medial sclerosis



ARTERY + HARDENING

ARTERIOSCLEROSIS

* artery thicker, harder, less elastic *

ATHEROSCLEROSIS

* hardening from PLAQUE *

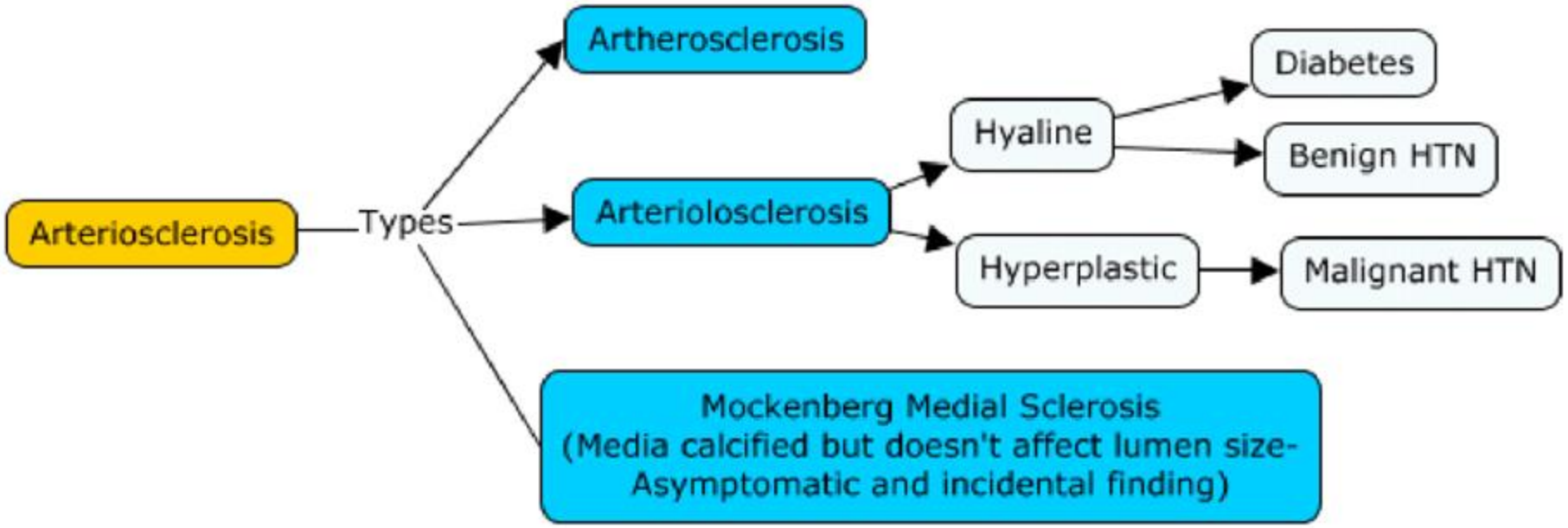
"ATHEROMATOUS PLAQUE"
↳ in

ARTERIOLES

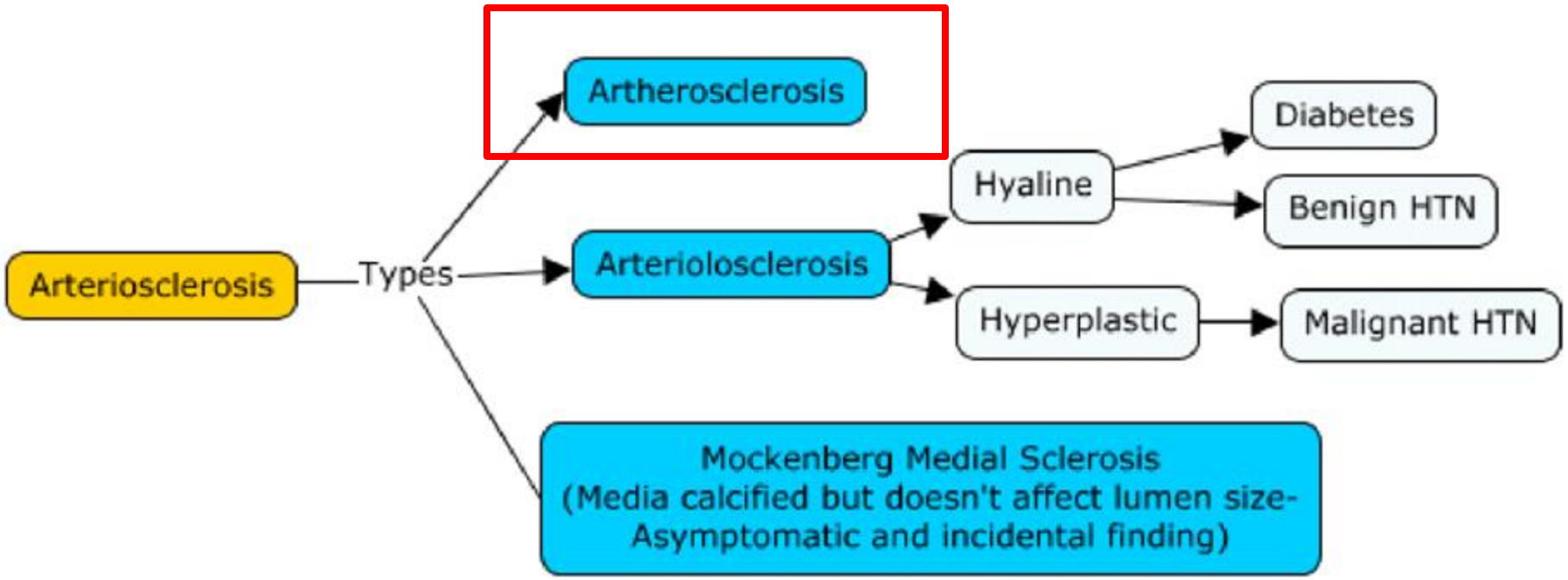
ARTERIOLOSCLEROSIS

* Hardening of ARTERIOLES *

Arteriosclerosis



Arteriosclerosis



Arteriosclerosis

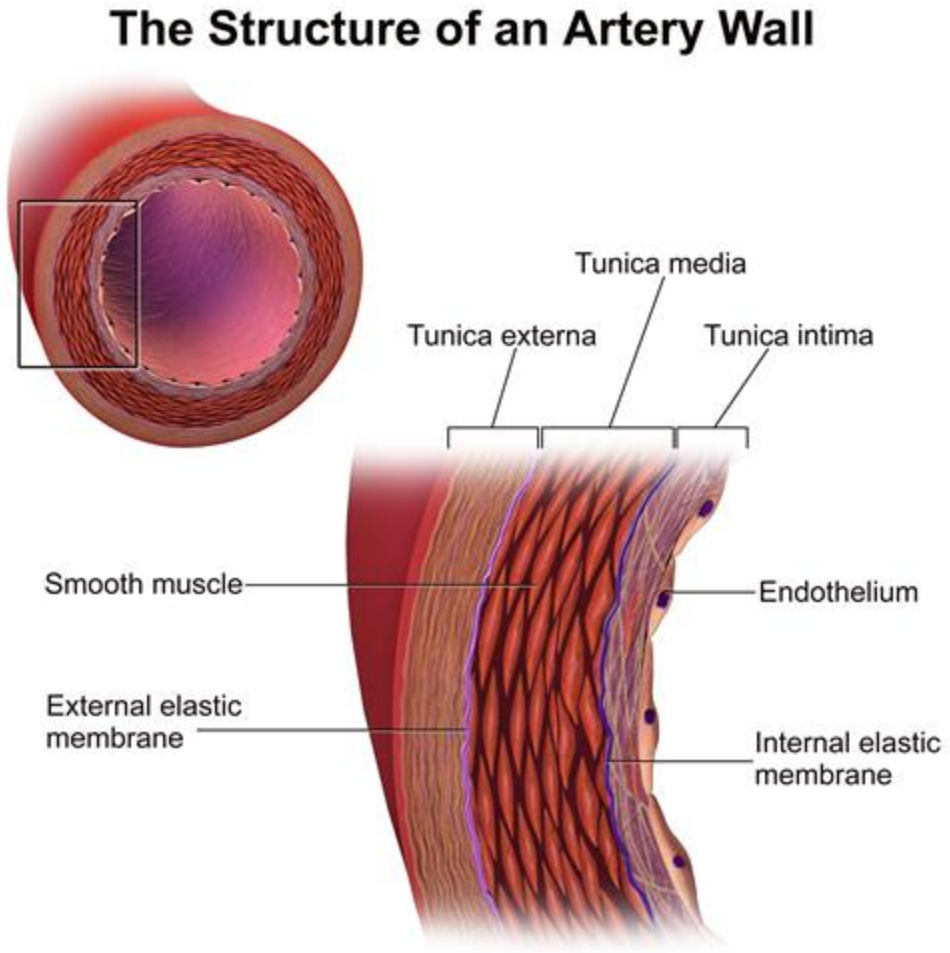
Arteriosclerosis **is hardening of arterial wall**

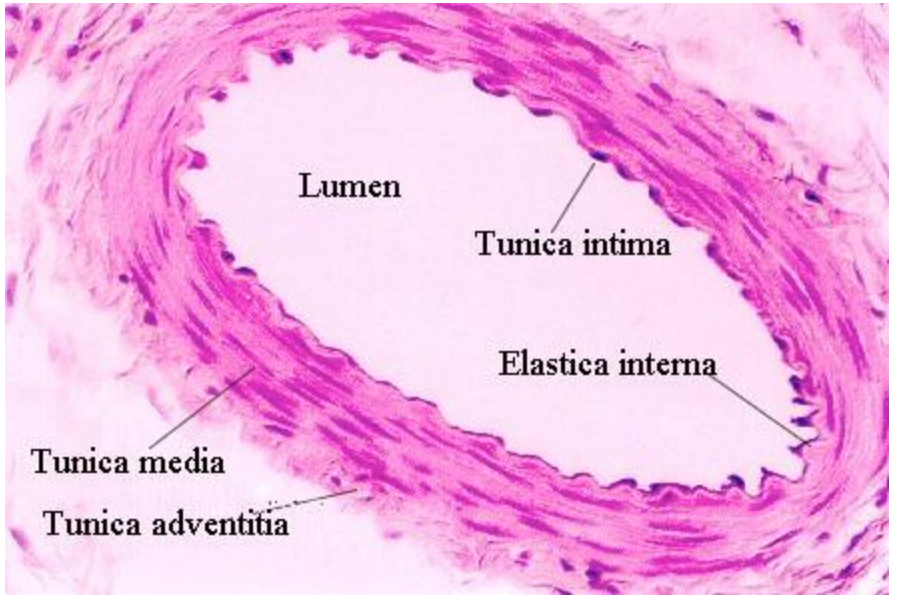
Three patterns

1. **Atherosclerosis - thickening of intima due to plaque (occurs in medium and large sized vessels)**

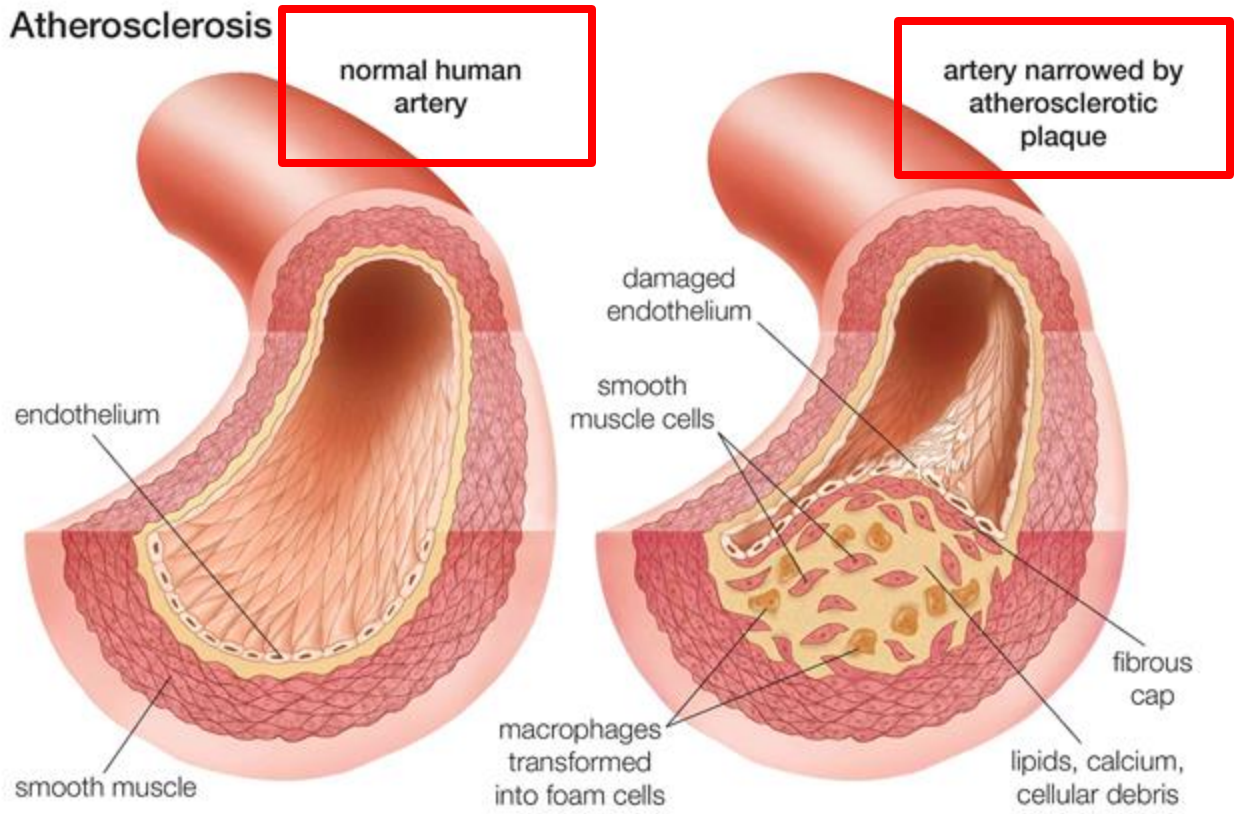
1. Arteriolosclerosis
2. Monckeberg medial sclerosis

Normal Artery structure

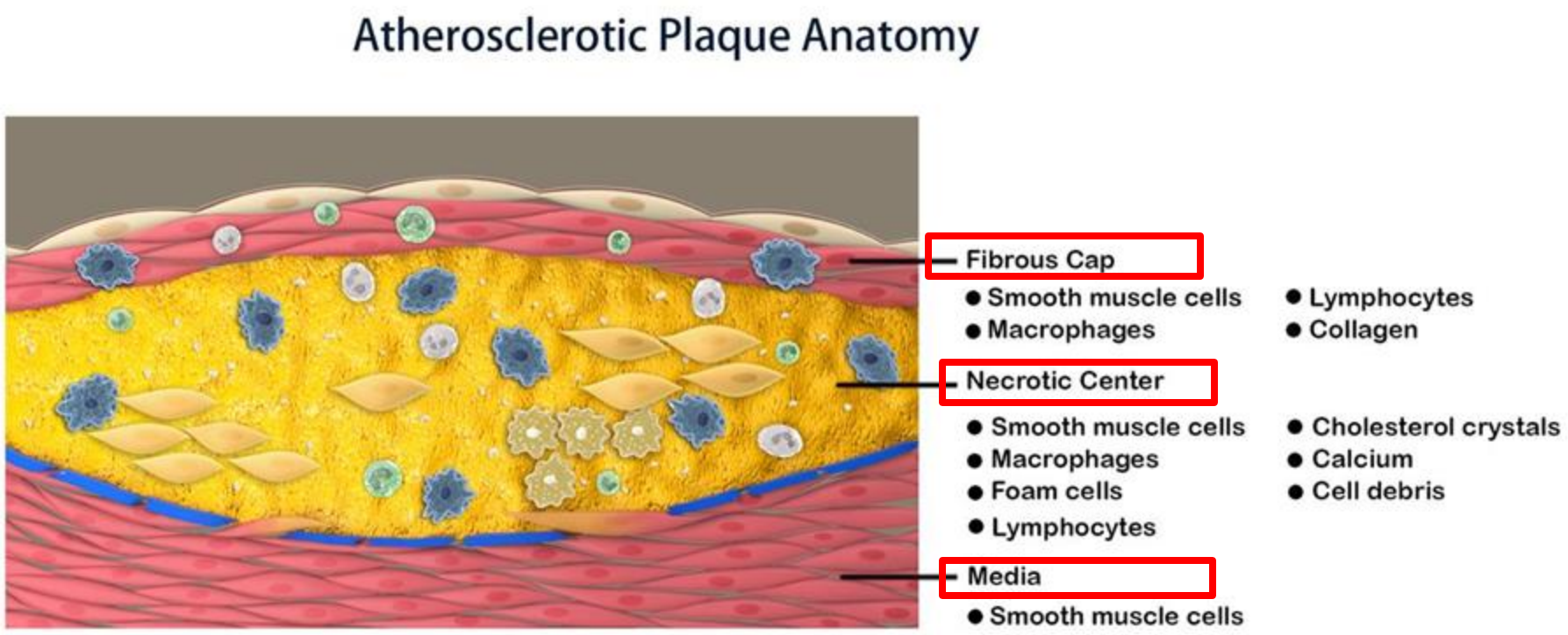




Atherosclerosis



Atherosclerosis

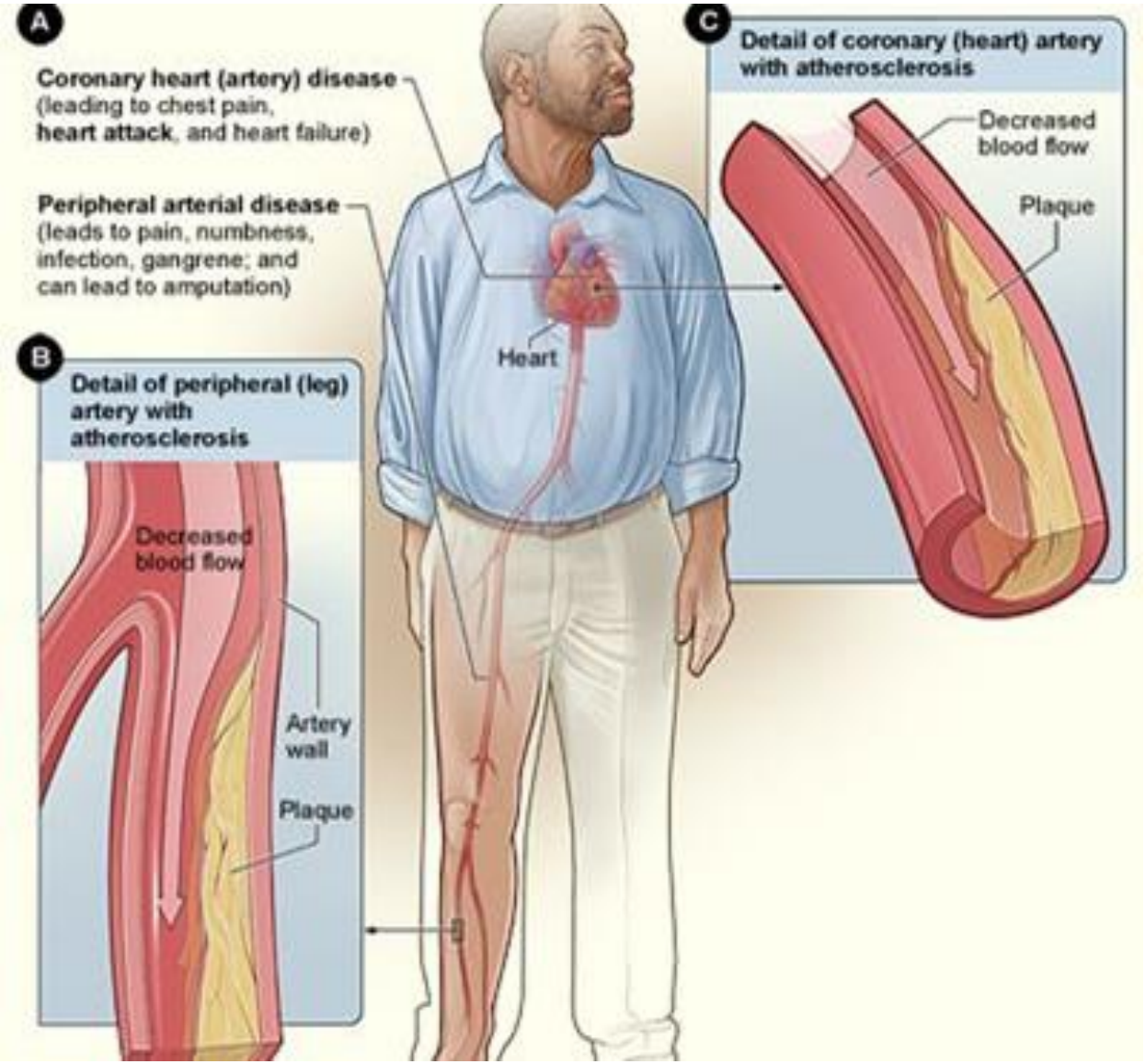


Atherosclerosis

Atheromas* = *atheromatous or ***atherosclerotic plaques***

Atheromas are **focal raised arterial intimal** lesion, **consisting** of soft yellow **core of lipid** (mainly cholesterol & cholesterol esters) covered by a firm, white **fibrous cap** , that protrude & obstruct the arterial lumina

Atheromas cause more morbidity & mortality (up to 50% of all deaths)



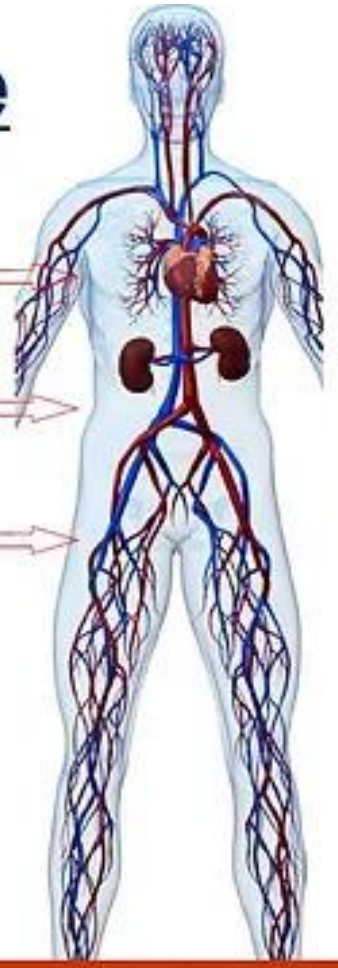
Atherosclerosis

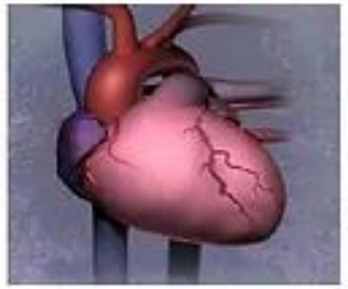
Atherosclerosis Risk Factors
Two types

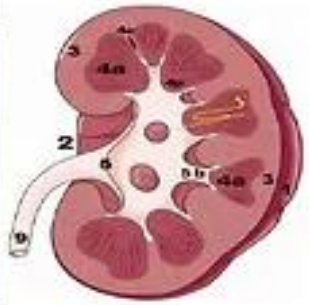
Modifiable	Non-modifiable
HTN	Age
Hypercholesteremia (LDL increases risk and HDL reduces)	Gender (male and postmenopausal females at high risk. Estrogen has protective effect on pre-menopausal females)
Smoking	Genetics (positive family history)
Diabetes	

Reversible HIGH

- Pressure
- Cholestrol
- Sugar
- Smoking
- Obesity
- Sedentary







Irreversible: Genetic, age, male, race, ?infections-flu

Atherosclerosis Risk Factors
Two types

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Modifiable Risk Factors
Hypercholesterolemia

1) Hypercholesterolemia - is a major risk factor for atherosclerosis.

LDL cholesterol (bad cholesterol);

LDL cholesterol which has an essential physiologic role of delivering cholesterol to peripheral tissues.

HDL (good cholesterol) mobilizes cholesterol from developing & existing atheromas & transports it to the liver for excretion in the bile.

So, higher levels of HDL correlate with reduced risk of atherosclerosis.

So, diet and drugs (ex: statins) that lower LDL or total serum cholesterol and raises serum HDL are **valuable**.

Also, Exercise raise HDL levels, whereas obesity & smoking lower it.

Modifiable Risk Factors

2) Hypertension

Hypertension increase the risk for Ischemic Heart disease (IHD) **60%** compared with normotensive.

Without treatment, 50% of hypertensive patients will die of IHD.

3) Cigarette Smoking

Prolonged (years) smoking of one pack of cigarettes or more daily increases the death rate from IHD by 200%. Smoking cessation reduces that risk substantially.

Modifiable Risk Factors

(4) Diabetes Mellitus "DM"

DM induces **hypercholesterolemia,** thus markedly **increases predisposition to atherosclerosis.**

The incidence of IHD is twice as high in diabetic as in nondiabetic, with increased risk of **strokes** and **gangrene of the lower extremities.**

Additional Risk Factors for IHD

20% of all cardiovascular events occur in the absence of any of the above factors (hyperlipidemia, hypertension, diabetes & smoking).

So, other "**nontraditional**" factors contribute to risk including:

Additional Risk Factors

- **Inflammation:** ~~CRP levels (Inflammation is present during all stages of atheroma plaque~~ formation & rupture)
- **Hyperhomocysteinemia:** abnormally high level of **homocysteine** in the blood
  - Elevated homocysteine promotes atherosclerosis through increased oxidant stress, impaired endothelial function, and induction of thrombosis.
  - Homocysteine is an amino acid. Vitamins B12, B6 and folate break down homocysteine to create other chemicals your body needs. High homocysteine levels may mean you have a vitamin deficiency. Without treatment, elevated homocysteine increases your risks for dementia, heart disease and stroke.
- **Lipoprotein(A) levels**: LDL-like particle
- **Factors Affecting Hemostasis:**

Hemostatic &/or fibrinolytic function markers are strong predictors of IHD & stroke risk.

- **Other Factors :** lack of exercise; obesity, competitive stressful lifestyle ("type A" personality) .

Atherosclerosis Risk Factors
Two types

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Diabetes	

Non-Modifiable risk factors

- **Age:** incidence of IHD increases 5-fold between 40 and 60 years of age.

- **Gender:**

  - premenopausal women are relatively protected against atherosclerosis in the absence of other risk factors due to estrogen. After menopause, incidence increases.
  - The hormone oestrogen is known for its protective effect on your heart. One of these benefits is its ability to reduce the levels of 'bad' cholesterol in your blood. This is a type of fat that can clog the arteries and increase the risk of heart attack, heart disease and stroke.
  - Estrogen **lowers plasma concentrations of LDL particles by stimulating hepatic synthesis of LDL receptors while increasing plasma concentrations of HDL particles via inhibition of hepatic triglyceride lipase activity.**
  - **Estrone (E1) is the primary form of estrogen that your body makes after menopause. Estradiol (E2) is the primary form of estrogen in your body during your reproductive years.**

- **Genetics: Familial predisposition to atherosclerosis may be related to familial clustering of other risk factors, (hypertension or DM), or to a well-defined genetic factor e.g. familial hypercholesterolemia.**

- **Familial combined hyperlipidemia (FCH) is a hereditary metabolic disorder characterized by elevated levels of total cholesterol, triglycerides, low-density lipoprotein (LDL) cholesterol, and decreased levels of high-density lipoprotein (HDL) cholesterol. FCH is one of the most common hereditary lipid disorders**
- **Familial hypercholesterolemia (FH) can be caused by inherited changes (mutations) in the LDLR, APOB, and PCSK9 genes, which affect how your body regulates and removes cholesterol from your blood. About 60-80% of people with FH have a mutation found in one of these three genes.**
- **It is an autosomal dominant-inherited genetic disorder that leads to elevated blood cholesterol levels. Typically, the patient inherits only 1 of the defective genes, making him heterozygous.**

- **Complications. People who have familial hypercholesterolemia** have a higher risk of heart disease and death at a younger age. Heart attacks may occur before age 50 in men and age 60 in women. The rarer and more severe variety of the condition, if undiagnosed or untreated, can cause death before age 20.S.

- **Q:What does familial hypercholesterolemia do to your body?**

  Coronary artery disease.

  Cerebrovascular disease.

  Aortic aneurysm.

  Peripheral artery disease.

  Xanthomas (skin bumps from cholesterol accumulating on the Achilles tendon, elbow, knee or hand tendons).

  Xanthelasmas (yellow cholesterol around the eyelids).

- Familial combined hyperlipidemia (FCH) is a complex genetic trait that results from the additive effect of several common genetic variants that lead to hepatic overproduction of very-low-density lipoprotein (VLDL) particles and an impaired clearance of apoB-containing particles.
-

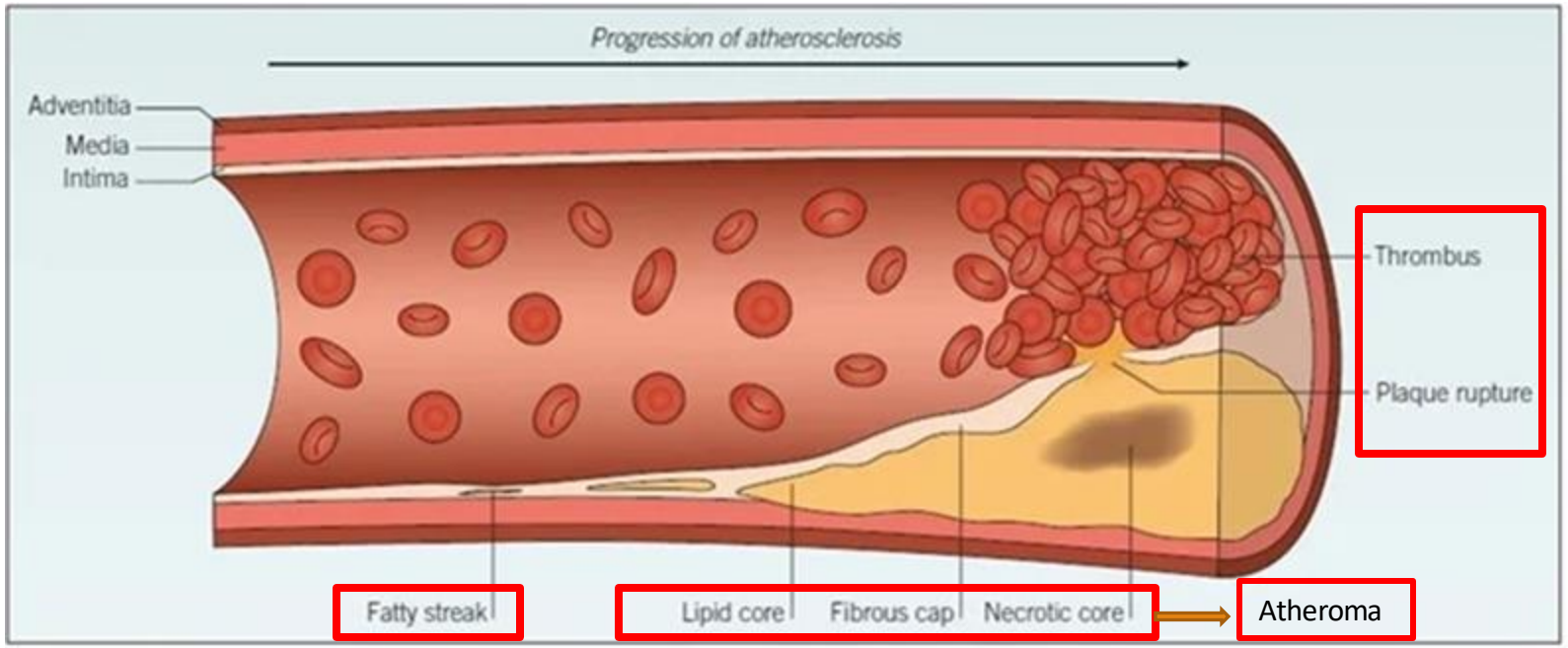
- Familial Hypercholesterolemia: Identification of a Defect in the Regulation of 3-Hydroxy-3-Methylglutaryl Coenzyme A Reductase Activity Associated with Overproduction of Cholesterol.

Q:What is the first line treatment for familial hypercholesterolemia?

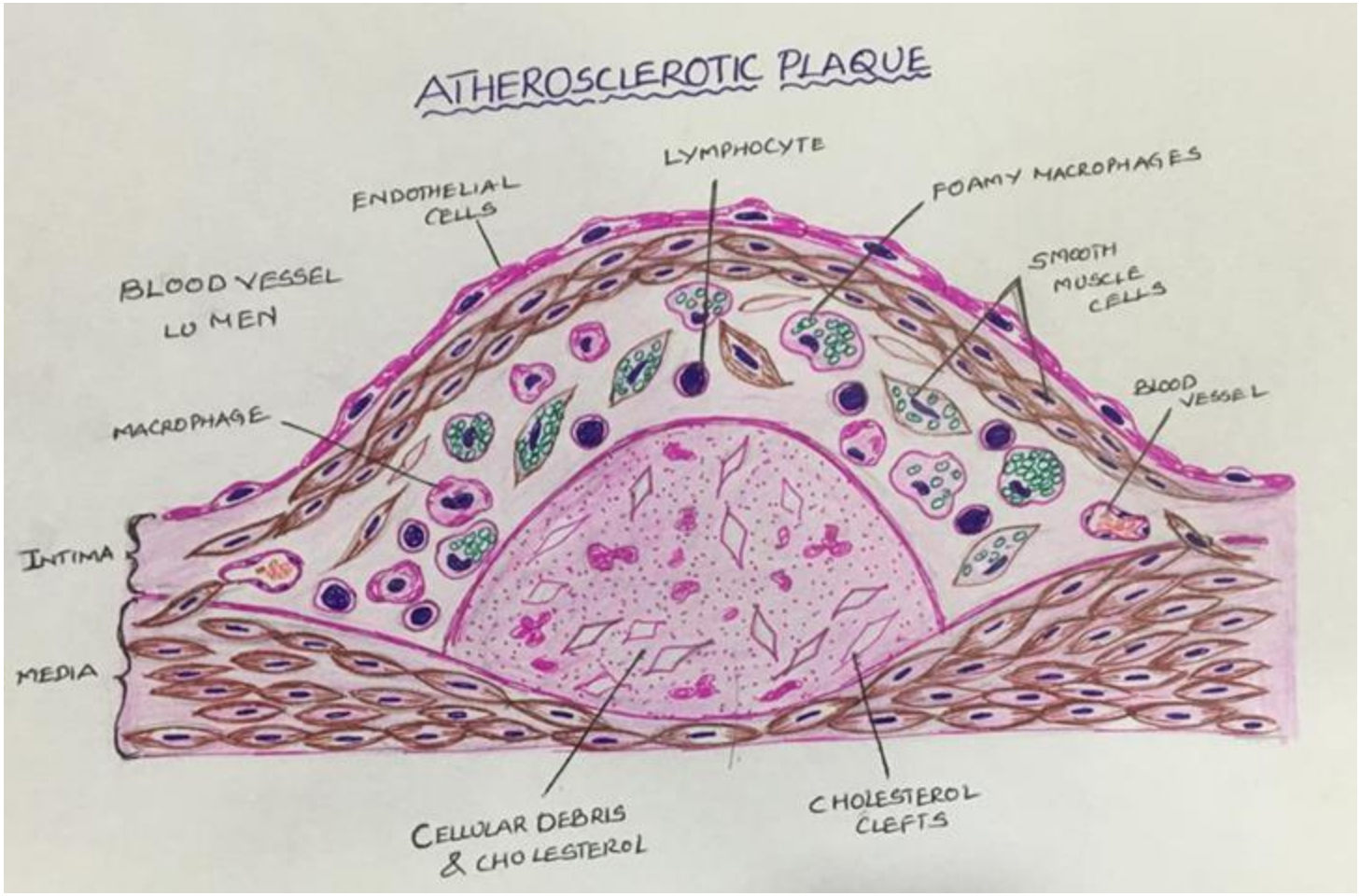
- Drug Therapy in HeFH. In many HeFH patients, adequate lipid management cannot be achieved through lifestyle habit interventions such as dietary therapy, exercise therapy, smoking cessation and anti-obesity measures alone, so drug therapy is usually combined with them. Statins are the first-line drugs for FH treatment.
- Treatment should be started as early age as possible (8 -10 years)

Pathogenesis of atherosclerosis

- Atherosclerosis forms as a result of **chronic inflammatory response of the arterial wall to endothelial cell injury**, followed by lipid accumulation & oxidation, and eventually thrombosis.



- Pathogenesis Endothelial injury Accumulation of lipoprotein (oxidized LDL) in vessel wall Monocyte adhesion to endothelium, migration into intima, transformation into foam cells Platelet adhesion, activation, release of factors Smooth muscle cell recruitment from media and proliferation Lipid accumulation Role of inflammation, cytokine and biomarkers Infection Genomics in CV diseases and atherosclerosis
- Role of inflammation ' Innate immunity in atherosclerosis Monocyte recruitment as an early event in atherogenesis Maturation of monocytes into macrophages, their multiplication, and production of mediators



Pathogenesis of atherosclerosis