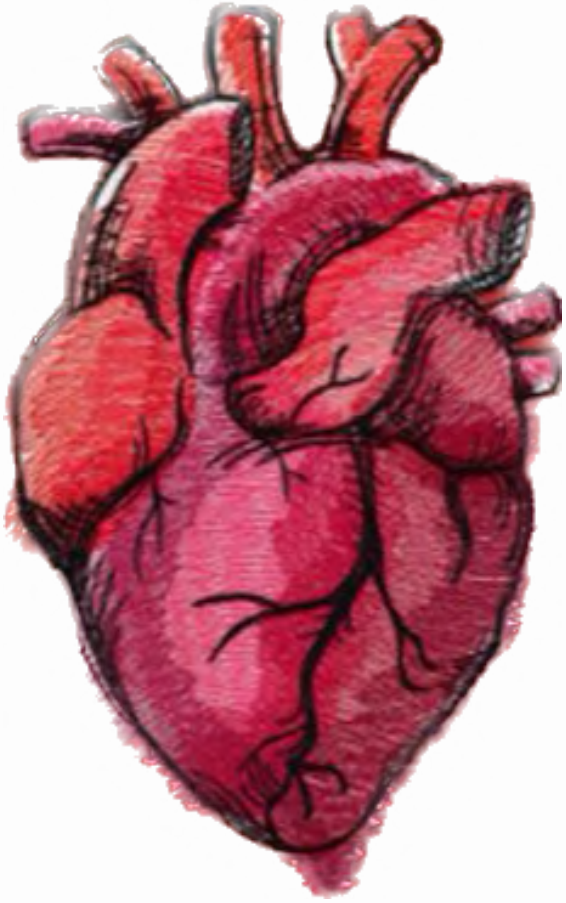
النادي الطبي

CARDIOVASCULAR SYSTEM



SUBJECT : Atherosclerosis

LEC NO. : 1

DONE BY : Khalida AlBaddawi 🤍

وَقُل رَّبِّ زِدْنِي عِلْمًا

GENITOURINARY SYSTEM

SCAN ME!

GUIDANCE | SLIDES | NOTES | RECORDS

في البداية قبل ما نبلش حابة أنصحكم
تشيكوا على الجدول السفاح يلي
موجود بال guidance
كثير رح تستفيدوا منه بخصوص
الشروحات الخارجية

شرح المادة لدفعة وريد

الدكتورة دعاء

Pathology-CVS

medical club | Sameh ghazi | Dr.MO. al.rakabi

Subject	Medical club	Sameh ghazi	Other videos
Atherosclerosis Lec 1+2		video	Dr.doaa -vein video 1 video 2
Ischemic heart disease Lec 3+4	Video 1 Video 2	MI	Dr.MO. al.rakabi **video 1** **video 2**

يلا بسم خلينا نبلش ❤️

Harding of arteries → narrowing the lumen → less blood supply to organs → Poor circulation → which may lead to hypoxia ,Ischemia

Arteriosclerosis

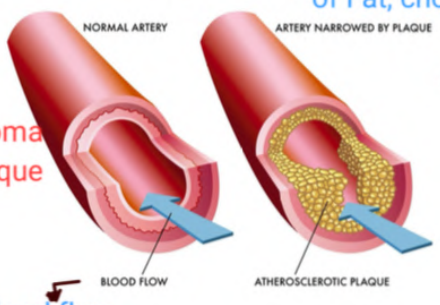
Arteriosclerosis is hardening and narrowing of the arterial wall, leading to poor circulation throughout the body

narrowing of lumen ← تصلب شرايين

it is Yellow becouse it is composed of Fat, cholesterol

Three patterns:

1. Atherosclerosis sclerosis due to presence of atheroma plaque
2. Arteriolosclerosis → Small artery
3. Monckeberg medial sclerosis



Normal lumen → normal blood flow

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تركيز يا جماعه تركيز رح ابلش أشرح الموضوع فيلا بسم الله
هسا نحن بأول محاضرتين رح نحكي عن ال arterioles side مش ال venous

ال sclerosis معناها تصلب يعني hardening يعني رح يصير عنا thicking لل BV
يعني ال BV رح تكون more harder وايضا less elastic رح يفقد المطاطيه يلي بتجيه من ال elastic lamina (internal + external)
طب أنا هون hardening من وين أجت ؟ نعم يا اعزائي أجت من plaques
طب شو هي أصلا ال plaques ؟ هي عبارة عن تجمعات الدهون (subintimal deposition)
هسا نحن بالأصل عنا أنواع عديده من الدهون بالجسم زي HDL ← كوليسترول جيد ، LDL ← كوليسترول سيئ يلي بحالو ينقلوا ال cholesterol للأوعية دموية (LDL أسم على مسمى واطي على قولت الدكتوره 😂 (low Density lipoprotein) هاد بذات بيموت بنقل الكولسترول من الكبد إلى (circulation
هسا إذا صار ونقلت ايش رح يصير ؟ برافو رح تترسب على الأوعية الدمويه ورح يؤدي زي ما حكينا لل hardening وايضاً poor blood supply يلي رح يأدي هيدا كله إلى ischemia (يلي هو نفسه decrease blood supply) ورح يصير كمان low perfusion وممكن يؤدي هاد الحكي كله إلى infarction لل tissue

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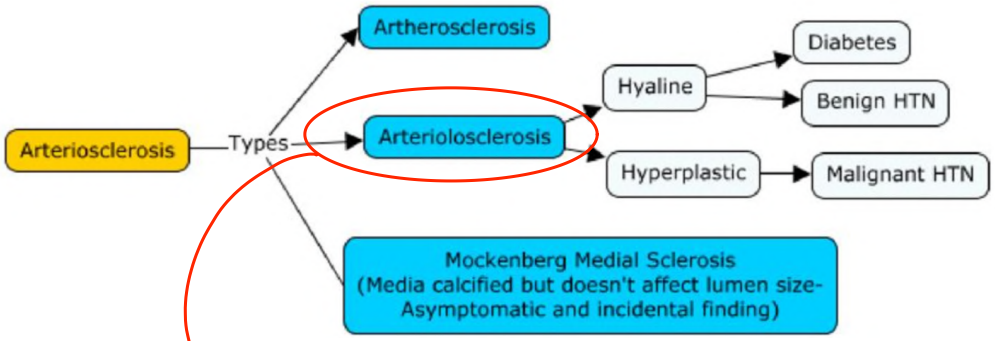
هون بدنا ننتبه انه ال hardening بصير على arterioles (الصغار) هون رح يزيد عنا peripheral resistance وهاد رح يؤدي إلى hypertension

Arteriosclerosis



عبارة عن مرض بصيب ال intima (منطقة بال arterial wall) ، هسا هاد مرض بصيب ال large + medium BV (معناها بصيب aorta يلي هي largest BV)
هسا هاد مرض بصير في arterioles يلي مثلا بتكون في نهايات ال BV يلي بال organs
بتكون على شكلين أما : HYALINE أو HYPERPLASTIC
ال hyaline بيكون أما في diabetes أو benign hypertension
(المريض يلي بيكون عنده benign HTN بيكون عنده long standing HTN وبيختلف عن malignant HTN يلي هاد بيكون sudden و rapid increase بال blood pressure)

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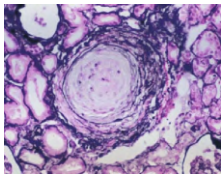


ملاحظة بسيطة ال skin appearance onion
مرتبط بال Hyperplastic arteriosclerosis يلي
بال kidney
وهاد شكل صار عندي من ورا fibrinoid necrosis

بالنسبة للنوع الثالث هون اهم اشي نعرفه حاليا انه المريض بجيني بدون أي أعراض لأنه هاد المرض بصير بال medium blood vessels

Mockenberg Medial Sclerosis
(Media calcified but doesn't affect lumen size- Asymptomatic and incidental finding)

Arteriosclerosis

Arteriosclerosis **is hardening of arterial wall**

Three patterns

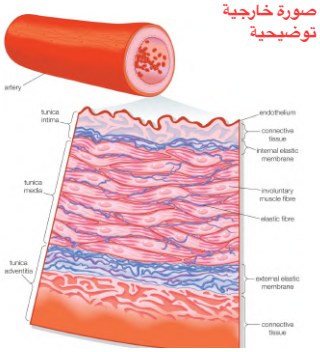
الطبقة الداخلية / أول طبقة.

cholestrol + Lipid

1. **Atherosclerosis - thickening of intima due to plaque (occurs in medium and large sized vessels)**
   Large blood v like aorta especially abdominal aorta , common iliac artery , cerebral artery that supply the brain
   e.x: Coronary artery that Supply the heart
   Popliteal artery that supply the leg
   Renal artery
2. Arteriolosclerosis → Small one
3. Monckeberg medial sclerosis

ال intima متكونه من endothelial cells و lining تبعه smooth
عشان رح يجري فيها الدم (وعشان هيك لما يصير عنا arteriosclerosis
في البدآية رح يصير endothelial cells injury)

صورة خارجية توضيحية



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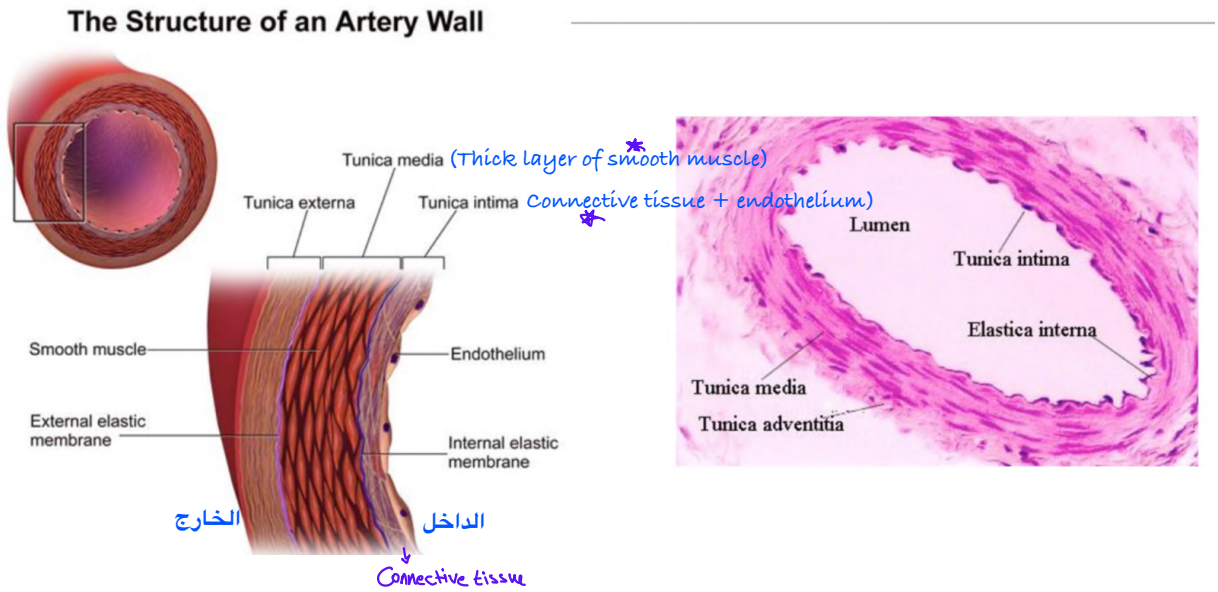
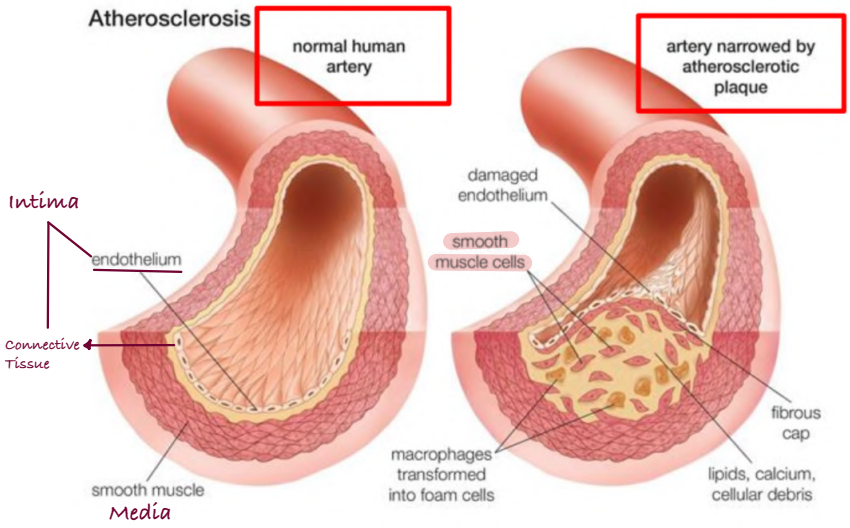
Normal Artery structure



Atherosclerosis



يلي صار عنا هون لاحظوا

Collection of lipid + calcium +macrophage + smooth muscle in intima ------>intima raised,protruding to lumen --->narrowed lumens --->less oxygen to tissue

وهون مع وجود LDL (كوليسترول سيء) يلي جاي من الكبد لهون
رح يزيد ال permeability لل BV
ورح تصير تدخل LDL جوا subintimal
هسا LDL إذا دخل ال BV ما رح يقدر يطلع لأنه رح يتحول ل LDL oxidized

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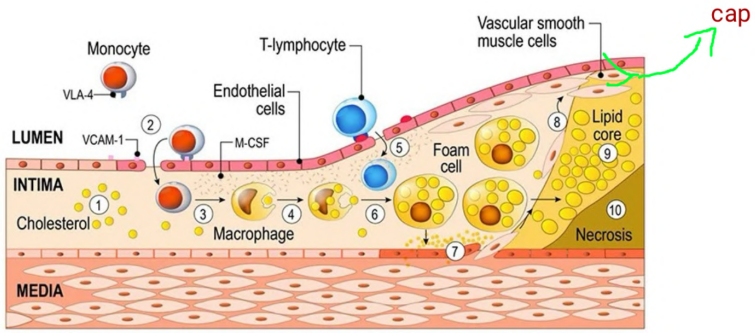
زي ما حكينا فوق إذا دخل ما رح يطلع ورح يترسب ونحن هيك هيك عنا damage أصلا
رح يصير عنا recruitment of inflammatory cells وعنا ال main one يلي monocytes يلي موجوده بال blood بس تدخل منطقة subintimal رح تصير macrophages هاي رح تأكل oxidized LDL فرح يتحول عنا ل foam cells (يلي هي عبارة lipid laden macrophages)
بالاضافة عنا endothelial cell injury يلي رح يصير aggregation of the platelets يلي رح يعطينا fibroblast growth factor يلي هدول رح يعطونا extra cellular deposition of substances
هاد كله توضيح لطريقة تكون plaque يلي رح يكون داخل BV

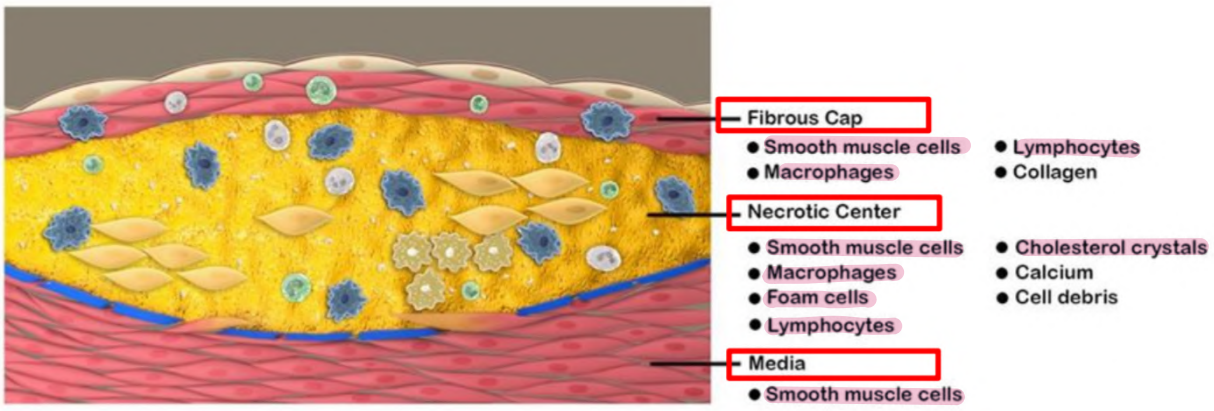
عنا هون ال (ATHEROMA) plaque رح يصير زي شكل tumor وهي طبعا (not truly mass) ولكن هي عبارة عن كتلة داخل BV



Atherosclerosis

Atherosclerotic Plaque Anatomy

توضيح لمكونات plaque



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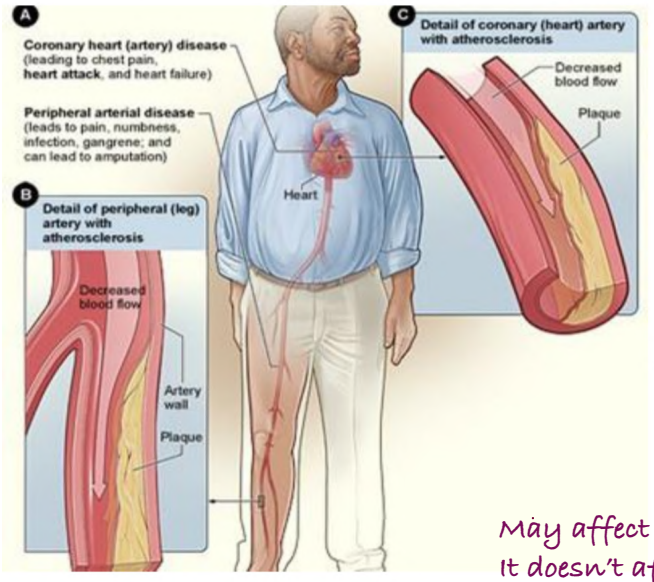
Atherosclerosis

Atheromas* = *atheromatous* or *atherosclerotic plaques

It's not a true tumor

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)



اكثر مكان بتصير فيه في ال aorta
وايضاً بال coronary هون بيكون اخطر لأنه زي
ما حكينا فوق بتكون medium فعلى سريع
يتراكم الدهون فيها
وايضاً في popliteal

هسا إذا صار بال peripheral arterioles
بال lower limbs رح يعملنا dry

Atherosclerosis

May affect heart and lower limbs
It doesn't affect upper limbs usually

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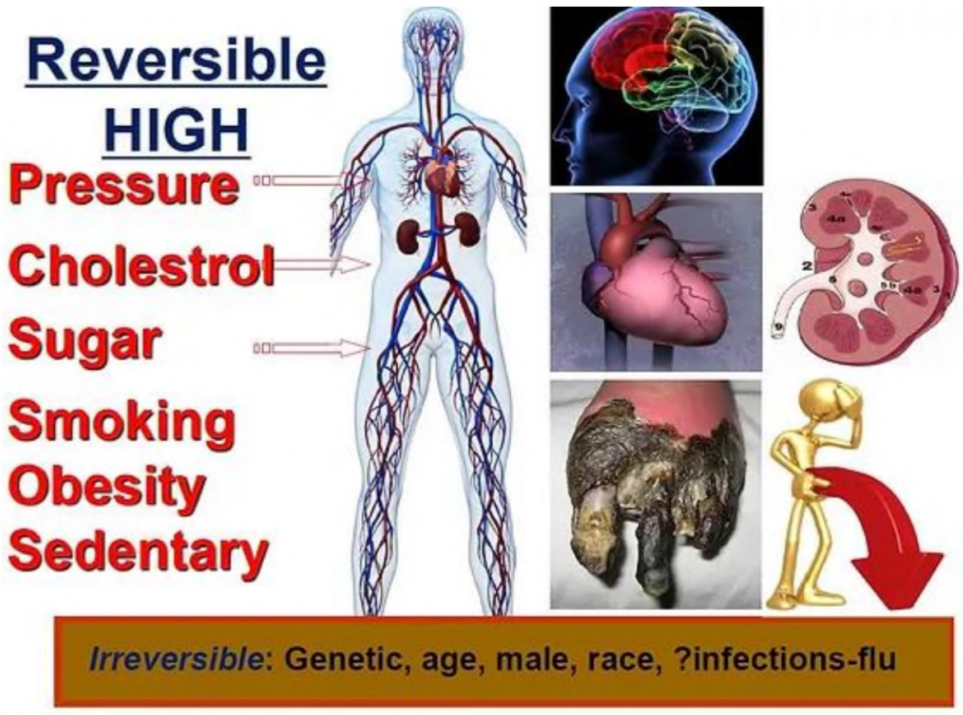
Atherosclerosis Risk Factors
Two types

Modifiable ممكن تعالج	Non-modifiable We can't deal with them, can't treat it
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	

في بدايه عنا HTN تؤدي إلى Atherosclerosis
وكأحد نتائج atherosclerosis رح تزود من موضوع HTN.

في حالة menopause رح يتساوون بسبب وجود deficiency of estrogen

لـ مرحلة انقطاع الدورة



نفس فكرة الجدول فوق

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Atherosclerosis Risk Factors
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Modifiable Risk Factors
Hypercholesterolemia

أساس الل Atherosclerosis plaqe هو وجود high cholesterol

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

LDL cholesterol (bad cholesterol); تساعد في ترسيب الكوليسترول في peripheral tissue

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.

Liver → gall bladder → bile → excreted by intestines as feces .

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

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

↓ LDL : statins, diet
↑ HDL : exercise
↓ HDL : obesity - smoking

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

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Modifiable Risk Factors

2) Hypertension

هون ممكن يصير تشققات بال BV من قوة ضغط دم

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

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

عشان هيك مرضى الضغط لازم دايما يكونوا critically treated و يكون الضغط دايما controled

3) Cigarette Smoking

هون عند ترك التدخين ممكن يعالج عشان هيك هو modifiable

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.

حكينا إنها بتفرز toxins و بتعمل direct injury on endothelial wall
و تدخين one pack or more daily رح تزيد الخطر للضعف 200%

Modifiable Risk Factors

ال diabetes is mutifactorial يعني في كثير طرق من السكري بتساهم انه يصير Atherosclerosis ومن هاي الطرق : hypercolestrolemia ,
وممكن تعمل chronic endothelial injury due to high sugar levels , وممكن تأثر على ال inflammatory responce

(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**.

مرضى السكري معرضين أكثر للإصابة ب stroke (cerebrovascular accidents CVA) و معرضين انهم يصير عندهم Gangrene

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:

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Additional Risk Factors

C reactive protein — Acute phase reactive Secreted from the liver when there is continuous inflammation

- **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 — Mainly composed of apolipoprotein which is homologus to plasminogen ,So it can increase the incident of thrombosis & Atherosclerosis
- **Factors Affecting Hemostasis:**

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

- **Other Factors :** 1 lack of exercise; 2 obesity, 3 competitive stressful lifestyle ("type A" personality) . — الأشخاص يلي دائما stressed و بدهم كل اشي straight

Atherosclerosis Risk Factors
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Non-Modifiable risk factors

- **Age:** incidence of IHD increases 5-fold between 40 and 60 years of age.
- **Gender:** Male > women بنسبة 4:1

مهم جدا نأكد على معلومه انه إستروجين بقلل من دهون بالدم

  - premenopausal women are relatively protected against atherosclerosis in the absence of other risk factors due to estrogen. After menopause, incidence increases.

Postmenopausal are not protected against Atherosclerosis even with hormonal (estrogen) therapy .
وهيك بتصير ال incident انه يصير عند المرأة من IHD هي نفسها عند الرجل

  - 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** ① **LDL receptors while increasing plasma concentrations of HDL particles via inhibition of** ② **hepatic triglyceride lipase activity.**

هدول mechanism تبعت إستروجين

  - **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**

عاده بيكون autosomal dominant

  - **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.**

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عادة هدول العائلات لازم يبلشوا علاج من عمر 8 - 10 بالإضافة
طبعا لتغيير lifestyle تبعهم مع تقليل نسبة دهون بالجسم عندهم

- **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.

بالحالة هاي بزيد تكوين وبيقل clearance

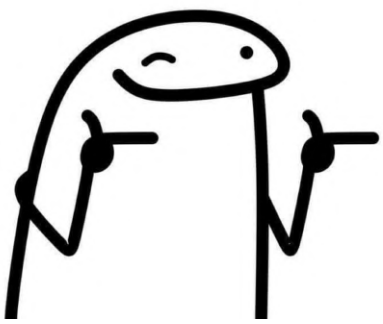
- Familial Hypercholesterolemia: Identification of a Defect in the Regulation of 3-Hydroxy-3-Methylglutaryl Coenzyme A Reductase Activity Associated with Overproduction of Cholesterol.

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.

العلاج هو الأساس بهاي الحالات

- Treatment should be started as early age as possible (8 -10 years)



خلص قربنا قربنا نخلص

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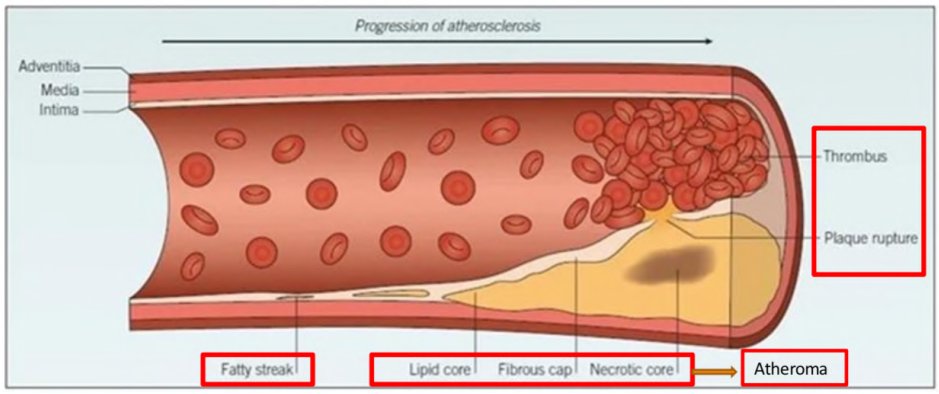
Pathogenesis of atherosclerosis

معناها انه صاير damage في مكان بالجسم وأدى ذلك لتراكم chronic inflammatory cells (زي مثلا lymphocytes + macrophages) وهدول بيلعبوا دور مهم في تطور 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.



مهم اول بصير عندي تشققات بعدين ببلشوا يدخلوا لجّوا

هون في damage بال first line لل BV

- 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

نفس يلي شرحناه فوق

- 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

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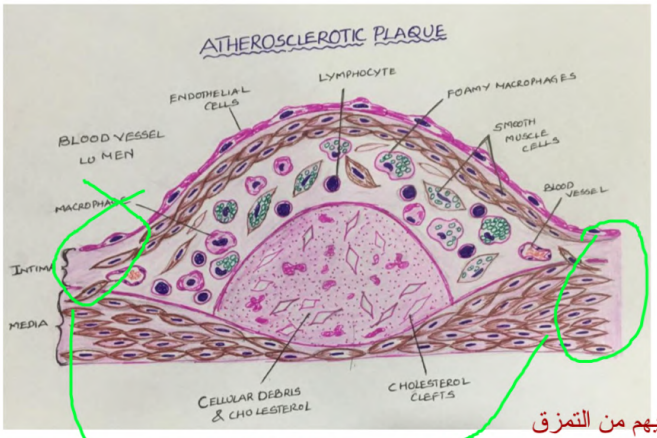
الصورة موجودة عنا بس جبت الشرح من سلايدات وريد

Pathogenesis of atherosclerosis Summary



A plaques have three principal components;

- ✓ **Cells** = SMCs + macrophages + T lymphocytes cells;
- ✓ **ECM** = collagen + elastic fibers
- ✓ **Lipids:** mainly oxidized LDL

AND COMPOSED MAINLY OF

(1) **Fibrous cap** (SMCs & collagen).

(2) **Necrotic core,** deep to the fibrous cap containing lipids + foam cells + debris from dead cells

حتى الي هون بخاف عليهم من التمزق

لو صار rupture

رح تكبر و تعمل occlusion

اللهم اني استودعتك ما حفظت و ما فهمت و ما مرت عليه عيني

الطبقة الفوق مكونه من : smooth muscle + connective tissue يلي كأنو
نتيجة extra cellular matrix يلي بزيد بسبب fibroblast growth factors
يلي انفرزوا من inflammatory cells

الطبقة الوسطية : عبارة عن cholesterol cleft

وقل رب زدني علماً