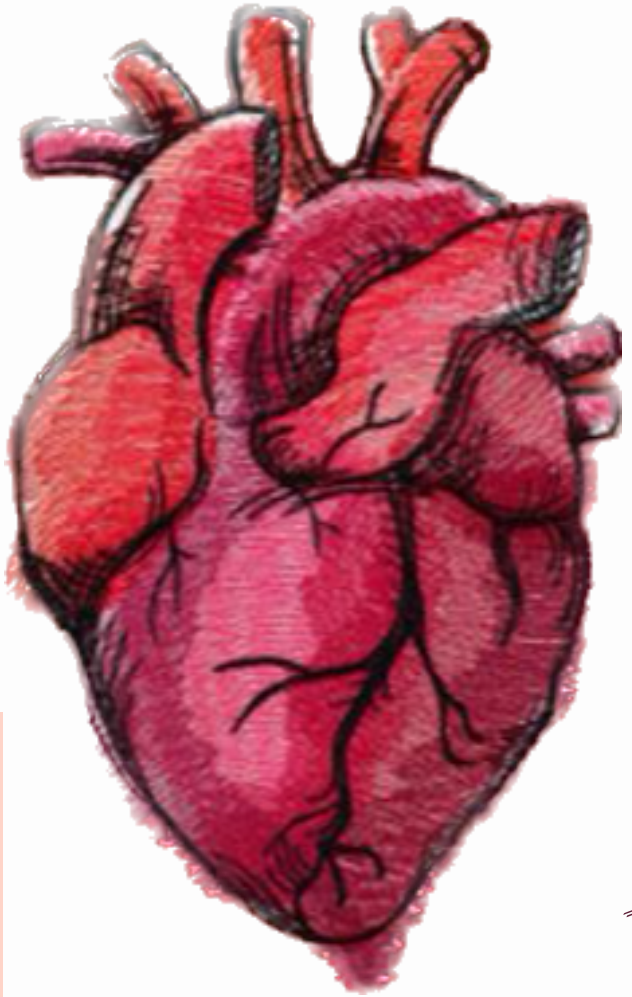


النادي الطبي

CARDIOVASCULAR SYSTEM

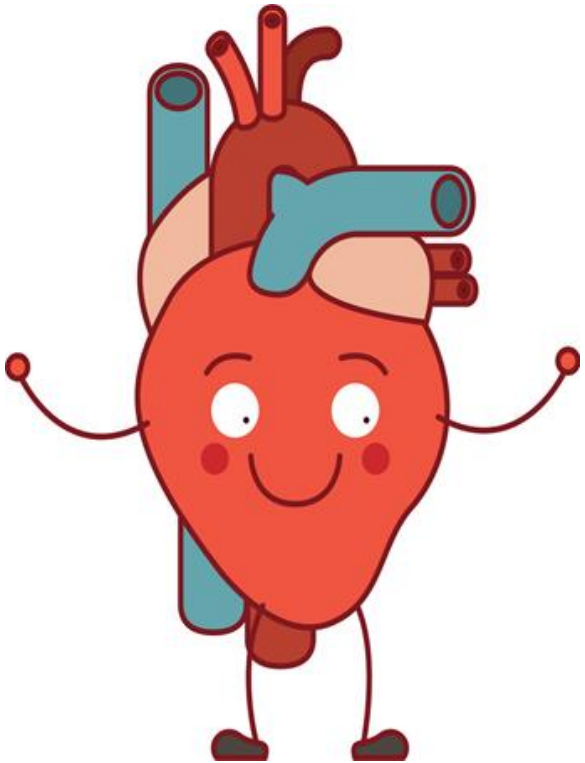
SUBJECT : Pathology

LEC NO. : "1"

DONE BY : Sadeel Alfageer

وَقُل رَّبِّ زِدْنِي عِلْمًا

SCAN ME!



بسم الله الرحمن الرحيم نبدأ

Arteriosclerosis
Cardiovascular Module 2024

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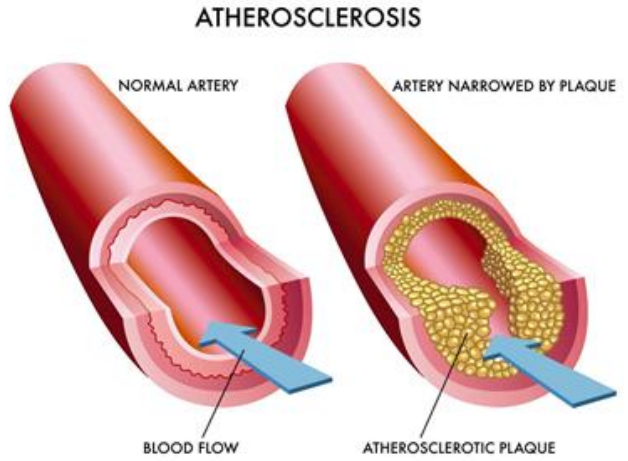
2024

Arteriosclerosis

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

Three patterns:

1. Atherosclerosis → The most common cause is plaque
2. Arteriolosclerosis → in arterioles
3. Monckeberg medial sclerosis



In this lecture we are taking about artery
من عنوان المحاضرة واضح

ARTERY + HARDENING or thickning

ARTERIOSCLEROSIS

* artery thicker, harder, less elastic *

بفقد المرونة يلي بكتسبها من ال internal & external elastic lamina

موضوع المحاضرة الجاي ↵

ATHEROSCLEROSIS

subintimal deposition of fat تجمعات الدهون

* hardening from PLAQUE *

"ATHEROMATOUS PLAQUE" in

fat

LDL (Low density lipoprotein like cholestrol) → HDL (High density lipoprotein)

ARTERIOLOSCLEROSIS

ARTERIOLES

* Hardening of ARTERIOLES *

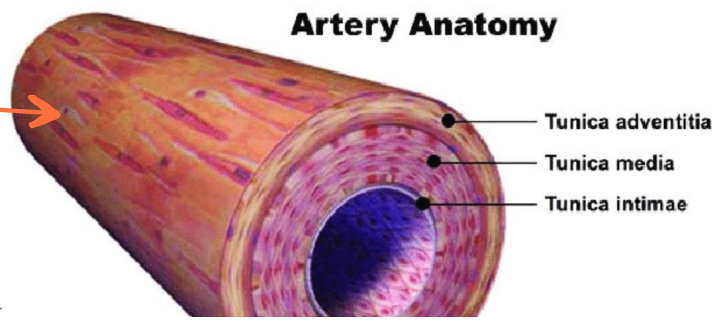
بهاي الحالة بزيد ال **perepheral resistance and lead mainly to the hypertension**

الكوليسترول منخفض الكثافة هو بروتين دهني يحمل الكوليسترول من الكبد لأنسجة الجسم عن طريق الدورة الدموية ، و زيادته تؤدي إلى ترسب الكوليسترول على جدران الأوعية الدموية و تضيقها ويصير عنا زيادة خطر الاصابة بأمراض القلب و الأوعية الدموية ، ممكن يصير عنا ischaemia and atherosclerosis

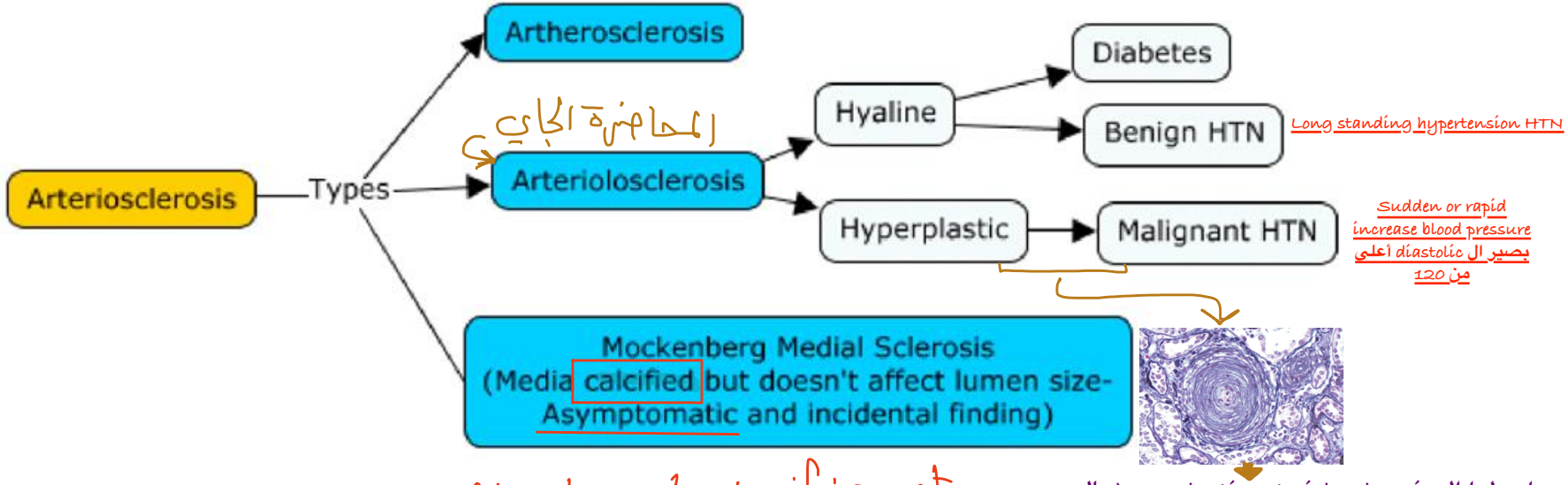
خلصنا المقدمة، و هلأ بدنا نحكي عن

Arteriosclerosis

الدكتورة ذكرتنا بال **main structure of artery**
و هي صورة خارجية للتذكير



اول شي بدنا نعرف انه arteriosclerosis
is a disease of intimae



اربطوا ال hyperplastic arteriolosclerosis **بال** onion skin appearence ، **و هاد المنظر بنشوفه بال** kidney **كتير**

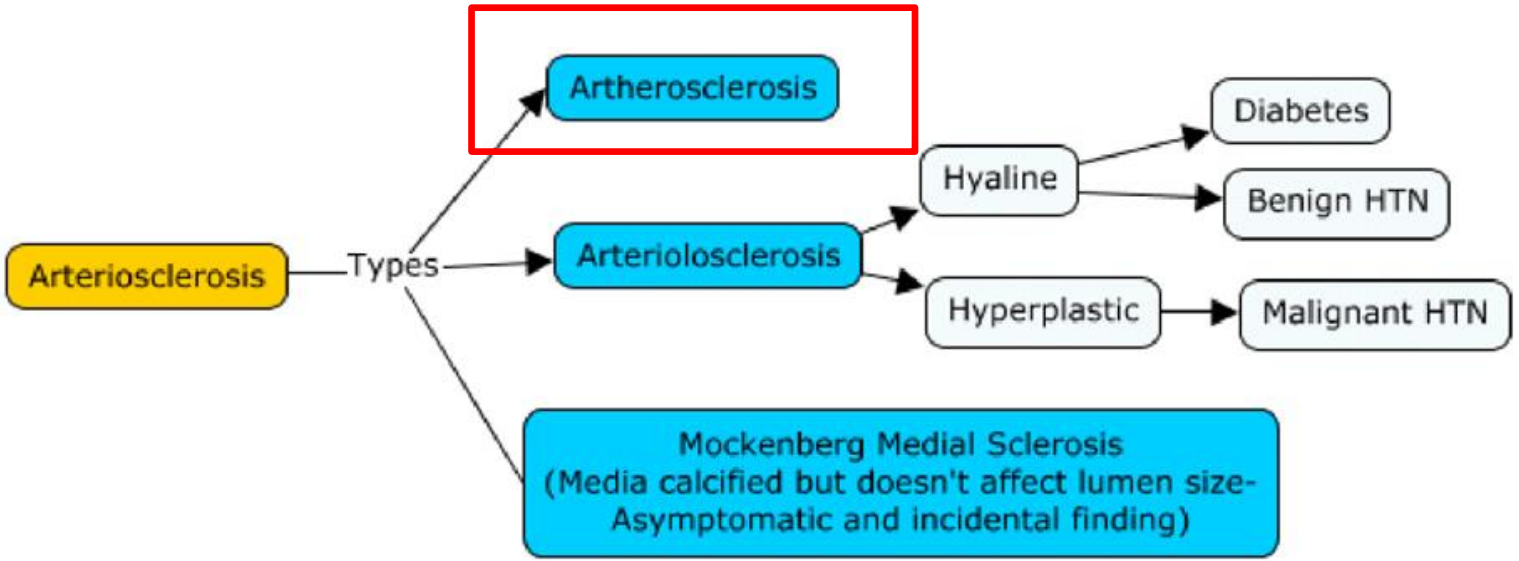
أول معلومة بدنا نعرفها انه ال atherosclerosis is a disease of intimae ،
بصير بال large & medium size blood vessels ← Aorta

ال Aorta ما رح يصيرله انسداد بال atheromatous plaque، لكن ممكن جزء من هاي ال plaques يصير الها dislodge من ال primary site و تروح لأماكن اخرى مسببة كوارث

Mockenberg medial sclerosis

- بصير عنا calcification of wall بدون التأثير على ال lumen size.
- اخف من يلي قبلها و أقل خطورة لأنها بتكون asymptomatic و بتيجي مع تقدم العمر

Arteriosclerosis



Arteriosclerosis

Arteriosclerosis **is hardening of arterial wall**

Three patterns

intima ال مكونة من endothelial cells which is smooth

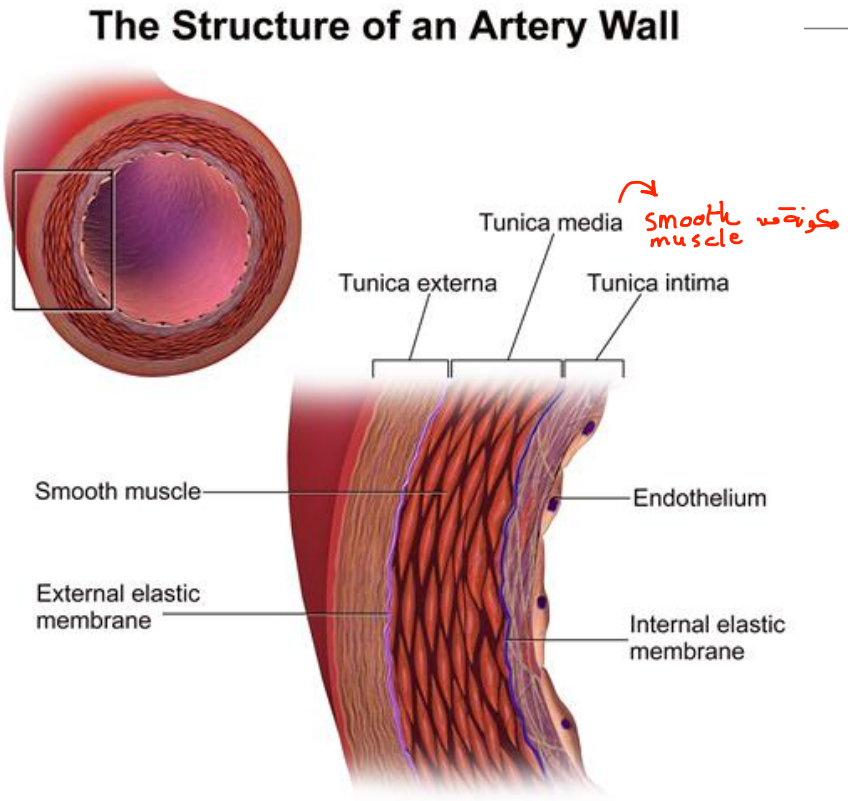
1. **Atherosclerosis - thickening of intima due to plaque (occurs in medium and large sized vessels)**

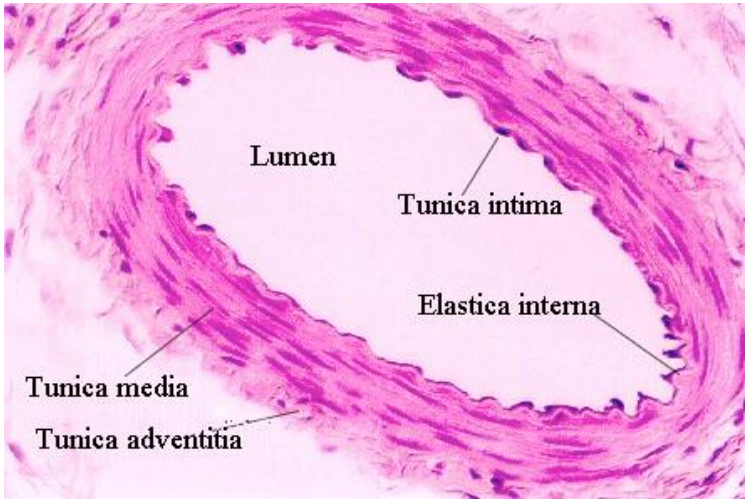
تجمعات الدهون بال intima جواها

Damage to the endothelial cells → Increase vascular permeability → Fats enter inside intima and aggregate → Recruiting of ~~the~~ inflammator → Increase ECM , fibrosis of CT

1. Arteriolosclerosis
2. Monckeberg medial sclerosis

Normal Artery structure





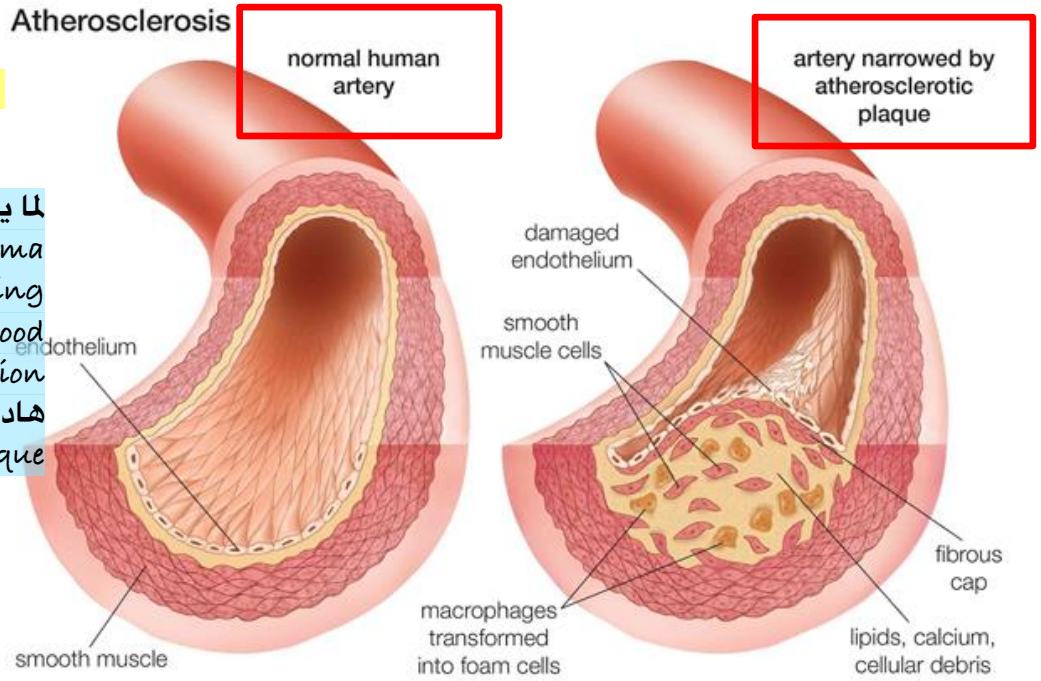
Atherosclerosis

كلام دكتورة دعاء .

شرح دكتورة غادة

Collection of lipid , macrophages , smooth muscle, calcium in the intima

لما يصير عندي هاد التجمع رح ترتفع ال intima و تزيد سماكتها ، بصير protruding جوا ال lumen و لو في blood بده يدخل رح يصير عنا oxigenation اقل و الشريان بتضيق و atherosclerosis هاد هو. مبدأ تكون ال plaque



Endothelial cell → Platelet adhesion → Exposed sub endothelial → vWF released → Platelet activation & aggregation → Secret many factor بتساعد في تكوين ال plaque → بدخل ال intima و بتجمع و بتحول لل oxidized form

في حال زيادة الكوليسترول السيئ LDL
يلي بطلع من الكبد للدم

Recruiting inflammation cells as monocyte monocyte enter in the intima then convert to microphage → بتحول ال oxidized LDL إلى foam cells → بصير aggregation للصفائح و بعطونا platelet derived growth factors زي ما حكينا

! اخر السلايد

بتعطينا deposition of substance و بصير عنا migration لل smooth muscle من وين ؟ من ال media (م احنا حكينا انها مكونة من smooth m) ، بتنتقل ال smooth muscle from media و بتروح تتجمع حول ال foam cells or oxidized LDL ، و بزيد ال ECM و هاد بسبب atheroma (هي tumor like mass يعني مش tumor حقيقي هي عبارة عن كتلة داخل ال blood vessle ، هاي الكتلة atherosclerotic plaque ، السلايد الجاي بوضح مكونات هاي الكتلة اكتر

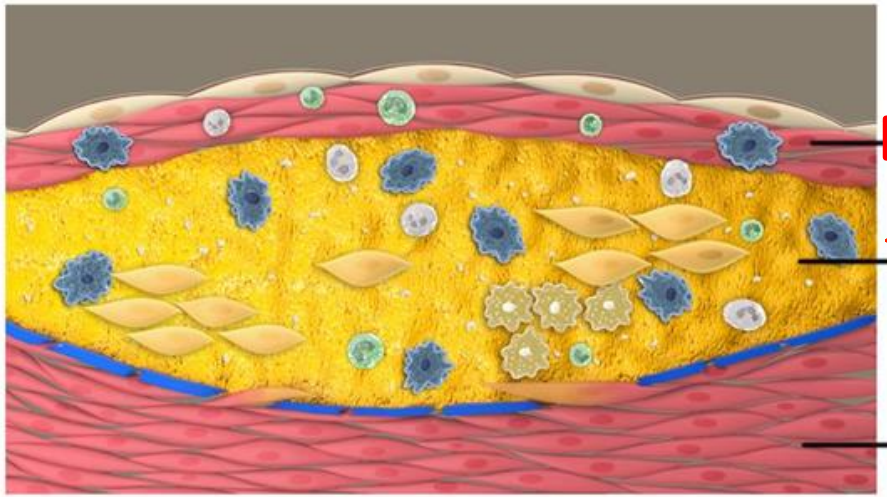
في الطب، تُعرف خلايا الفوام (Foam Cells) بأنها خلايا تتشكل عندما تتم حماية الخلايا الليفية العضلية الناعمة للأوعية الدموية بطبقة دهنية. تتشكل هذه الخلايا عادةً في عملية تعرف بتصلب الشرايين (Atherosclerosis)، حيث تتجمع الدهون والكوليسترول في جدران الشرايين، مما يؤدي إلى تكوين البلاك الدهني. وتظهر خلايا الفوام كخلايا دهنية كبيرة الحجم تحتوي على ترسبات دهنية، وهي جزء من عملية التهاب الأوعية الدموية التي تلعب دورًا مهمًا في تطور تصلب الشرايين ومضاعفاته.

لن تحصُل أبداً على شيء كامل، ستحصُل على أشياءٍ ناقِصة تكتمل برِضاك بها.

- أحمد خالد توفيق

Atherosclerosis

Atherosclerotic Plaque Anatomy



بكون عندي endothelium بعدين بيجي smooth muscle & collagen و هو المفروض ما يكونوا موجودين بال intima و بكونوا fibrous cap

1- **Fibrous Cap**
- Smooth muscle cells
- Macrophages
- Lymphocytes
- Collagen

2- **Necrotic Center**
- Smooth muscle cells
- Macrophages
- Foam cells
- Lymphocytes
- Cholesterol crystals
- Calcium
- Cell debris

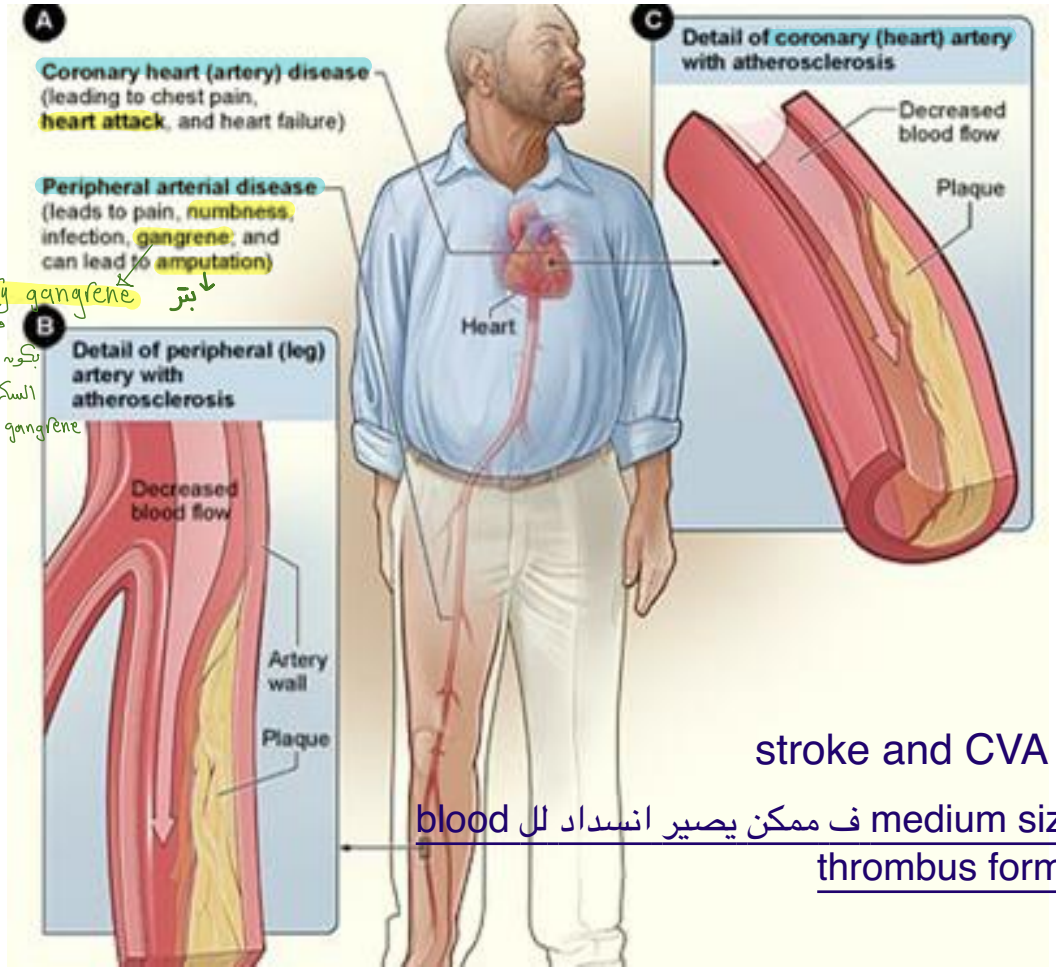
3- **Media**
- Smooth muscle cells

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

- بتصير بال aorta
- بتصير بال cerebral blood vessels و ممكن تعمل stroke and CVA
- بال coronary arteries و ممكن تسبب مشاكل كبيرة لأنهم medium sized ف ممكن يصير انسداد لل blood vessels ، ممكن ischemic heart disease or MI ، thrombus formation
- Popletial BV
- Prepheral blood vessels

Atherosclerosis Risk Factors
Two types

يعني أشياء بنقدر نعدل فيها و نعالجها

ما بنقدر نعدل عليها

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	

عادة ال male دائماً عنده النسبة أعلى لكن بس توصل الwomen سن اليأس

يعني just male more than female before menopause

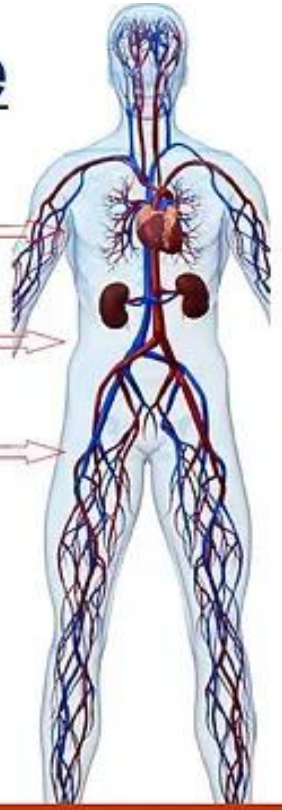
بال pre menopause بكون ال estrogen عامل حماية ، لكن هل معناته انه أعطي estrogen لل post menopause عشان اتجنب المشكلة؟ عملوا دراسة على الموضوع و ما نجحت

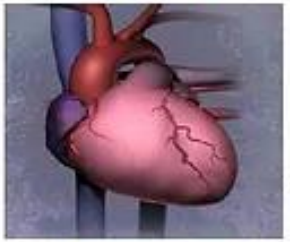
معلومة هبه د. دعاء

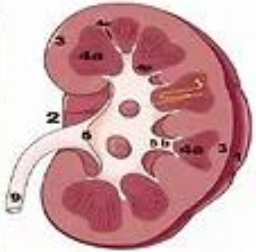
Reversible

HIGH

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







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

← حا ينقدر نغيّر فيهم بشكل عام

Atherosclerosis Risk Factors
Two types

* الكلام بـ شرحته الدكتوره هوه كل بكتوب بالسلايدات تحت

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)
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دكتورة غادة ما شرحت هاد السلايد، بس. المعلومات يلي موجودة حكيناها و للتأكيد فرغته من شرح دكتورة دعاء لوريد 👩

Modifiable Risk Factors

Hypercholesterolemia

لأنه اساس الatherosclerosis هو وجود high colestrol

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

LDL cholesterol (bad cholesterol); → لأنها بتساعد في ترسيب الكوليسترول بال peripheral tissued

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

بالعكس بتحرك الكوليسترول و ممكن تبعته لل gall bladder بعدين لل bile و بطلع الكوليسترول الزائد من ال intestine مع ال feces ، و هيك بنتخلص من الكوليسترول الزايد عن طريق ال bile

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**.

المناسف و الكنافة و الشبس و المقالي و القصص هاي كلها بترفع ال LDL ، فهي سيئة جداً لازم نتجنبها قدر الإمكان

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

Modifiable Risk Factors

Which one lead to other about to Hypertension and atherosclerosis ?

بالبداية ارتفاع الضغط بعمل ضغط على endothelial cell و بسبب damage الها بعمل cracking مش ulcer انتبهوايؤدي الى increase vascular permeapility which lead to accumulation of LDL in sub intima و هاد بزيد الضغط جوا كمان (يعني بدايةً ال HTN يؤدي لل atherosclerosis لكن بعدين برضو ال atherosclerosis بزيد الضغط

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.

اول خطوة بال pathogenesis هي انه يصير عنا injury &damage endothelial cell زي ما حكينا ، وال smoking بساعد بهاد الموضوع بصورة كبيرة ، لأنه بحتوي على oxidizing substances بتعمل injury بال endothelial cell و كذلك السكري

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.

حكيناه وحسبناه بال cs .

Modifiable Risk Factors

، imparement the metabolism of lipid and suger بصير عنا diabetes بال
بالتالي بتزيد نسبة حدوث ال atherosclerosis

(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

(C-reactive protein)

لو كان ال CRP عالي معناته عنا high risk ، لأنه ال

- **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.

ما حكتله الدكتورة

  - 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) .

الحمد لله حياتنا مش stressful أبداً

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	

Non-Modifiable risk factors

- **Age:** incidence of IHD increases 5-fold between 40 and 60 years of age. علاقة طردية
- **Gender:** ما لحقنا ننسى ، حكيناه بأول المحاضرة

- 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' LDL 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.** Atherogenic actually
- **Estradiol (E2) is the primary form of estrogen in your body during your reproductive years.** Non atherogenic

- **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.

↳ autosomal dominant

- 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

يعني بزيد السيئ وبقلل الجيّد.

- 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.

هدول الناس لازم يتعالجوا ، و العلاج ببدأمن عمر 8-10 سنين ، و لازم يغيروا و يحسنوا من life style
و اهم شي بدؤوا العلاج و ما يتأخروا

- **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.

بزيد انتاج الكوليسترول و بقل ال

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.

حكيناها قبل شوي انه العلاج جداً مهم ، ما بكفي اغير و احسن ال life style و بس ، لازم drug therapy

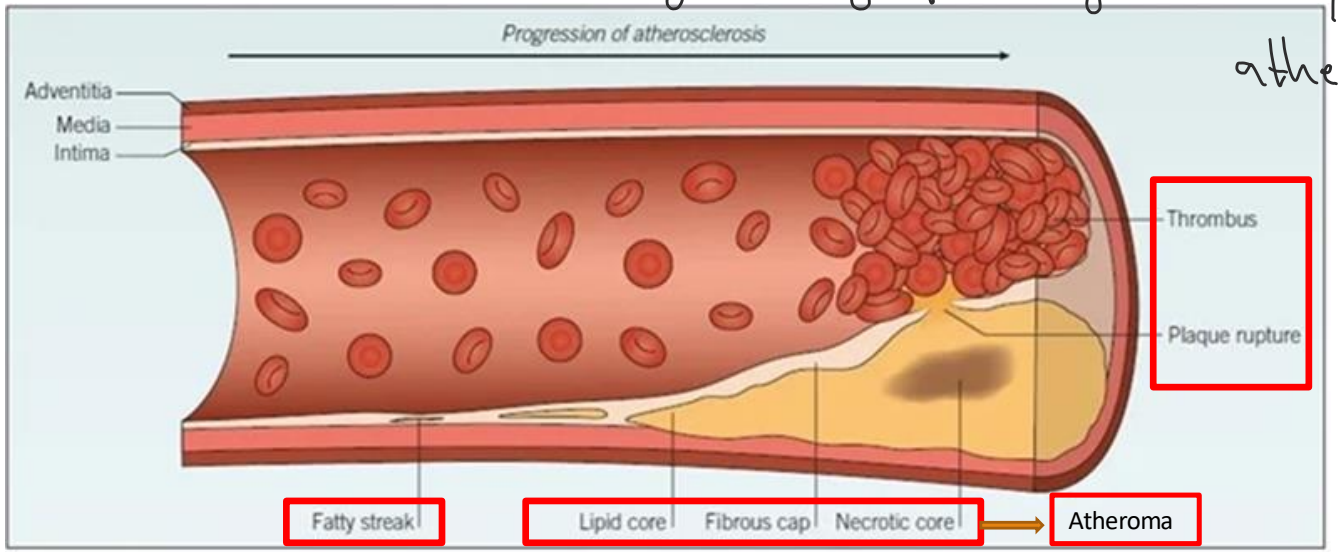
- Treatment should be started as early age as possible (8 -10 years)

Pathogenesis of atherosclerosis

دكتنا عن موضوع الـ inflammation فوق

- 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.

macrophages & lymphocyte → الهم دور مهم بتطور الـ atherosclerosis



First line protective of CV.

- 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

بس لسا وصلنا thrombus formation

- 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

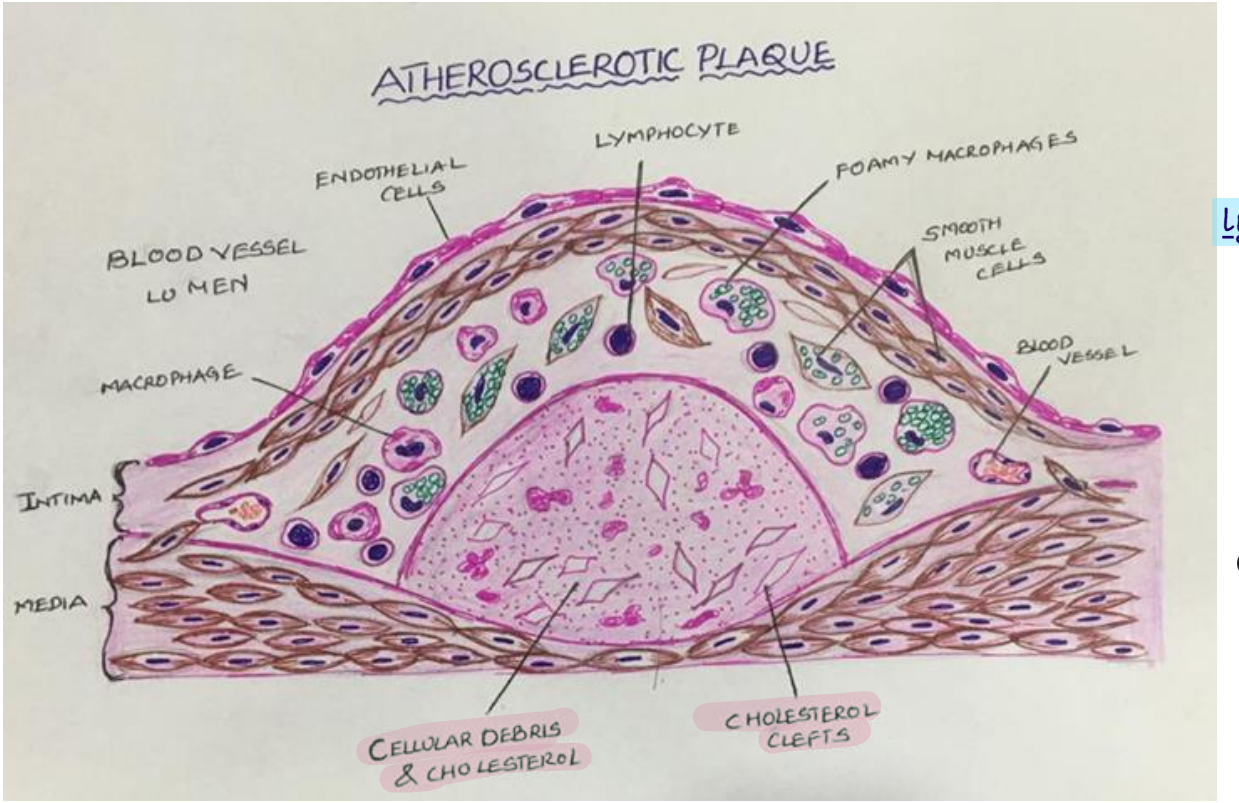
ارجعوا لسلايد ١١ شرحناها هناك 👀

(برخو شرحناها)

نتذكر انه كان عنا intima و تحتها ال media و هاد بالوضع الطبيعي

اما الشي يلي مش طبيعي هو يلي بنشوفه بالصورة ، عنا endothelium و تحتها smooth muscle انتقلت من ال media (طلعت من عندها) و عملت CAP ، و بعدين عنا core مكون من : lymphocyte , smooth muscle , macrophages and

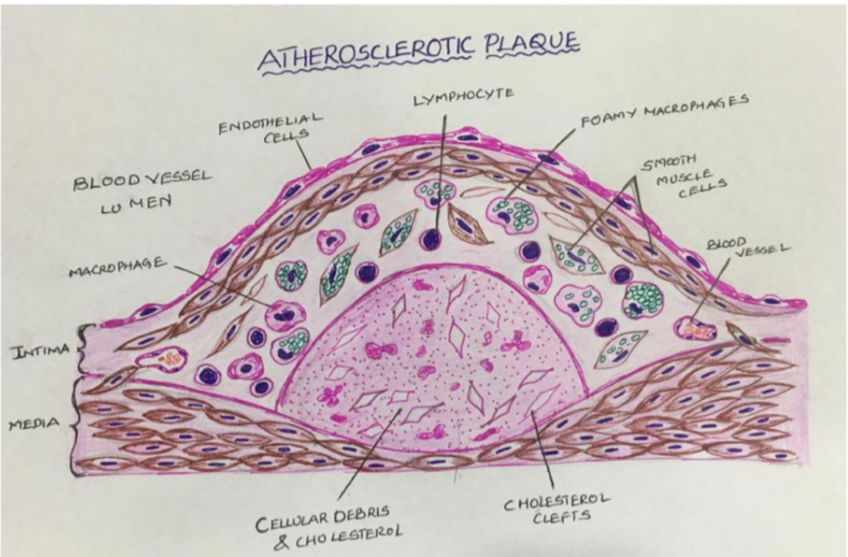
هاد كلام د. دعاء .



Pathogenesis of atherosclerosis

★ هاد السلايد تزويدي مه وربه .

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

ی macrophages and inside them there is oxidised LDD.

شرح المادة لدفعة وريد

الدكتورة دعاء

Pathology-CVS

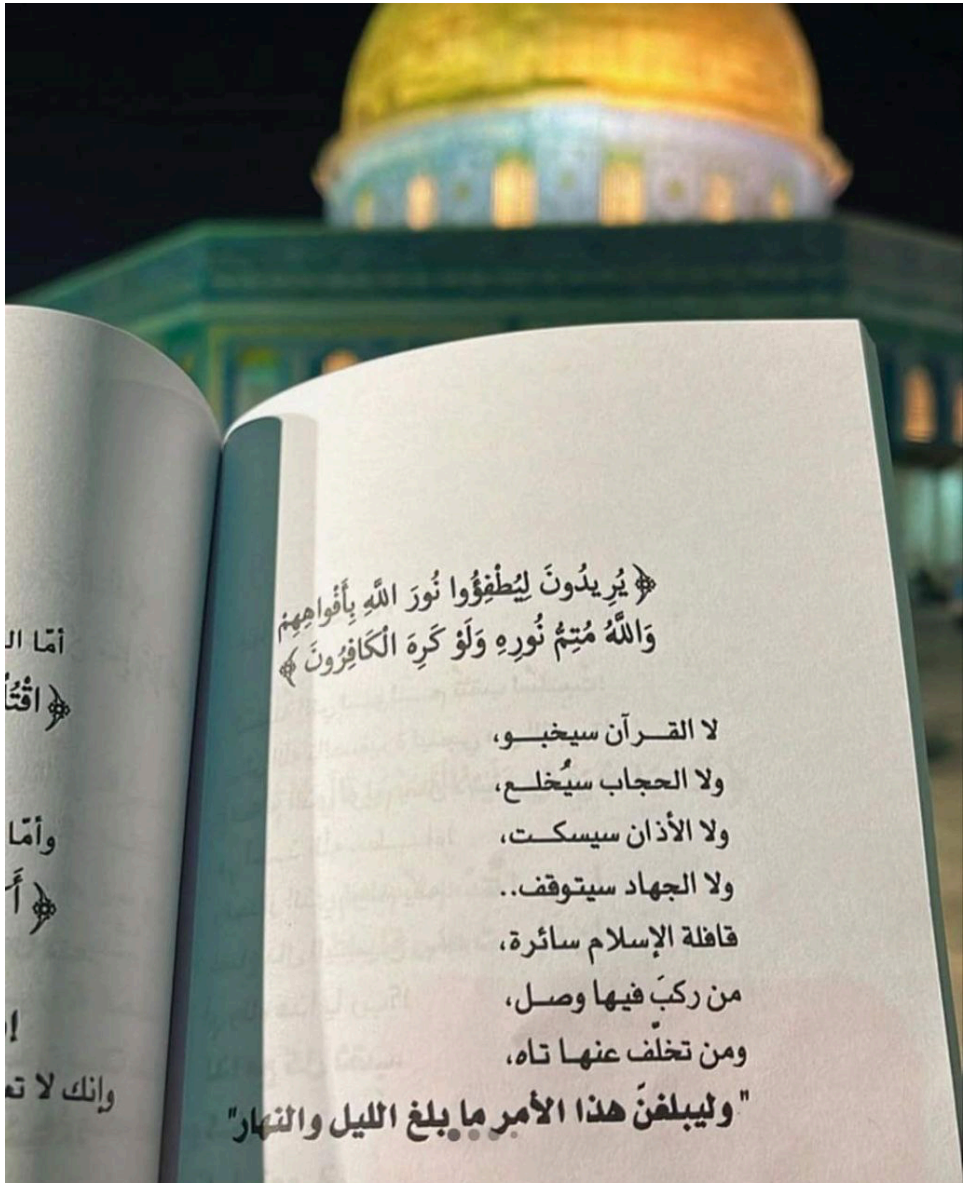
شرح خارجي

Medical club | Dr.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**

ضفنالكم على خانه ال Guidance جداول بتحتوي على فيديوهات بتساعدكم بفهم مواضيع البائو بشكل أكبر ولتسهل عليكم الحفظ بتلاقوهم من (دفعة حياة .. CVS .. بائو .. Guidance)

Thank You


﴿يُرِيدُونَ لِيُطْفِؤُوا نُورَ اللَّهِ بِأَفْوَاهِهِمْ
وَاللَّهُ مُتِمُّ نُورِهِ وَلَوْ كَرِهَ الْكَافِرُونَ﴾
لا القــرآن سيخبــو،
ولا الحجاب سيُخلــع،
ولا الأذان سيسكــت،
ولا الجهاد سيتوقف..
قافلة الإسلام سائرة،
من ركبَ فيها وصــل،
ومن تخلّف عنهـا تاه،
"وليبلغنّ هذا الأمر ما بلغ الليل والنهار"