ΚΑΡΔΙΟΜΕΤΑΒΟΛΙΚΗ ΙΑΤΡΙΚΗ

ΕΛΛΗΝΙΚΗ ΔΗΜΟΚΡΑΤΙΑ
Εθνικόν και Καποδιστριακόν Πανεπιστήμιον Αθηνών
ΙΔΡΥΘΕΝ ΤΟ 1837
ΙΑΤΡΙΚΗ ΣΧΟΛΗ ΑΘΗΝΩΝ

ΠΜΣ: Καρδιομεταβολική Ιατρική
Παθογένεια και σχηματισμός αθηρωματικής πλάκας

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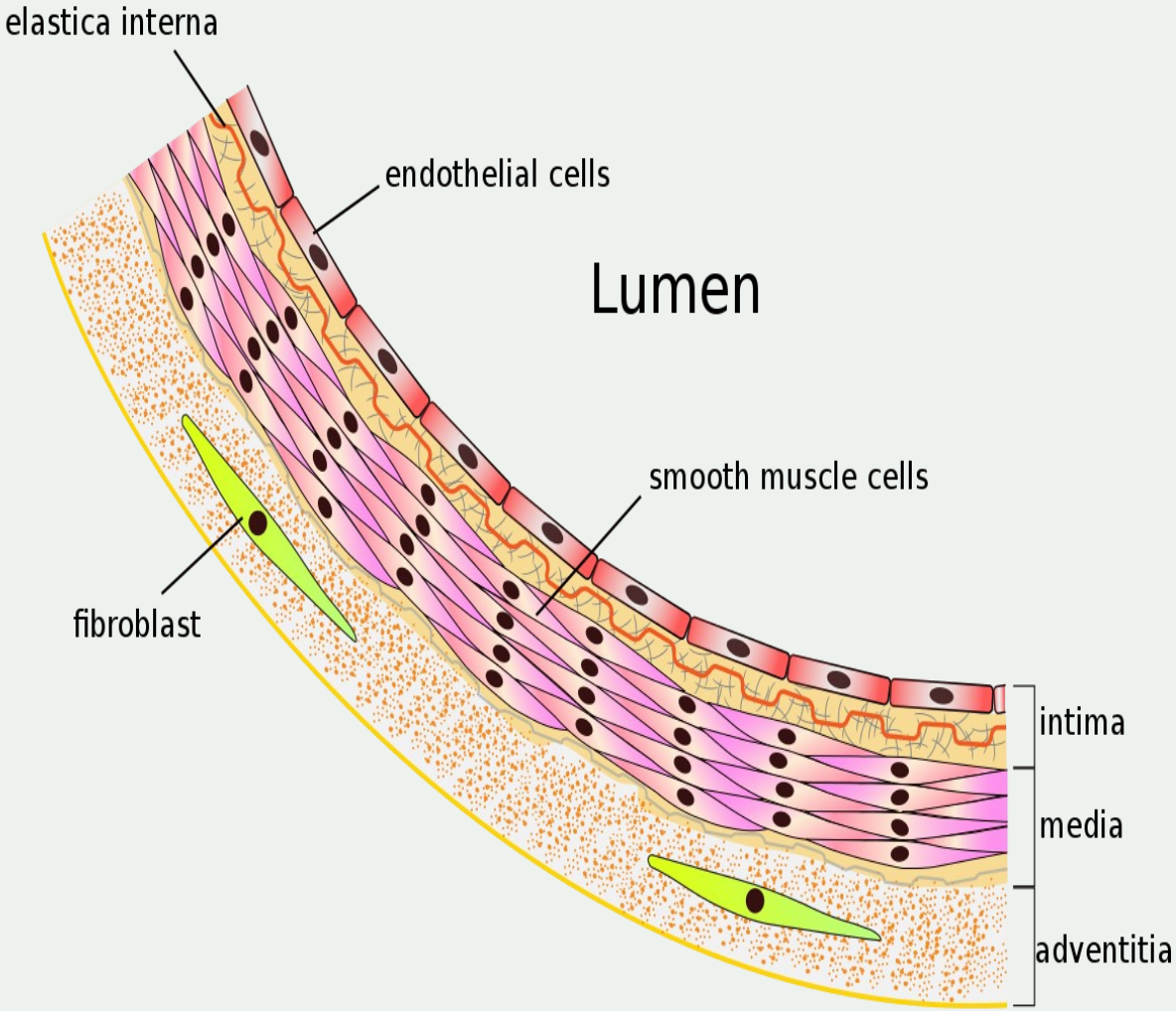
Καρδιολόγος, ΕΠΙΜΕΛΗΤΗΣ Β' ΕΣΥ
ΠΓΝ ΑΤΤΙΚΟΝ

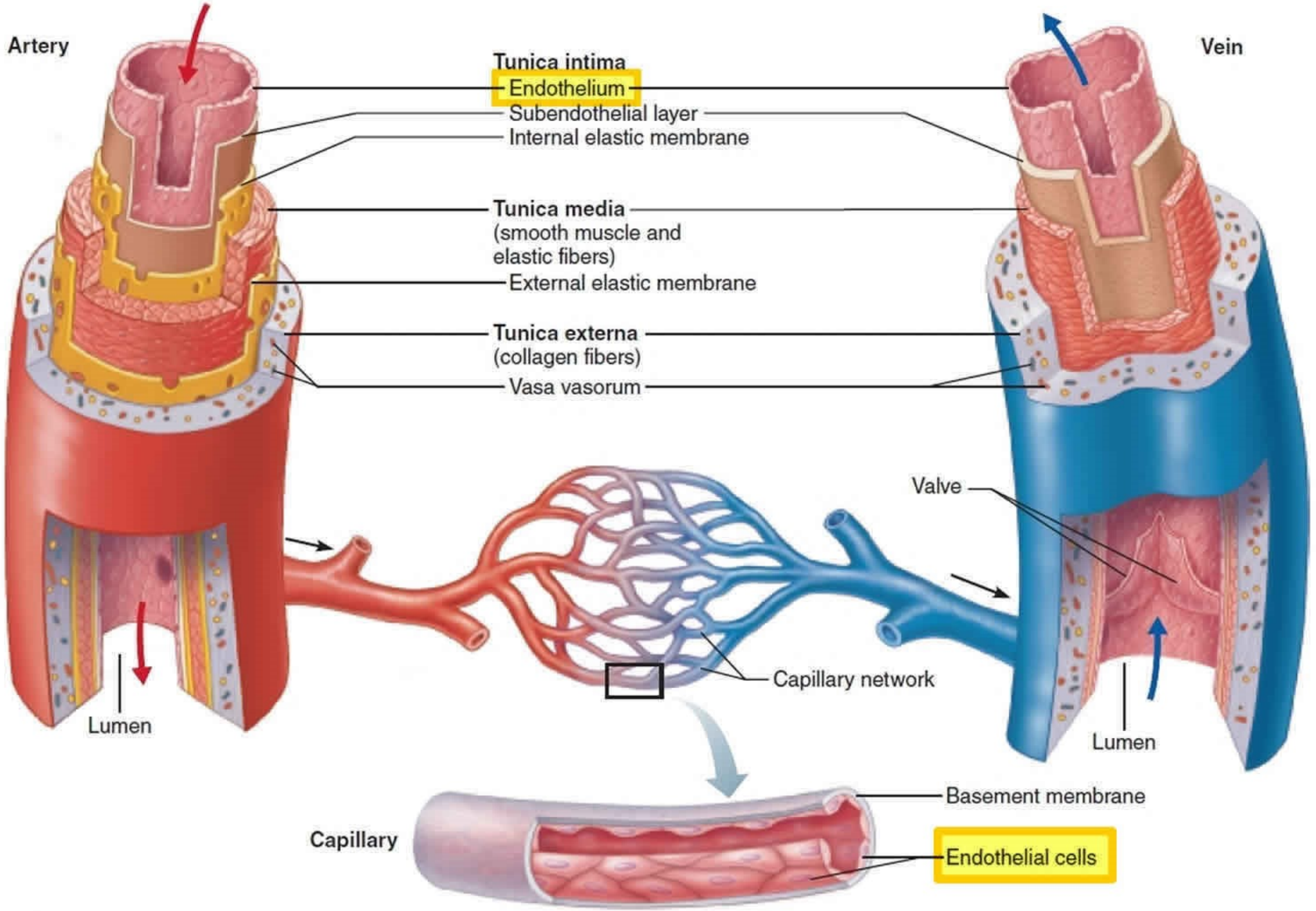
ΜΟΡΦΟΛΟΓΙΚΑ ΧΑΡΑΚΤΗΡΙΣΤΙΚΑ ΑΡΤΗΡΙΑΚΟΥ ΤΟΙΧΩΜΑΤΟΣ

- Έσω χιτών

[Ενδοθήλιο, βασική μεμβράνη, υπενδοθηλιακή στοιβάδα, έσω ελαστική μεμβράνη]

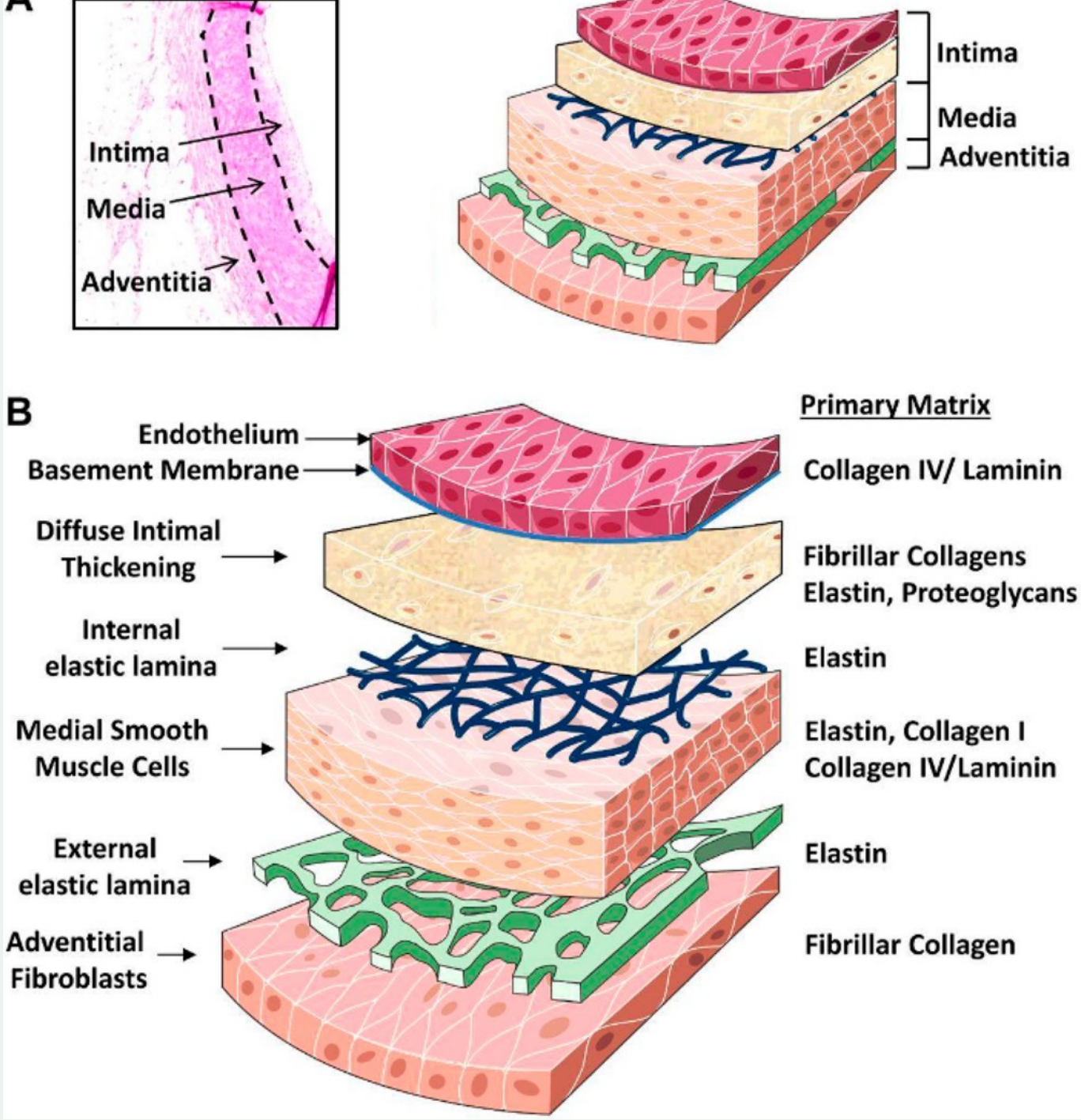
- Μέσος χιτών
- Έξω χιτών



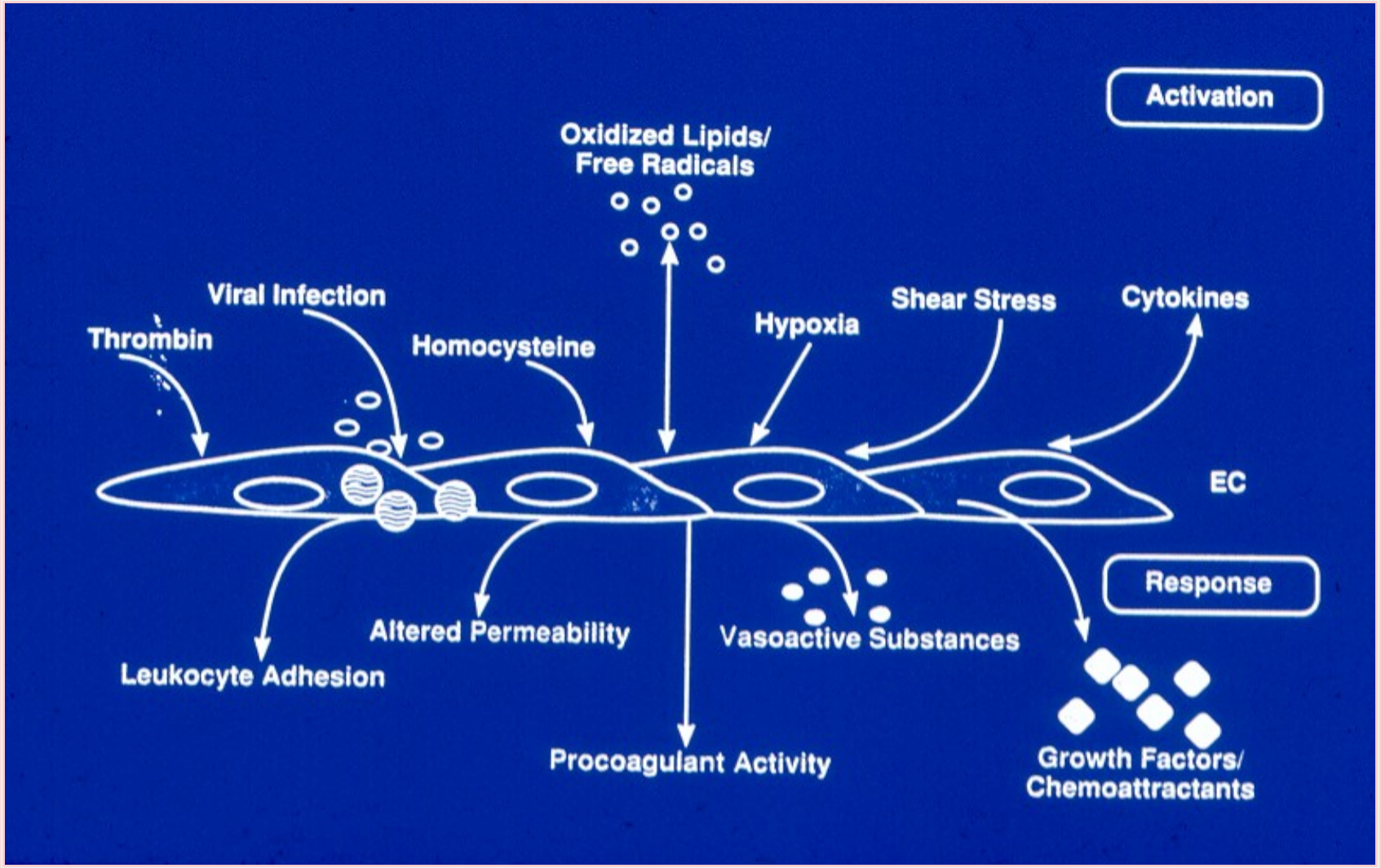

Artery
Vein
Tunica intima
Endothelium
Subendothelial layer
Internal elastic membrane
Tunica media
(smooth muscle and
elastic fibers)
External elastic membrane
Tunica externa
(collagen fibers)
Vasa vasorum
Valve
Capillary network
Lumen
Lumen
Capillary
Basement membrane
Endothelial cells

ΕΝΔΟΘΗΛΙΟ

- Μονή στοιβάδα κυττάρων
- Κύτταρα επιμηκυμένα κατά τη ροή του αίματος
- Μεσοκυττάριοι χώροι 15-20 nm
- Κυτταρικοί δεσμοί
- Χαμηλός ρυθμός πολλαπλασιασμού [1-2/1000 κύτταρα/ημέρα]
- Χαμηλή διαπερατότητα πρωτεϊνών [1-10%]



Factors affecting endothelial function



Substances Released by Endothelium

Vasoactive Substances

- **Vasodilators**
  - —Nitric oxide/EDRF
  - —EDHF
  - —Prostacyclin (PGI_2)
  - —Bradykinin
  - —Acetylcholine, serotonin, histamine, substance P, etc
- **Vasoconstrictors**
  - —Endothelin
  - —Angiotensin II
  - —Thromboxane A_2, acetylcholine, arachidonic acid, prostaglandin H_2, etc

Growth Mediators/Modulators

- Growth promotors
- Growth inhibitors

Inflammatory Mediators/ Modulators

Hemostasis and Thrombosis

Redox State

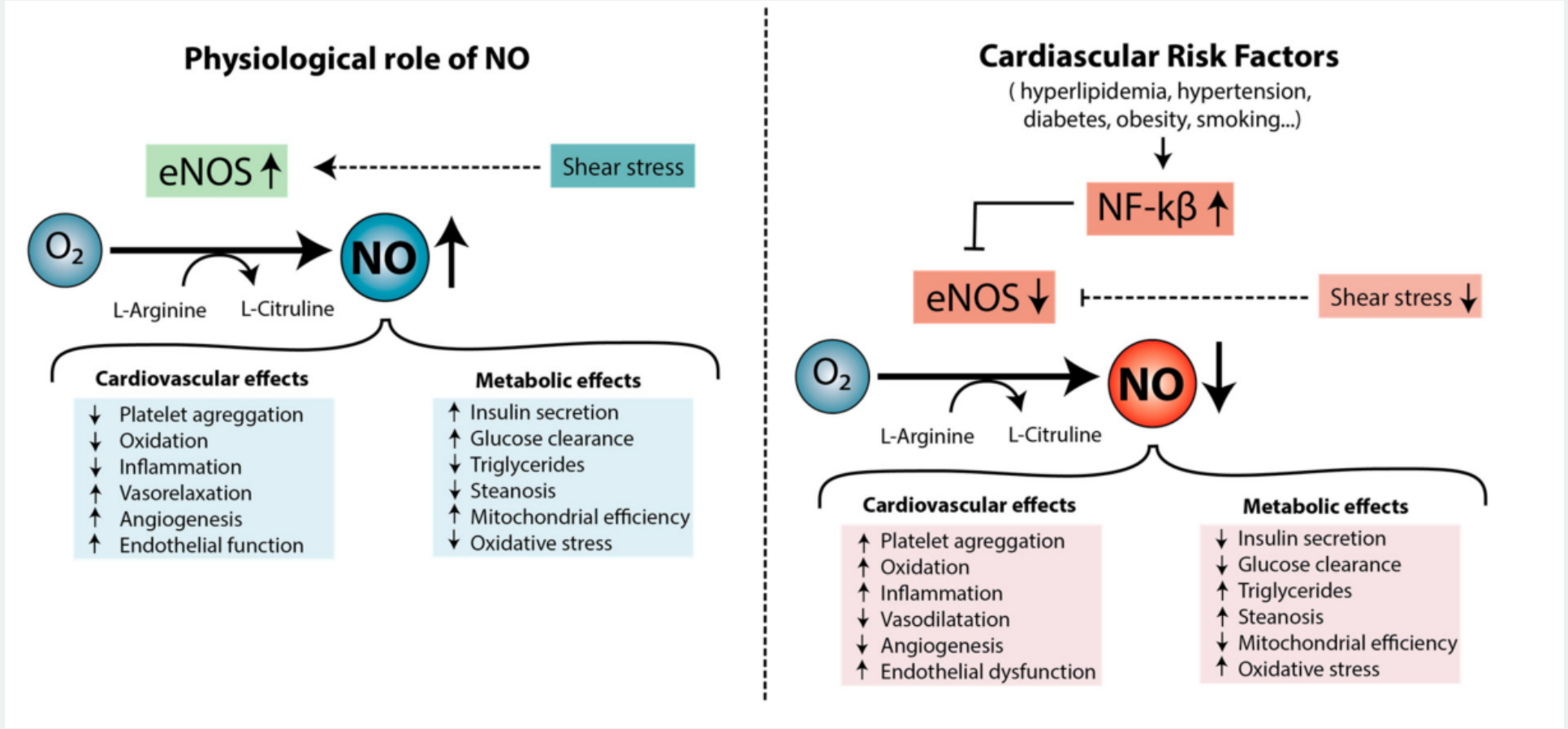
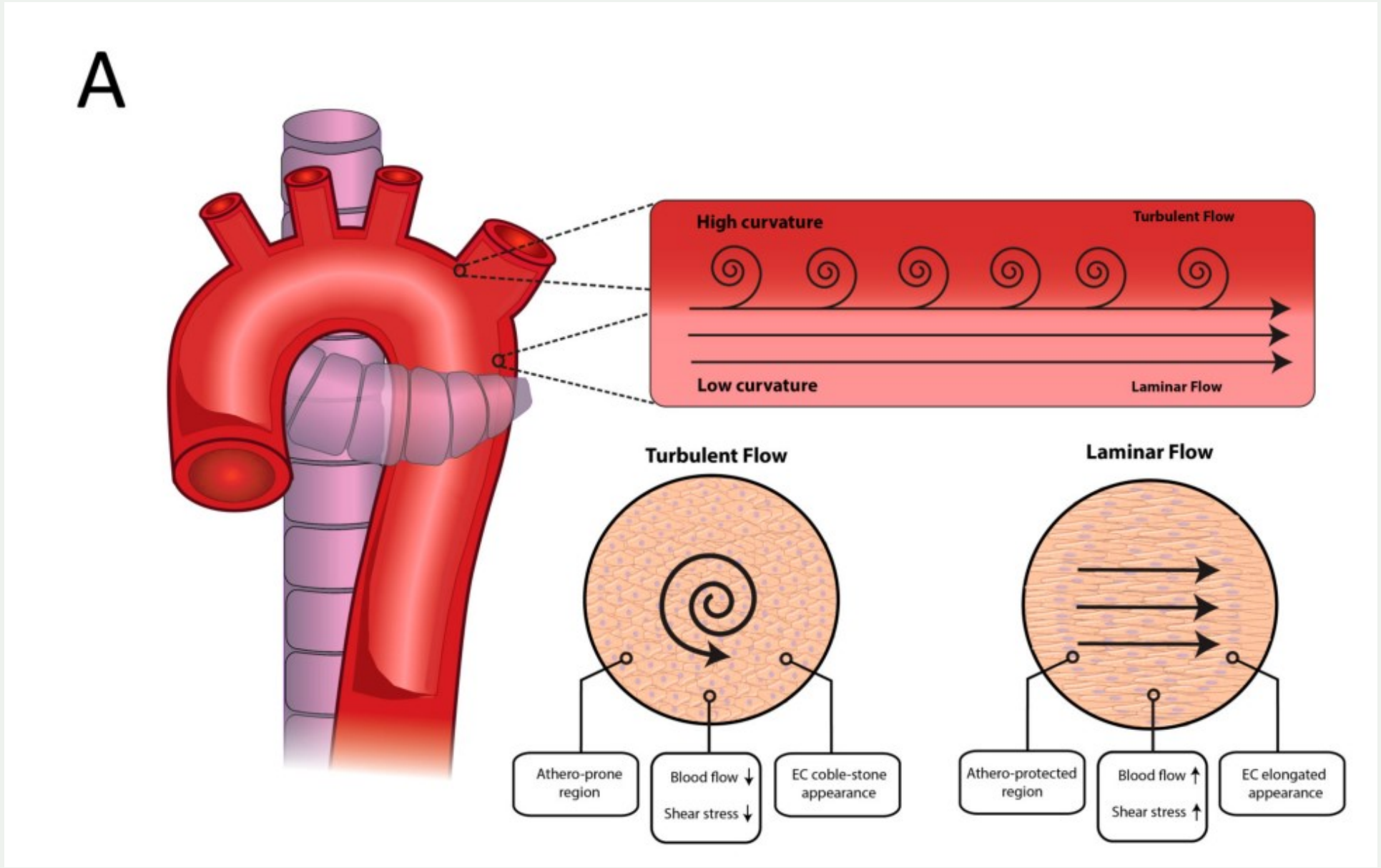


Figure 2. Nitric oxygen regulates cardiovascular metabolism and is compromised in the presence of cardiovascular risk factors. eNOS catalyzes the production of NO from L-arginine. NO is an essential metabolite that inhibits the progression of atherosclerosis improving vasorelaxation, angiogenesis, endothelial function, insulin secretion, glucose clearance, and mitochondrial efficiency. On the other hand, it reduces oxidative stress, inflammation, plasma lipid levels, and stenosis. Cardiovascular risk factors, such as hyperlipidemia, hypertension, and diabetes, inhibit eNOS activity upon NF-kβ induction, reducing NO and promoting atherosclerosis development.

Int. J. Mol. Sci. 2022, 23, 3346. doi.org/10.3390/ ijms23063346

ΠΡΟΔΙΑΘΕΣΙΚΟΙ ΠΑΡΑΓΟΝΤΕΣ

- Υπερλιπιδαιμια
- Σακχαρωδης διαβητης
- Υπερταση
- Καπνισμα
- Ομοκυστεινη
- Ινωδογονο
- Οιστρογονα
- CRP
- Παχυσαρκια-Φυσικη δραστηριοτητα-Γενετικοι παραγοντες



Int. J. Mol. Sci. 2022, 23, 3346. doi.org/10.3390/ ijms23063346

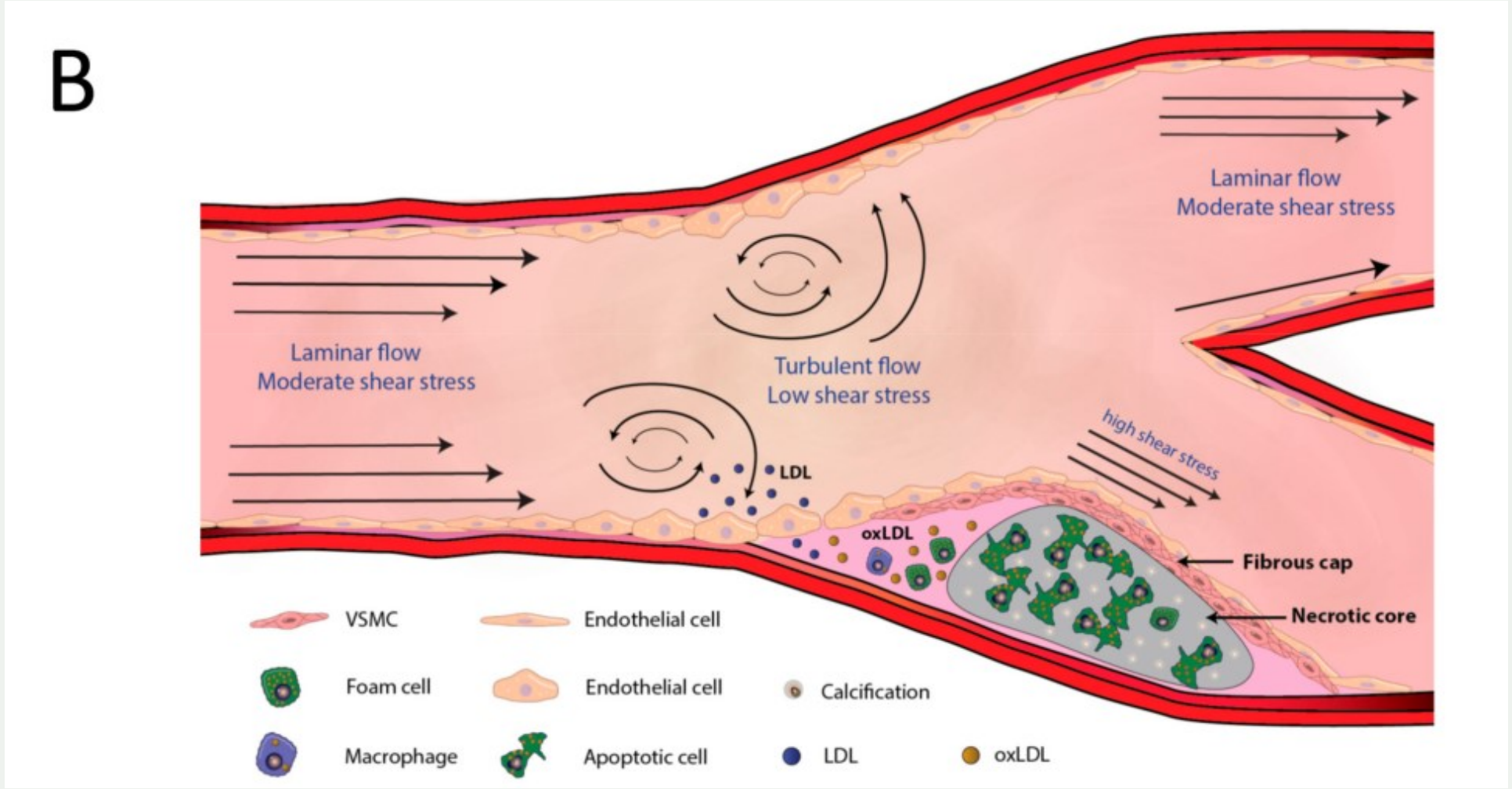


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Figure 1. Effect of flow and WSS patterns at arterial bifurcations on atherosclerotic plaque development. (**A**) In straight vessel segments, physiological WSS with laminar flow leads to ECs and shows a quiescent characteristic flattened shape when flow disturbance occurs. Lower WSS at the outer vessel wall causes ECs to adopt a cobblestone appearance. (**B**) Turbulent flow occurs at bifurcations and branch points where the arterial curvature is higher due to flow separation. Disturbed laminar flow or turbulent flow reduces WSS and promotes endothelial dysfunction and LDL infiltration, which constitutes the first step of atheroma plaque formation. On the contrary, low curvature areas of the vascular system subjected to higher shear stress are athero-protected.

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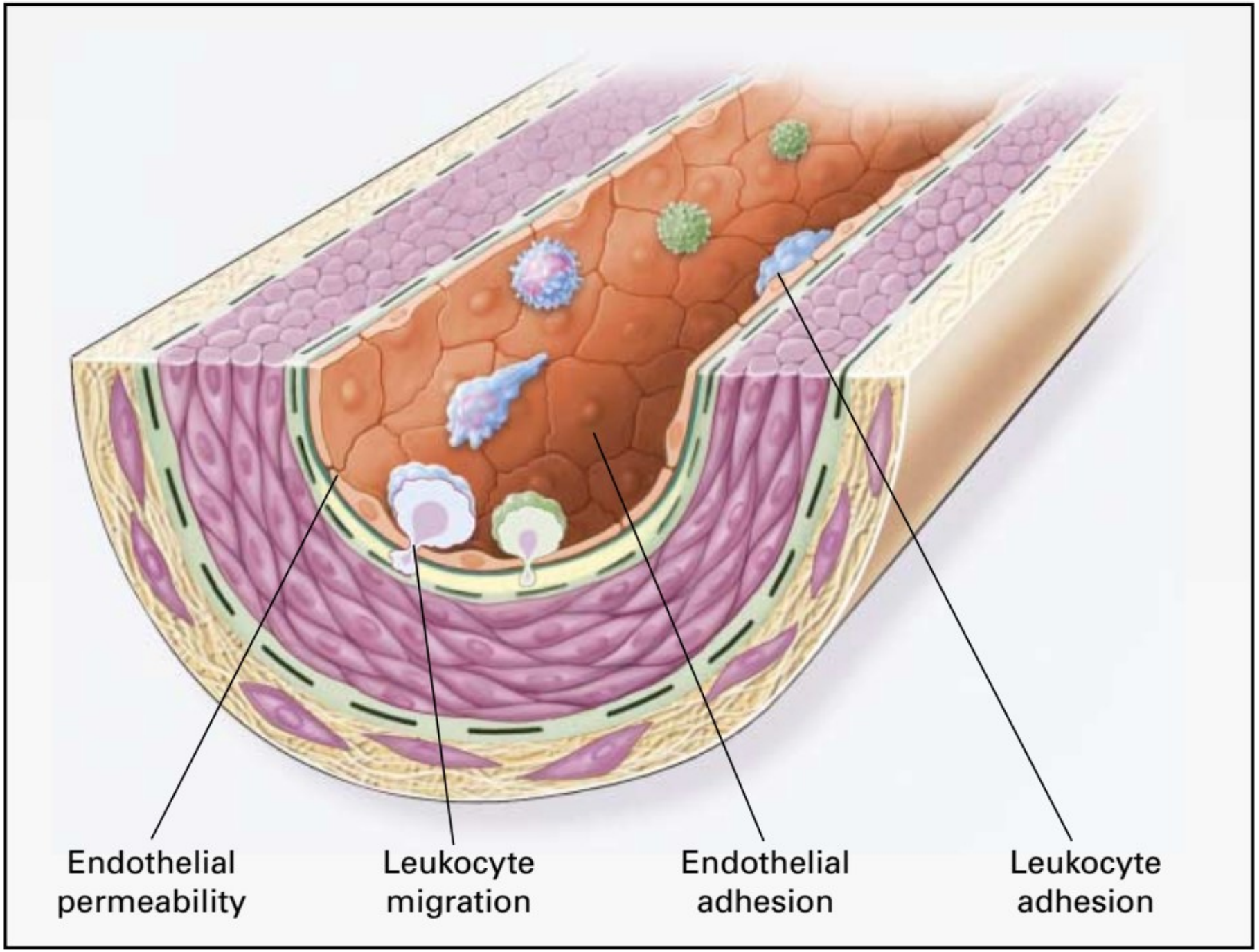
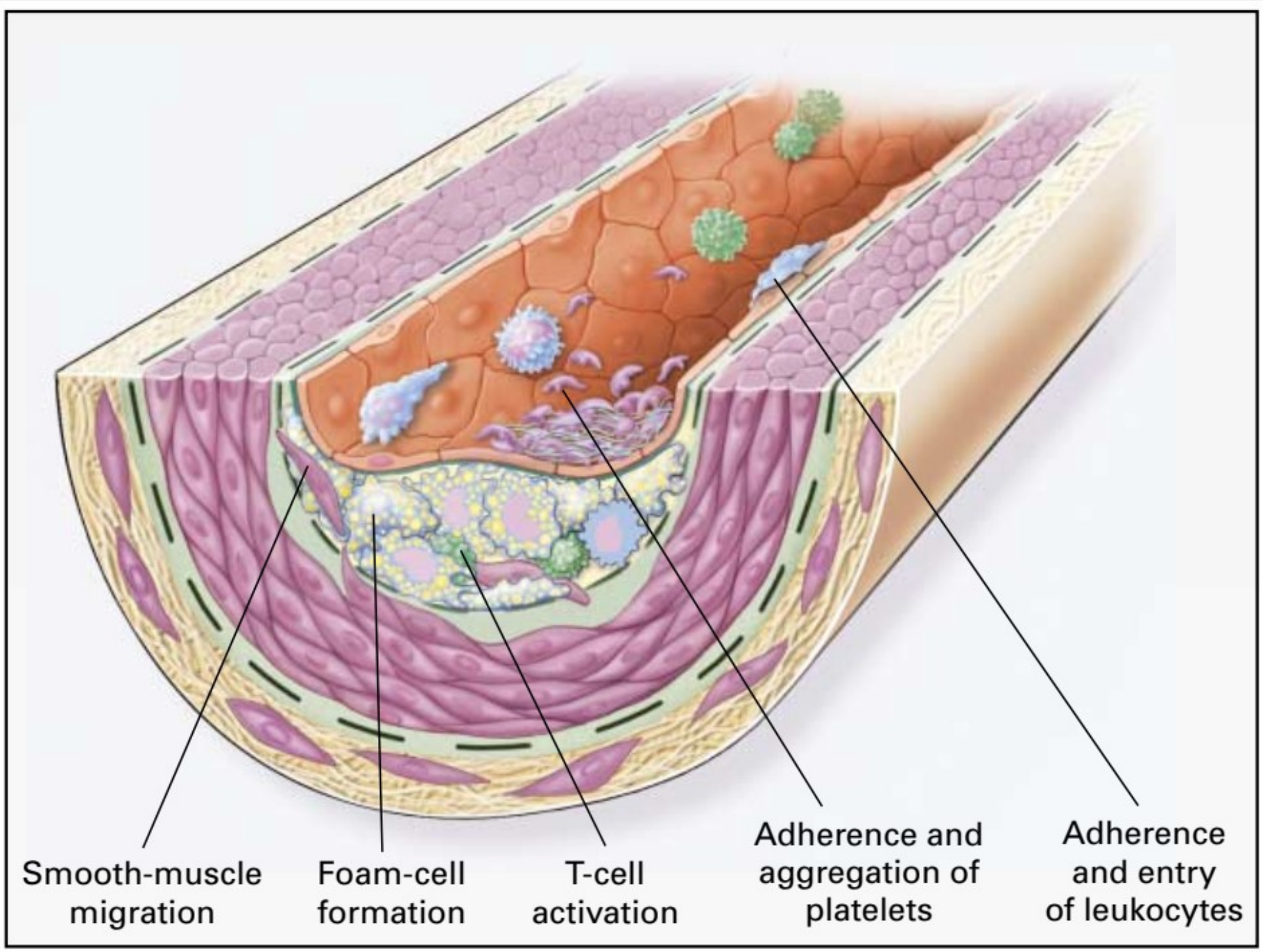


N Engl J Med 1999; 340:115-126. DOI: 10.1056/NEJM199901143400207

Endothelial Dysfunction in Atherosclerosis.

The earliest changes that precede the formation of lesions of atherosclerosis take place in the endothelium. These changes include increased endothelial permeability to lipoproteins and other plasma constituents, which is mediated by nitric oxide, prostacyclin, platelet-derived growth factor, angiotensin II, and endothelin; up-regulation of leukocyte adhesion molecules, including L-selectin, integrins, and platelet–endothelial-cell adhesion molecule 1, and the up-regulation of endothelial adhesion molecules, which include E-selectin, P-selectin, intercellular adhesion molecule 1, and vascular-cell adhesion molecule 1; and migration of leukocytes into the artery wall, which is mediated by oxidized low-density lipoprotein, monocyte chemotactic protein 1, interleukin-8, platelet-derived growth factor, macrophage colony-stimulating factor, and osteopontin.

N Engl J Med 1999; 340:115-126. DOI: 10.1056/NEJM199901143400207

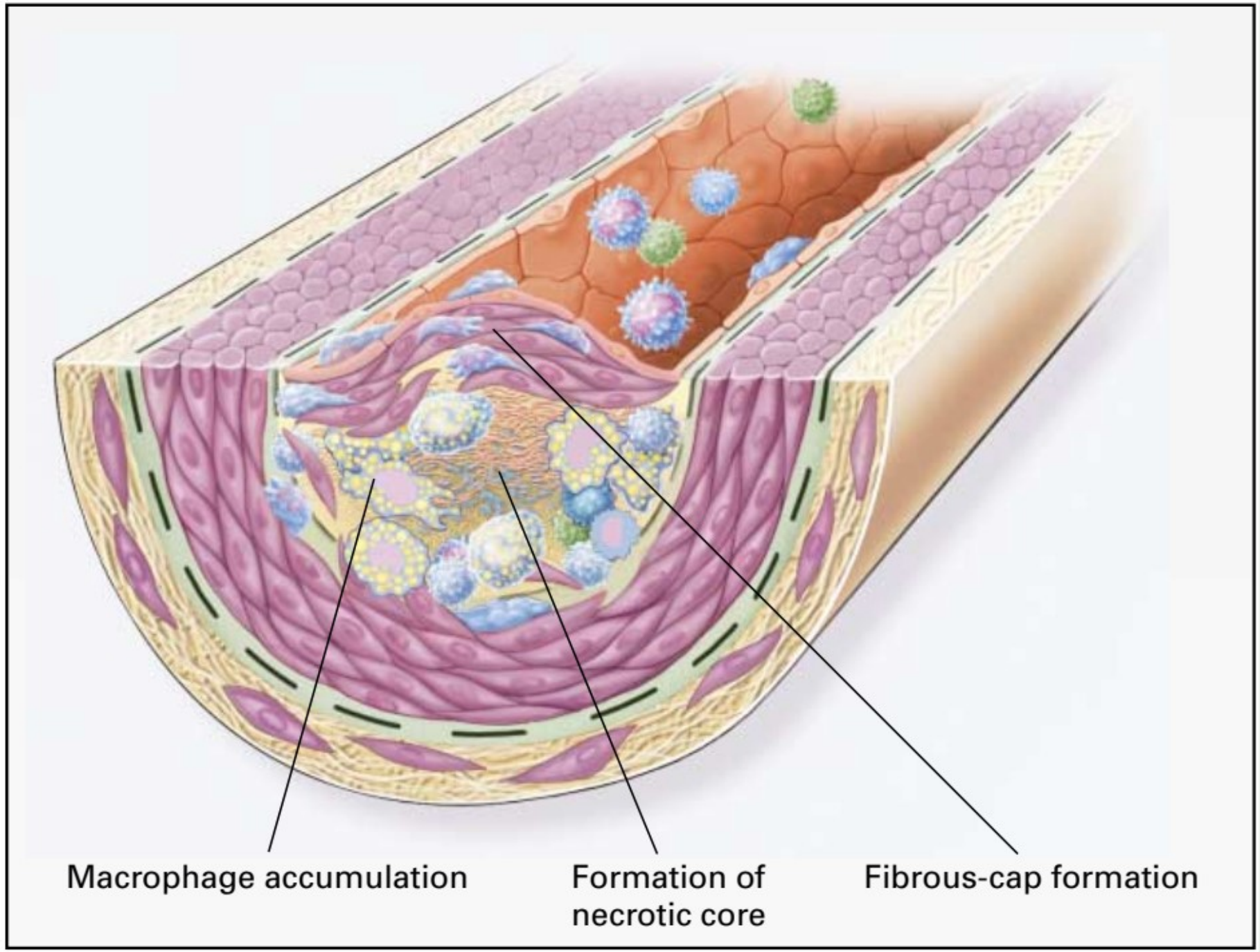


N Engl J Med 1999; 340:115-126. DOI: 10.1056/NEJM199901143400207

Fatty-Streak Formation in Atherosclerosis.

Fatty streaks initially consist of lipid-laden monocytes and macrophages (foam cells) together with T lymphocytes. Later they are joined by various numbers of smooth-muscle cells. The steps involved in this process include smooth-muscle migration, which is stimulated by platelet-derived growth factor, fibroblast growth factor 2, and transforming growth factor β; T-cell activation, which is mediated by tumor necrosis factor α, interleukin-2, and granulocyte–macrophage colony-stimulating factor; foam-cell formation, which is mediated by oxidized low-density lipoprotein, macrophage colony-stimulating factor, tumor necrosis factor α, and interleukin-1; and platelet adherence and aggregation, which are stimulated by integrins, P-selectin, fibrin, thromboxane A_2, tissue factor, and the factors described in Figure 1 as responsible for the adherence and migration of leukocytes.

N Engl J Med 1999; 340:115-126. DOI: 10.1056/NEJM199901143400207

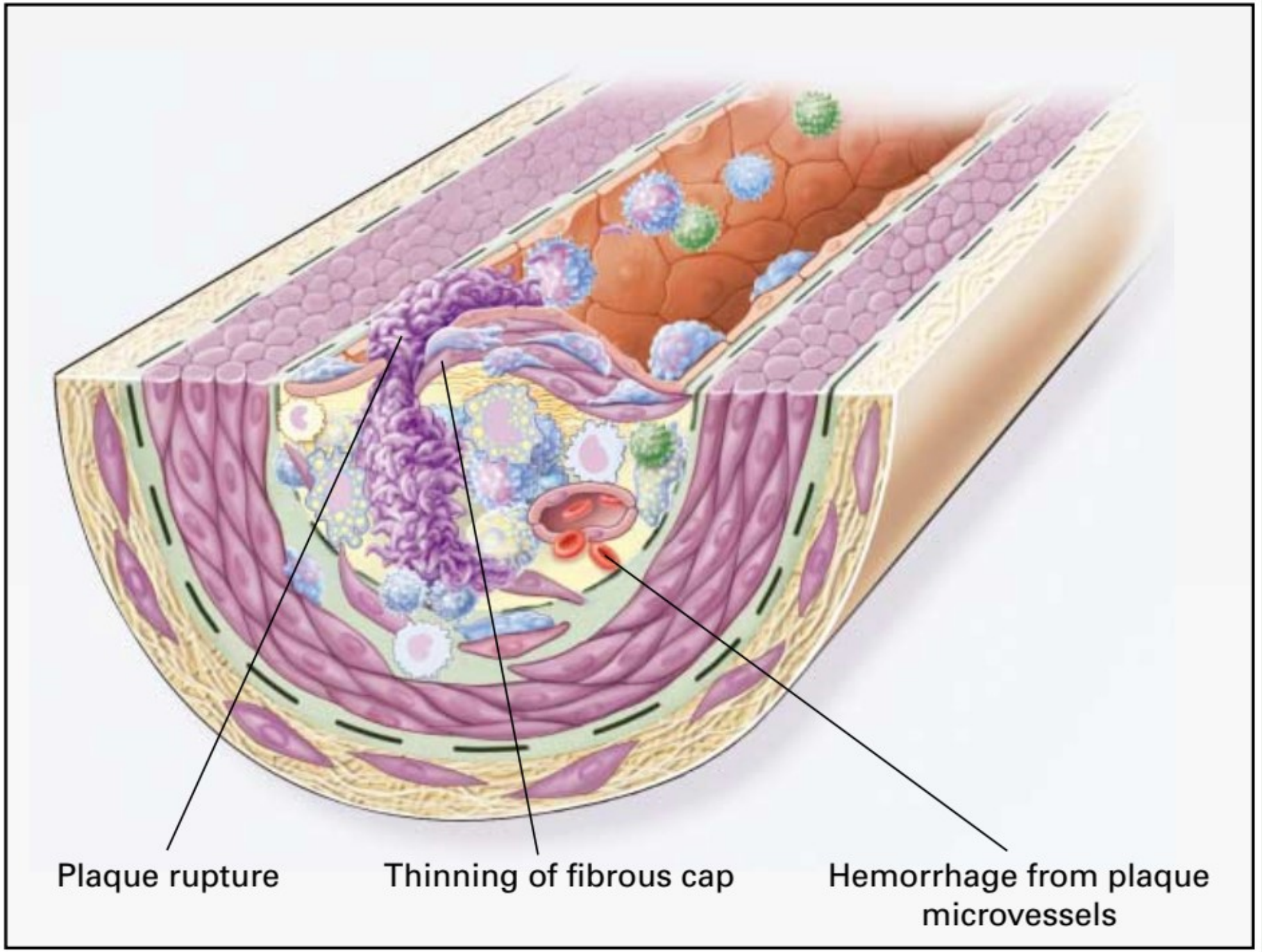


N Engl J Med 1999; 340:115-126. DOI: 10.1056/NEJM199901143400207

Formation of an Advanced, Complicated Lesion of Atherosclerosis.

As fatty streaks progress to intermediate and advanced lesions, they tend to form a fibrous cap that walls off the lesion from the lumen. This represents a type of healing or fibrous response to the injury. The fibrous cap covers a mixture of leukocytes, lipid, and debris, which may form a necrotic core. These lesions expand at their shoulders by means of continued leukocyte adhesion and entry caused by the same factors as those listed in Figures 1 and 2. The principal factors associated with macrophage accumulation include macrophage colony-stimulating factor, monocyte chemotactic protein 1, and oxidized low-density lipoprotein. The necrotic core represents the results of apoptosis and necrosis, increased proteolytic activity, and lipid accumulation. The fibrous cap forms as a result of increased activity of platelet-derived growth factor, transforming growth factor β, interleukin-1, tumor necrosis factor α, and osteopontin and of decreased connective-tissue degradation.

N Engl J Med 1999; 340:115-126. DOI: 10.1056/NEJM199901143400207

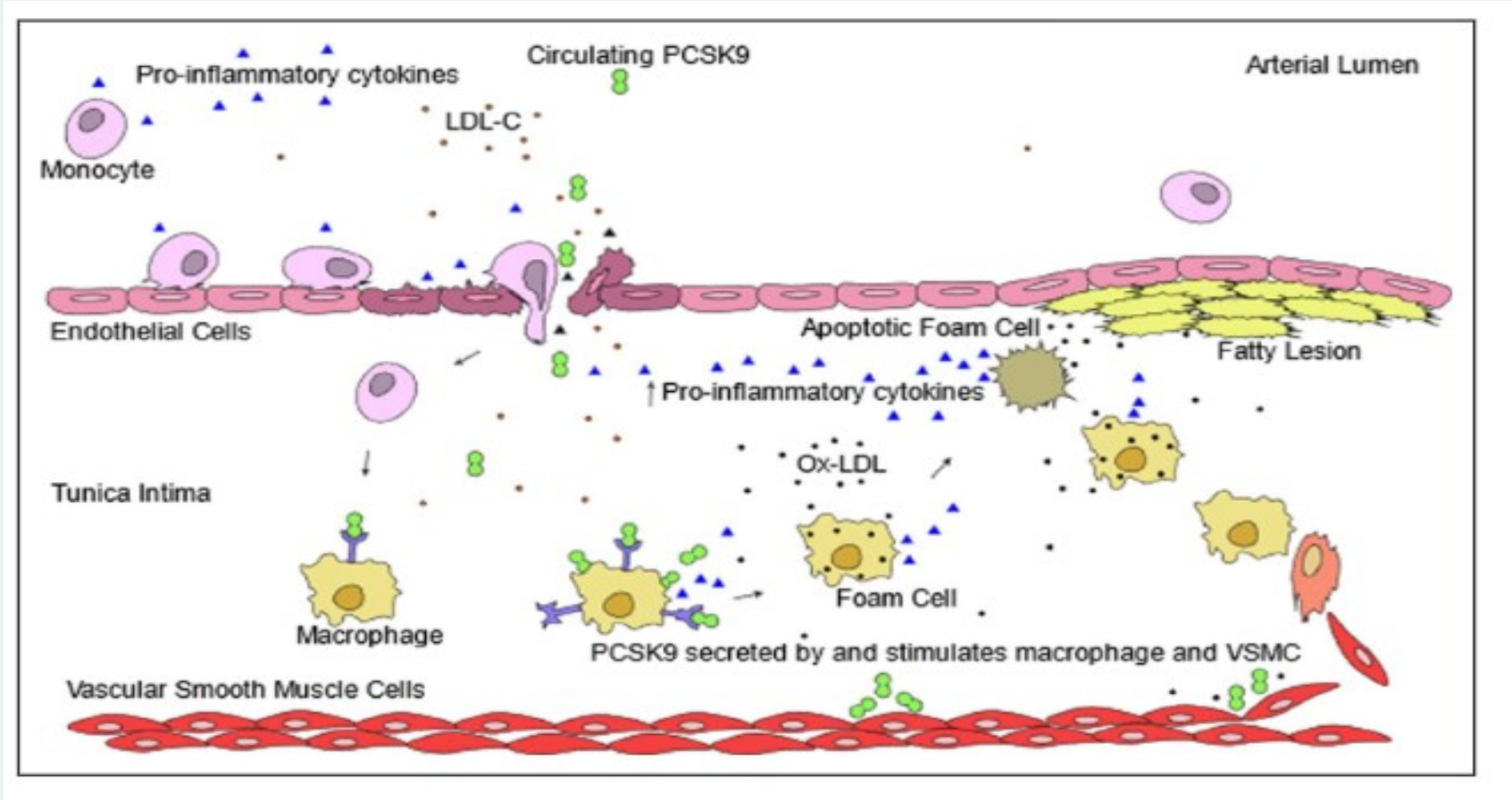


N Engl J Med 1999; 340:115-126. DOI: 10.1056/NEJM199901143400207

Unstable Fibrous Plaques in Atherosclerosis.

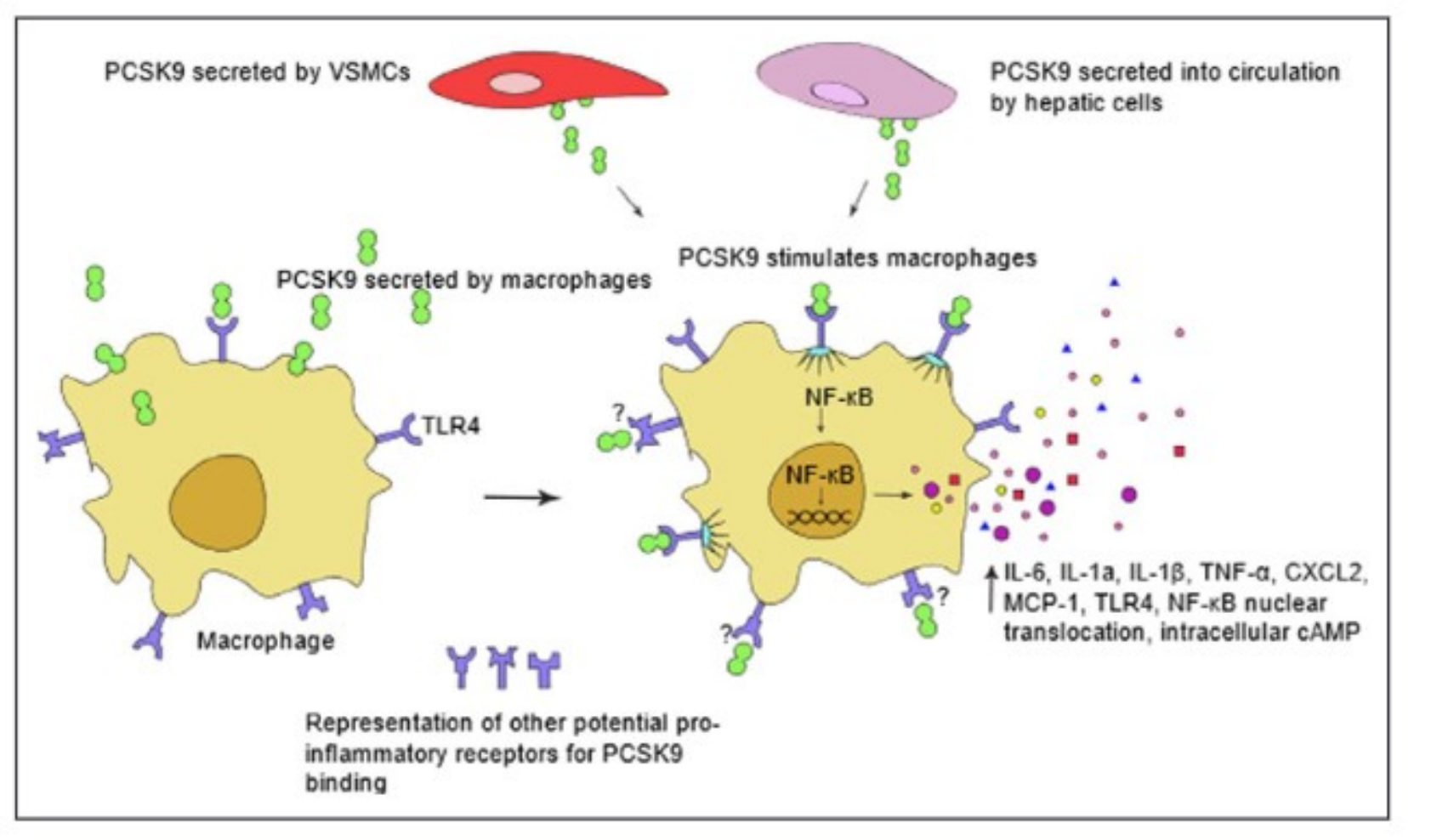
Rupture of the fibrous cap or ulceration of the fibrous plaque can rapidly lead to thrombosis and usually occurs at sites of thinning of the fibrous cap that covers the advanced lesion. Thinning of the fibrous cap is apparently due to the continuing influx and activation of macrophages, which release metalloproteinases and other proteolytic enzymes at these sites. These enzymes cause degradation of the matrix, which can lead to hemorrhage from the vasa vasorum or from the lumen of the artery and can result in thrombus formation and occlusion of the artery.

N Engl J Med 1999; 340:115-126. DOI: 10.1056/NEJM199901143400207



Schematic representation of PCSK9s involvement in atherosclerotic plaque development. Endothelial cell damage allows infiltration of circulating LDL-C and to the intimal space. Oxidation of LDL-C in the intimal space stimulates proinflammatory activation and phagocytosis of macrophages. Engulfment of excess Ox-LDL by macrophages generates foam cells, which contributes to fatty deposits in the arterial wall, proinflammatory cytokine release, and apoptosis. Circulating PCSK9 secreted from hepatic cells also enters the intimal space, where it stimulates macrophage cells to produce proinflammatory cytokines and VSMC migration and transformation to macrophages, which in turn become apoptotic foam cells. Atherosclerotic macrophages and VSMCs also secrete PCSK9 within the plaque, contributing to increased inflammation and fatty deposition. Collectively, the proinflammatory stimulation within the plaque drives recruitment and infiltration of more circulating monocytes, feeding the cycle. LDL-C indicates low-density lipoprotein cholesterol; Ox-LDL, oxidized low-density lipoprotein; PCSK9, protein proprotein convertase subtilisin/kexin 9; and VSMC, vascular smooth muscle cells.

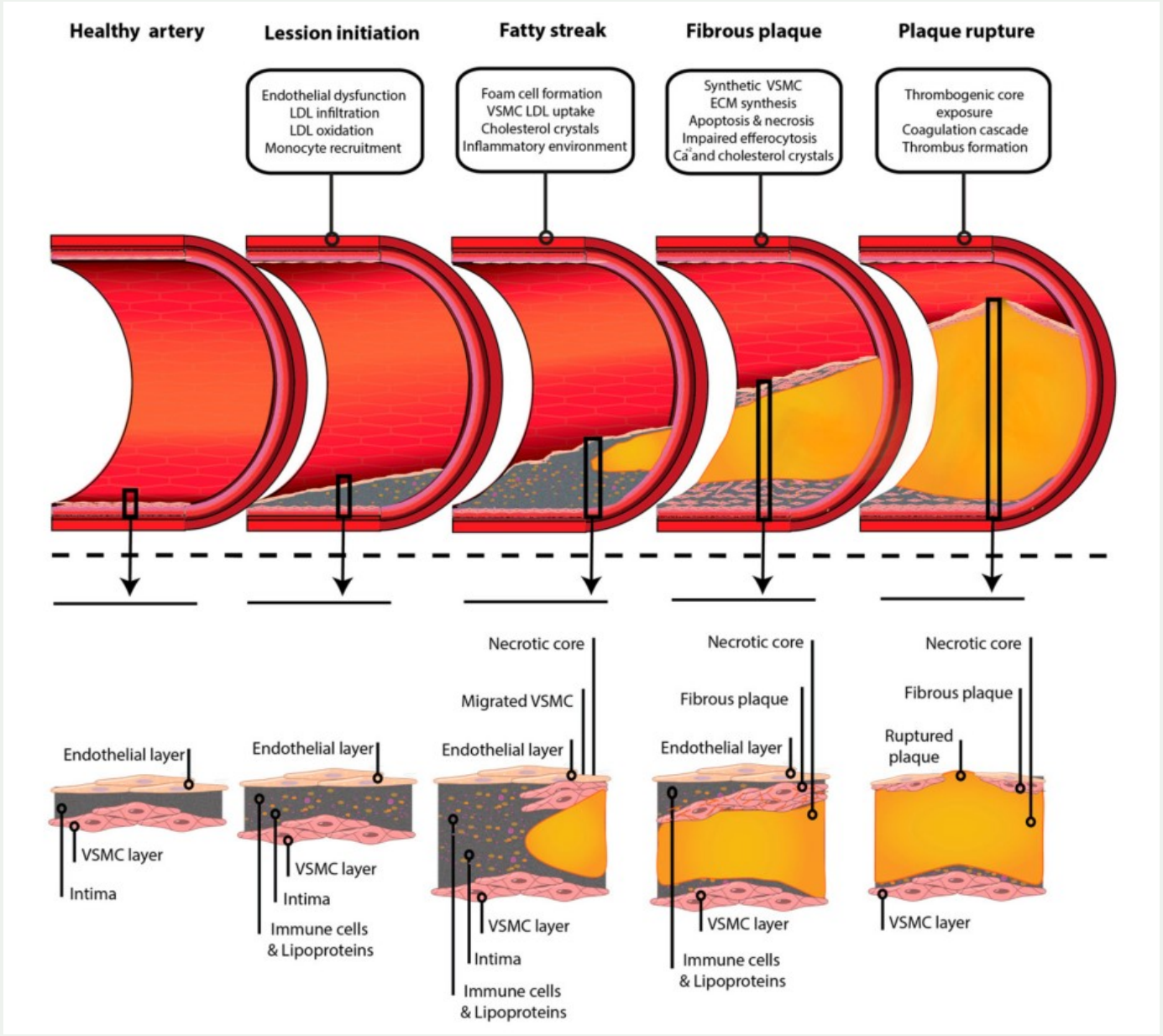
J Am Heart Assoc. 2022;11:e023328. doi: 10.1161/JAHA.121.023328.



Activation of macrophages within atherosclerotic plaque by interaction with PCSK9. PCSK9 is now known to stimulate proinflammatory effects within an atherosclerotic plaque. PCSK9 is expressed and secreted by hepatic cells, macrophages, and vascular smooth muscle cells. PCSK9 activates macrophage proinflammatory effects by cell surface receptor binding of TLR4 and potentially several other inflammatory stimulating receptors. This graphic represents the binding of PCSK9 to and activation of TLR4, triggering NF-κB activation and nuclear translocation. Nuclear translocation of the transcription factor NF-κB stimulates the expression and secretion of a variety of proinflammatory cytokines, contributing to increased monocyte infiltration and plaque deposition. Other receptors on the macrophage represent additional proinflammatory-stimulating binding partners for PCSK9 within cells in the atherosclerotic plaque. CXCL2 indicates CXC motif chemokine ligand 2; IL-1a, interleukin-1a; IL-1β, interleukin- 1β; IL-6, interleukin-6; MCP-1, monocyte chemoattractant protein-1; NF-κB, nuclear factor- kappa B; PCSK9, protein proprotein convertase subtilisin/kexin 9; TLR4, toll-like receptor 4; TNF-α, tumor necrosis factor-α; and VSMCs, vascular smooth muscle cells

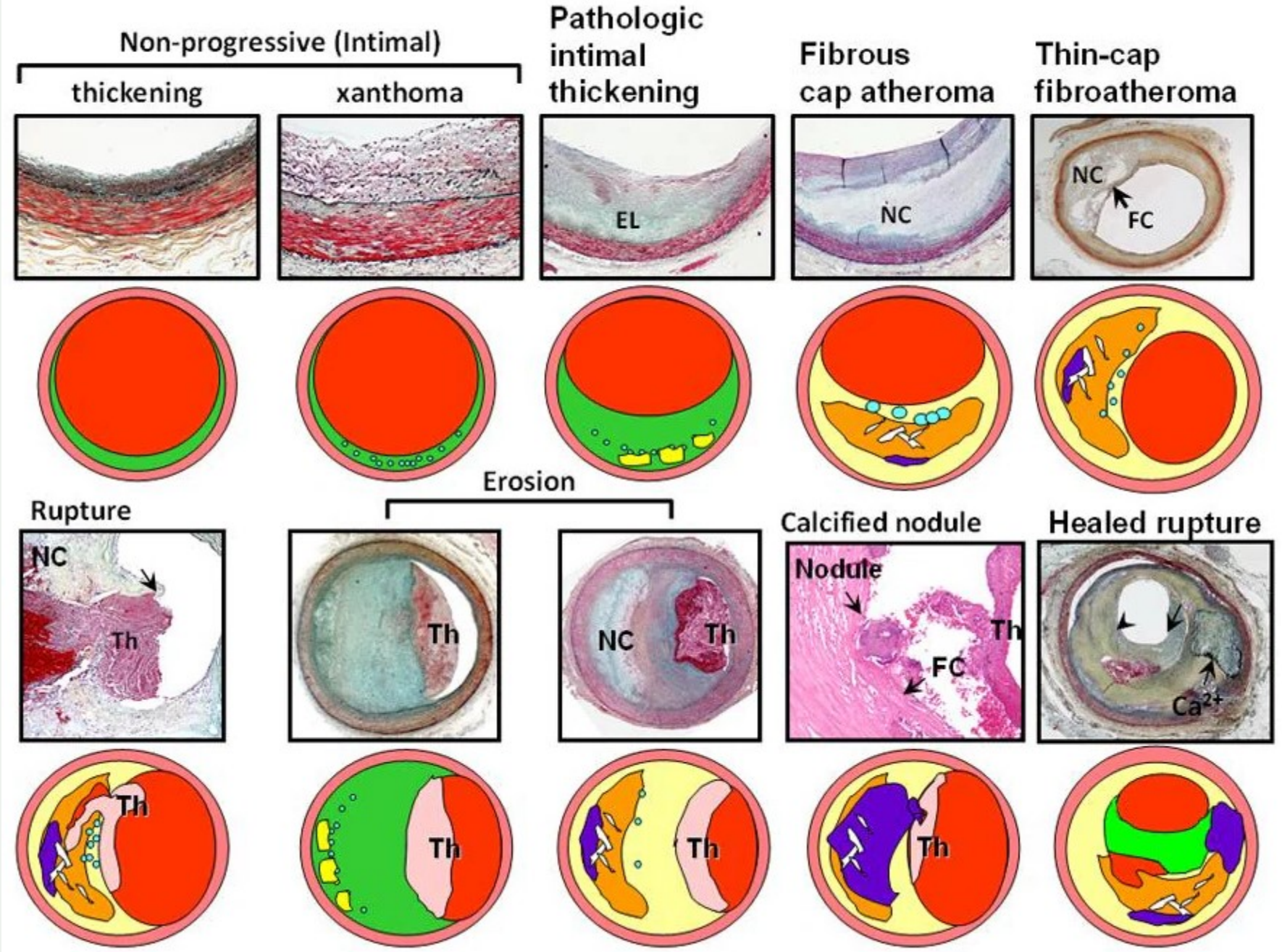
J Am Heart Assoc. 2022;11:e023328. doi: 10.1161/JAHA.121.023328.

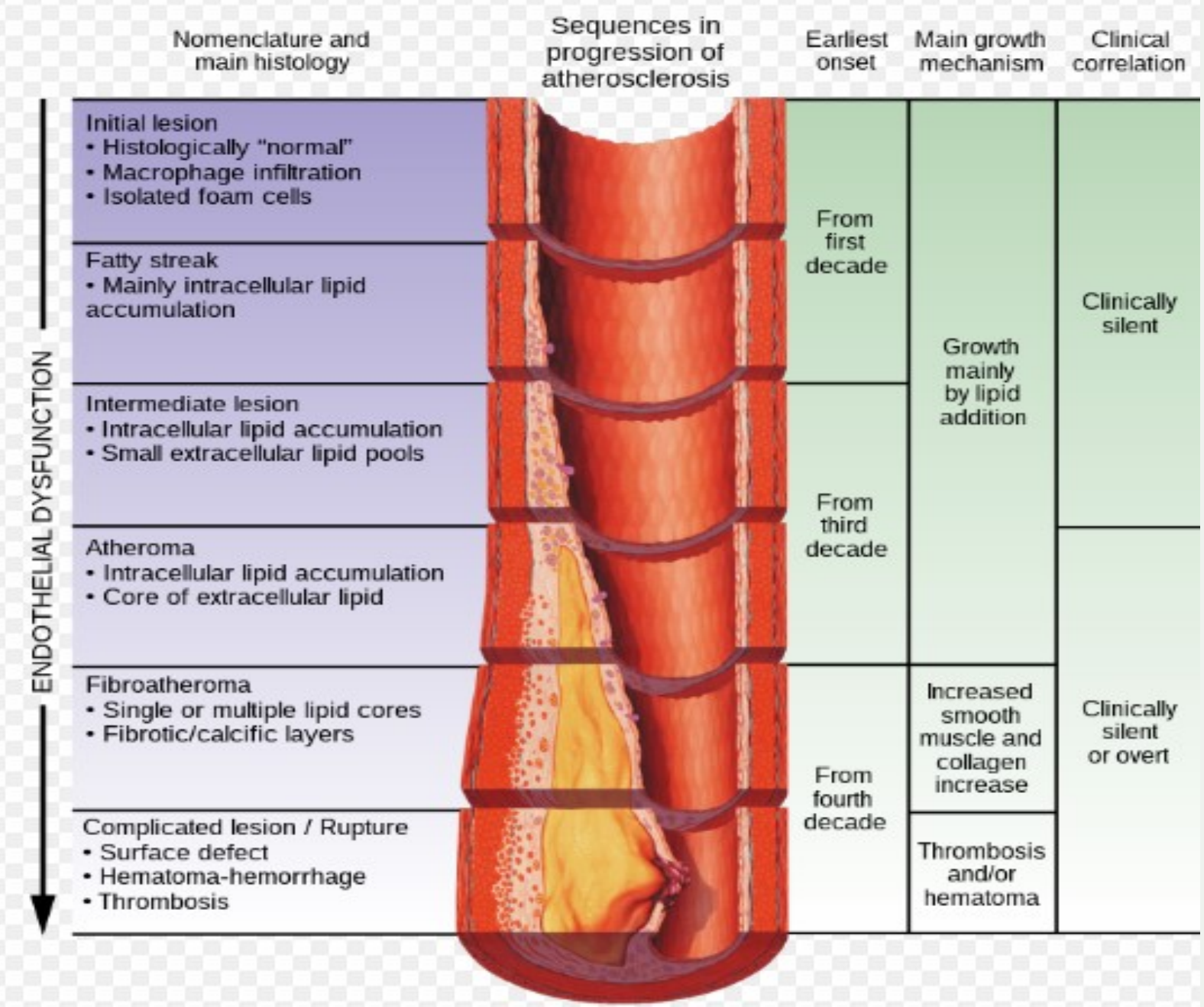
Schematic representation of atheroma plaque formation from a healthy artery to plaque rupture



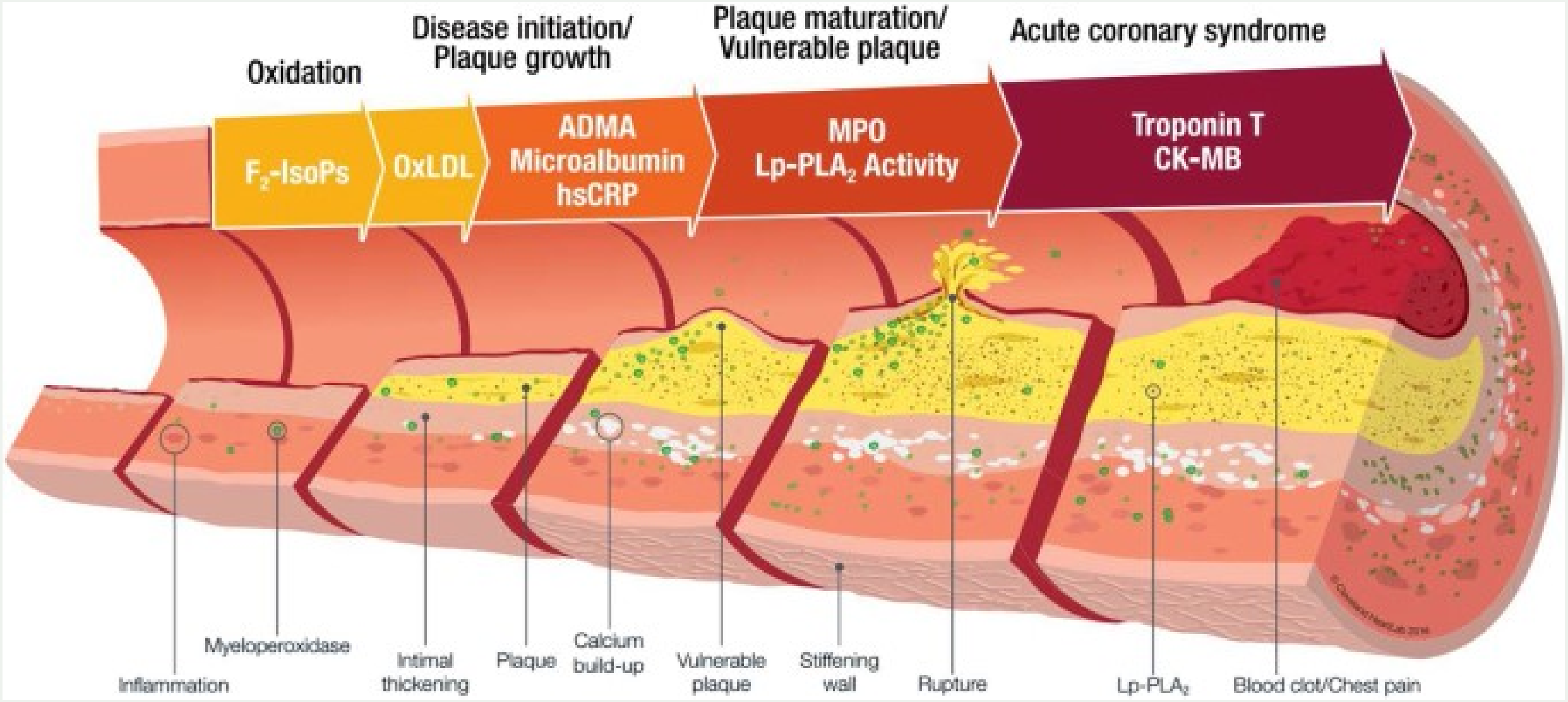
Int. J. Mol. Sci. 2022, 23, 3346. doi.org/10.3390/ ijms23063346

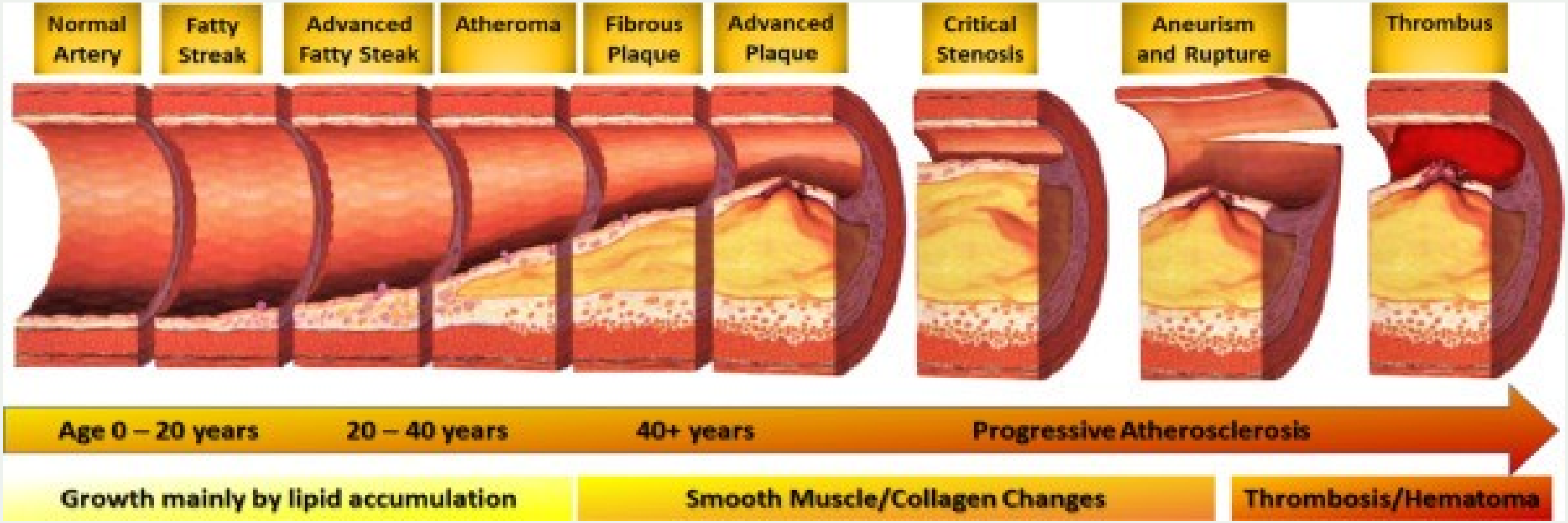
Progression of Human Coronary Atherosclerosis

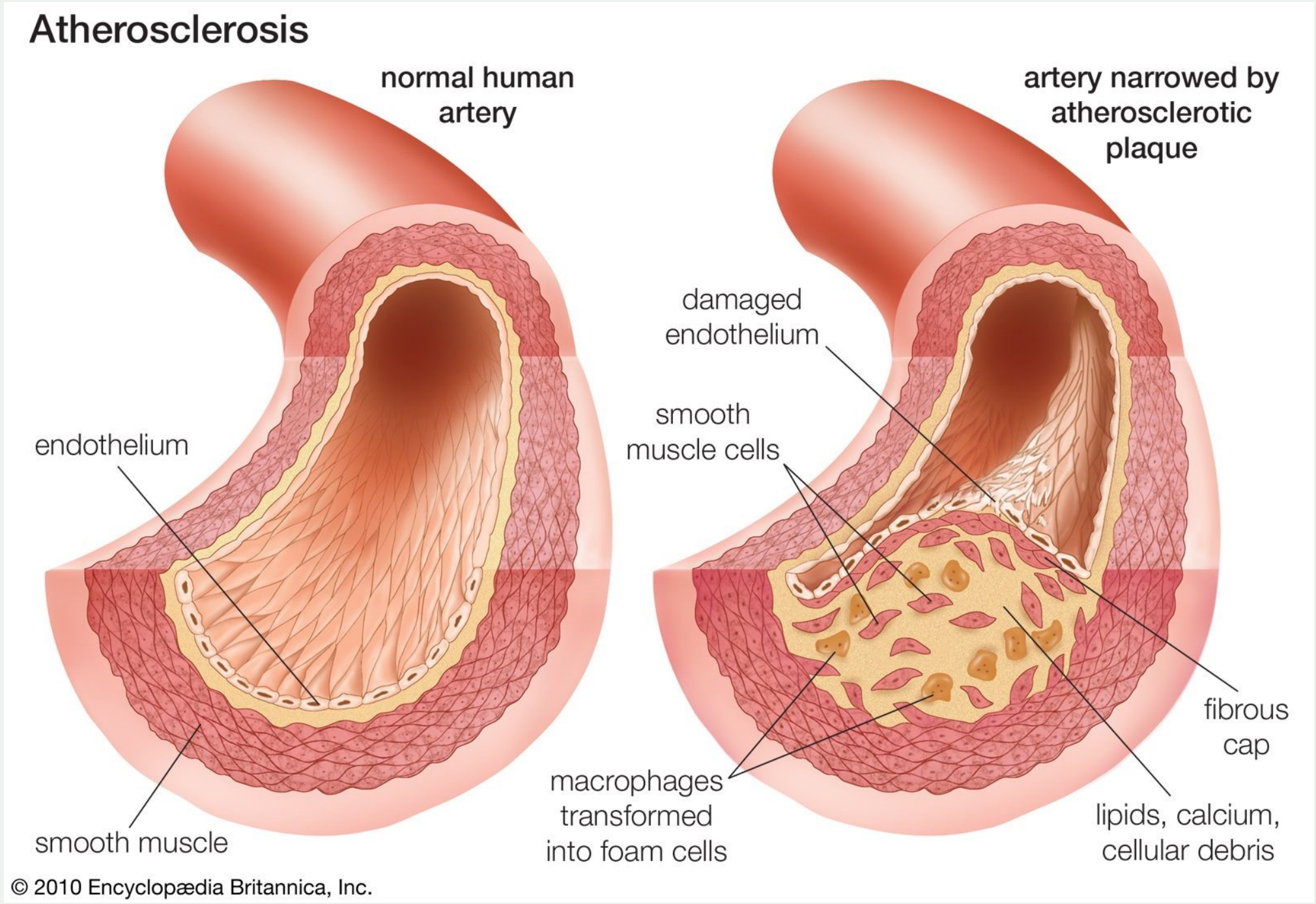


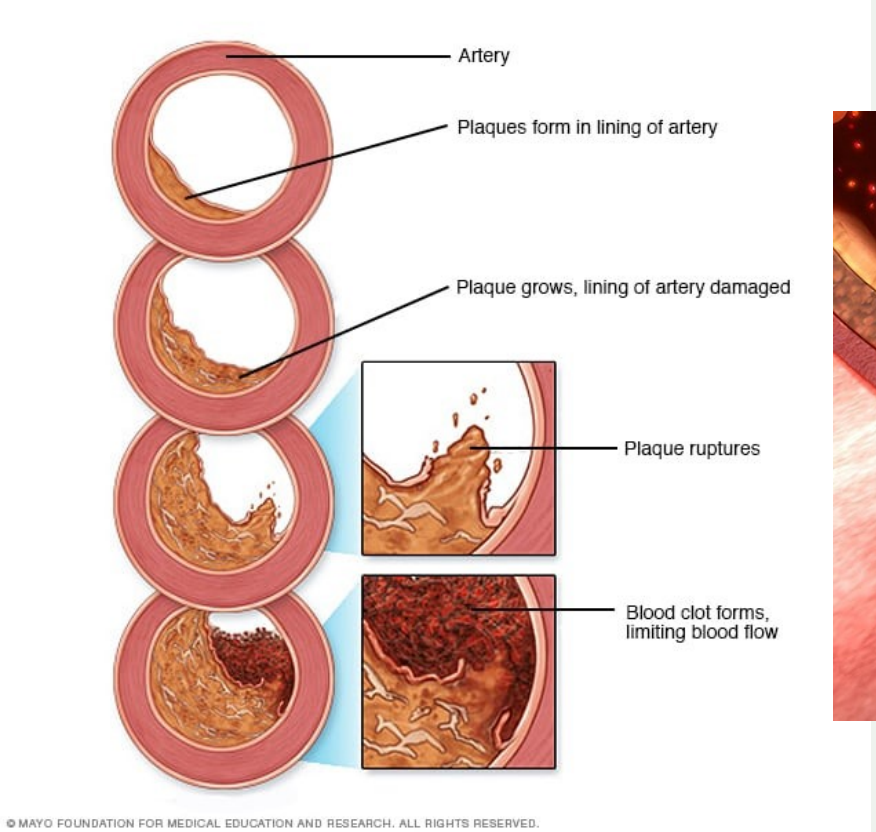


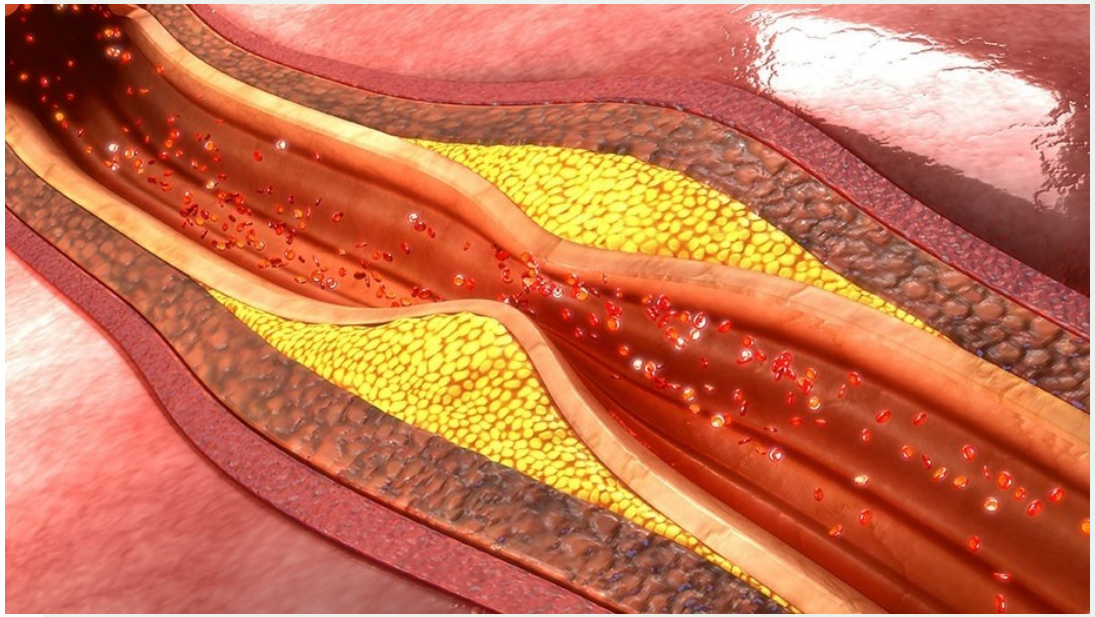
YitzhakNat - Own work and based on. Made with MS Visio.

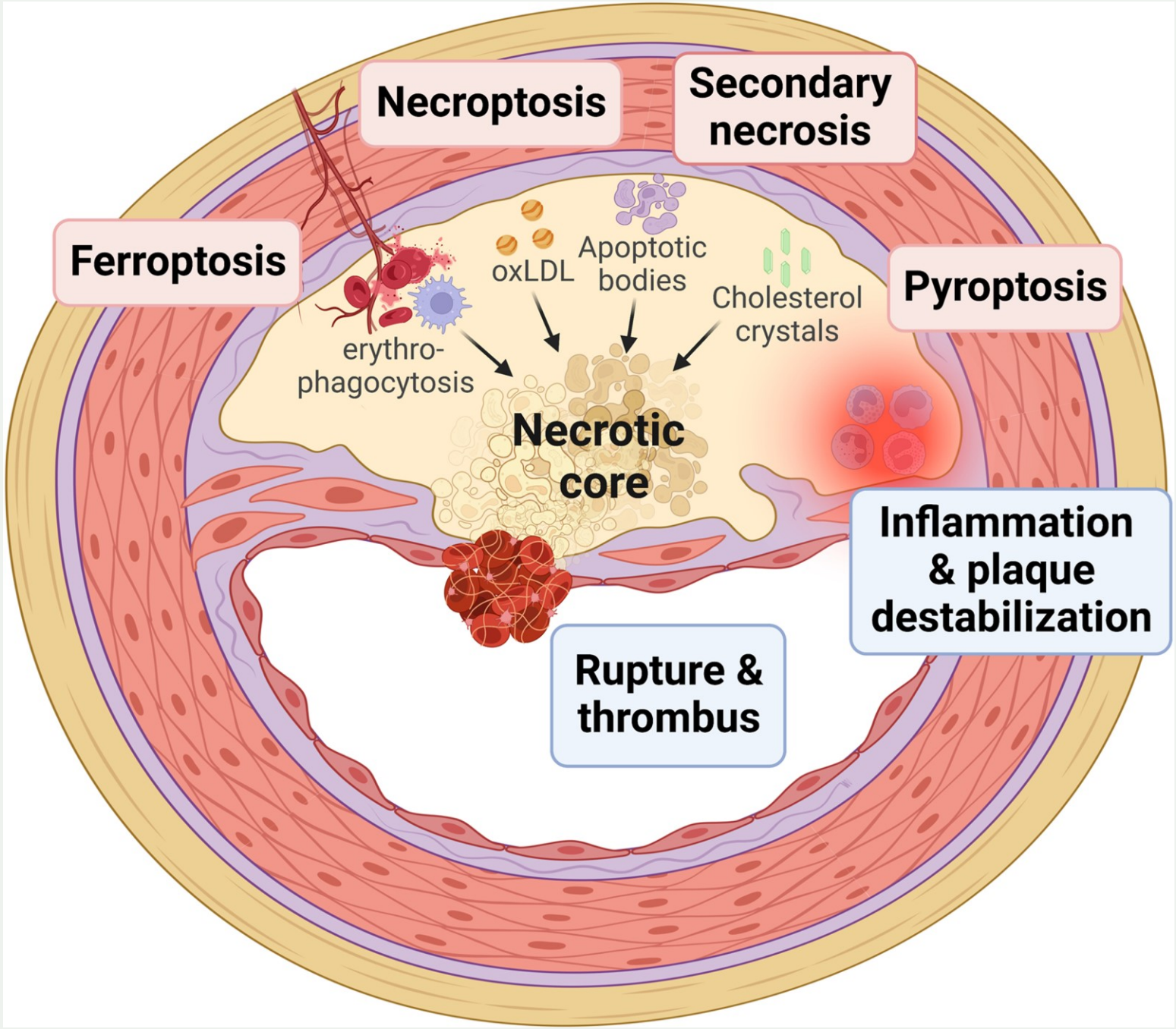

Oxidation
Disease initiation/
Plaque growth
Plaque maturation/
Vulnerable plaque
Acute coronary syndrome
F2-IsoPs
OxLDL
ADMA
Microalbumin
hsCRP
MPO
Lp-PLA2 Activity
Troponin T
CK-MB
Inflammation
Myeloperoxidase
Intimal
thickening
Plaque
Calcium
build-up
Vulnerable
plaque
Stiffening
wall
Rupture
Lp-PLA2
Blood clot/Chest pain

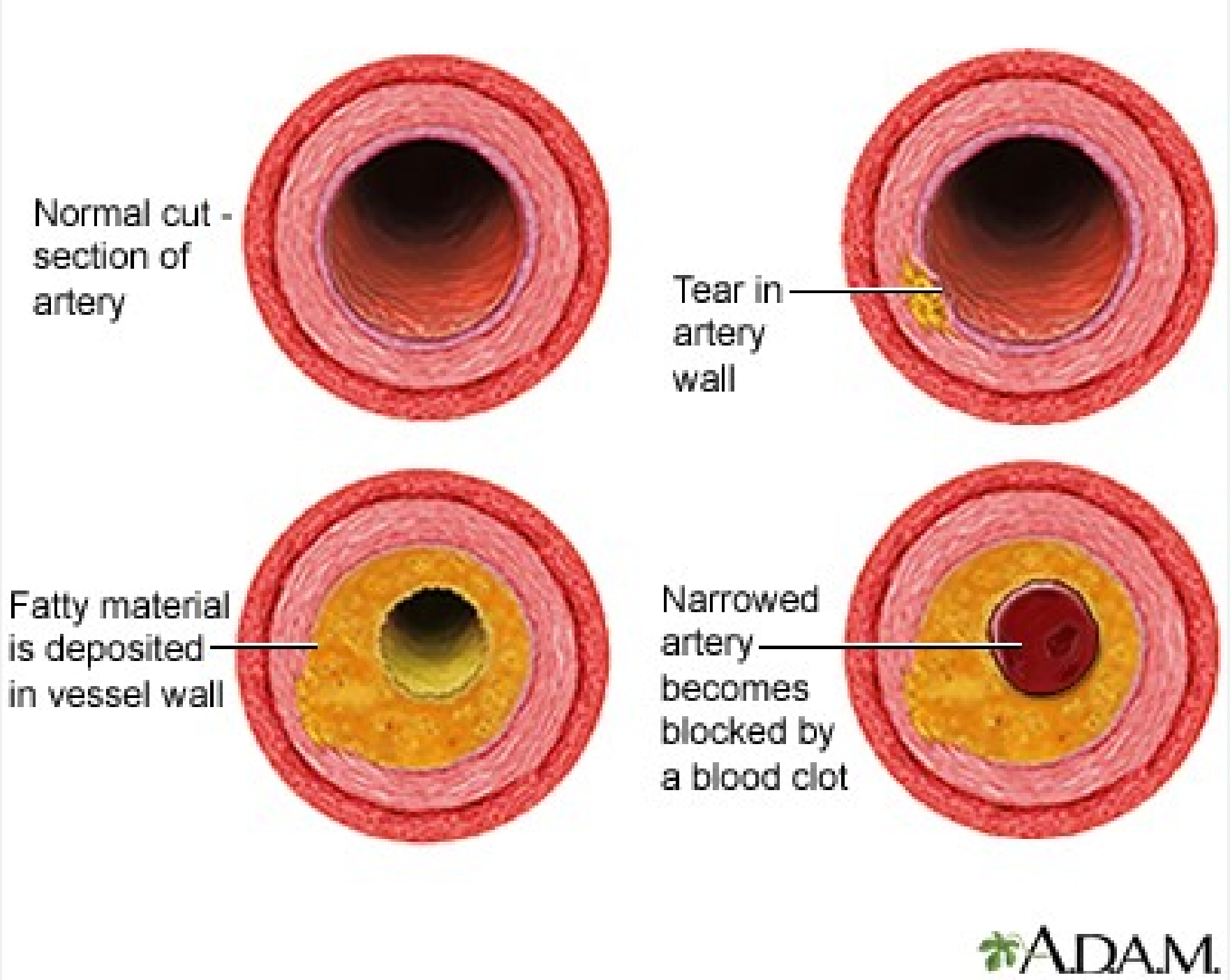

Normal Artery
Fatty Streak
Advanced Fatty Steak
Atheroma
Fibrous Plaque
Advanced Plaque
Critical Stenosis
Aneurism and Rupture
Thrombus
Age 0 – 20 years
20 – 40 years
40+ years
Progressive Atherosclerosis
Growth mainly by lipid accumulation
Smooth Muscle/Collagen Changes
Thrombosis/Hematoma


Atherosclerosis
normal human artery
artery narrowed by atherosclerotic plaque
endothelium
smooth muscle
damaged endothelium
smooth muscle cells
fibrous cap
macrophages transformed into foam cells
lipids, calcium, cellular debris
© 2010 Encyclopædia Britannica, Inc.



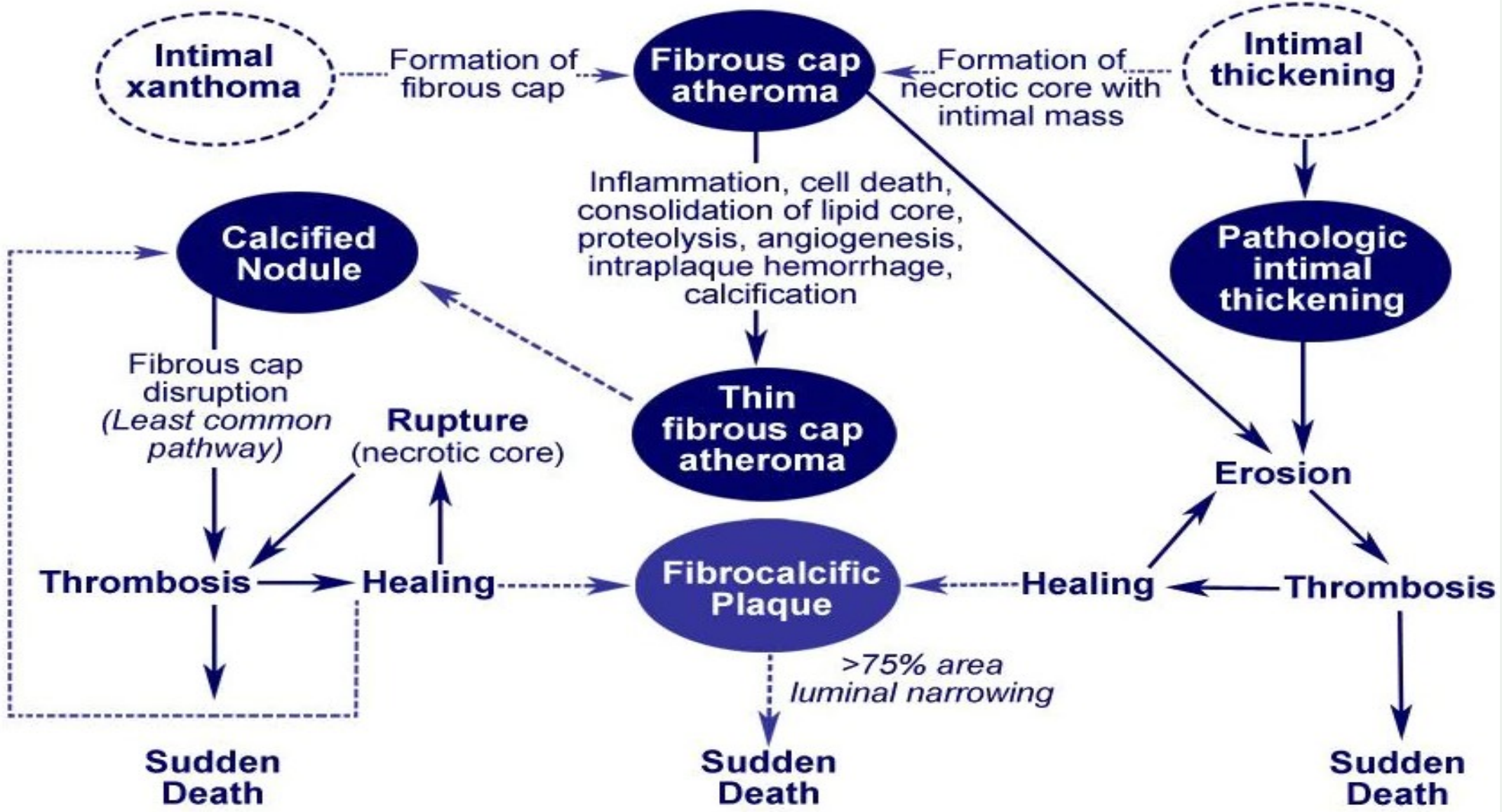



Necroptosis
Secondary necrosis
Ferroptosis
Pyroptosis
oxLDL
Apoptotic bodies
Cholesterol crystals
erythro-phagocytosis
Necrotic core
Inflammation & plaque destabilization
Rupture & thrombus


Normal cut - section of artery
Tear in artery wall
Fatty material is deposited in vessel wall
Narrowed artery becomes blocked by a blood clot
A.D.A.M.

Conventional AHA Classification	Modified AHA Classification for MRI
Type I: initial lesion with foam cells Type II: fatty streak with multiple foam cell layers	Type I–II: near-normal wall thickness, no calcification
Type III: preatheroma with extracellular lipid pools	Type III: diffuse intimal thickening or small eccentric plaque with no calcification
Type IV: atheroma with a confluent extracellular lipid core Type V: fibroatheroma	Type IV–V: plaque with a lipid or necrotic core surrounded by fibrous tissue with possible calcification
Type VI: complex plaque with possible surface defect, hemorrhage, or thrombus	Type VI: complex plaque with possible surface defect, hemorrhage, or thrombus
Type VII: calcified plaque	Type VII: calcified plaque
Type VIII: fibrotic plaque without lipid core	Type VIII: fibrotic plaque without lipid core and with possible small

Simplified scheme for classifying atherosclerotic lesions modified from the current AHA recommendations

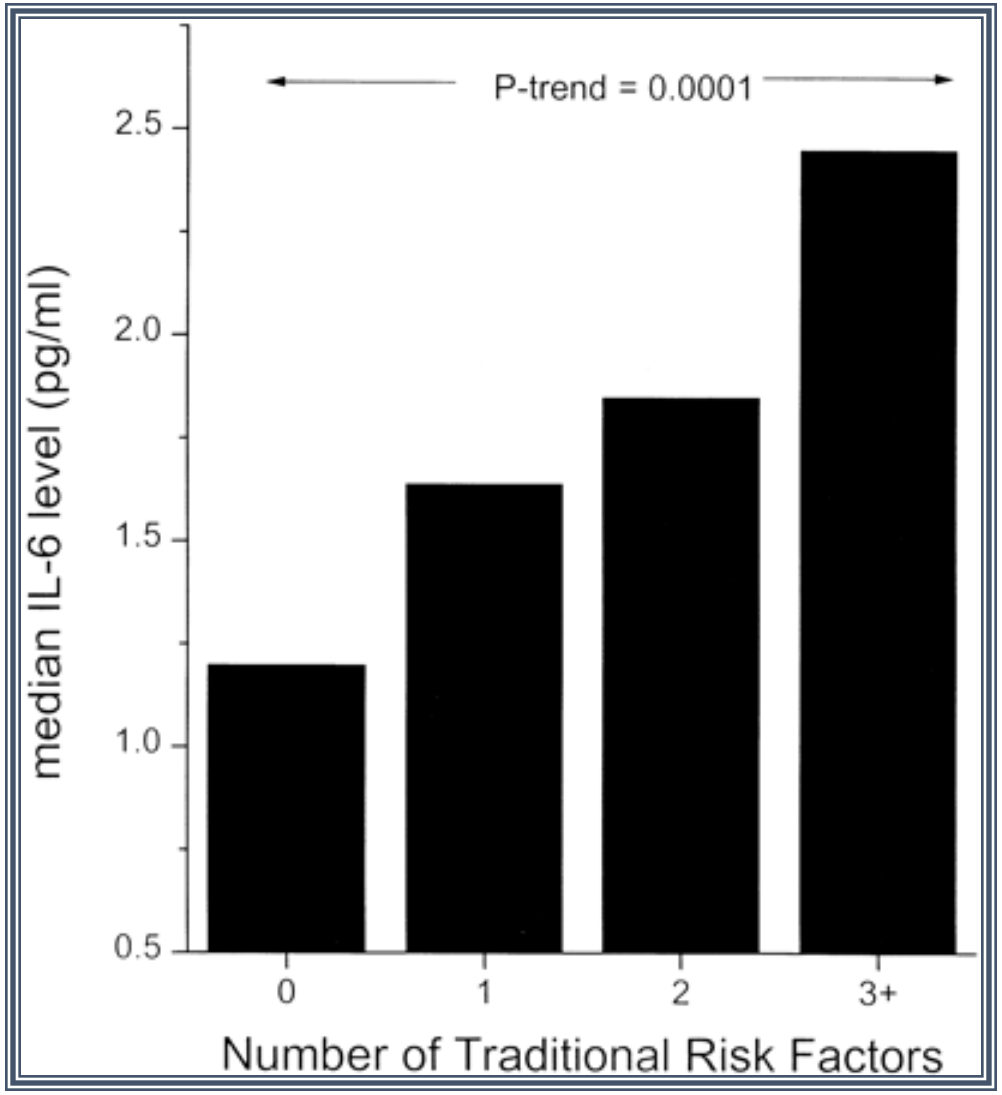


- A major event in atherosclerotic plaque progression is thrombosis, which may occur in any arterial bed (coronary, aorta, carotid, etc.)
- Three different morphologies (rupture, erosion and calcified nodule) may give rise to acute coronary thrombosis.
- The development of plaque and its rupture are hallmarks of atherosclerotic vascular disease.

Plaque rupture is defined by fibrous cap disruption or fracture, whereby the overlying thrombus is in continuity with the underlying ***necrotic core***.
Plaque erosion is identified when serial sectioning through a thrombus ***fails to show communication with a necrotic core*** or deep intima; the endothelium is absent, and the thrombus is superimposed on a plaque substrate primarily composed of smooth muscle cells and proteoglycans.
Calcified nodules are characterized by eruptive dense calcified bodies protruding into the luminal space and represent the least frequent morphology associated with luminal thrombosis.

- Atherosclerosis occurs in elastic and muscular arteries and may occur iatrogenically in vein grafts interposed in the arterial circulation.
- The aorta is affected earliest, followed by the carotid arteries, coronary arteries and iliofemoral arteries.
- Initially, lesions are most common at branch points, at sites of low shear, where a predilection to plaque formation has been observed.
- **Coronary lesions**, including thrombi occurring at atherosclerotic sites, are most prevalent in the proximal coronary arteries: the proximal left anterior descending coronary artery, followed by the right and left circumflex coronary arteries.

Risk factors and cytokines



Median baseline IL-6 levels according to number of traditional risk factors present

- ✓Hypertension
- ✓hyperlipidemia
- ✓smoking
- ✓Diabetes
- ✓age >60 years
- ✓family history

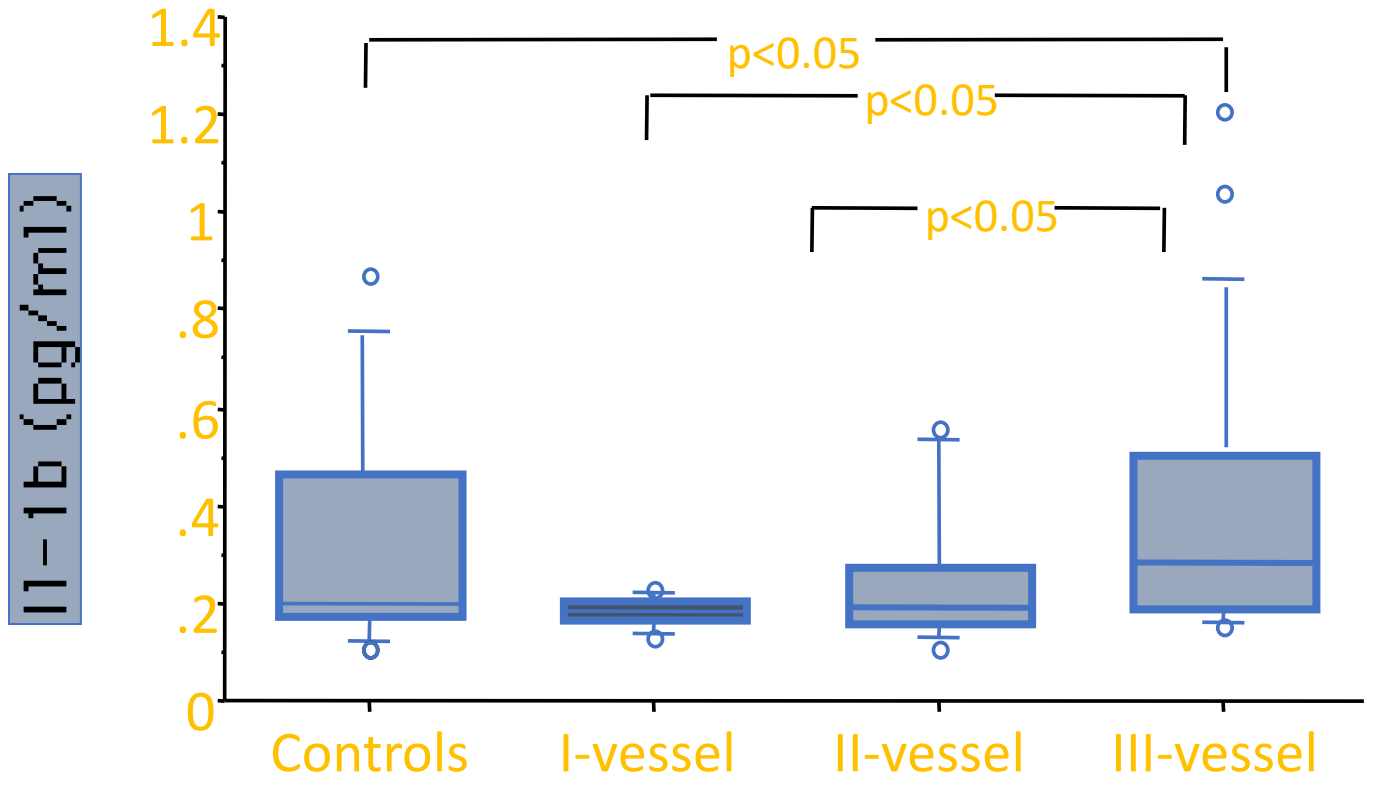
Ridker et al Circulation 2000

Proinflammatory Cytokines and CRP plasma levels in Patients with CSA vs. normal controls

	Patients (n=60)	Controls (n=24)	p
MCSF	991(459-1476)	372 (265-770)	<0.01
IL6	3.9 (3.2-4.6)	1.7 (1.3-2.5)	<0.01
CRP	1.5 (0.5-4.05)	0.23 (0.17-1.4)	<0.01

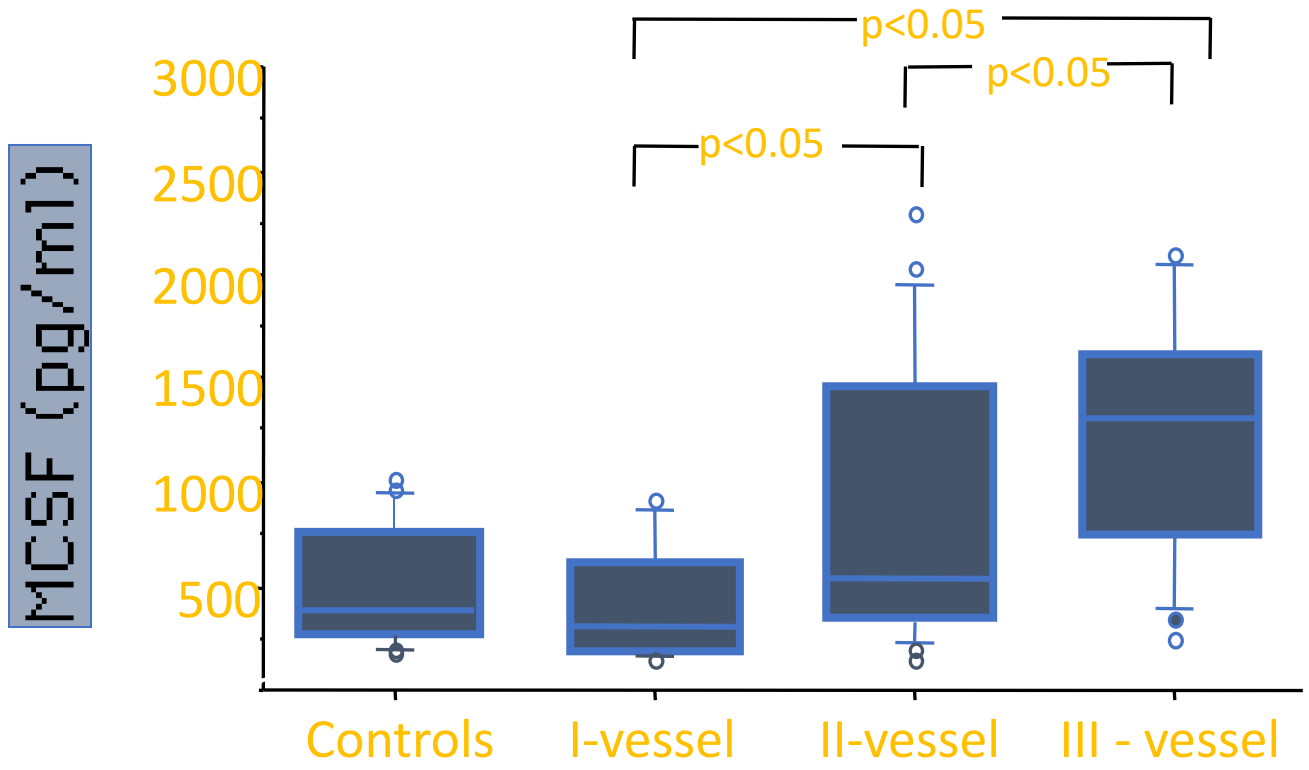
Ikonomidis et al Circulation 1999

Relation of cytokines to extent of CAD



Ikonomidis et al Circulation 1999

Relation of cytokines with the extent of CAD



Ikonomidis et al Circulation 1999

TABLE 1. CHARACTERISTICS OF ATHEROSCLEROSIS AND OTHER CHRONIC INFLAMMATORY DISEASES.*

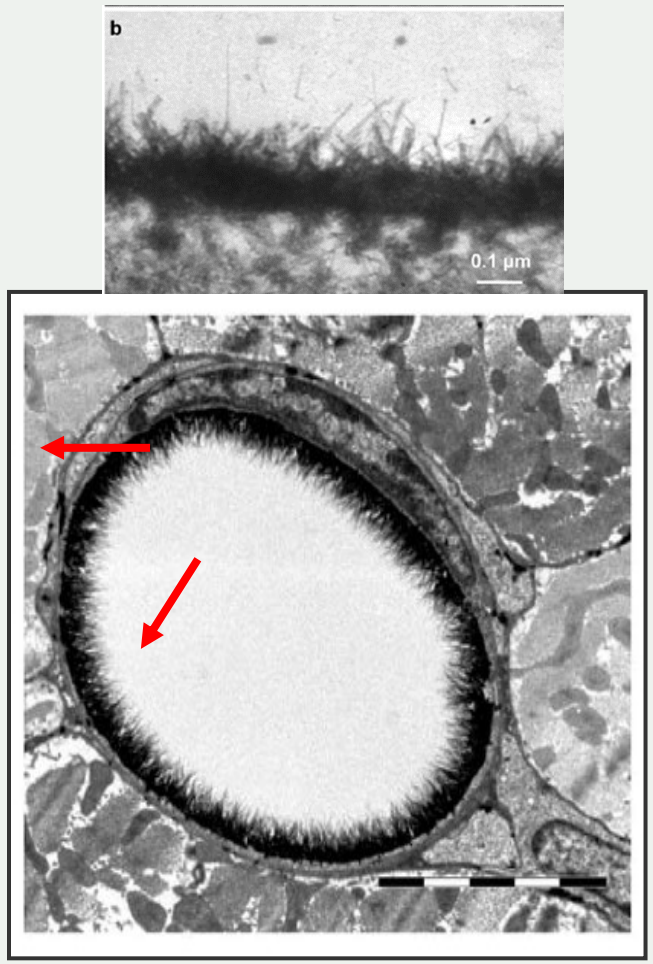
DISEASE	MONOCYTES AND MACROPHAGES	LYMPHOCYTES	GRANULOCYTES	CONNECTIVE-TISSUE CELLS	EXTRACELLULAR MATRIX	PATHOGENETIC MECHANISMS	STUDIES
Atherosclerosis	+	+	−	Smooth-muscle cells	Collagen types I, III, and IV, elastin, fibronectin, proteoglycan	Endothelial-cell injury and dysfunction; fibrous cap; new matrix formation and degradation; necrotic core	Ross,[9] Libby and Hansson,[109] Ross and Fuster[110]
Cirrhosis	+	+	−	Fibroblasts, Ito cells	Collagen types I and III	Parenchymal-cell injury; new matrix and scarring replacing necrotic parenchyma	Maher,[111] Anthony et al.[112]
Rheumatoid arthritis	+	+	+/−	Synovial fibroblasts	Collagen types I and III, fibronectin, proteoglycan	Synovial-cell injury; erosion of cartilage; new matrix scarring (pannus)	Sewell and Trentham,[113] Harris [114]
Glomerulosclerosis	+	+	−	Mesangial cells	Collagen types I and IV, fibronectin	Epithelial- and endothelial-cell injury and dysfunction; decrease in glomerular filtration; new matrix formation	Johnson,[115] Magil and Cohen[116]
Pulmonary fibrosis	+	+	+/−	Smooth-muscle cells, fibroblasts	Collagen types III and IV, fibronectin	Inflammatory exudate in alveoli and bronchi, organized by extensive matrix deposition and scarring	Kuhn et al.,[117] Lukacs and Ward,[118] Brody et al.[119]
Chronic pancreatitis	+	+	−	Fibroblasts	Collagen, fibronectin, proteoglycan	Epithelial (ductal) injury; periductal inflammation; interstitial fat necrosis; new matrix formation	lSarles et al.,[120] 2 DiMagno et al.[121]

N Engl J Med 1999; 340:115-126. DOI: 10.1056/NEJM199901143400207

Endothelial Glycocalyx

Damage to the endothelial glycocalyx is associated with

- **influx of lipoproteins,**
- **leakage of macromolecules**
- **adhesion of circulating cells to the endothelium.**
- **to an imbalance in enzymatic systems such as coagulation and antioxidant defence as well as an impaired NO release.**



Lekakis J, Ikonomidis I,Vlachopoulos C Eur J Cardiovasc Prev Rehabil. 2011 Dec;18(6):775-89

IMAGING: Assessment of endothelial function

Sublingual endothelial glycocalyx

Sideview Darkfield imaging (Microscan, Glycocheck)

Perfuse Boundary Region (PBR): a non-invasive accurate index of endothelial glycocalyx thickness in sublingual microvessels with a diameter 5-25μm

Peripheral arterial tonometry (EndoPAT)

Measurement of **reactive hyperemia index** using fingertip peripheral arterial tonometry (PAT) technology

IMAGING: Assessment of endothelial function, carotid arteries and coronary microcirculation

Endothelial-dependent flow-mediated dilation (FMD)

Carotid intima-media thickness (cIMT)

Coronary flow reserve (CFR)

Laboratory of Preventive Cardiology and Echocardiography Department

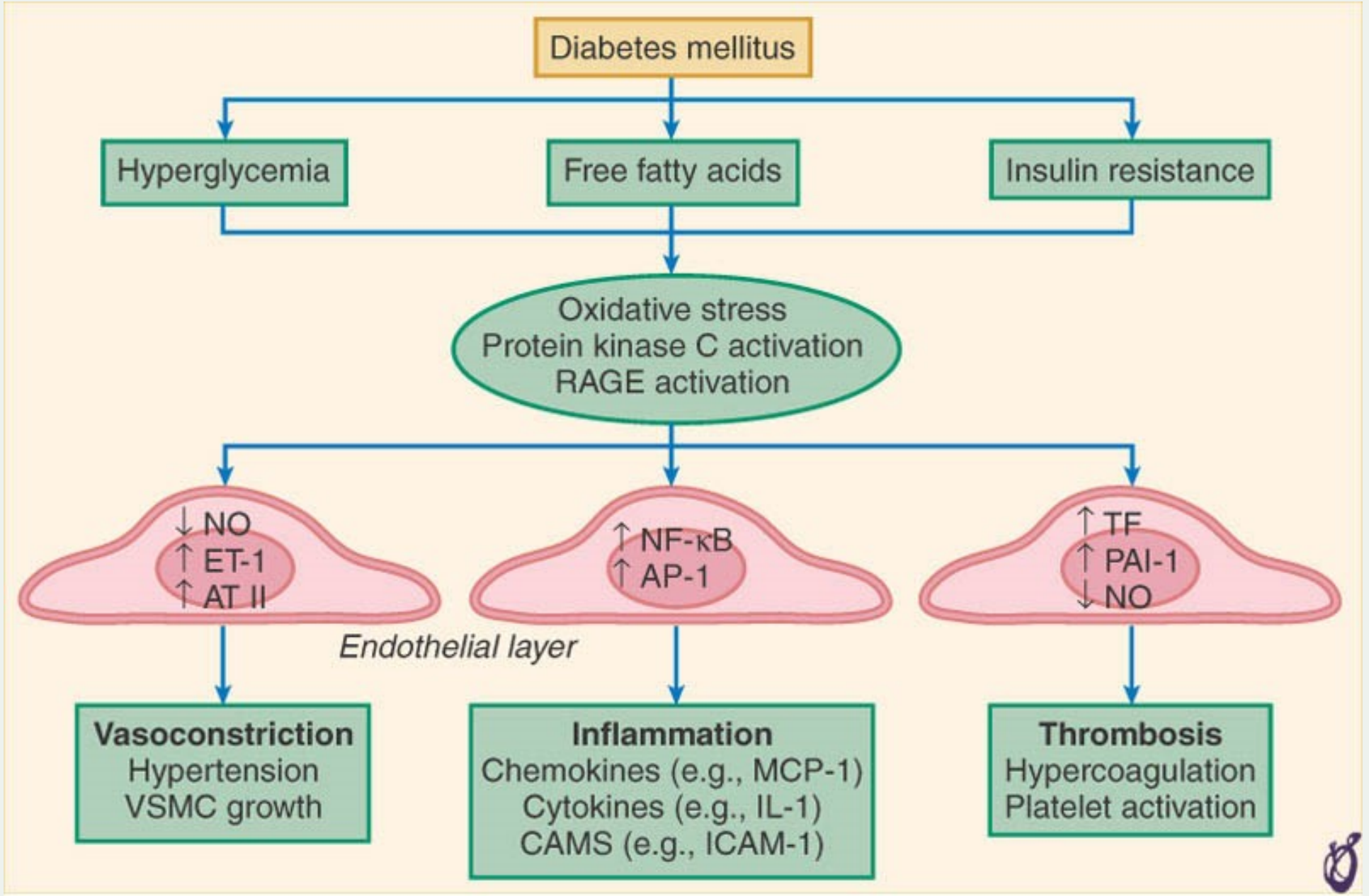
Equipment:

- **VIVID E95**, VIVID 7, VIVID S70, VIVID 3, VSCAN, PHILIPS I33
- **ECHOPAC 203**, QLAB, XCELERA, STORAGE 20 TB

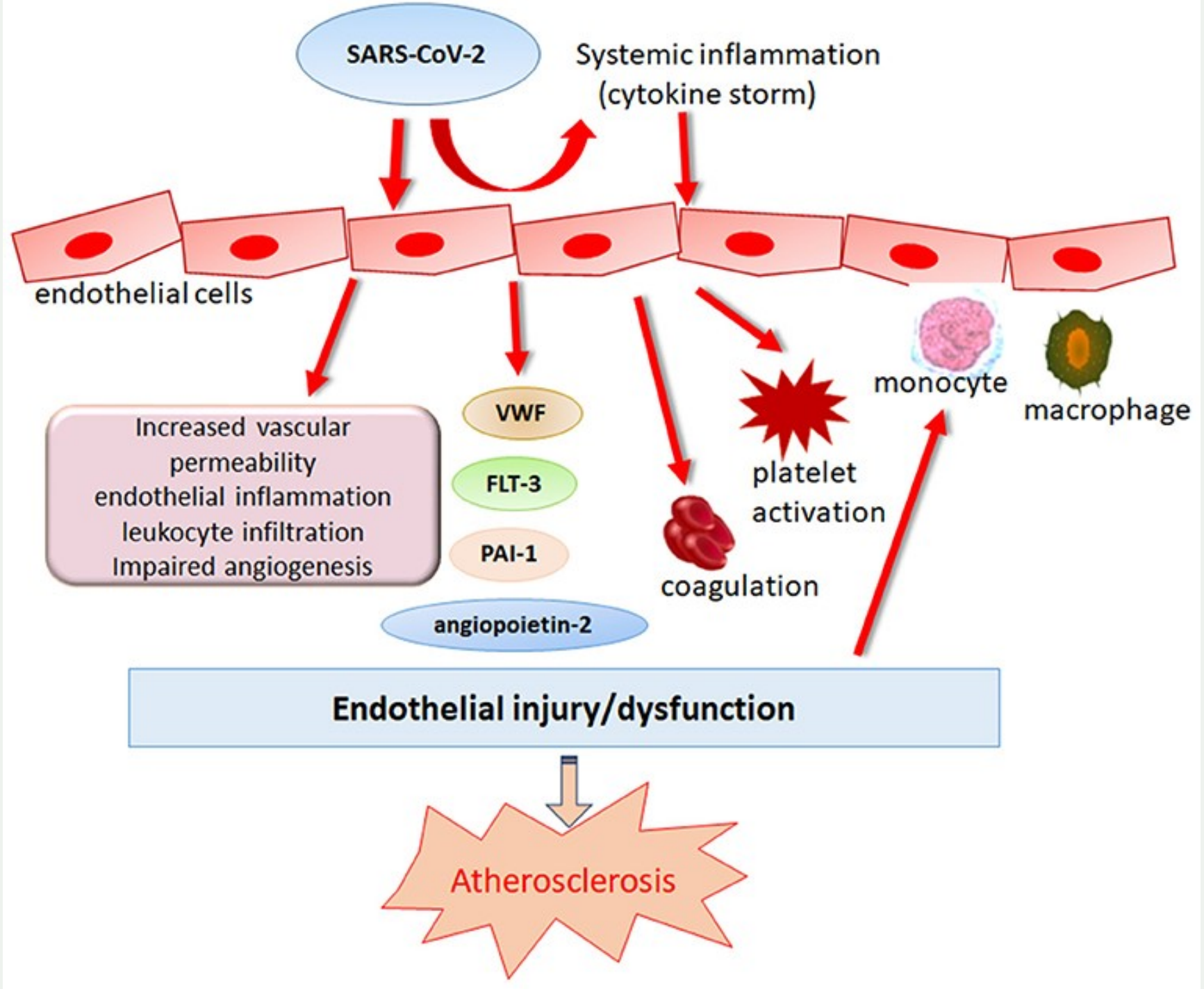
Differential microRNA expression levels in atherosclerotic arteries.

Location	Upregulated	Downregulated
Coronary arteries	miR-29, miR-100, miR-155, miR-199, miR-221, miR-363, miR-497, miR-508 and miR-181 [264–266].	miR-1273, miR-490, miR-24 and miR-1284 [264–266].
Aorta, femoral, and carotid arteries	miR-21, miR-34, miR-146 and miR-210 [267]. Only in carotid plaques: miR-15, miR-26, miR-30, miR-98, miR-125, miR-152, miR-181, miR-100, miR-127, miR-133, miR-145 and miR-422 [268,269].	Only in carotid plaques: miR-520, miR-105 [268,269].

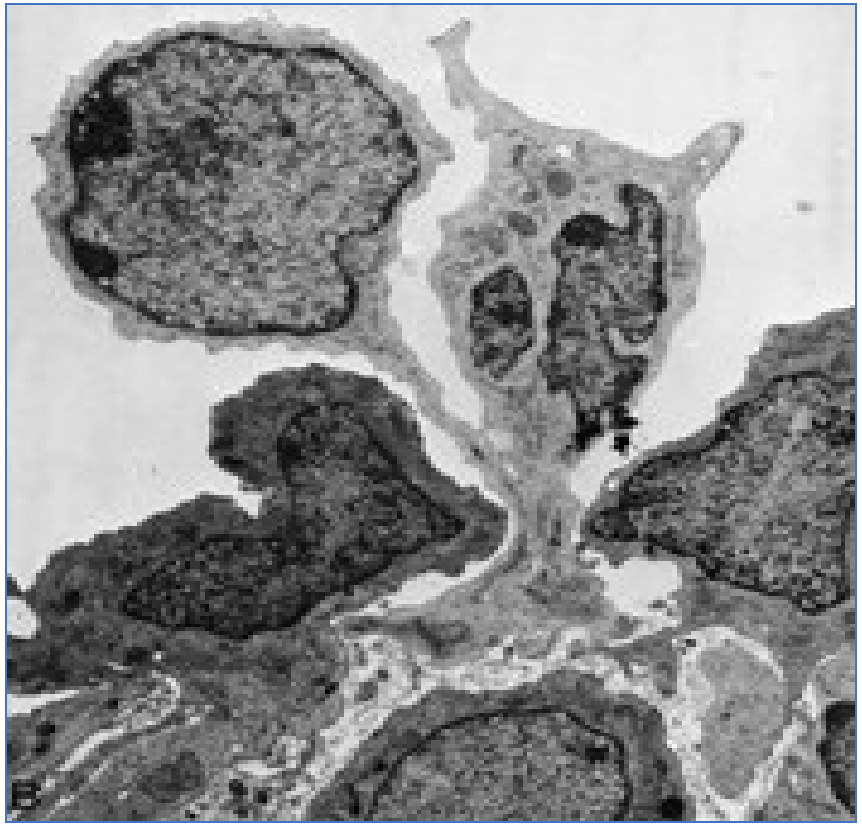
Int. J. Mol. Sci. 2022, 23, 3346. doi.org/10.3390/ ijms23063346

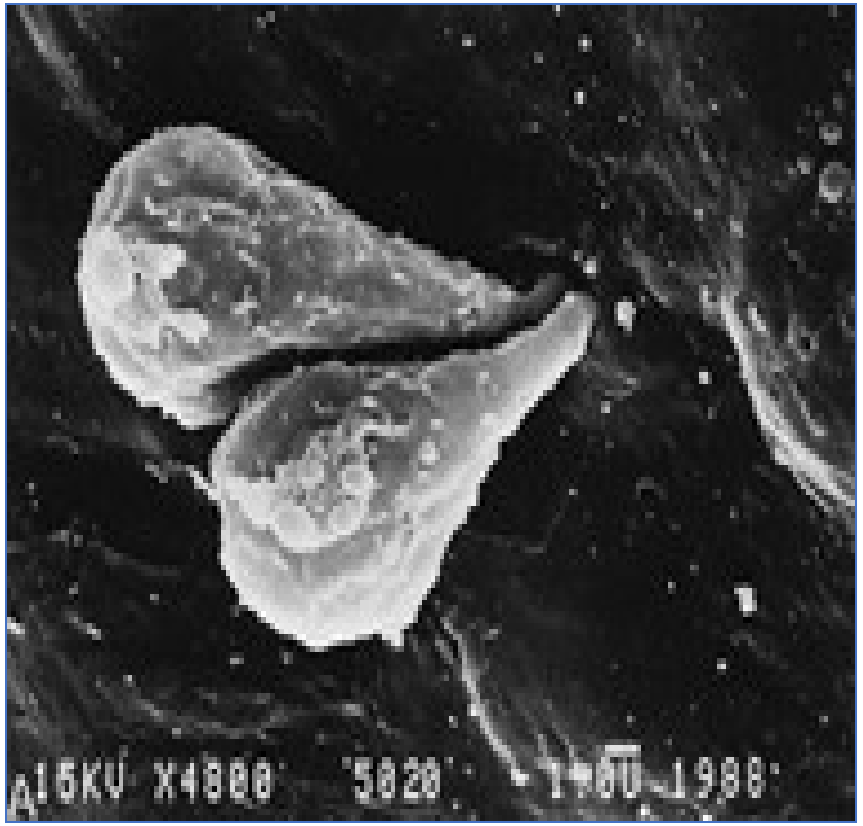


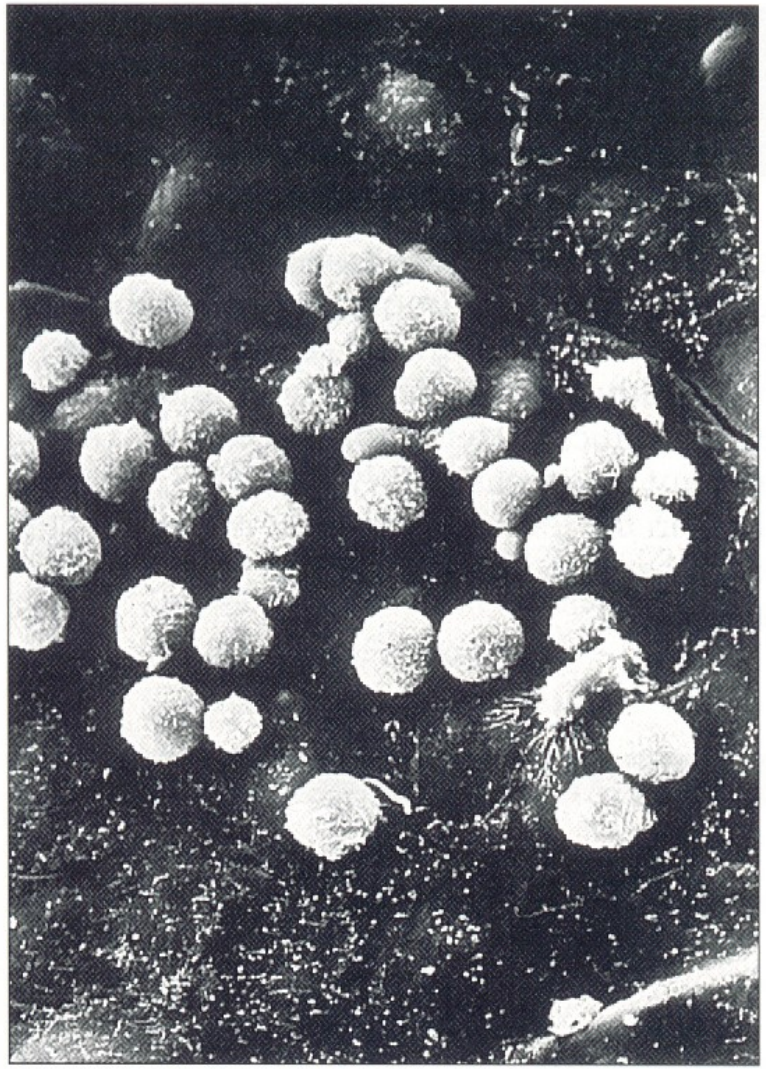
(From Creager MA, Luscher TF, Cosentino F, Beckman JA: Diabetes and vascular disease: Pathophysiology, clinical consequences, and medical therapy: Part I. Circulation 108:1527, 2003.)

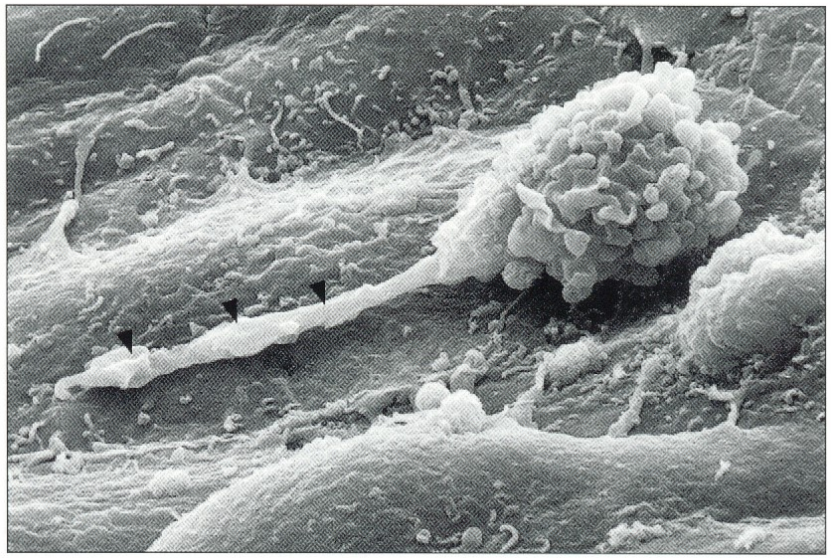

SARS-CoV-2
Systemic inflammation
(cytokine storm)
endothelial cells
Increased vascular
permeability
endothelial inflammation
leukocyte infiltration
Impaired angiogenesis
VWF
FLT-3
PAI-1
angiopoietin-2
platelet
activation
coagulation
monocyte
macrophage
Endothelial injury/dysfunction
Atherosclerosis

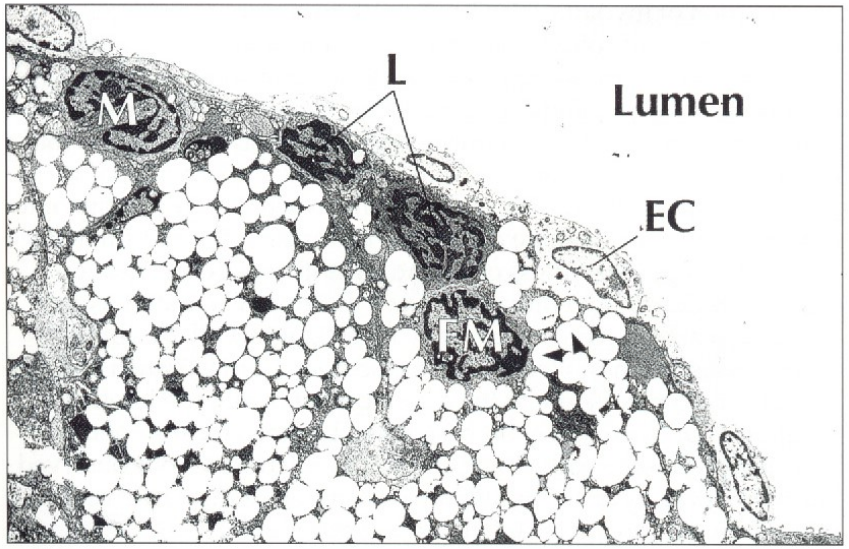
Pathophysiology

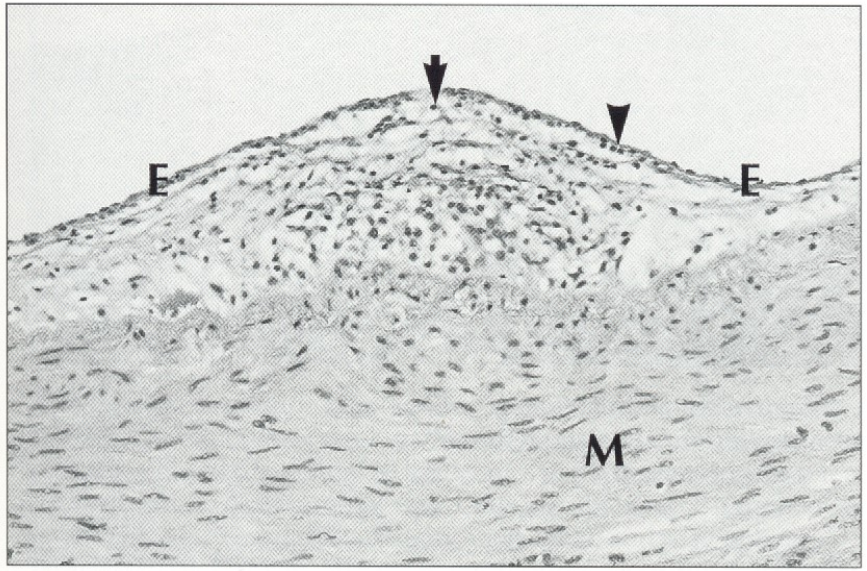




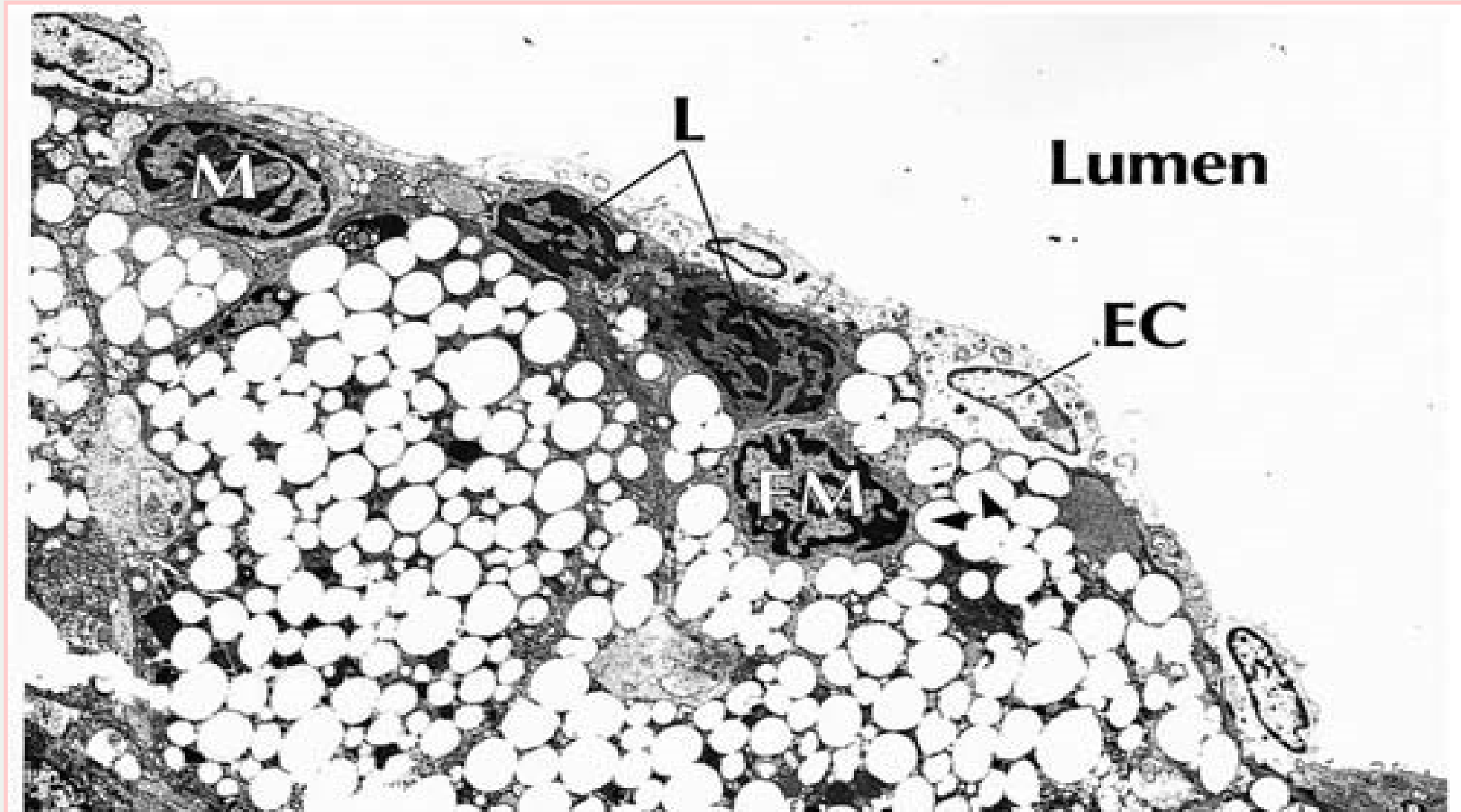


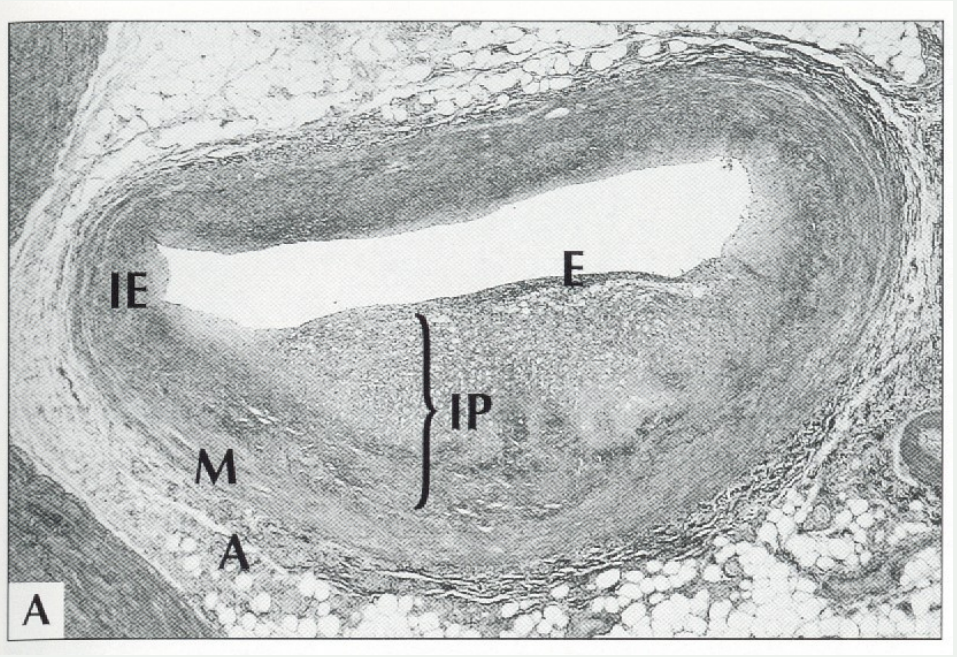


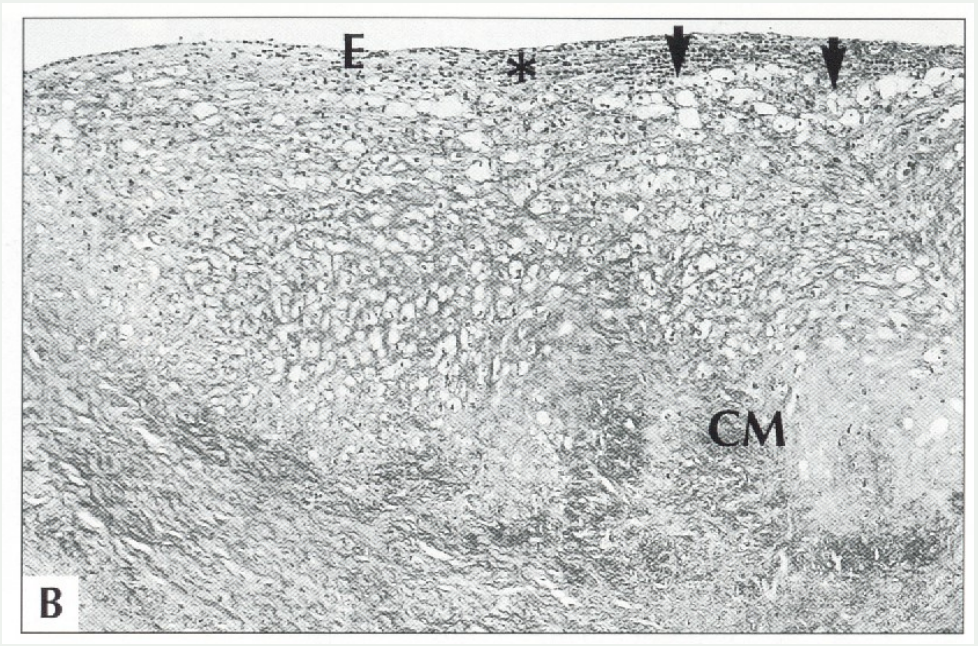

L
M
Lumen
EC
FM

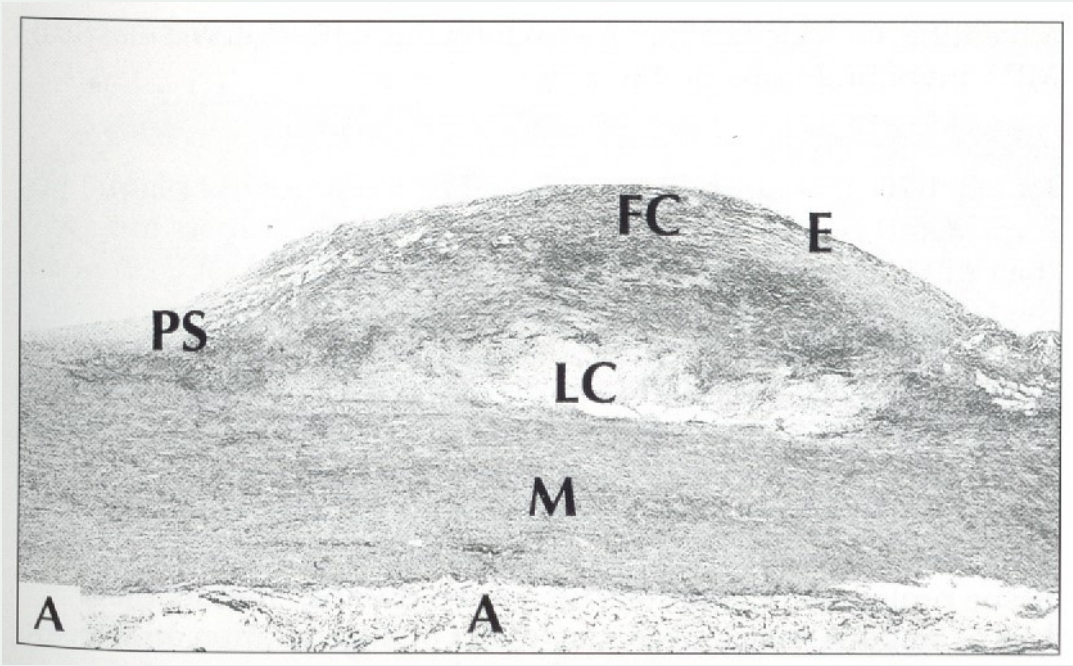

E
E
M

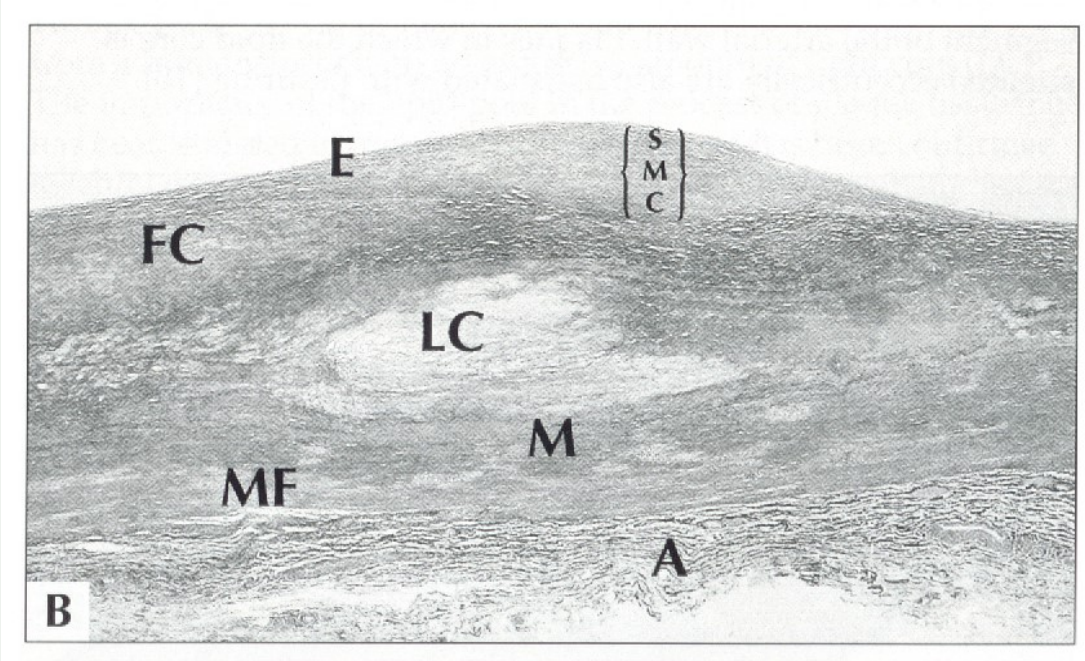
Fatty streak

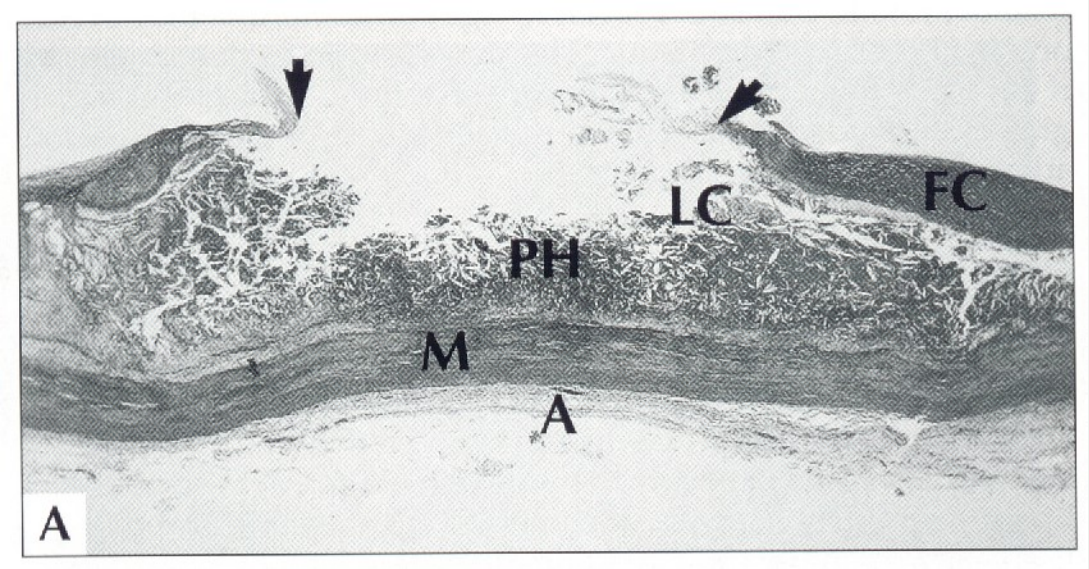



IE
E
IP
M
A
A


E
*
CM
B


FC
E
PS
LC
M
A
A


E
S
M
C
FC
LC
M
MF
A
B


LC
FC
PH
M
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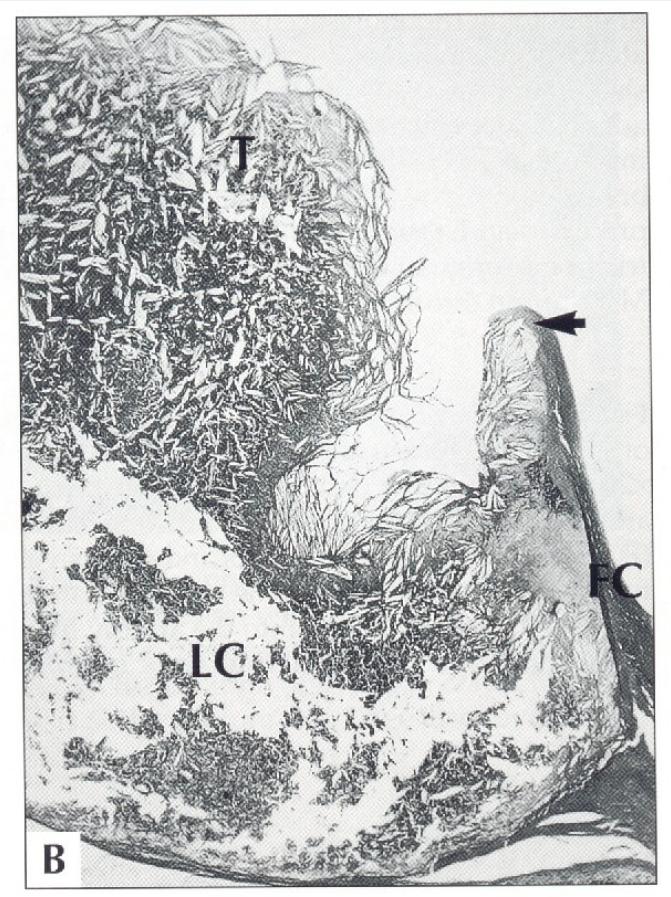
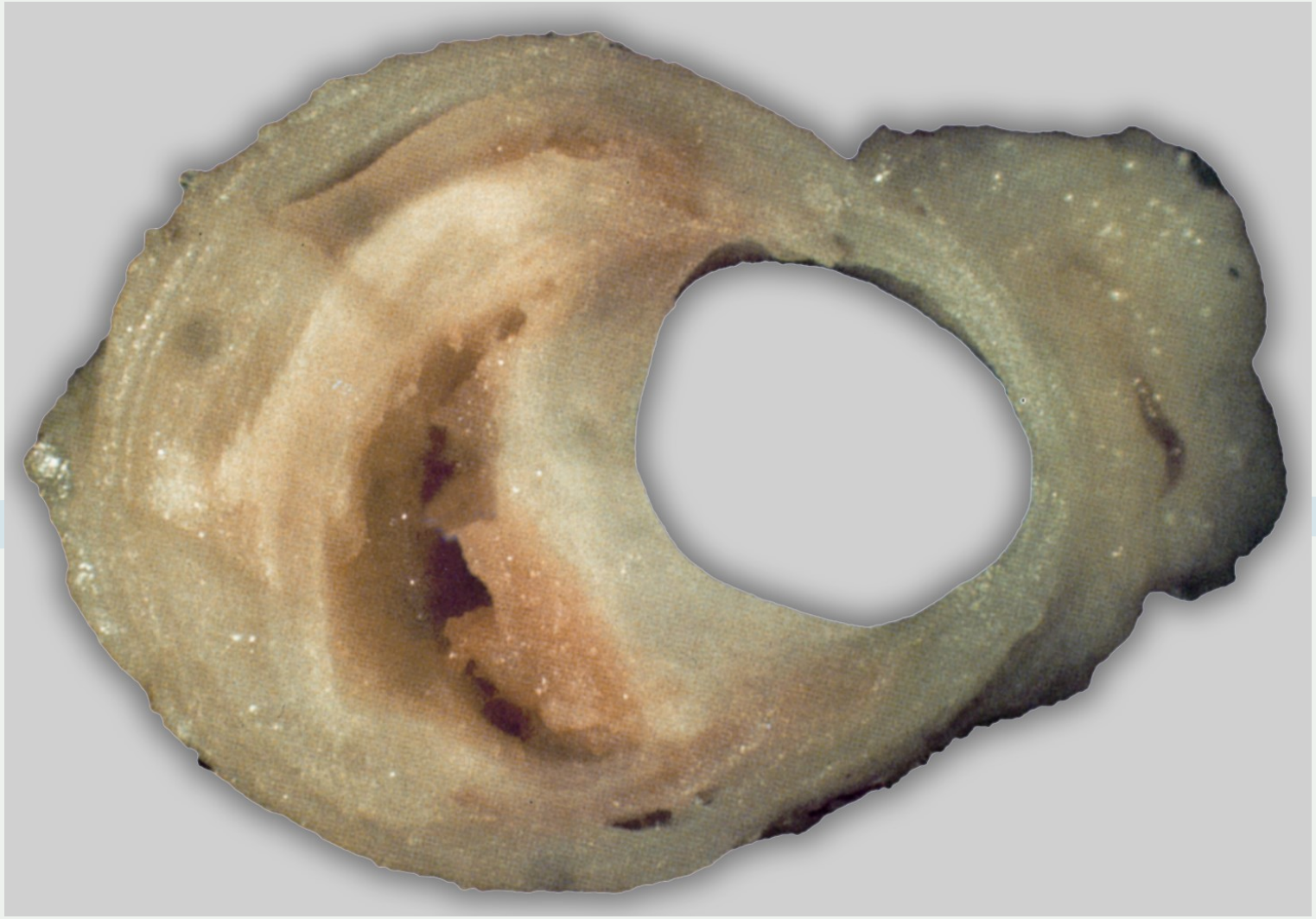
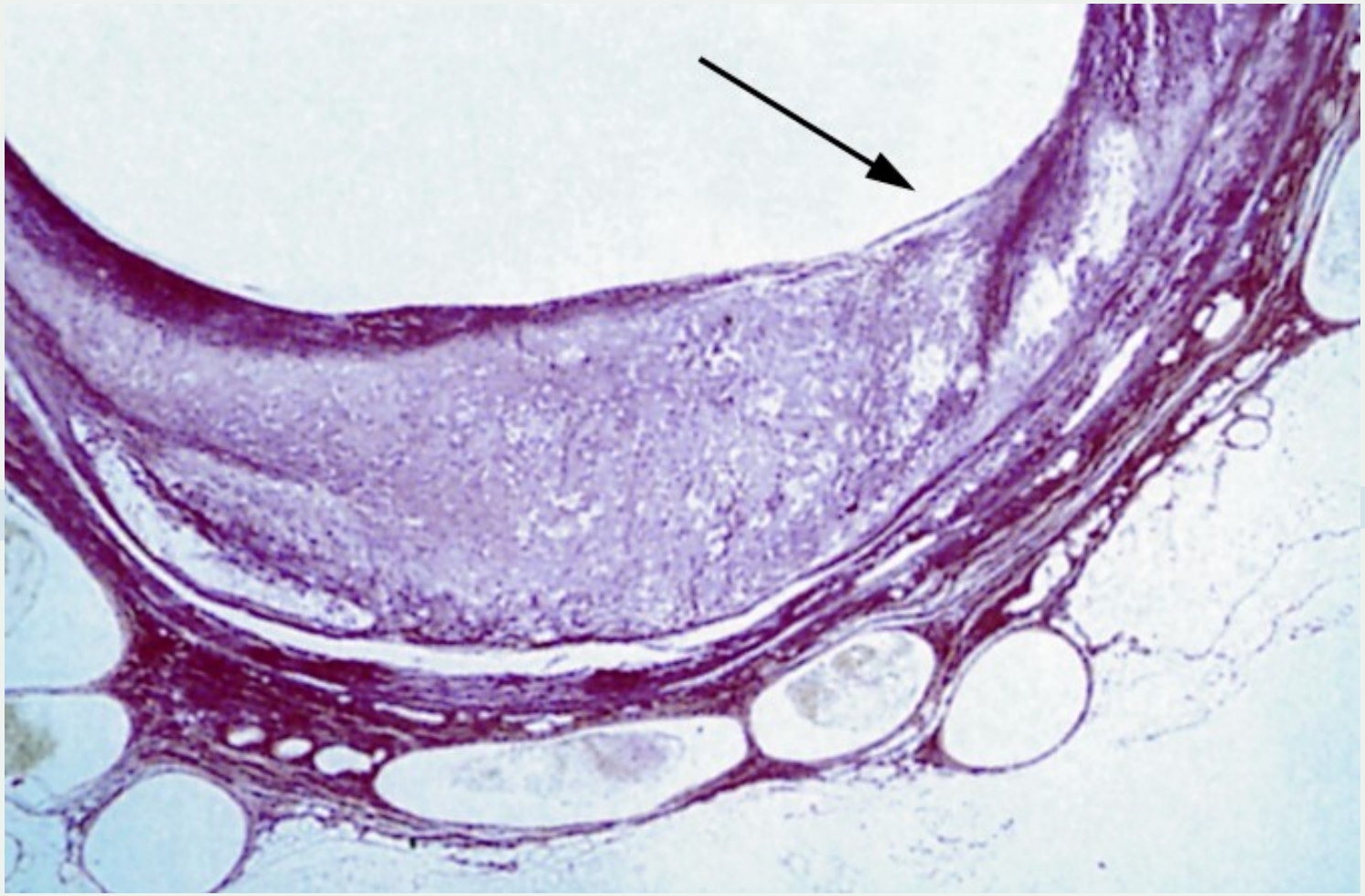
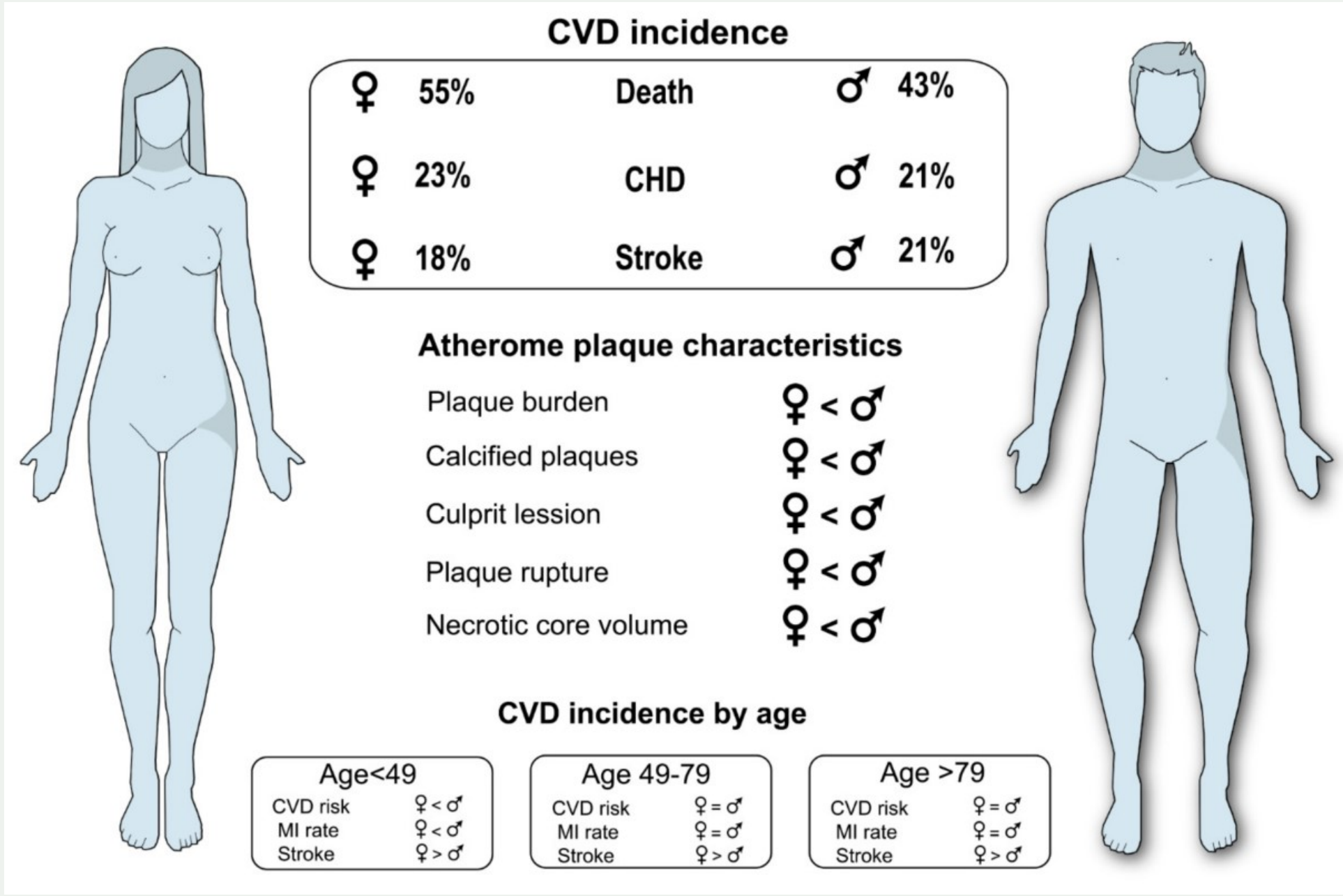
A


T
FC
LC
B







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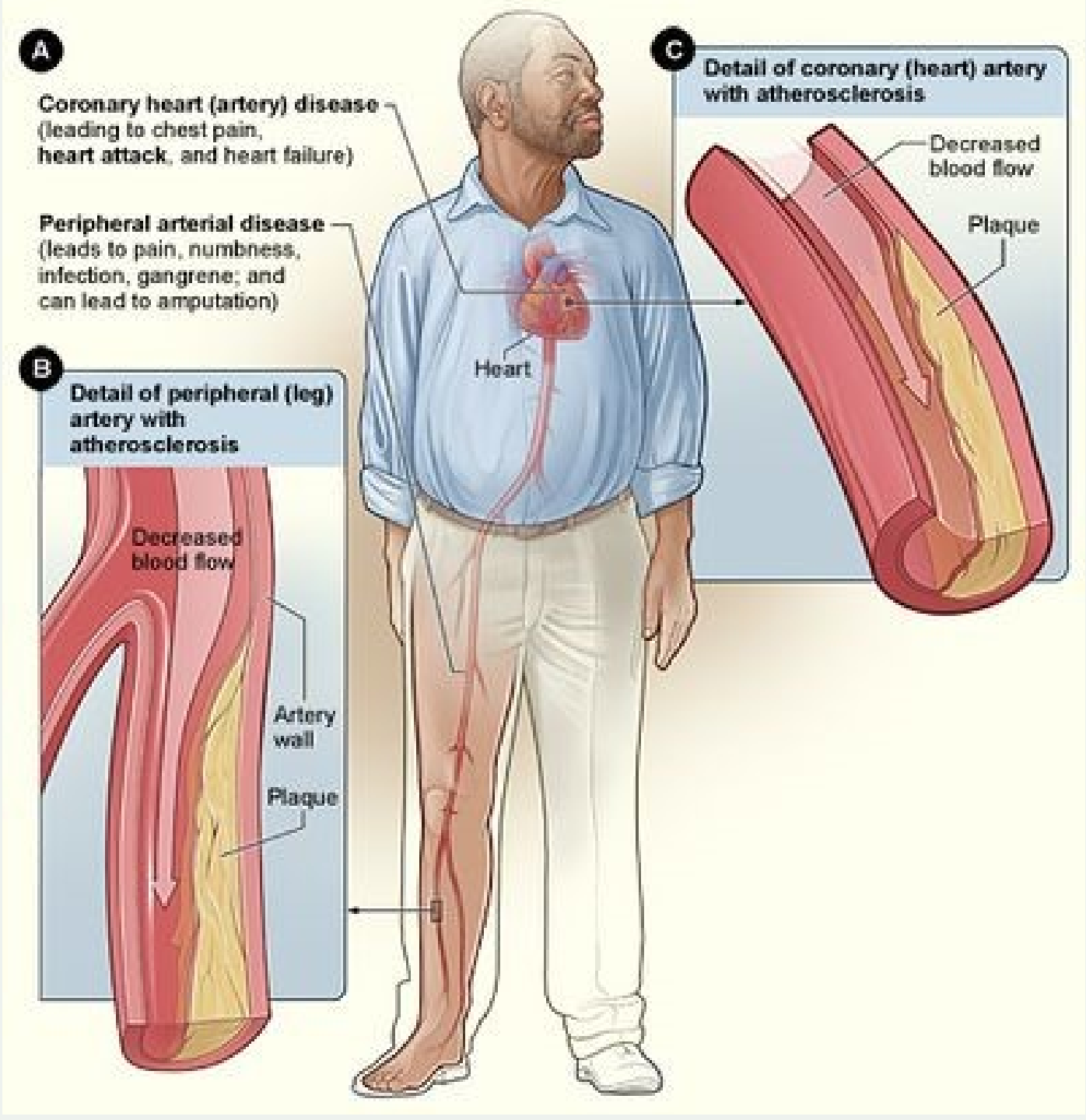
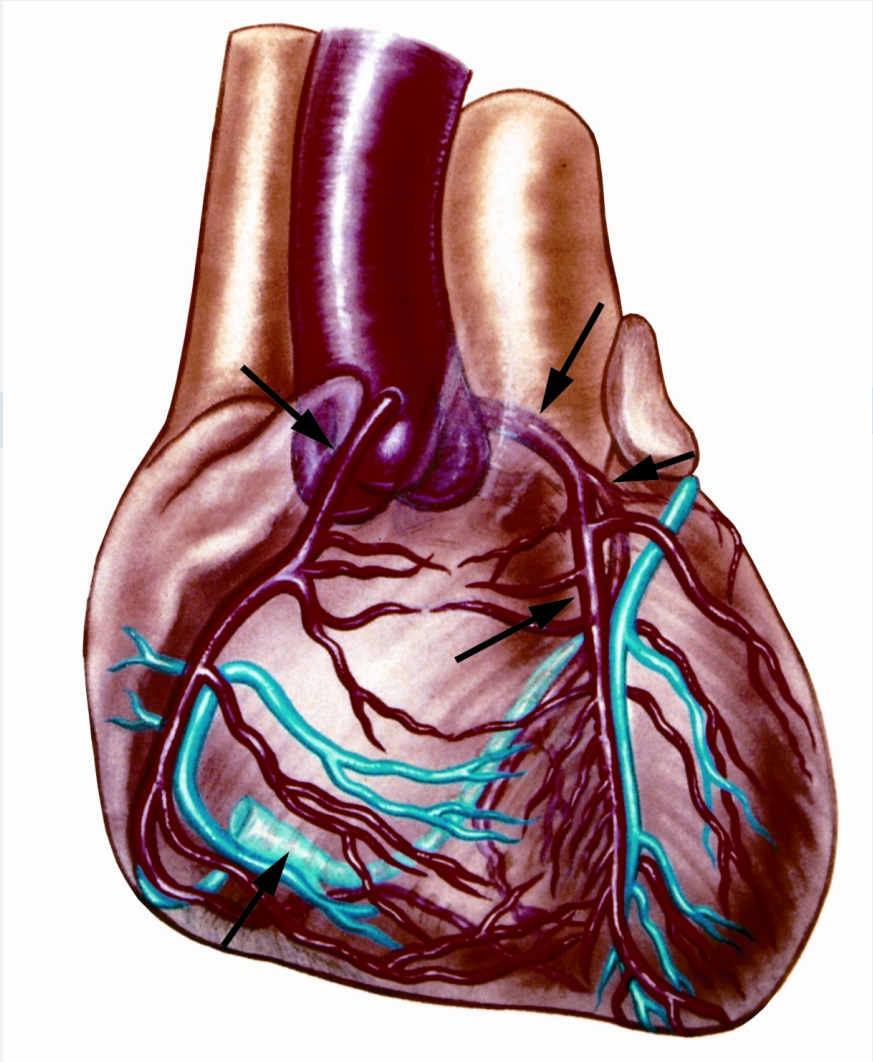
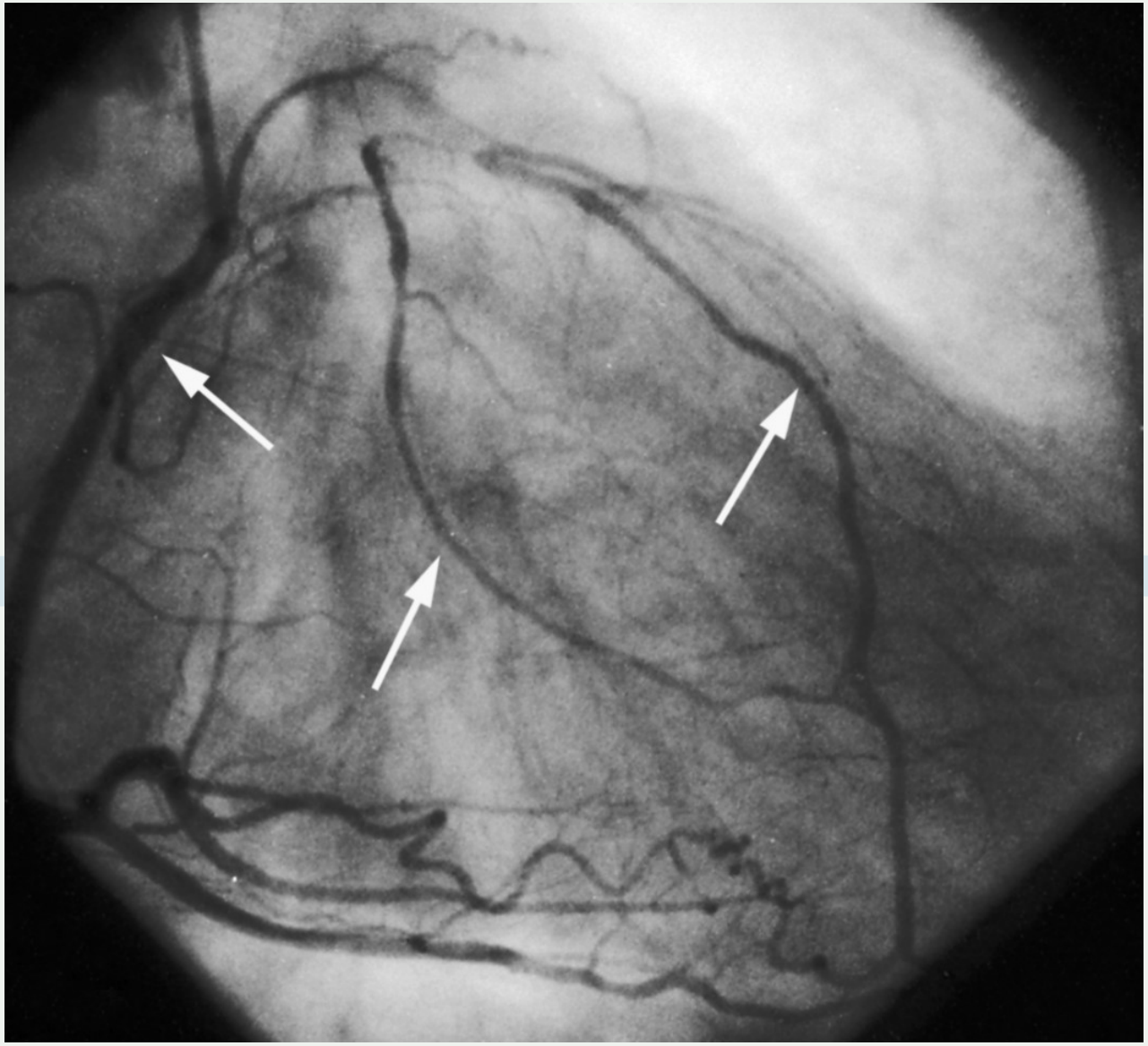
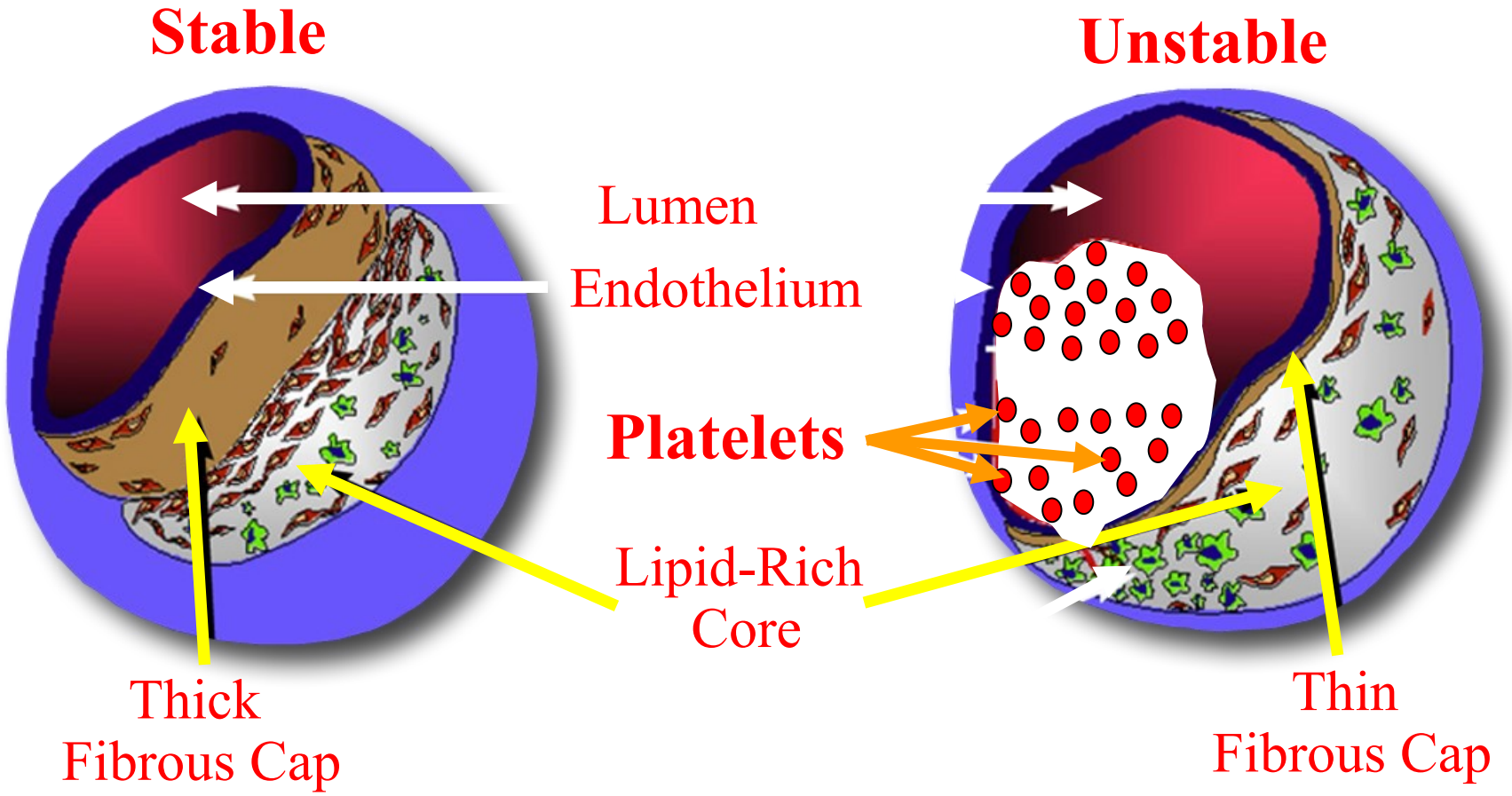

A
Coronary heart (artery) disease
(leading to chest pain,
heart attack, and heart failure)
Peripheral arterial disease
(leads to pain, numbness,
infection, gangrene; and
can lead to amputation)
Heart
B
Detail of peripheral (leg)
artery with
atherosclerosis
Decreased
blood flow
Artery
wall
Plaque
C
Detail of coronary (heart) artery
with atherosclerosis
Decreased
blood flow
Plaque

ΧΡΟΝΙΑ ΣΤΕΦΑΝΙΑΙΑ ΝΟΣΟΣ





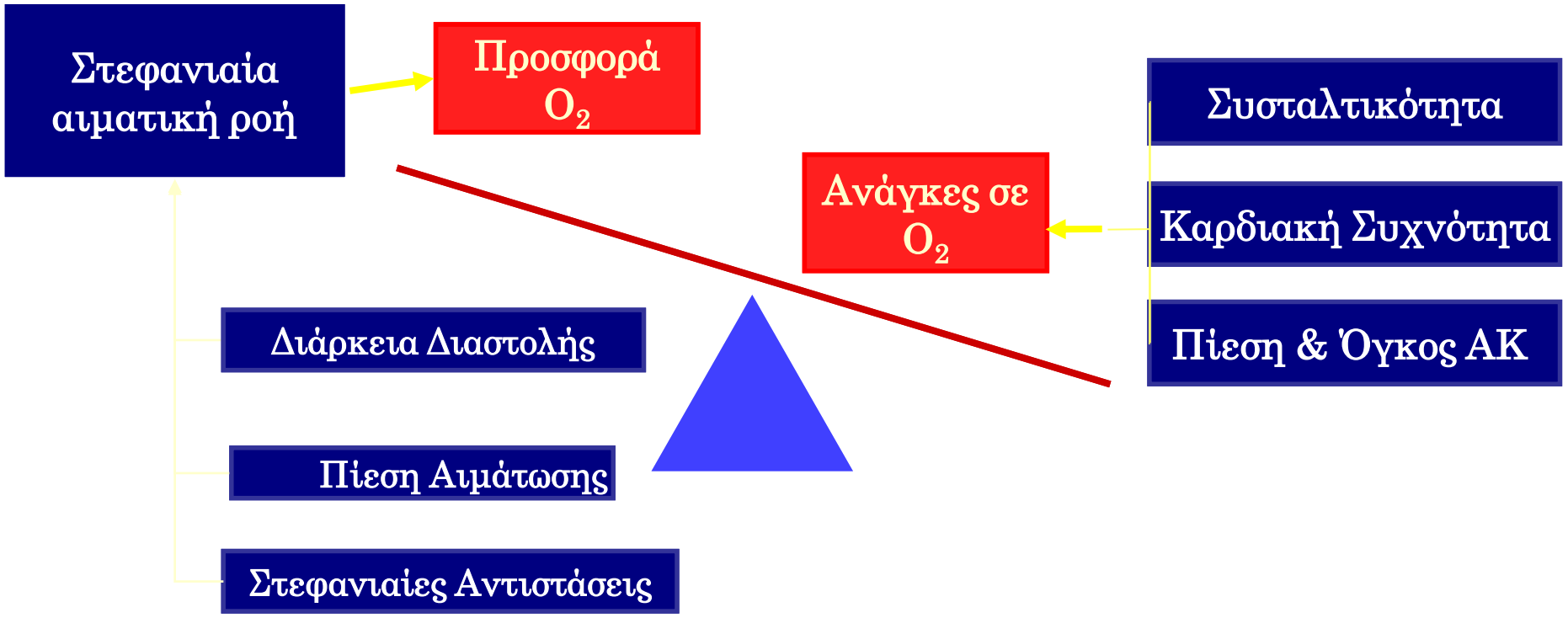
What Types of Atherothrombotic Lesions Cause MI and Stable Angina?



MI = myocardial infarction.

Adapted with permission from Falk E, et al. *Circulation*. 1995;92:657-671.

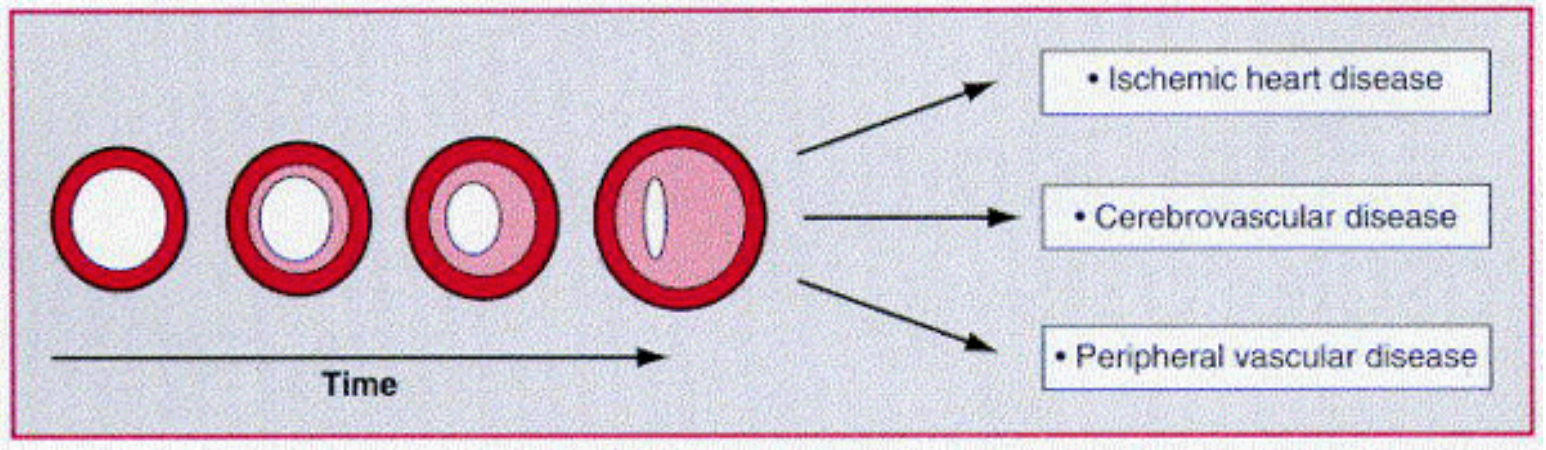
Ισχαιμία του μυοκαρδίου



Crossman DC. Heart. 2004;90:576-580 - Gersh BJ et al. In: Braunwald E et al. Heart Disease. 6th ed. 2001

Παθολογική ανατομία

- Στένωση στεφανιαίων αγγείων
- Μειωμένη στεφανιαία εφεδρεία στη άσκηση
- Δυσαναλογία μεταξύ αυξημένων αναγκών και μειωμένης παροχής O2



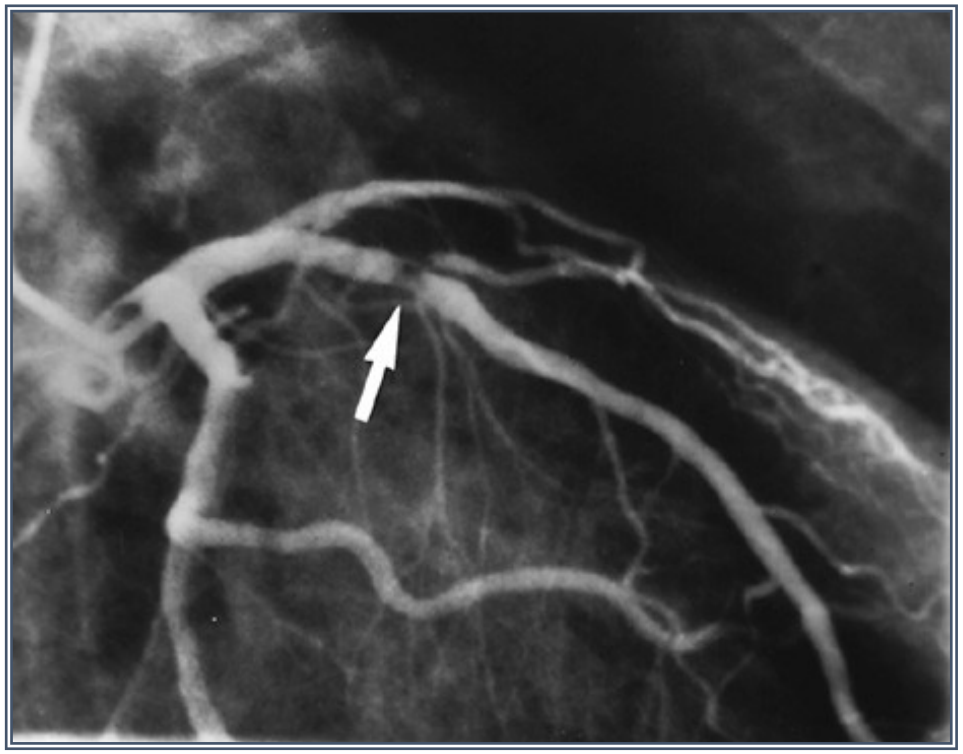
Αυξημένες ανάγκες Ο2

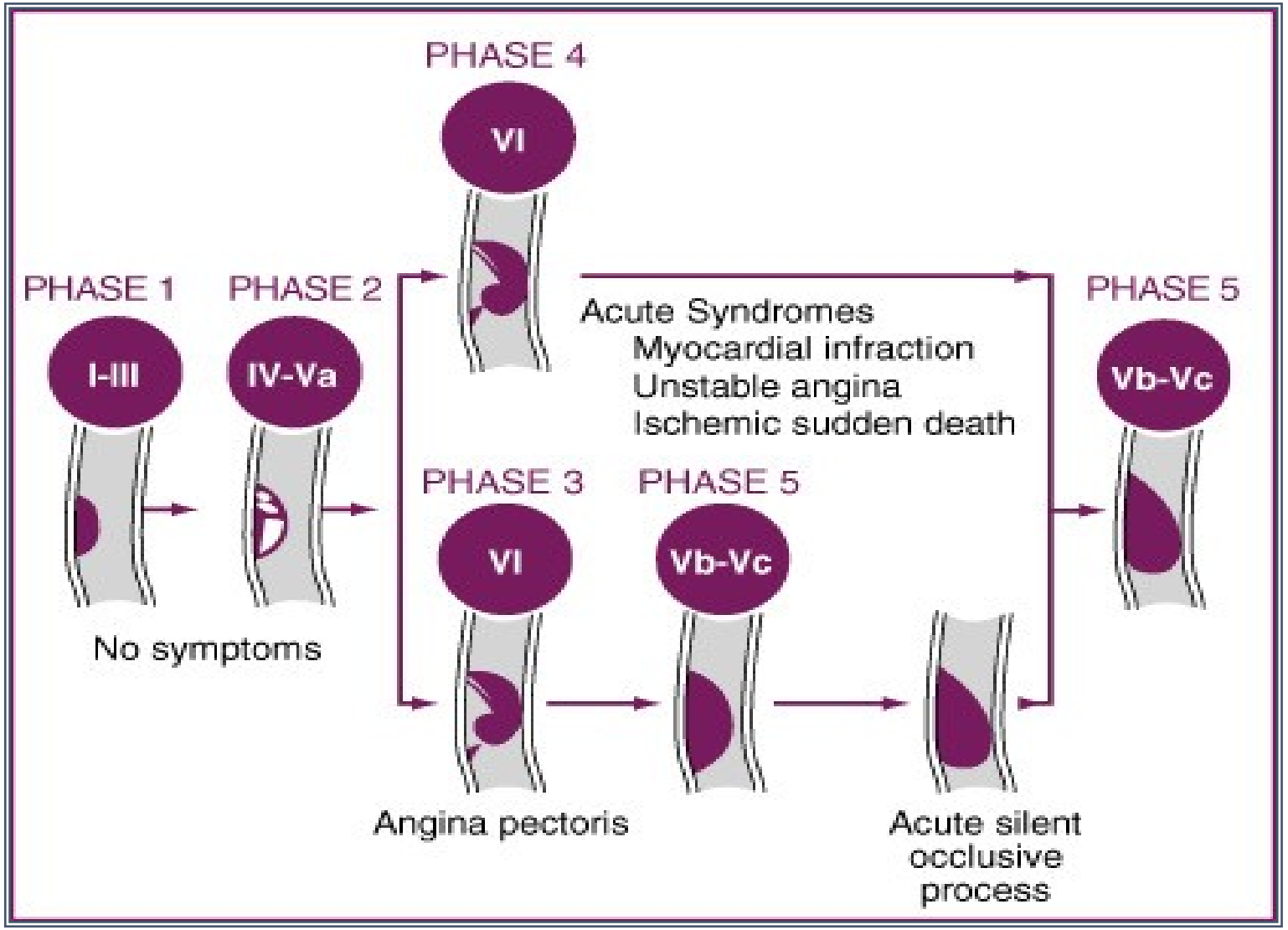
- Αύξηση κατεχολαμινων (άσκηση, έντονα συναισθήματα, πνευματική καταπόνηση)
- Χρονοτροπη, ινότροπη απάντηση

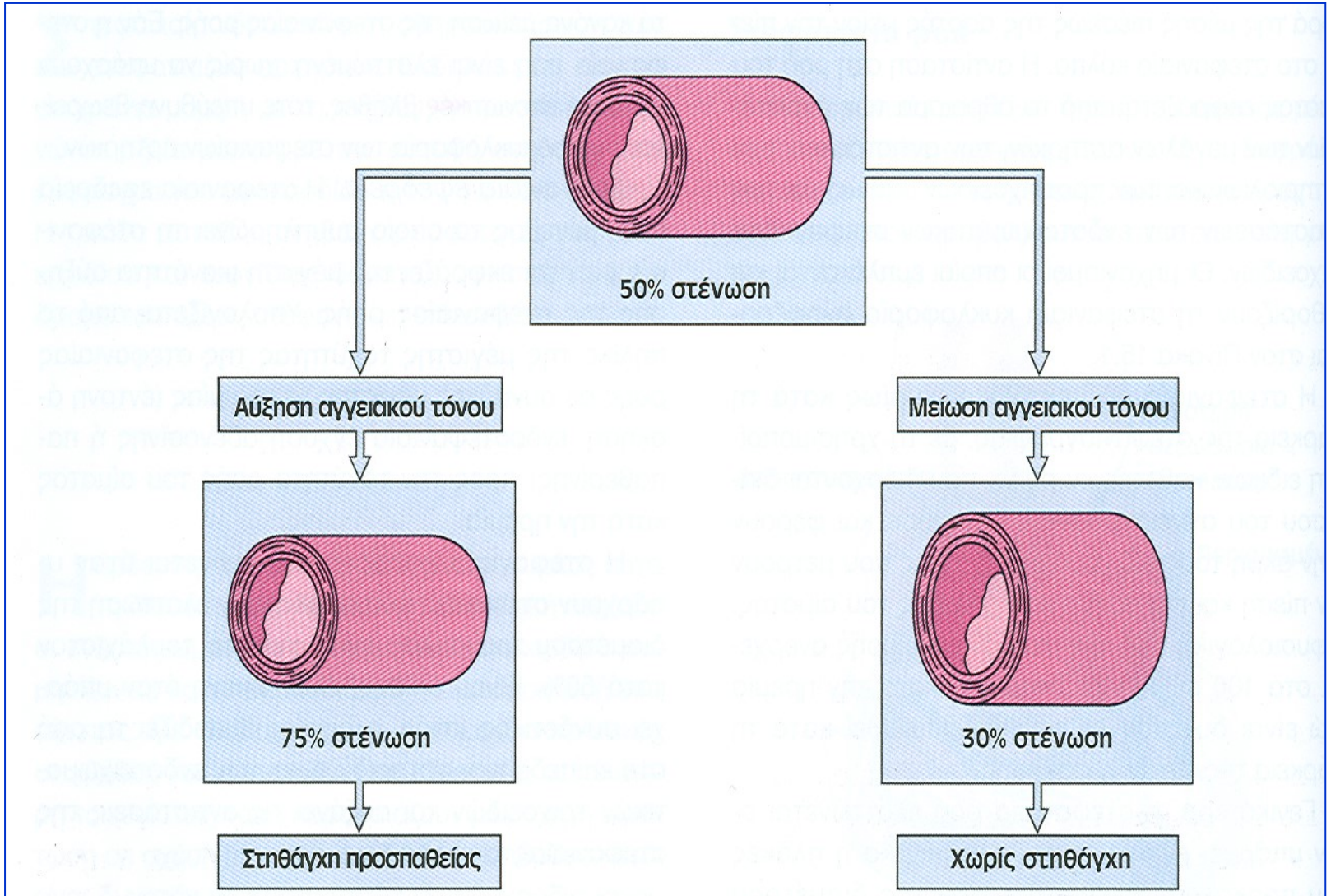
Παροδική μείωση της παροχής O2

- Δυσλειτουργία ενδοθηλίου= μειωμένη παραγωγή αγγειοδιασταλτικών ουσιών (NO, προστακυκλινη)
- Ενεργοποίηση αιμοπεταλίων –φλεγμονή= αγγειοσυσπαστικες ουσίες
- Σε σοβαρή στενωση και μικρή μόνο αύξηση του αγγειακού τόνου =ισχαιμία

Παθοφυσιολογία





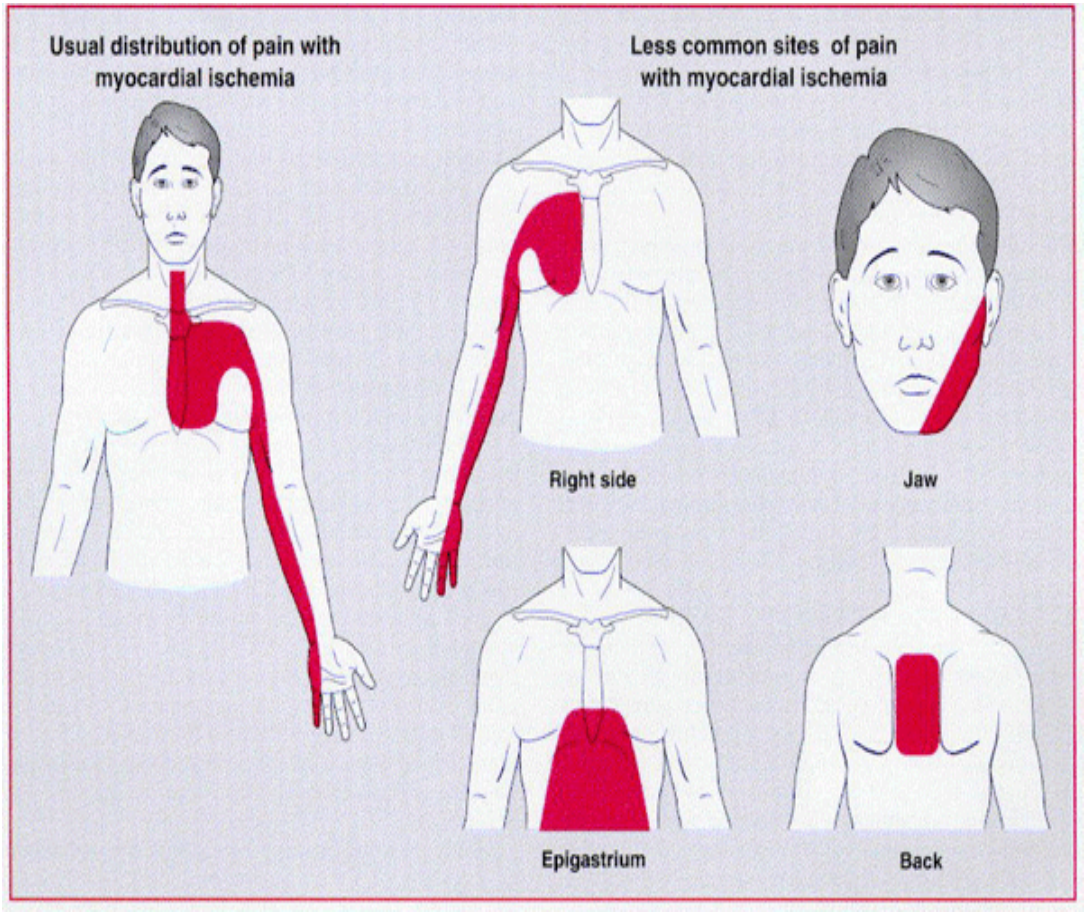


ΕΙΚΟΝΑ 15.2. Λειτουργικές μεταβολές της στεφανιαίας αρτηρίας επί εδάφους αθηροσκληρωτικής πλάκας. Αθηροσκληρωτική π
κα με ανατομική στένωση 50% είναι δυνατόν να εκφράζεται αιμοδυναμικά ως στένωση π.χ. 30% ή ως στένωση π.χ. 75% ανάλ
με τον τόνο του στεφανιαίου αγγείου. Οι μεταβολές αυτές είναι δυνατόν να παρατηρηθούν είτε στην ηρεμία ή κατά την άσκηση.

Στηθάγχη

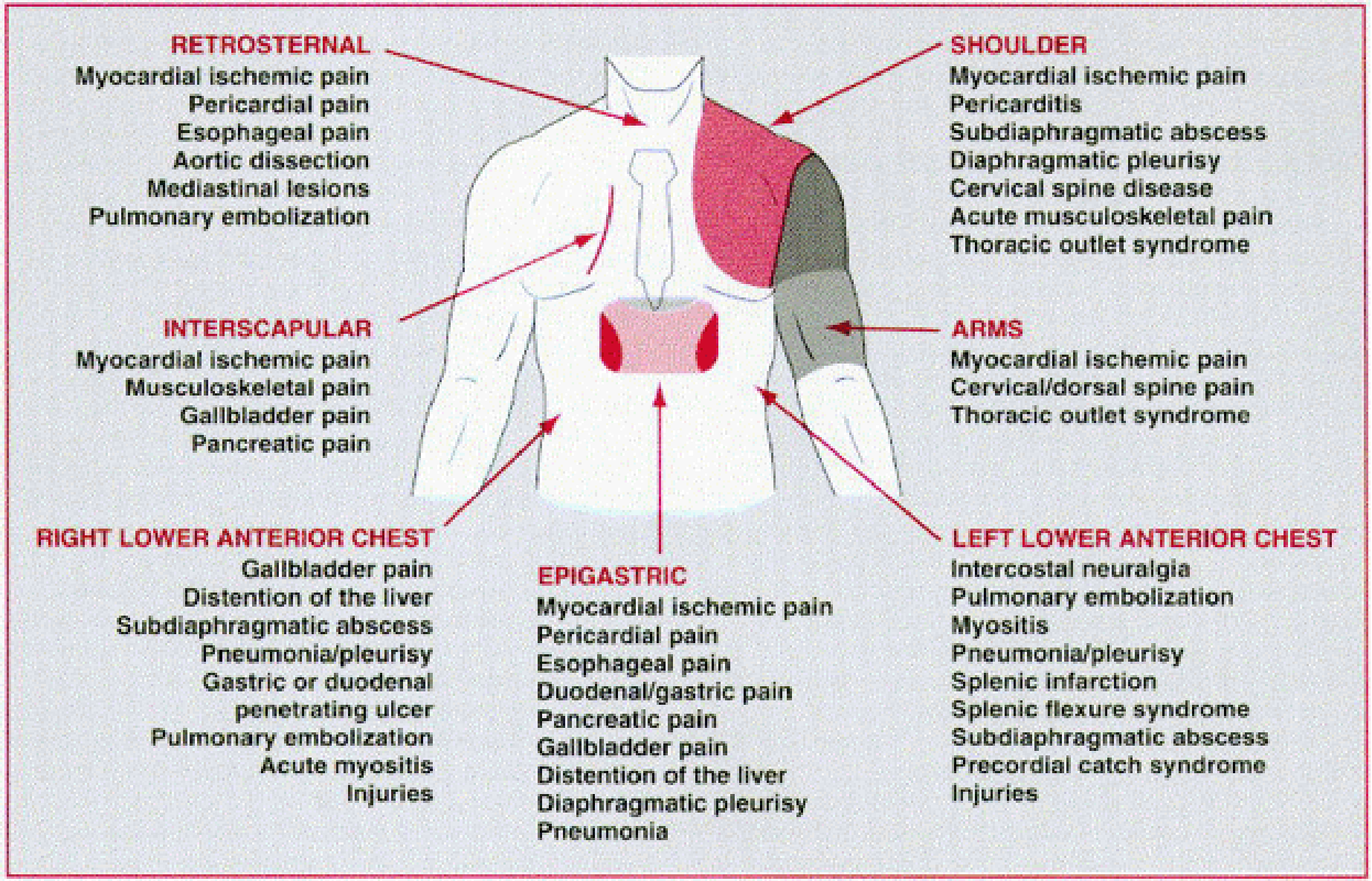
- Ασυμπτωματική ΣΝ
- Σταθερός ουδός έκλυσης
- Μεταβαλλόμενος ουδός έκλυσης στηθάγχης (μεταγευματική στηθάγχη)
- ‘Μεικτή’ στηθάγχη
- Στηθάγχη Prinzmetal

Κλινική εικόνα



- Στηθάγχη
- Εκσεσημασμένη δύσπνοια στη προσπάθεια
  - Ποιότητα
  - Διάρκεια
  - Εκλυτικοί παράγοντες
  - Συνοδά συμπτώματα

Διαφορική διάγνωση



Επιδημιολογία

- 12,200,000 Americans have CAD,
  - 6,300,000 of whom have angina pectoris
  - 7,200,000 have had myocardial infarction
- The economic cost of CAD and stroke in the United States in 2000 is estimated at $326.6 billion ($118.2 billion for CAD).

American Heart Association: 2000 Heart and Stroke Statistical Update. Dallas, American Heart Association, 1999.

ΜΕΓΕΘΟΣ ΠΡΟΒΛΗΜΑΤΟΣ

- 30 ασθενείς με σταθερή στηθάγχη για κάθε ΟΕΜ
- 550.000 ΟΕΜ (ΗΠΑ)
- 16.500.000 άτομα με σταθερή στηθάγχη
- 20.000-40.000/1.000.000 πληθυσμού
- ΕΛΛΑΣ- 30 . 10.000 ΟΕΜ - 300.000 άτομα με σταθερή στηθάγχη

ΕΠΙΔΗΜΙΟΛΟΓΙΑ-ΦΥΣΙΚΗ ΙΣΤΟΡΙΑ

- Ετήσια θνητότητα 0.9-1.4%
- Ετήσια επίπτωση εμφράγματος μυοκαρδίου 0.5% (INVEST 2003)-2.6%(TIBET 1996)
- Πρόγνωση ποικίλλει ευρέως

Παροδική μείωση της παροχής O2

- Δυσλειτουργία ενδοθηλίου= μειωμένη παραγωγή αγγειοδιασταλτικών ουσιών (NO, προστακυκλινη)
- Ενεργοποίηση αιμοπεταλίων –φλεγμονή= αγγειοσυσπαστικες ουσίες
- Σε σοβαρή στενωση και μικρή μόνο αύξηση του αγγειακού τόνου =ισχαιμία

ΧΡΟΝΙΑ ΣΤΕΦΑΝΙΑΙΑ ΝΟΣΟΣ

- Ασυμπτωματική
- Σταθερή στηθάγχη

ΚΛΙΝΙΚΗ ΕΞΕΤΑΣΗ

- 4ος τόνος
- Συστολικό φύσημα
- Έκτοπη καρδιακή ώση

ΕΡΓΑΣΤΗΡΙΑΚΗ ΔΙΕΡΕΥΝΗΣΗ

- Ανάδειξη ισχαιμουσών περιοχών
- Ανάδειξη νεκρωμένων περιοχών
- Ανάδειξη αποφρακτικών βλαβών
- Εκτίμηση λειτουργικότητας αριστερής κοιλίας
- Εκτίμηση αρρυθμιών

ΔΙΕΡΕΥΝΗΣΗ ΣΤΕΦΑΝΙΑΙΑΣ ΝΟΣΟΥ

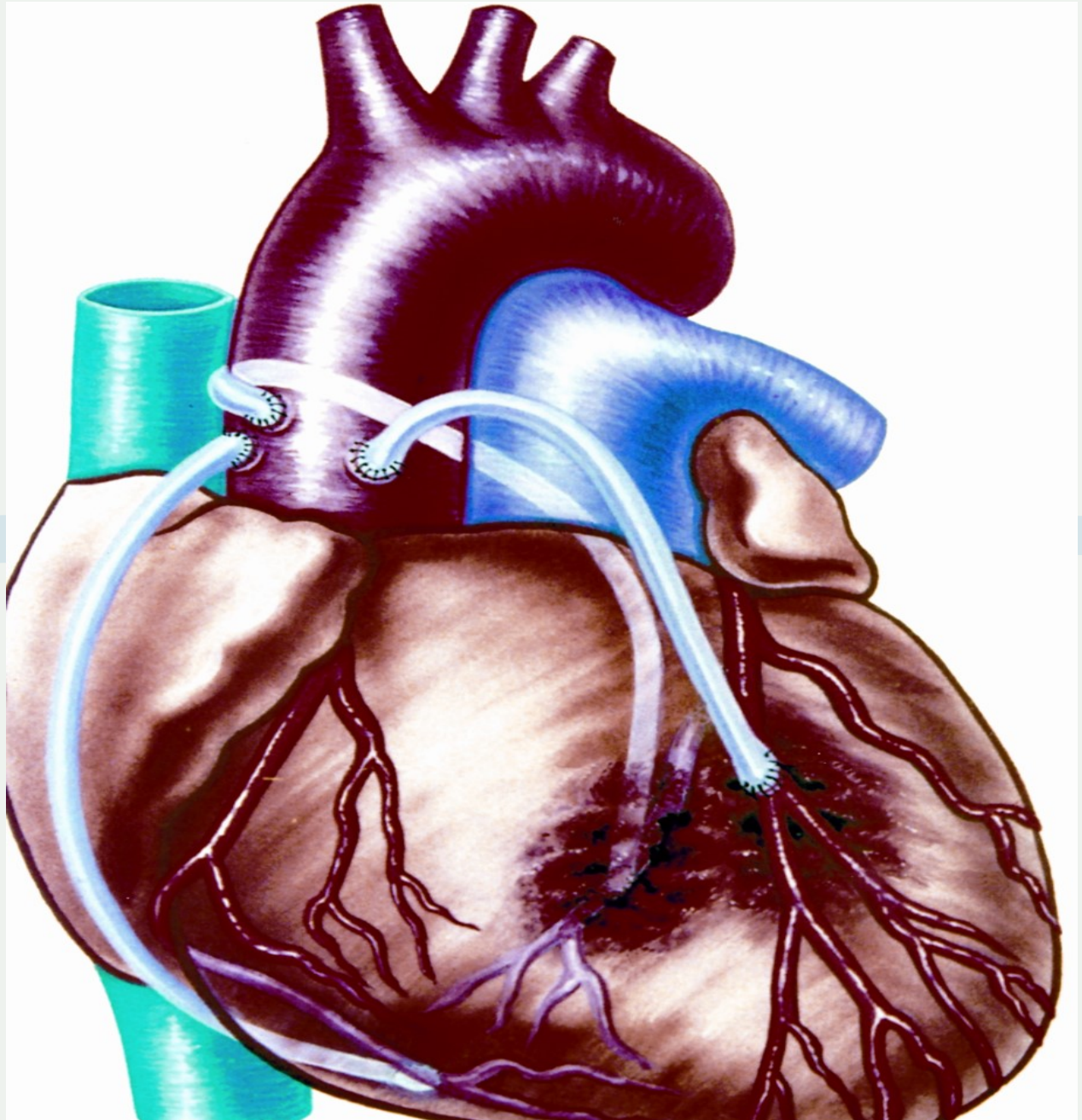
- Δοκιμασία κοπώσεως
- Σπινθηρογράφημα μυοκαρδίου
- Υπερηχογράφημα
- Ηλεκτροκαρδιογράφημα-Holter
- MRI
- PET
- Στεφανιογραφία
- ΗΦΜ

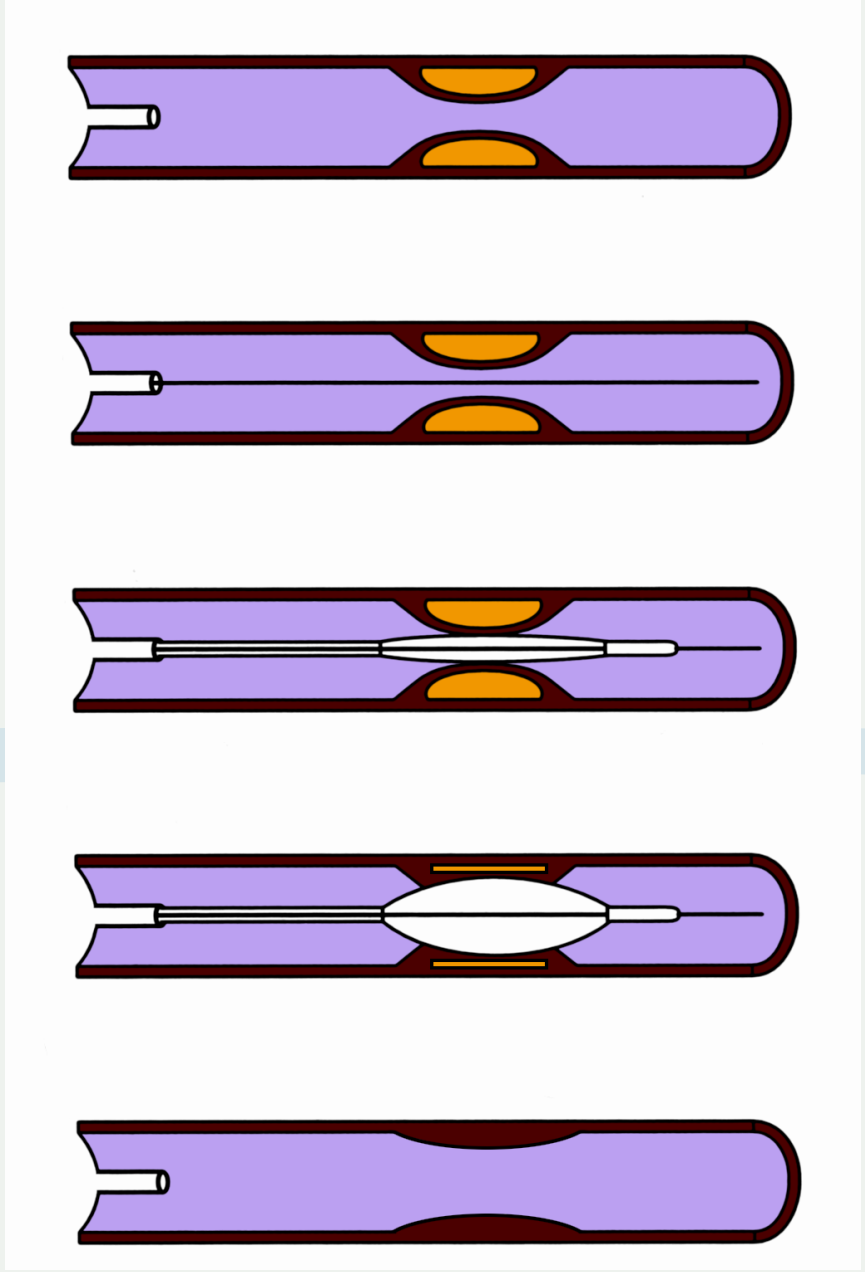
ΣΥΝΤΗΡΗΤΙΚΗ ΘΕΡΑΠΕΙΑ

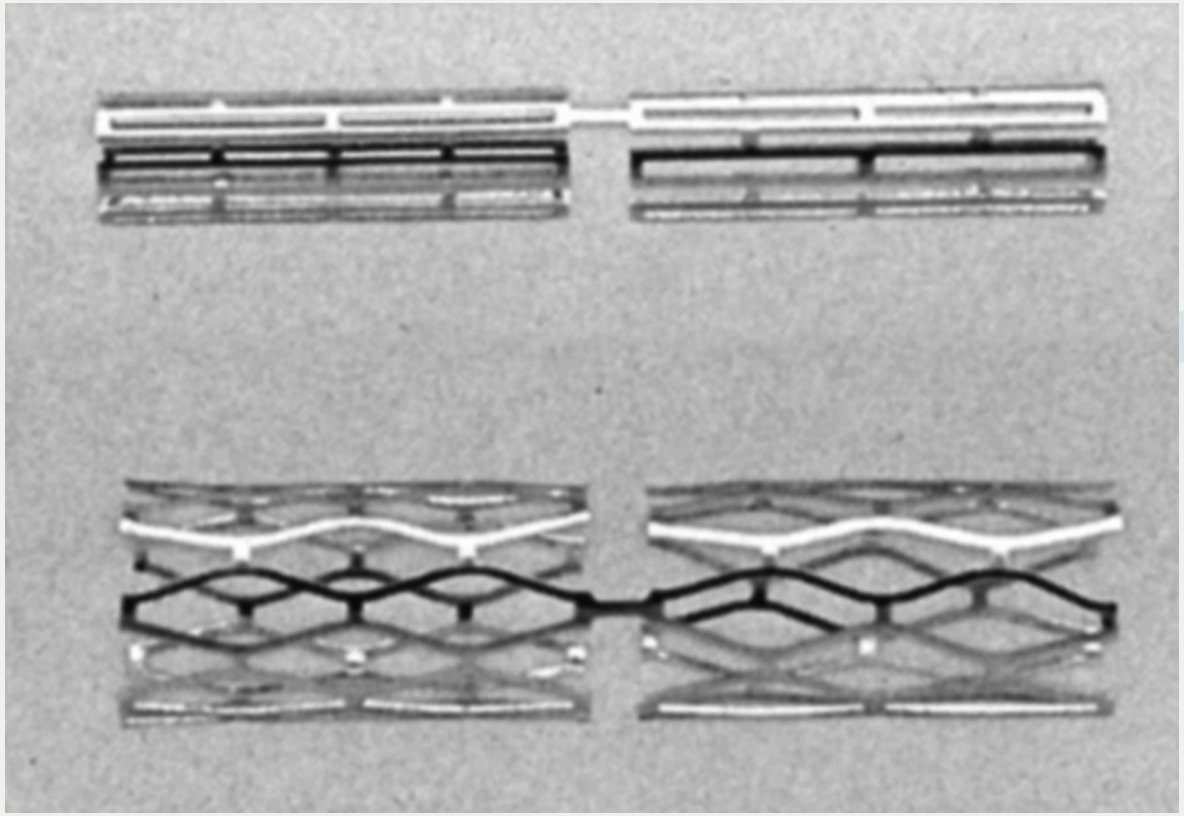
- Γενικά μέτρα
- Ασπιρίνη
- Νιτρώδη
- Β-αναστολείς
- Ανταγωνιστές ασβεστίου
- Στατίνες
- Αναστολείς μετατρεπτικού ενζύμου

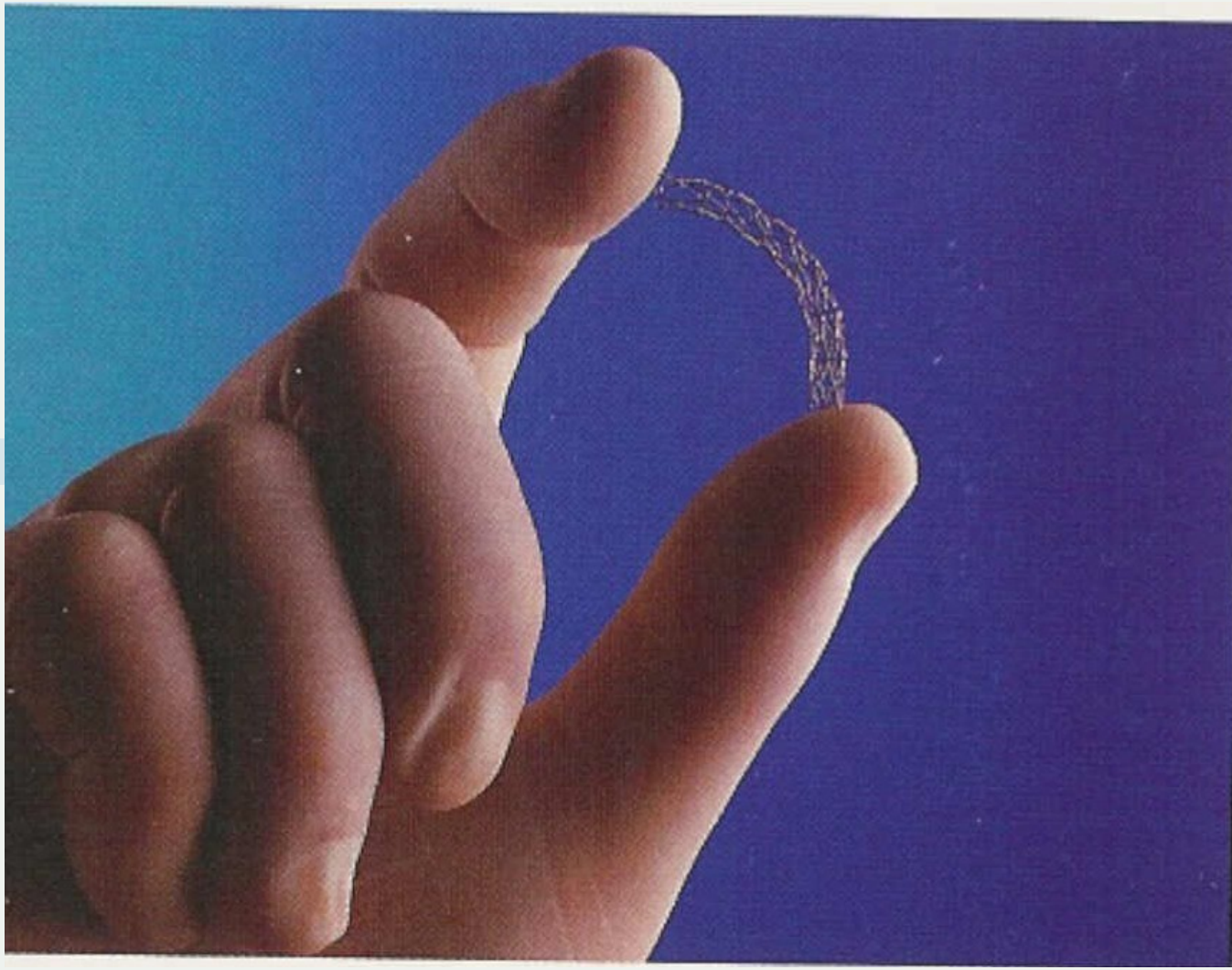
ΕΠΕΜΒΑΤΙΚΗ ΘΕΡΑΠΕΙΑ

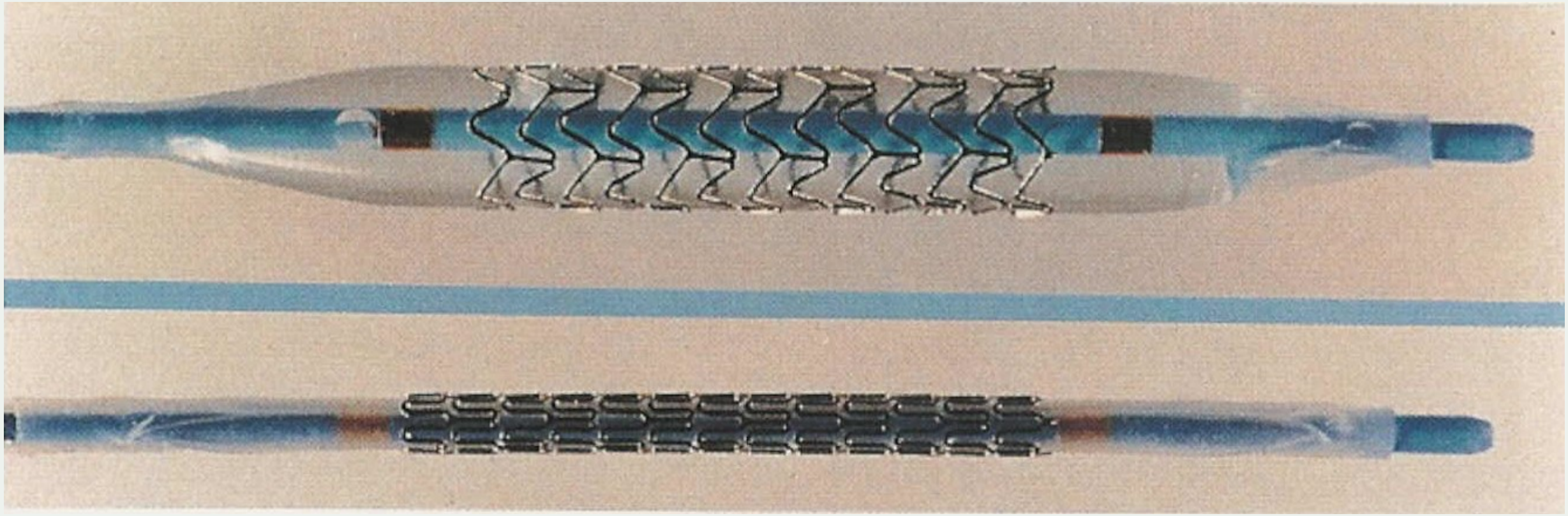
- Αορτοστεφανιαία παράκαμψη
- Αγγειοπλαστική

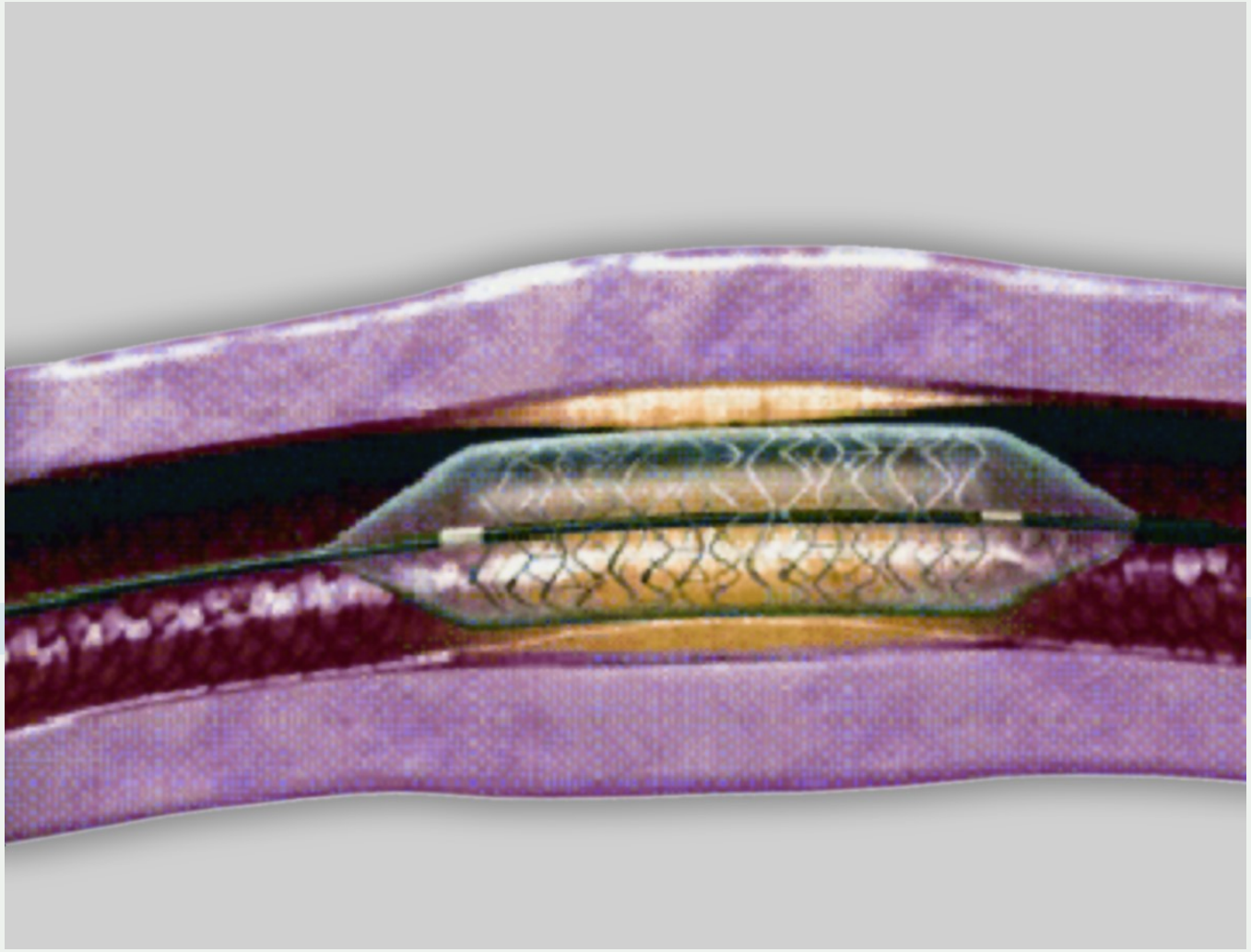












ΝΕΑ ΙΣΧΑΙΜΙΚΑ ΣΥΝΔΡΟΜΑ

- Ισχαιμική προετοιμασία μυοκαρδίου
- Χειμάζον μυοκάρδιο
- Παροδική δυσλειτουργία μυοκαρδίου

Περιστατικό 1

- 1.Άνδρας 58 ετών, παχύσαρκος με σακχαρώδη διαβήτη τύπου 2. Θα λάβει ασπιρίνη για πρωτογενή πρόληψη;

CV risk categories in patients with DM

ESC
European Society of Cardiology

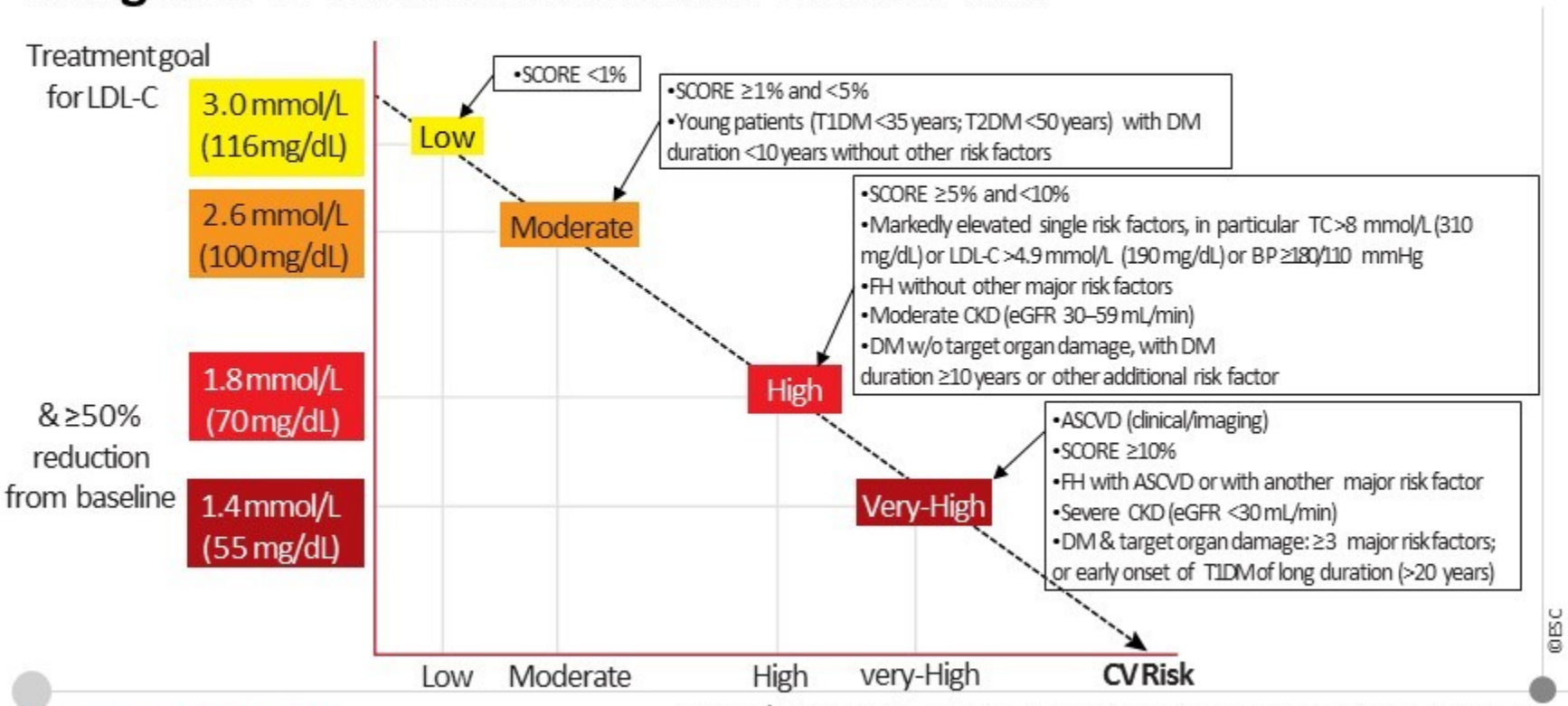
Very high-risk	Patients with DM **and** established CVD **or** other target organ damage[a] **or** three or more major risk factors[b] **or** early onset T1DM of long duration (>20 years)
High-risk	Patients with DM duration ≥10 years without target organ damage plus any other additional risk factor
Moderate-risk	Young patients (T1DM <35 years; T2DM <50 years) with DM duration <10 years, without other risk factors

[a]Proteinurea, renal impairment defined as eGFR < 30mL /min/1.73m², left ventricular hypertrophy, or retinopathy.
[b]Age, hypertension, dyslipidaemia, smoking, obesity

ESC Guidelines on Diabetes, pre-diabetes and cardiovascular diseases in collaboration with EASD (European Heart Journal 2019 - doi/10.1093/eurheartj/ehz486)

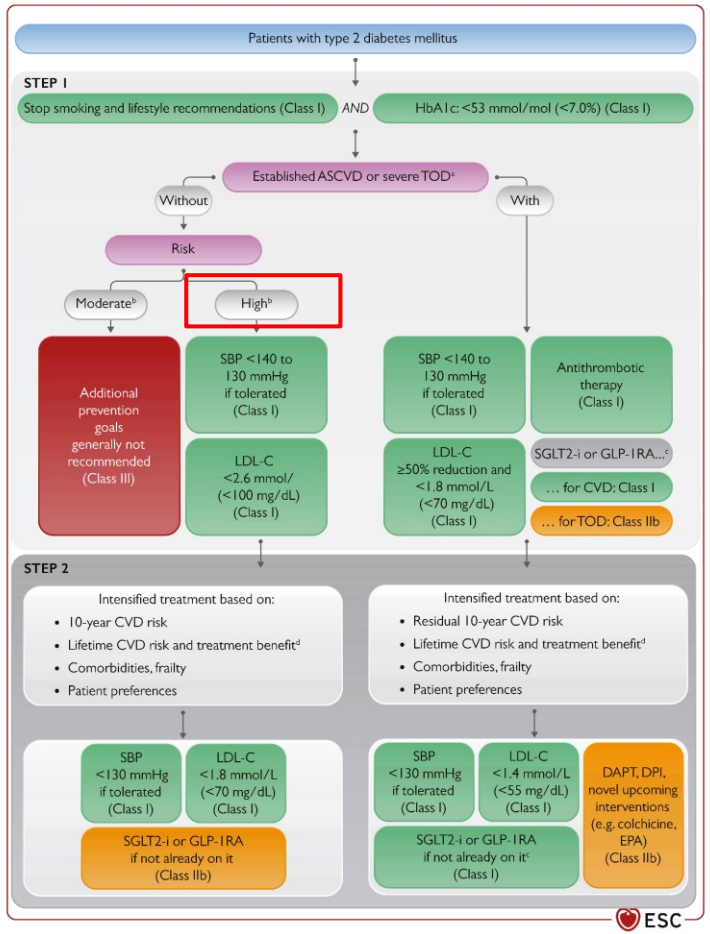
Central Illustration Upper panel Treatment goals for low-density lipoprotein cholesterol (LDL-C) across categories of total cardiovascular disease risk

EAS ESC European Society of Cardiology



www.escardio.org/guidelines

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)



Cardiovascular risk and risk factor treatment in patients with type 2 diabetes mellitus

www.escardio.org/guidelines

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice
(European Heart Journal 2021 – doi:10.1093/eurheartj/ehab484)

New recommendations (12)

Recommendations	Class
Risk factors and interventions at the individual level (continued)	
Statin therapy may be considered in persons aged ≤40 years with type 1 or type 2 DM with evidence of TOD and/or an LDL-C level >2.6 mmol/L (100 mg/dL), as long as pregnancy is not being planned.	IIb
In patients with DM at high or very high CVD risk, low-dose aspirin may be considered for primary prevention in the absence of clear contraindications.	IIb
Home-based CR, telehealth, and mHealth interventions may be considered to increase patient participation and long-term adherence to healthy behaviours.	IIb
In patients with HF and major depression, SSRIs, SNRIs, and tricyclic antidepressants are not recommended.	III
In patients with dialysis-dependent CKD who are free of ASCVD, commencing statin therapy is not recommended.	III

High-risk	Patients with DM duration ≥10 years without target organ damage plus any other additional risk factor

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice
(European Heart Journal 2021 – doi:10.1093/eurheartj/ehab484)

Recommendations for the diagnosis and management of PAD in patients with DM

ESC European Society of Cardiology

Recommendations	Class	Level
LEAD management		
In case of CLTI, revascularization is indicated whenever feasible, for limb salvage.	I	C
In patients with DM with CLTI, optimal glycaemic control should be considered to improve foot outcome.	IIa	C
In patients with DM and chronic symptomatic LEAD without a high bleeding risk, a combination of low-dose rivaroxaban (2.5 mg twice daily) and aspirin (100 mg once daily) should be considered.	IIa	B

NEW

ESC Guidelines on Diabetes, pre-diabetes and cardiovascular diseases in collaboration with EASD (European Heart Journal 2019 - doi/10.1093/eurheartj/ehz486)

Περιστατικό 2

- 2.Άνδρας 42 ετών με ιστορικό STEMI υπό rosuvastatin/ezetimibe 40/10 με LDL 60 mg/dl και τριγλυκερίδια 280 mg/dl. Υπάρχει λόγος μείωσης των τριγλυκεριδίων και, αν ναι, με ποιον τρόπο

Triglyceride-Related ASCVD Risk

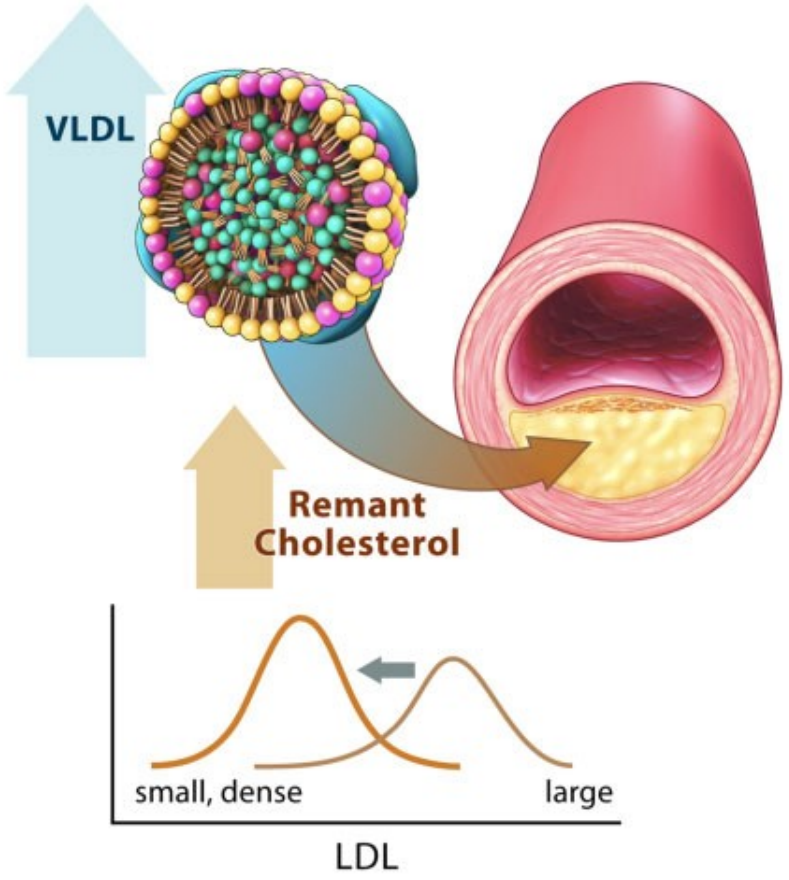
Marker of Cardiometabolic Risk in Insulin Resistance

Associated with:

1. Obesity
2. ↓HDL
3. Hypertension
4. ↑Glycemia
5. Diabetes Risk

Implications: Marker of insulin resistance and cardiometabolic risk. Reductions in triglyceride may indicate reductions in cardiometabolic risk?

Direct Atherogenic Effects



Implications: Lowering triglycerides may clinically reduce risk of atherosclerosis?

Potential therapeutic options: PPAR modulators (fibrates, e.g., pemafibrate) and omega-3 preparations (e.g., icosapent ethyl)

Risk categories

Very high-risk	Subjects with any of the following: • Documented CVD, clinical or unequivocal on imaging. Documented clinical CVD includes previous AMI, ACS, coronary revascularization and other arterial revascularization procedures, stroke and TIA, aortic aneurysm and PAD. Unequivocally documented CVD on imaging includes significant plaque on coronary angiography or carotid ultrasound. It does NOT include some increase in continuous imaging parameters such as intima–media thickness of the carotid artery. • DM with target organ damage such as proteinuria or with a major risk factor such as smoking or marked hypercholesterolaemia or marked hypertension. • Severe CKD (GFR <30 mL/min/1.73 m^2). • A calculated SCORE ≥10%.
High-risk	Subjects with: • Markedly elevated single risk factors, in particular cholesterol >8 mmol/L (>310 mg/dL) (e.g. in familial hypercholesterolaemia) or BP ≥180/110 mmHg. • Most other people with DM (with the exception of young people with type 1 DM and without major risk factors that may be at low or moderate risk). • Moderate CKD (GFR 30–59 mL/min/1.73 m^2). • A calculated SCORE ≥5% and <10%.
Moderate-risk	SCORE is ≥1% and <5% at 10 years. Many middleaged subjects belong to this category.
Low-risk	SCORE <1%.

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European Heart Journal 2016;37:2315–2381-doi:10.1093/eurheartj/ehw106

Patient categories and associated cardiovascular disease risk (2)

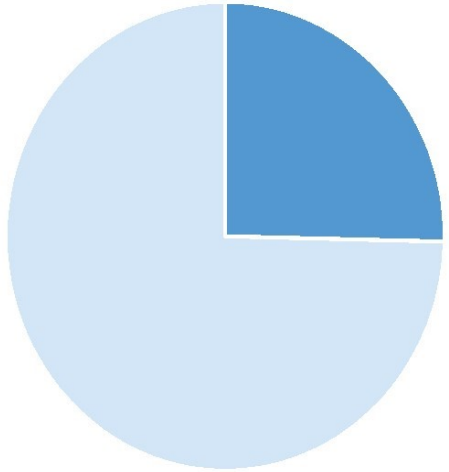
Patient category	Subgroups	Risk categories	CVD risk and therapy benefit estimation
Patients with type 2 diabetes mellitus (continued)			
	Patients with DM with established ASCVD and/or severe TOD: • eGFR <45 mL/min/1.73 m^2 irrespective of albuminuria • eGFR 45-59 mL/min/1.73 m^2 and microalbuminuria (ACR 30 mg/g – 300 mg/g) • Proteinuria (ACR >300 mg/g) • Presence of microvascular disease in at least 3 different sites (e.g. microalbuminuria plus retinopathy plus neuropathy)	**Very high-risk**	Residual 10-year CVD risk estimation after general prevention goals (e.g. with the SMART risk score for established CVD or with the ADVANCE risk score or with the DIAL model). Consider lifetime CVD risk and benefit estimation of risk factor treatment (e.g. DIAL model).
Patients with established ASCVD			
Documented ASCVD, clinical or unequivocal on imaging. Documented clinical ASCVD includes previous AMI, ACS, coronary revascularization and other arterial revascularization procedures, stroke and TIA, aortic aneurysm and PAD. Unequivocally documented ASCVD on imaging includes plaque on coronary angiography or carotid ultrasound or on CTA. It does NOT include some increase in continuous imaging parameters such as intima–media thickness of the carotid artery.	N/A	**Very high-risk**	Residual CVD risk estimation after general prevention goals (e.g. 10-year risk with the SMART risk score for patients with established CVD or 1- or 2-year risk with EUROASPIRE risk score for patients with CHD). Consider lifetime CVD risk and benefit estimation of risk factor treatment (e.g. SMART-REACH model; or DIAL model if diabetes).

Recommendations for drug treatments of patients with hypertriglyceridaemia

Recommendations	Class	Level
Statin treatment is recommended as the first drug of choice for reducing CVD risk in high-risk individuals with hypertriglyceridaemia (triglycerides >2.3 mmol/L [200 mg/dL]).	I	A
In patients taking statins who are at LDL-C goal with triglycerides >2.3 mmol/L (200 mg/dL), fenofibrate or bezafibrate may be considered.	IIb	B
In high-risk (or above) patients with triglycerides >1.5 mmol/L (135 mg/dL) despite statin treatment and lifestyle measures, n-3 PUFAs (icosapent ethyl 2 x 2 g/day) may be considered in combination with a statin.	IIb	B

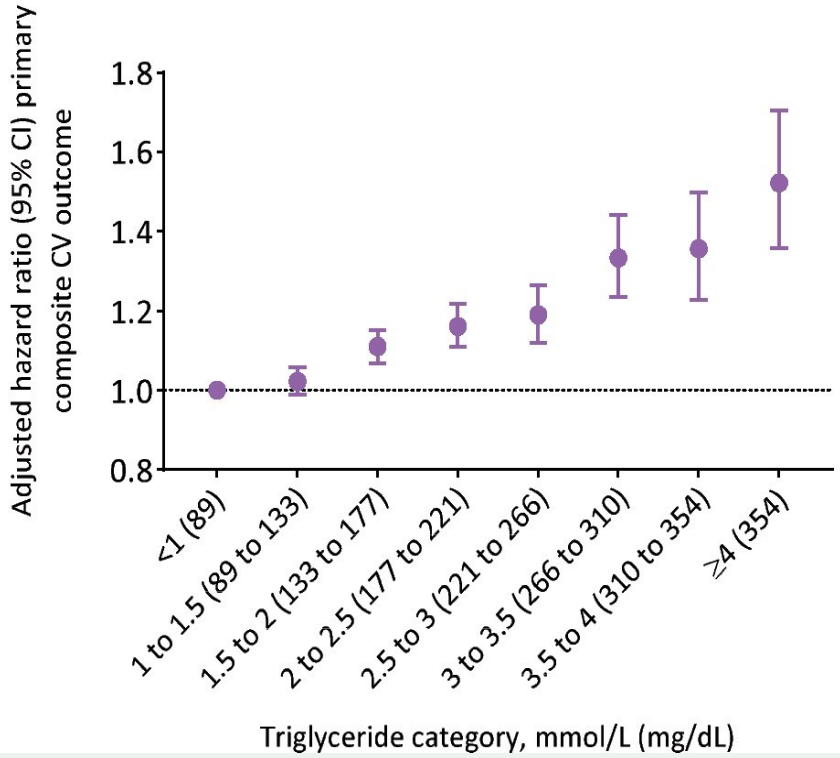
2021 ESC Guidelines on cardiovascular disease prevention in clinical practice
(European Heart Journal 2021 – doi:10.1093/eurheartj/ehab484)

Approximately 1 in 4 patients with ASCVD in the general population may have hypertriglyceridemia and controlled LDLc*



*defined as triglyceride 1.52-5.63 mmol/L (135-499 mg/dL) and LDLc 1.06-2.59 mmol/L (41-100 mg/dL)

Risk of ASCVD events associated with triglyceride level among 196,717 patients with prevalent ASCVD in the population

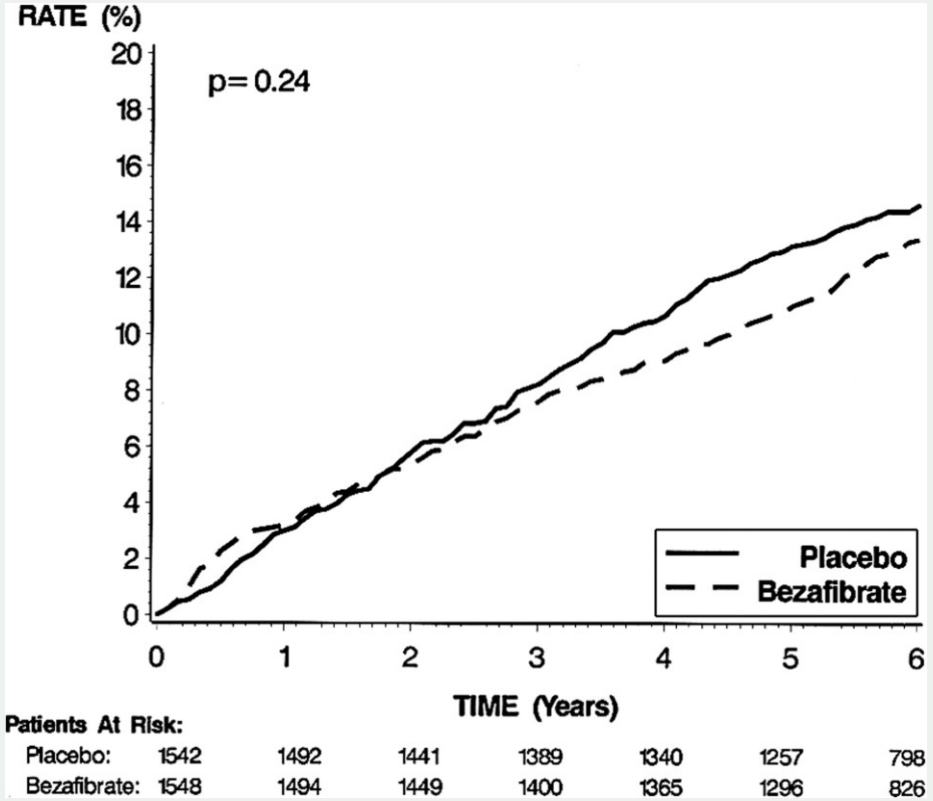


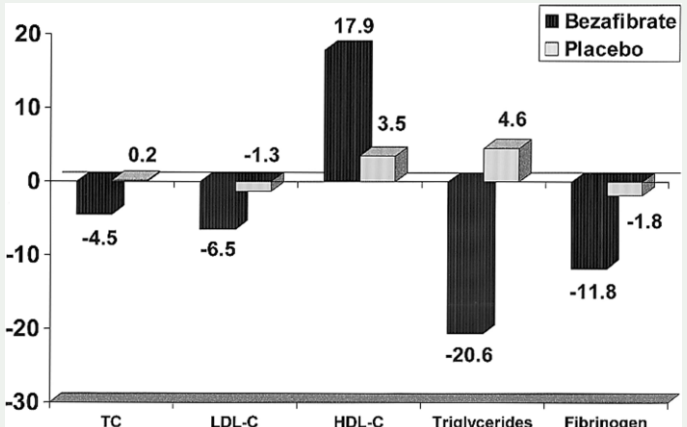
Eur Heart J, Volume 41, Issue 1, 1 January 2020, Pages 86–94, https://doi.org/10.1093/eurheartj/ehz767

The Bezafibrate Infarction Prevention (BIP) Study

Circulation. 2000;102:21-27.

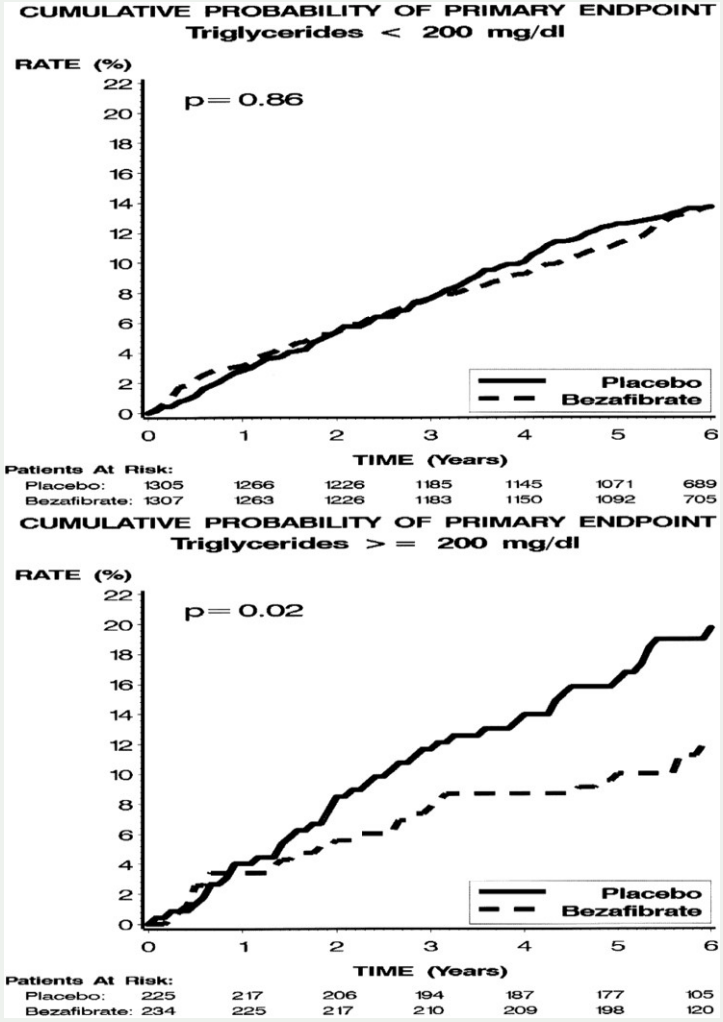
- ***3090 patients with a previous myocardial infarction or stable angina, 6 years f/u***
  - Total cholesterol of 180 to 250 mg/dL, HDL-C <45 mg/dL, triglycerides <300 mg/dL, and low-density lipoprotein cholesterol <180 mg/dL
- were randomized to receive either 400 mg of bezafibrate per day or placebo
- The primary end point was fatal or nonfatal myocardial infarction or sudden death.





The Bezafibrate Infarction Prevention (BIP) Study

- *3090 patients with a previous myocardial infarction or stable angina 6 years f/u*
- *The primary end point was fatal or nonfatal myocardial infarction or sudden death.*



. Circulation. Secondary Prevention by Raising HDL Cholesterol and Reducing Triglycerides in Patients With Coronary Artery Disease , Volume: 102, Issue: 1, Pages: 21-27, DOI: (10.1161/01.CIR.102.1.21)

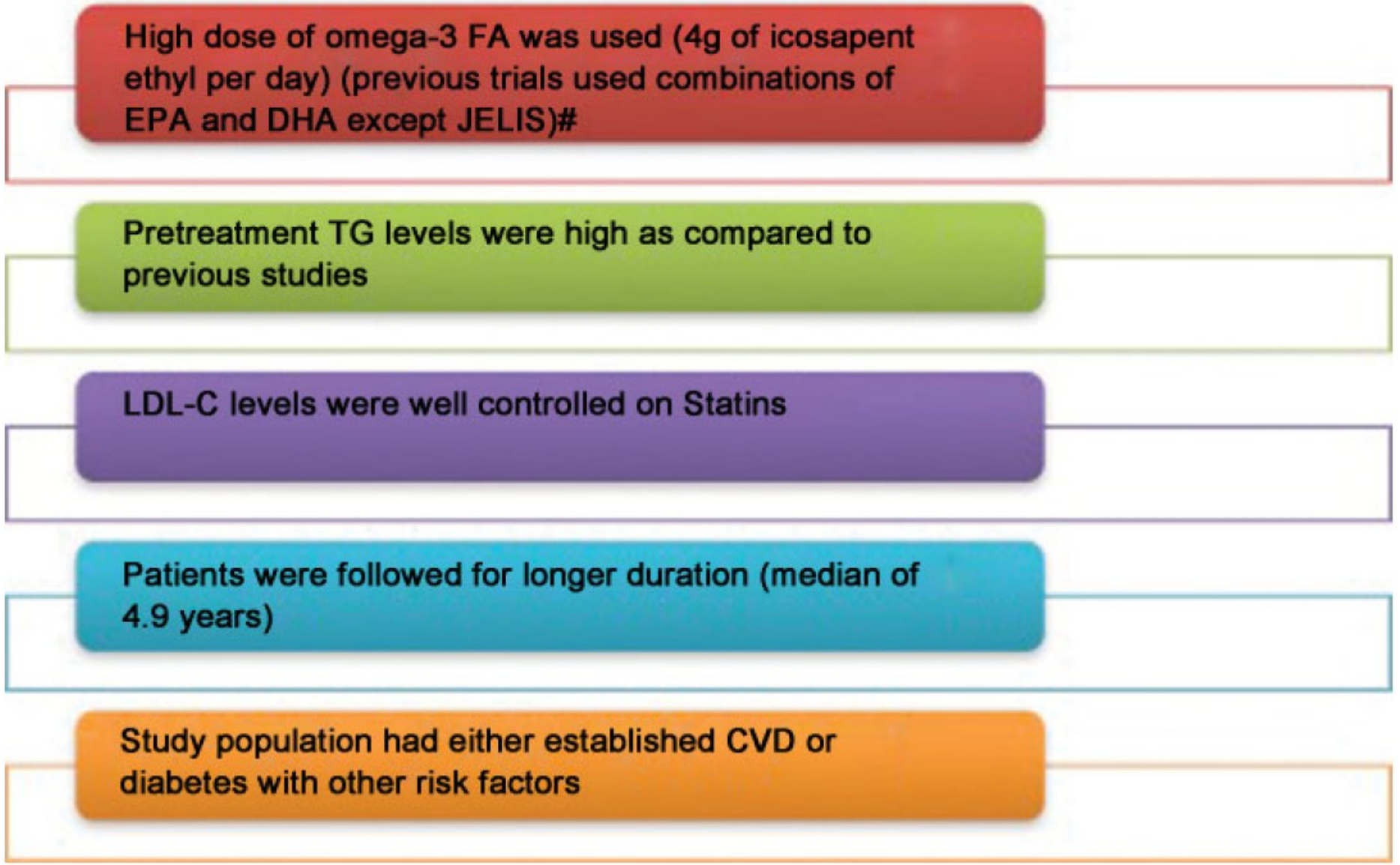
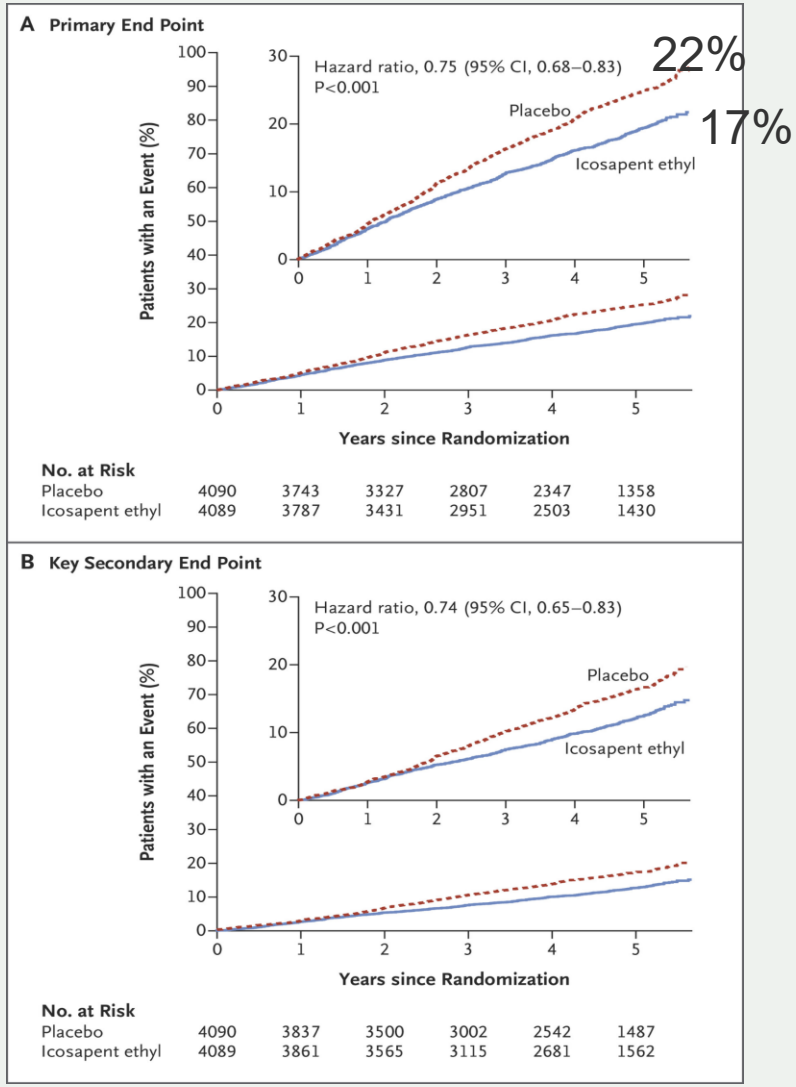


Fig. 3 Salient features of REDUCE-IT. CVD, cardiovascular disease; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; JELIS, Japan EPA Lipid Intervention Study; LDL-C, low-density lipoprotein cholesterol; REDUCE-IT, Reduction of Cardiovascular Events with Icosapent Ethyl-Intervention Trial.

Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia

- **a fasting triglyceride level of 135 to 499** mg per deciliter and a low-density lipoprotein cholesterol level of 41 to 100 mg per deciliter
- 8179 patients were randomly assigned to receive 2 g of icosapent ethyl twice daily (total daily dose, 4 g) or placebo.
- The primary end point was a composite of cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, coronary revascularization, or unstable angina.
- The key secondary end point was a composite of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke. Median F/U of 4.9 years



N Engl J Med 2019; 380:11-22
DOI: 10.1056/NEJMoa1812792

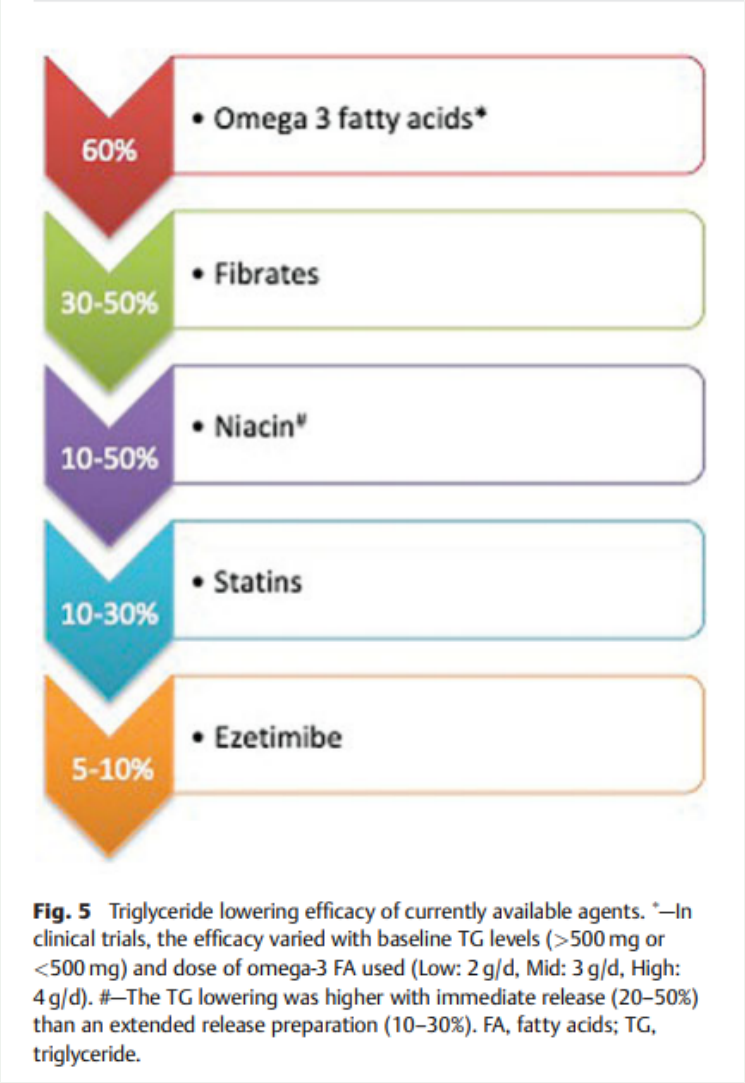


Fig. 5 Triglyceride lowering efficacy of currently available agents. *—In clinical trials, the efficacy varied with baseline TG levels (>500 mg or <500 mg) and dose of omega-3 FA used (Low: 2 g/d, Mid: 3 g/d, High: 4 g/d). #—The TG lowering was higher with immediate release (20–50%) than an extended release preparation (10–30%). FA, fatty acids; TG, triglyceride.

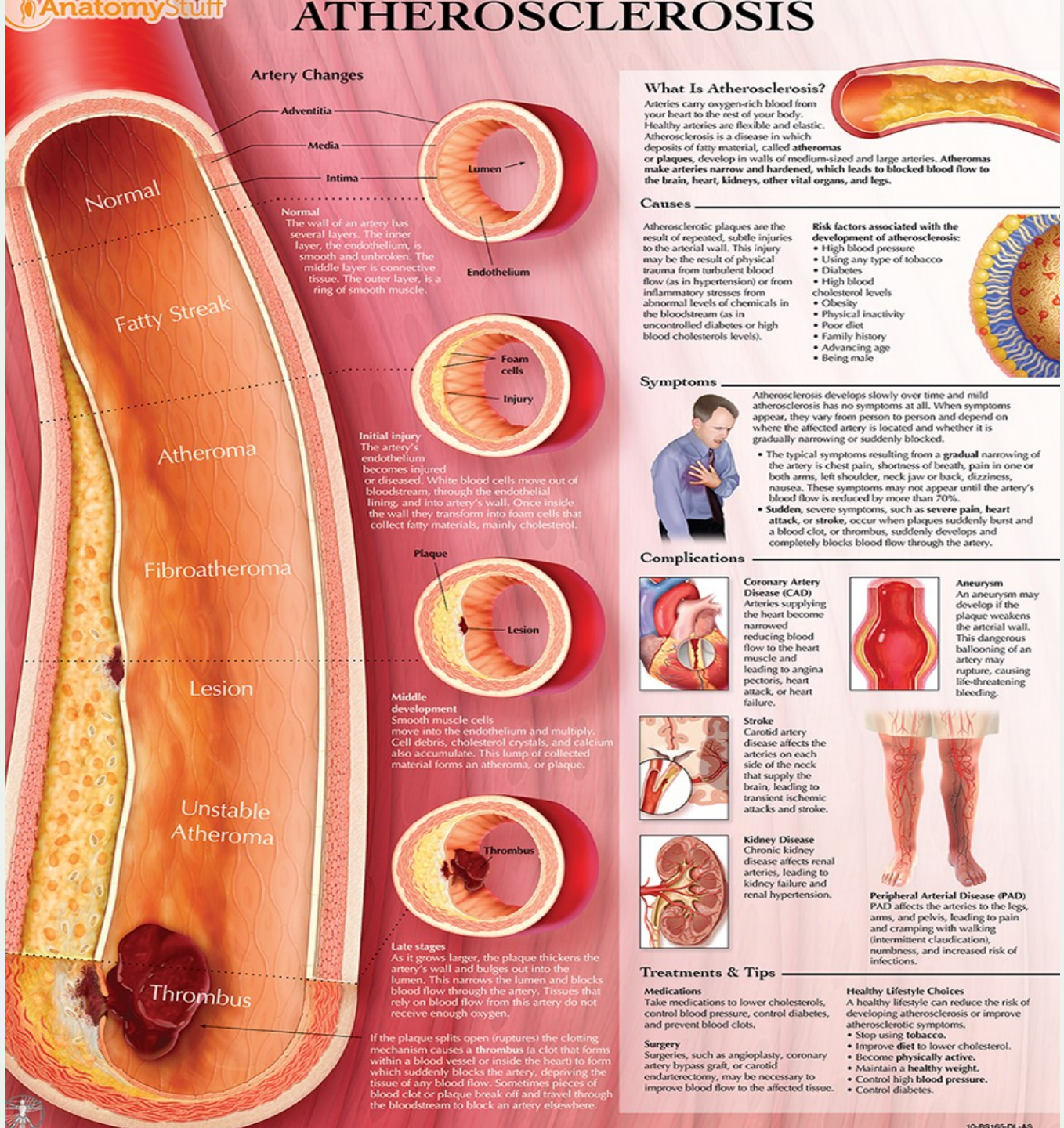
Int J Angiol 2020;29:2–11.

New recommendations (11)

Recommendations	Class
Risk factors and interventions at the individual level (continued)	
In patients with type 2 DM and TOD, the use of an SGLT2 inhibitor or GLP-1RA with proven outcome benefits may be considered to reduce future CVD and total mortality.	IIb
For primary prevention patients at very high risk, but without FH, if the LDL-C goal is not achieved on a maximum tolerated dose of a statin and ezetimibe, combination therapy including a PCSK9 inhibitor may be considered.	IIb
In high-risk (or above) patients with triglycerides >1.5 mmol/L (135 mg/dL) despite statin treatment and lifestyle measures, n-3 PUFAs (icosapent ethyl 2 X 2 g/day) may be considered in combination with a statin.	IIb
Initiation of statin treatment for primary prevention in older people aged ≥70 may be considered, if at high risk or above.	IIb

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice
(European Heart Journal 2021 – doi:10.1093/eurheartj/ehab484)

ATHEROSCLEROSIS



Artery Changes

Normal
The wall of an artery has several layers. The inner layer, the endothelium, is smooth and unbroken. The middle layer is connective tissue. The outer layer, is a ring of smooth muscle.

Initial injury
The artery's endothelium becomes injured or diseased. White blood cells move out of bloodstream, through the endothelial lining, and into artery's wall. Once inside the wall they transform into foam cells that collect fatty materials, mainly cholesterol.

Middle development
Smooth muscle cells move into the endothelium and multiply. Cell debris, cholesterol crystals, and calcium also accumulate. This lump of collected material forms an atheroma, or plaque.

Late stages
As it grows larger, the plaque thickens the artery's wall and bulges out into the lumen. This narrows the lumen and blocks blood flow through the artery. Tissues that rely on blood flow from this artery do not receive enough oxygen.

If the plaque splits open (ruptures) the clotting mechanism causes a **thrombus** (a clot that forms within a blood vessel or inside the heart) to form which suddenly blocks the artery, depriving the tissue of any blood flow. Sometimes pieces of blood clot or plaque break off and travel through the bloodstream to block an artery elsewhere.

What Is Atherosclerosis?

Arteries carry oxygen-rich blood from your heart to the rest of your body. Healthy arteries are flexible and elastic. Atherosclerosis is a disease in which deposits of fatty material, called **atheromas** or **plaques**, develop in walls of medium-sized and large arteries. **Atheromas make arteries narrow and hardened, which leads to blocked blood flow to the brain, heart, kidneys, other vital organs, and legs.**

Causes

Atherosclerotic plaques are the result of repeated, subtle injuries to the arterial wall. This injury may be the result of physical trauma from turbulent blood flow (as in hypertension) or from inflammatory stresses from abnormal levels of chemicals in the bloodstream (as in uncontrolled diabetes or high blood cholesterols levels).

Risk factors associated with the development of atherosclerosis:
- High blood pressure
- Using any type of tobacco
- Diabetes
- High blood cholesterol levels
- Obesity
- Physical inactivity
- Poor diet
- Family history
- Advancing age
- Being male

Symptoms

Atherosclerosis develops slowly over time and mild atherosclerosis has no symptoms at all. When symptoms appear, they vary from person to person and depend on where the affected artery is located and whether it is gradually narrowing or suddenly blocked.

- The typical symptoms resulting from a **gradual** narrowing of the artery is chest pain, shortness of breath, pain in one or both arms, left shoulder, neck jaw or back, dizziness, nausea. These symptoms may not appear until the artery's blood flow is reduced by more than 70%.
- **Sudden**, severe symptoms, such as **severe pain**, **heart attack**, or **stroke**, occur when plaques suddenly burst and a blood clot, or thrombus, suddenly develops and completely blocks blood flow through the artery.

Complications

Coronary Artery Disease (CAD)
Arteries supplying the heart become narrowed reducing blood flow to the heart muscle and leading to angina pectoris, heart attack, or heart failure.

Aneurysm
An aneurysm may develop if the plaque weakens the arterial wall. This dangerous ballooning of an artery may rupture, causing life-threatening bleeding.

Stroke
Carotid artery disease affects the arteries on each side of the neck that supply the brain, leading to transient ischemic attacks and stroke.

Peripheral Arterial Disease (PAD)
PAD affects the arteries to the legs, arms, and pelvis, leading to pain and cramping with walking (intermittent claudication), numbness, and increased risk of infections.

Kidney Disease
Chronic kidney disease affects renal arteries, leading to kidney failure and renal hypertension.

Treatments & Tips

Medications
Take medications to lower cholesterols, control blood pressure, control diabetes, and prevent blood clots.

Surgery
Surgeries, such as angioplasty, coronary artery bypass graft, or carotid endarterectomy, may be necessary to improve blood flow to the affected tissue.

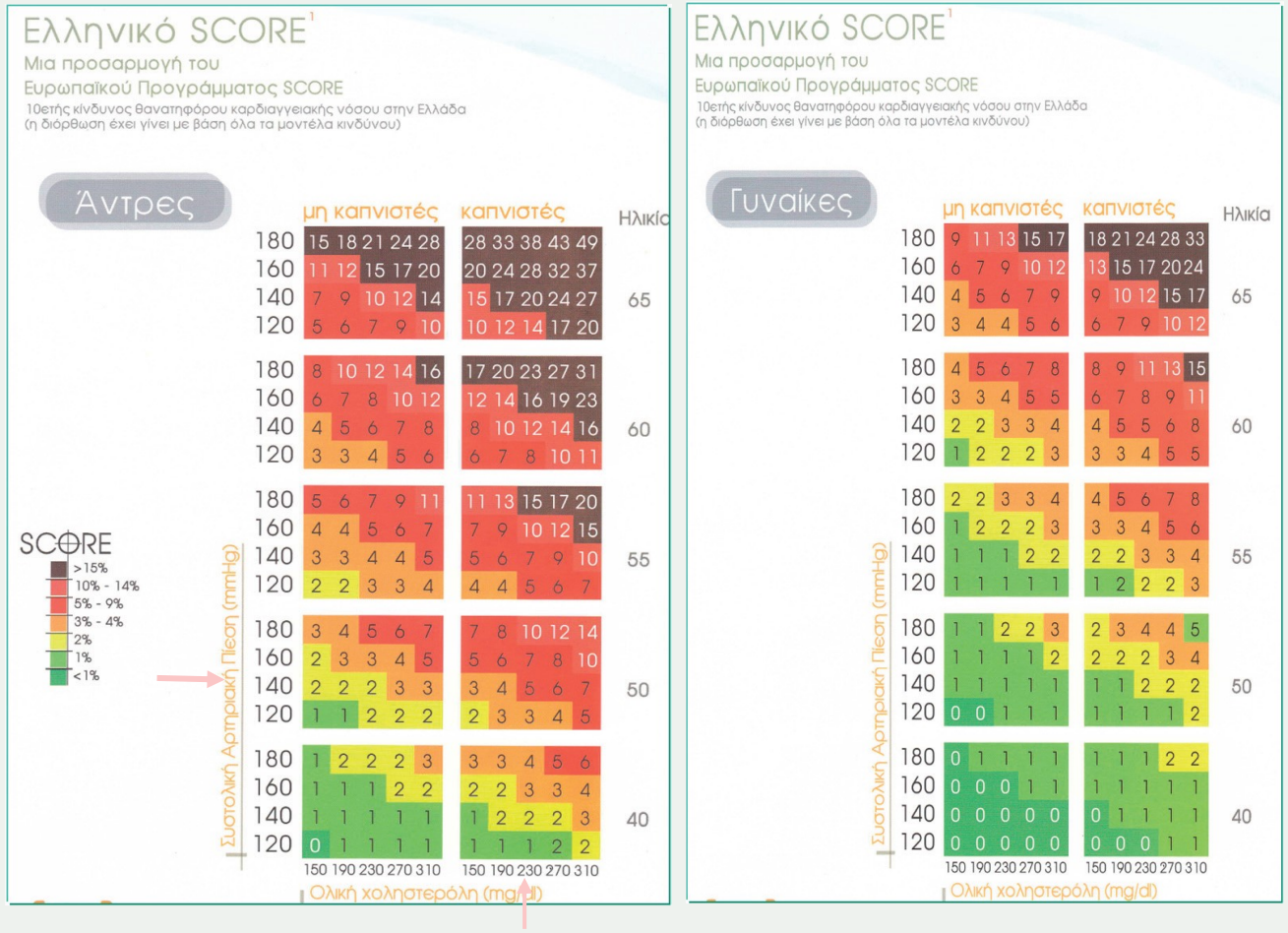
Healthy Lifestyle Choices
A healthy lifestyle can reduce the risk of developing atherosclerosis or improve atherosclerotic symptoms.
- Stop using **tobacco.**
- Improve **diet** to lower cholesterol.
- Become **physically active.**
- Maintain a **healthy weight.**
- Control high **blood pressure.**
- Control diabetes.

Περιστατικό 3

- 3.Ασθενής 45 ετών, καπνιστής με υψηλό Calcium Score.

  Πώς θα τον αντιμετωπίσουμε

Εκτίμηση κινδύνου σε ασθενή με σοβαρές συννοσηρότητες



Ann Rheum Dis 2010;69:325–331. doi:10.1136/ard.2009.113696

Risk categories

Very high-risk	Subjects with any of the following: • Documented CVD, clinical or unequivocal on imaging. Documented clinical CVD includes previous AMI, ACS, coronary revascularization and other arterial revascularization procedures, stroke and TIA, aortic aneurysm and PAD. Unequivocally documented CVD on imaging includes significant plaque on coronary angiography or carotid ultrasound. It does NOT include some increase in continuous imaging parameters such as intima–media thickness of the carotid artery. • DM with target organ damage such as proteinuria or with a major risk factor such as smoking or marked hypercholesterolaemia or marked hypertension. • Severe CKD (GFR <30 mL/min/1.73 m^2). • A calculated SCORE ≥10%.
High-risk	Subjects with: • Markedly elevated single risk factors, in particular cholesterol >8 mmol/L (>310 mg/dL) (e.g. in familial hypercholesterolaemia) or BP ≥180/110 mmHg. • Most other people with DM (with the exception of young people with type 1 DM and without major risk factors that may be at low or moderate risk). • Moderate CKD (GFR 30–59 mL/min/1.73 m^2). • A calculated SCORE ≥5% and <10%.
Moderate-risk	SCORE is ≥1% and <5% at 10 years. Many middleaged subjects belong to this category.
Low-risk	SCORE <1%.

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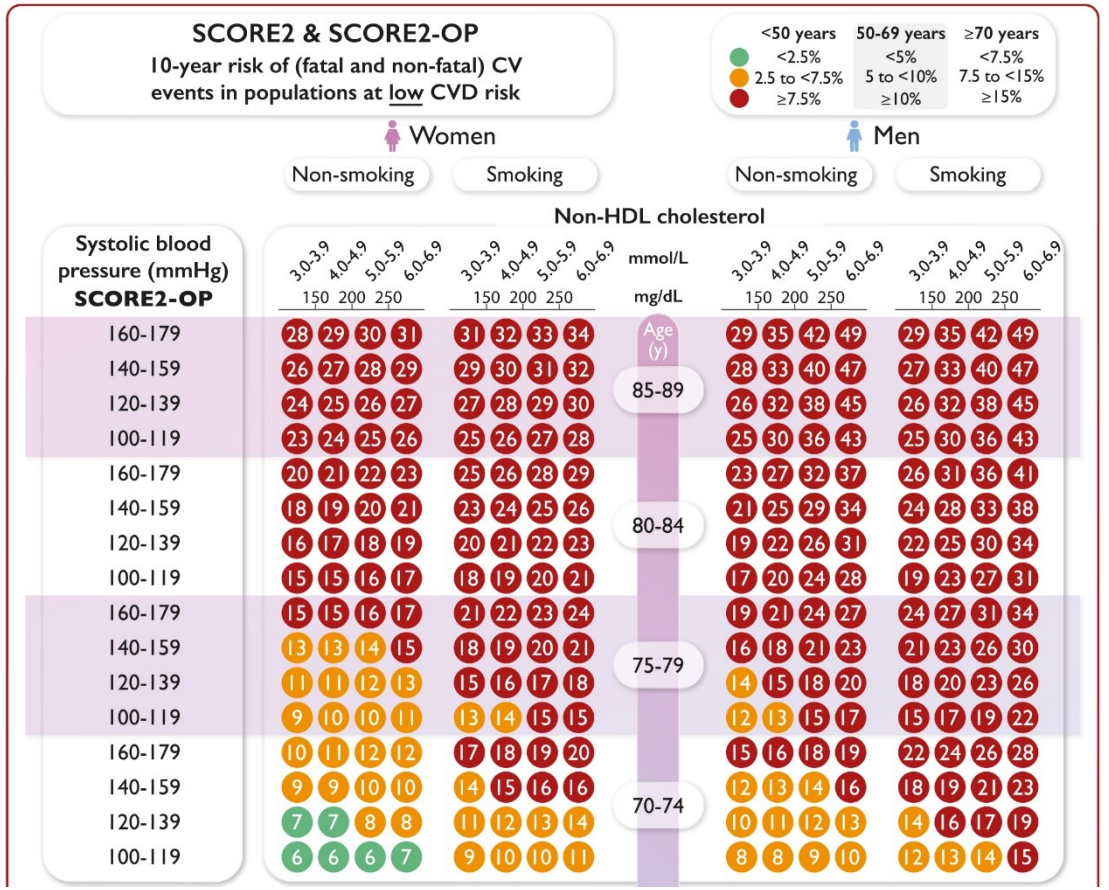
European Heart Journal 2016;37:2315–2381-doi:10.1093/eurheartj/ehw106

New recommendations (1)

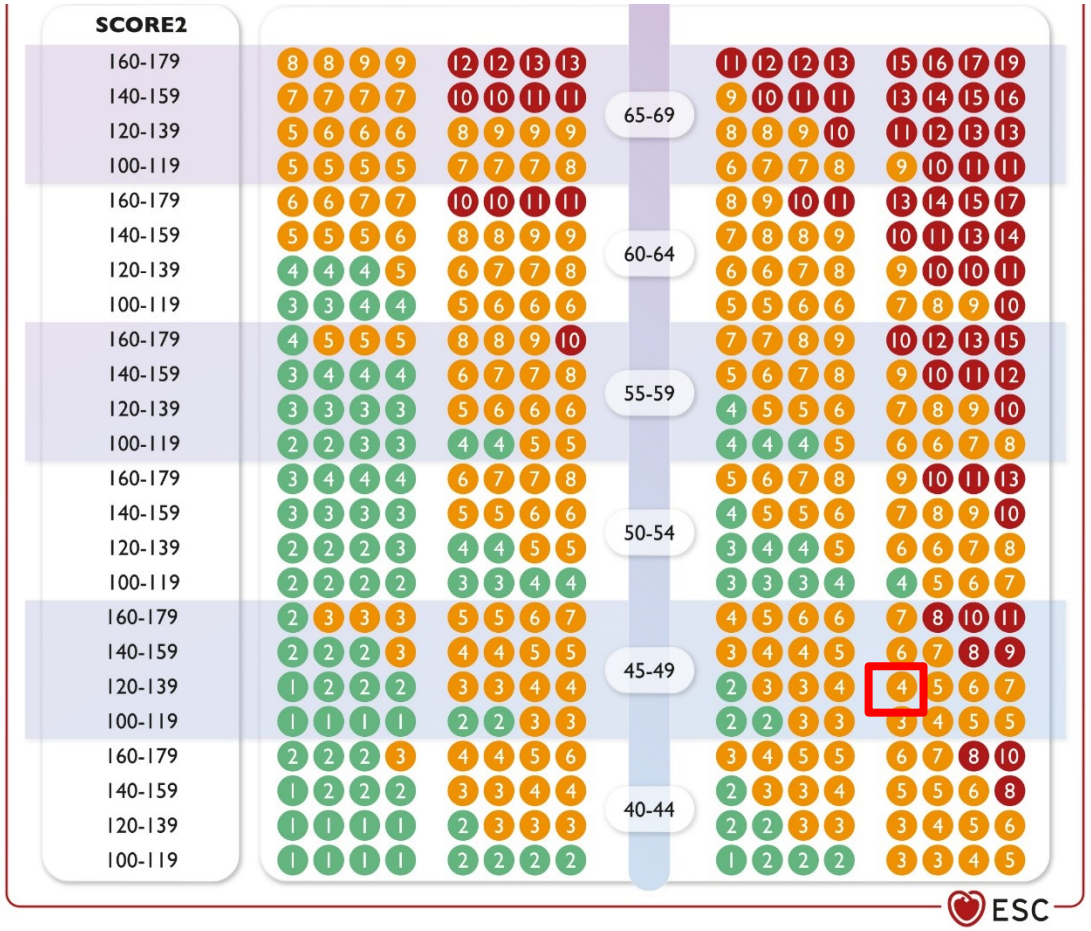
Recommendations	Class
Risk factors and clinical conditions	
In apparently healthy people <70 years of age without established ASCVD, DM, CKD, genetic/rarer lipid or BP disorders, estimation of 10-year fatal and nonfatal CVD risk with SCORE2 is recommended.	I
In apparently healthy people ≥70 years of age without established ASCVD, DM, CKD, genetic/rarer lipid or BP disorder, estimation of 10-year fatal and nonfatal CVD risk with SCORE2-OP is recommended.	I
Patients with established ASCVD and/or DM and/or moderate-to-severe renal disease and/or genetic/rarer lipid or BP disorders are to be considered at high or very high CVD risk.	I



SCORE2 and SCORE2-OP risk chart for fatal and non-fatal (MI, stroke) ASCVD

Low CVD Risk (1)

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice
(European Heart Journal 2021 – doi:10.1093/eurheartj/ehab484)



SCORE2 and SCORE2-OP risk chart for fatal and non-fatal (MI, stroke) ASCVD

Low CVD Risk (2)

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Recommendations for CVD risk assessment (1)

Recommendations	Class	Level
Systematic global CVD risk assessment is recommended in individuals with any major vascular risk factor (i.e. family history of premature CVD, FH, CVD risk factors such as smoking, arterial hypertension, DM, raised lipid level, obesity, or comorbidities increasing CVD risk).	I	C
Systematic or opportunistic CV risk assessment in the general population in men >40 years of age and in women >50 years of age or postmenopausal with no known ASCVD risk factors may be considered.	IIb	C
In those individuals who have undergone CVD risk assessment in the context of opportunistic screening, a repetition of screening after 5 years (or sooner if risk was close to treatment thresholds) may be considered.	IIb	C

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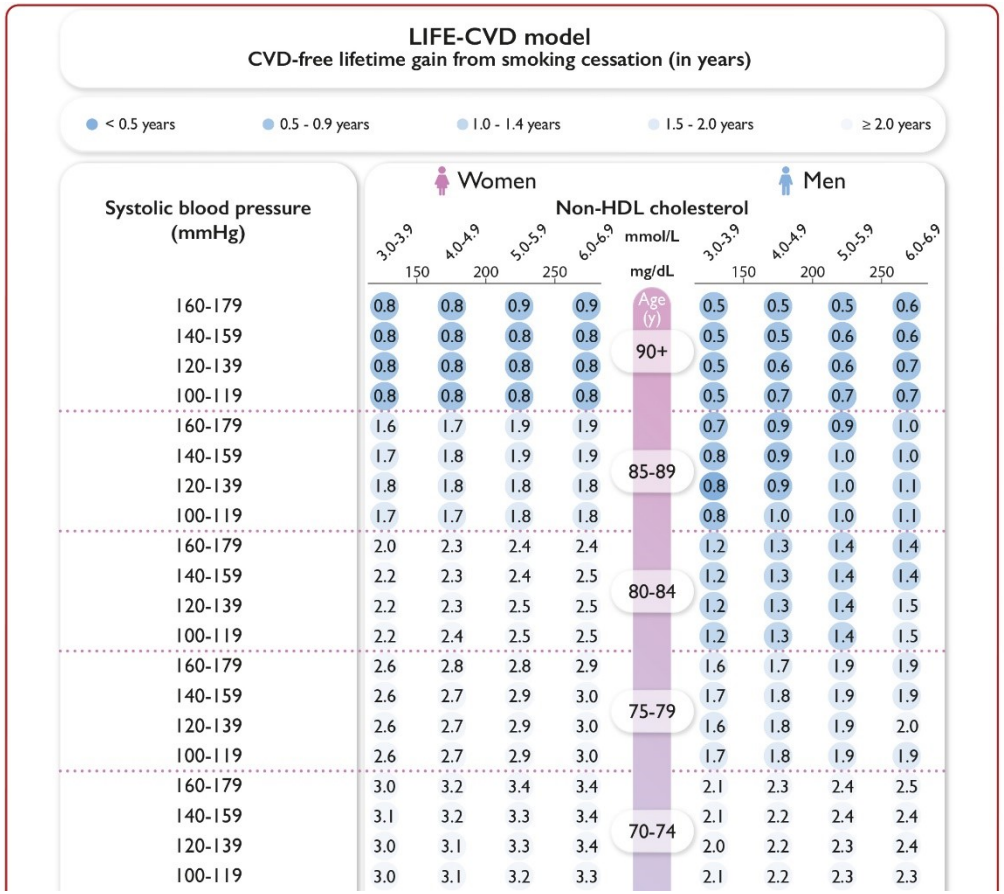

Lifetime CVD benefit from smoking cessation for apparently healthy persons (1)

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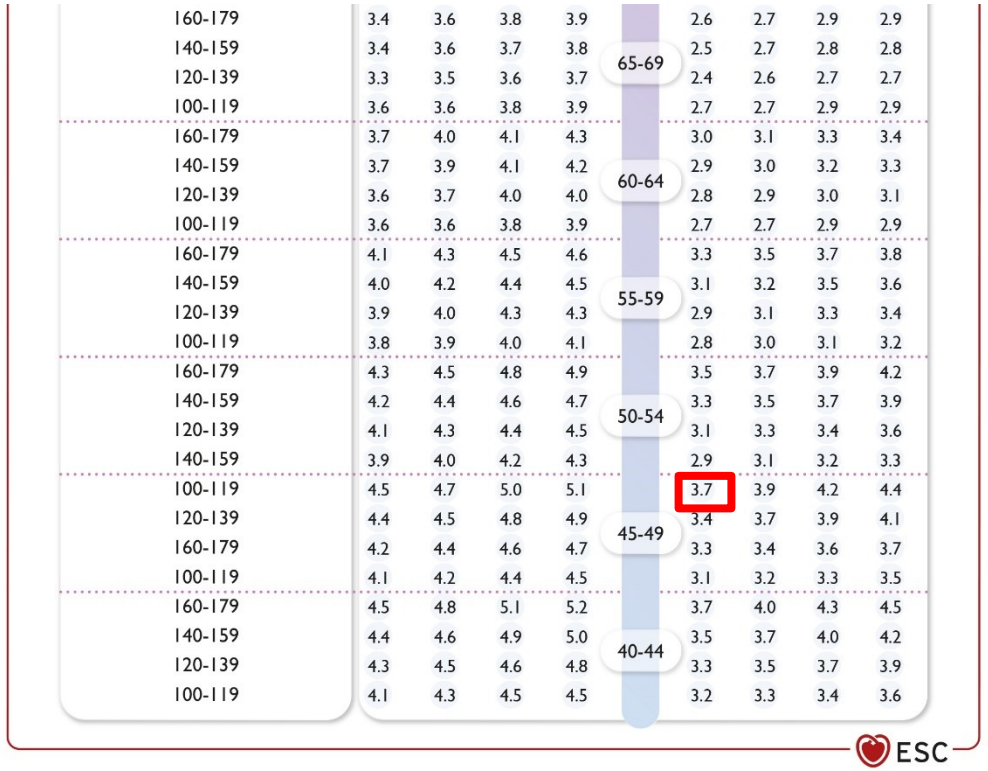
Lifetime CVD benefit from smoking cessation for apparently healthy persons (2)



160-179	3.4	3.6	3.8	3.9		2.6	2.7	2.9	2.9
140-159	3.4	3.6	3.7	3.8	65-69	2.5	2.7	2.8	2.8
120-139	3.3	3.5	3.6	3.7		2.4	2.6	2.7	2.7
100-119	3.6	3.6	3.8	3.9		2.7	2.7	2.9	2.9
160-179	3.7	4.0	4.1	4.3		3.0	3.1	3.3	3.4
140-159	3.7	3.9	4.1	4.2	60-64	2.9	3.0	3.2	3.3
120-139	3.6	3.7	4.0	4.0		2.8	2.9	3.0	3.1
100-119	3.6	3.6	3.8	3.9		2.7	2.7	2.9	2.9
160-179	4.1	4.3	4.5	4.6		3.3	3.5	3.7	3.8
140-159	4.0	4.2	4.4	4.5	55-59	3.1	3.2	3.5	3.6
120-139	3.9	4.0	4.3	4.3		2.9	3.1	3.3	3.4
100-119	3.8	3.9	4.0	4.1		2.8	3.0	3.1	3.2
160-179	4.3	4.5	4.8	4.9		3.5	3.7	3.9	4.2
140-159	4.2	4.4	4.6	4.7	50-54	3.3	3.5	3.7	3.9
120-139	4.1	4.3	4.4	4.5		3.1	3.3	3.4	3.6
140-159	3.9	4.0	4.2	4.3		2.9	3.1	3.2	3.3
100-119	4.5	4.7	5.0	5.1		3.7	3.9	4.2	4.4
120-139	4.4	4.5	4.8	4.9	45-49	3.4	3.7	3.9	4.1
160-179	4.2	4.4	4.6	4.7		3.3	3.4	3.6	3.7
100-119	4.1	4.2	4.4	4.5		3.1	3.2	3.3	3.5
160-179	4.5	4.8	5.1	5.2		3.7	4.0	4.3	4.5
140-159	4.4	4.6	4.9	5.0	40-44	3.5	3.7	4.0	4.2
120-139	4.3	4.5	4.6	4.8		3.3	3.5	3.7	3.9
100-119	4.1	4.3	4.5	4.5		3.2	3.3	3.4	3.6

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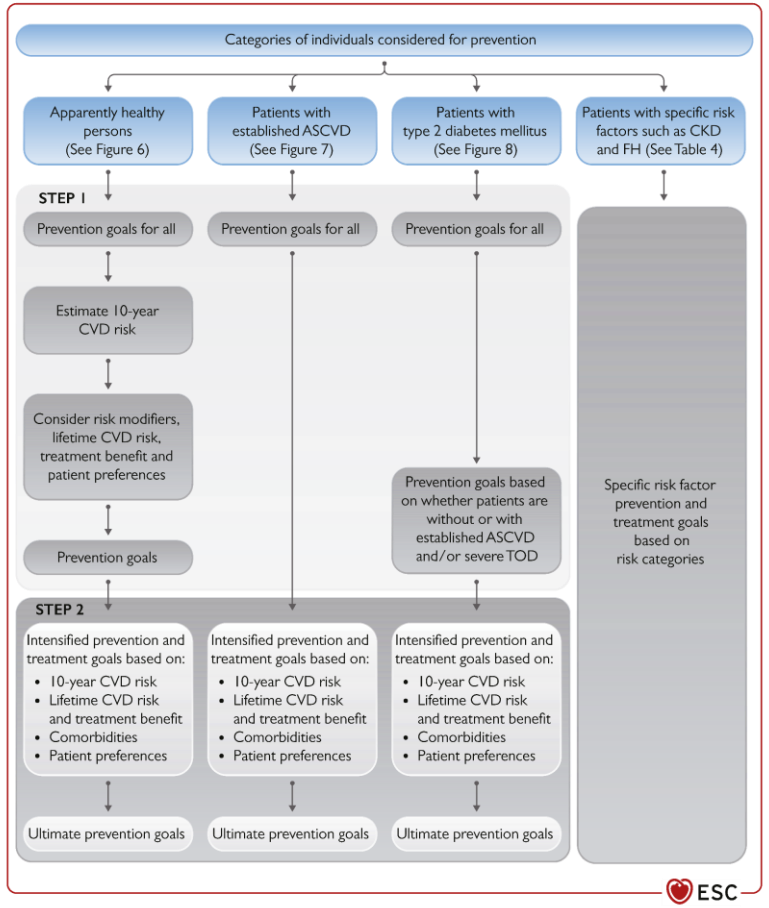

Examples of a stepwise approach to risk stratification and treatment options

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Recommendations for risk modifiers

Recommendations	Class	Level
Stress symptoms and psychosocial stressors modify CVD risk. Assessment of these stressors should be considered.	IIa	C
CAC scoring may be considered to improve risk classification around treatment decision thresholds. Plaque detection by carotid ultrasound is an alternative when CAC scoring is unavailable or not feasible.	IIb	C
Multiplication of calculated risk by RR for specific ethnic subgroups should be considered.[c]	IIa	B
The routine collection of other potential modifiers, such as genetic risk scores, circulating or urinary biomarkers, or vascular tests or imaging methods (other than CAC scoring or carotid ultrasound for plaque determination), is not recommended.	III	B

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Recommendations for cardiovascular imaging for risk assessment of atherosclerotic cardiovascular disease

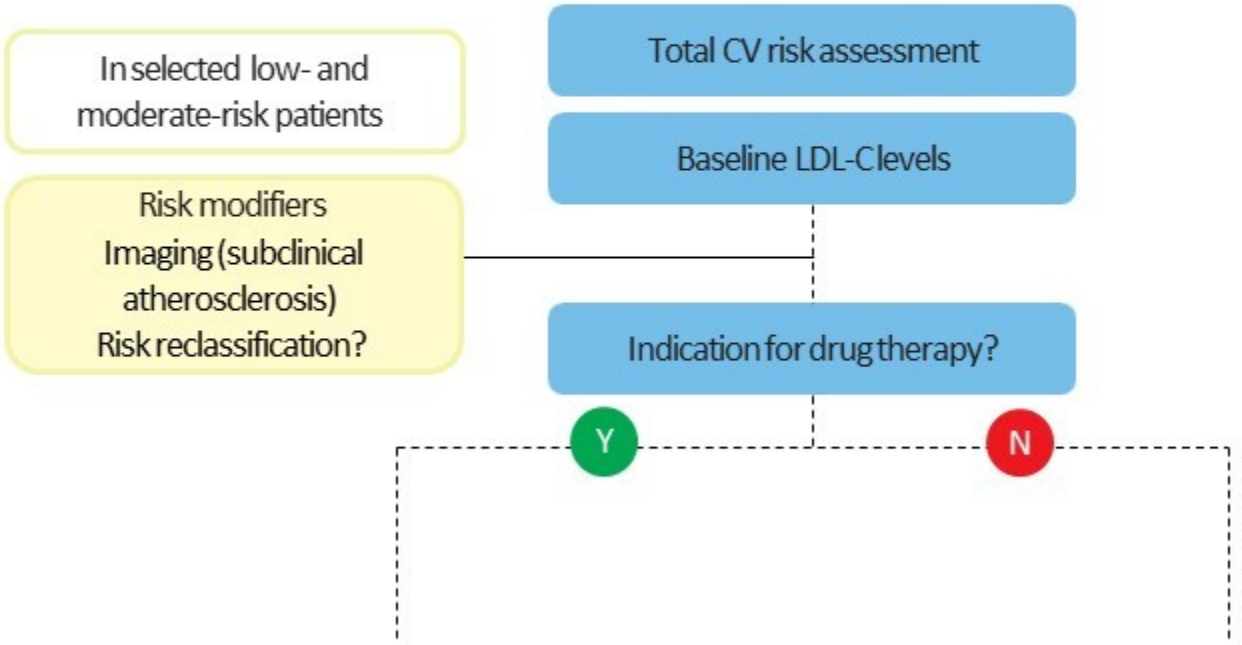
EAS ESC European Society of Cardiology

Recommendations	Class	Level
Arterial (carotid and/or femoral) plaque burden on ultrasonography should be considered as a risk modifier in individuals at low or moderate risk.	IIa	B
CAC score assessment with CT may be considered as a risk modifier in the CV risk assessment of asymptomatic individuals at low or moderate risk.	IIb	B

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Central Illustration Lower panel: Treatment algorithm for pharmacological LDL-C lowering (1)

EAS ESC European Society of Cardiology

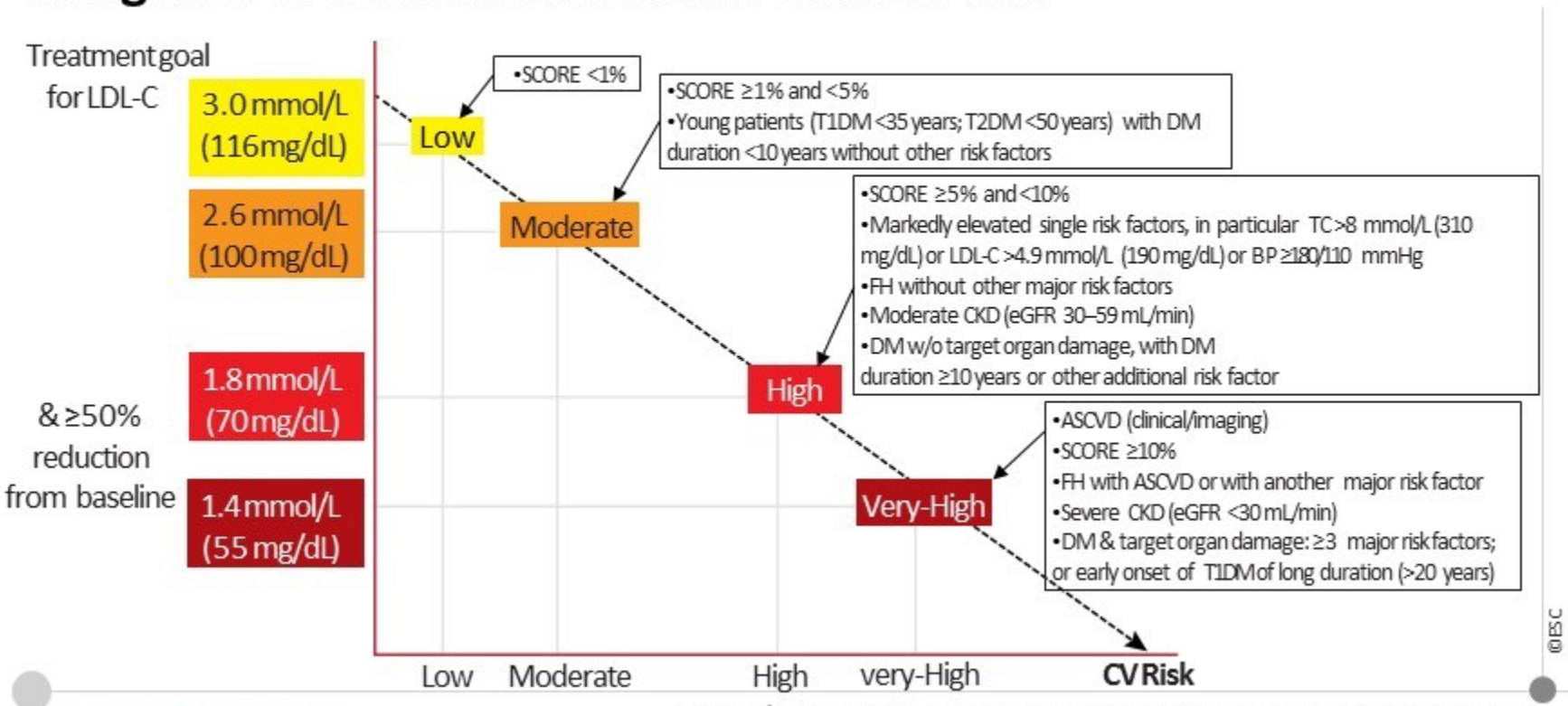


www.escardio.org/guidelines

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Central Illustration Upper panel Treatment goals for low-density lipoprotein cholesterol (LDL-C) across categories of total cardiovascular disease risk

EAS ESC European Society of Cardiology



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2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Cardiovascular disease risk categories based on SCORE2 and SCORE2-OP in apparently healthy people according to age

	<50 years	50-69 years	≥70 years[a]
Low-to-moderate CVD risk: risk factor treatment generally not recommended	<2.5%	<5%	<7.5%
High CVD risk: risk factor treatment should be considered	2.5 to <7.5%	5 to <10%	7.5 to <15%
Very high CVD risk: risk factor treatment generally recommended[a]	≥7.5%	≥10%	≥15%

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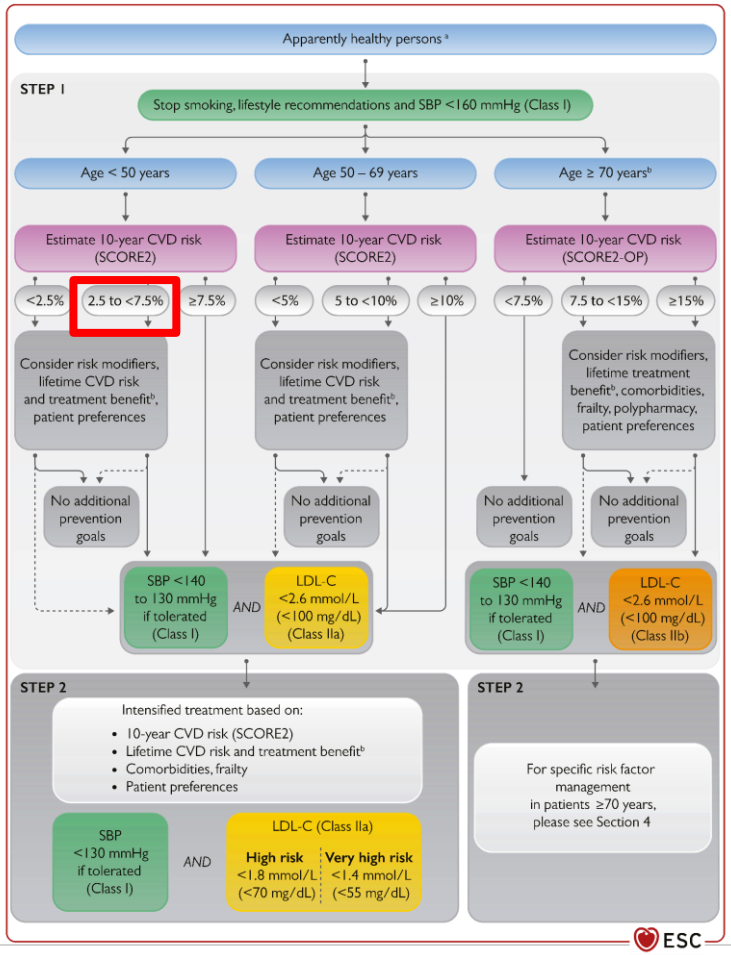
Cardiovascular risk and risk factor treatment in apparently healthy persons



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Recommendations for cardiovascular disease risk estimation (2)

Recommendations	Class	Level
A stepwise treatment-intensification approach aiming at intensive risk factor treatment is recommended for apparently healthy people at high or very high CVD risk, as well as patients with established ASCVD and/or DM, with consideration of CVD risk, treatment benefit of risk factors, risk modifiers, comorbidities, and patient preferences.	I	B
Treatment of ASCVD risk factors is recommended in apparently healthy people without DM, CKD, genetic/rarer lipid, or BP disorders who are at very high risk (SCORE2 ≥7.5% for age under 50; SCORE2 ≥10% for age 50–69; SCORE2-OP ≥15% for age ≥70 years).	I	C
Treatment of ASCVD risk factors should be considered in apparently healthy people without DM, CKD, genetic/rarer lipid, or BP disorders who are at high risk (SCORE2 2.5 to <7.5% for age under 50; SCORE2 5 to <10% for age 50–69; SCORE2-OP 7.5 to <15% for age ≥70 years), taking CVD risk modifiers, lifetime risk and treatment benefit, and patient preferences into account.	IIa	C

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