Coronary Artery Atherosclerosis (Coronary Artery Disease)

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Background

Atherosclerosis is a chronic inflammatory disease of the arteries characterized by the deposition of lipids, particularly cholesterol, along with other substances in the arterial wall. Atherosclerosis involves any elastic or muscular artery (e.g. renal, carotid, cerebral). Coronary artery atherosclerosis is a leading cause of morbidity and mortality globally and the most common cause of death in the USA. Autopsies play a crucial role in documenting and understanding atherosclerosis. The pathological evaluation of atherosclerosis at autopsy provides insights into the severity of the disease, its complications, and in many cases, the underlying cause of death.

Although “coronary artery disease” (CAD) technically refers to any of a number of arterial pathologies (e.g. atherosclerosis, Kawasaki disease, coronary artery dissection, and vasculitis) in this article, as is commonly practiced in medicine, the term CAD will refer to coronary artery atherosclerosis.

Quick Tips at Time of Autopsy

Clinical History

- Risk factors for CAD which can be identified in the history include systemic hypertension, diabetes mellitus, tobacco smoking, hyperlipidemia, and obesity.
- The patient may have a family history of CAD.
- Medications can be clues to the presence of underlying CAD or its risk factors (e.g. statins, antihypertensive drugs, or anti-diabetic medications).
- A history of prior cardiac interventions may be present (e.g., angioplasty, stenting, or bypass surgeries).

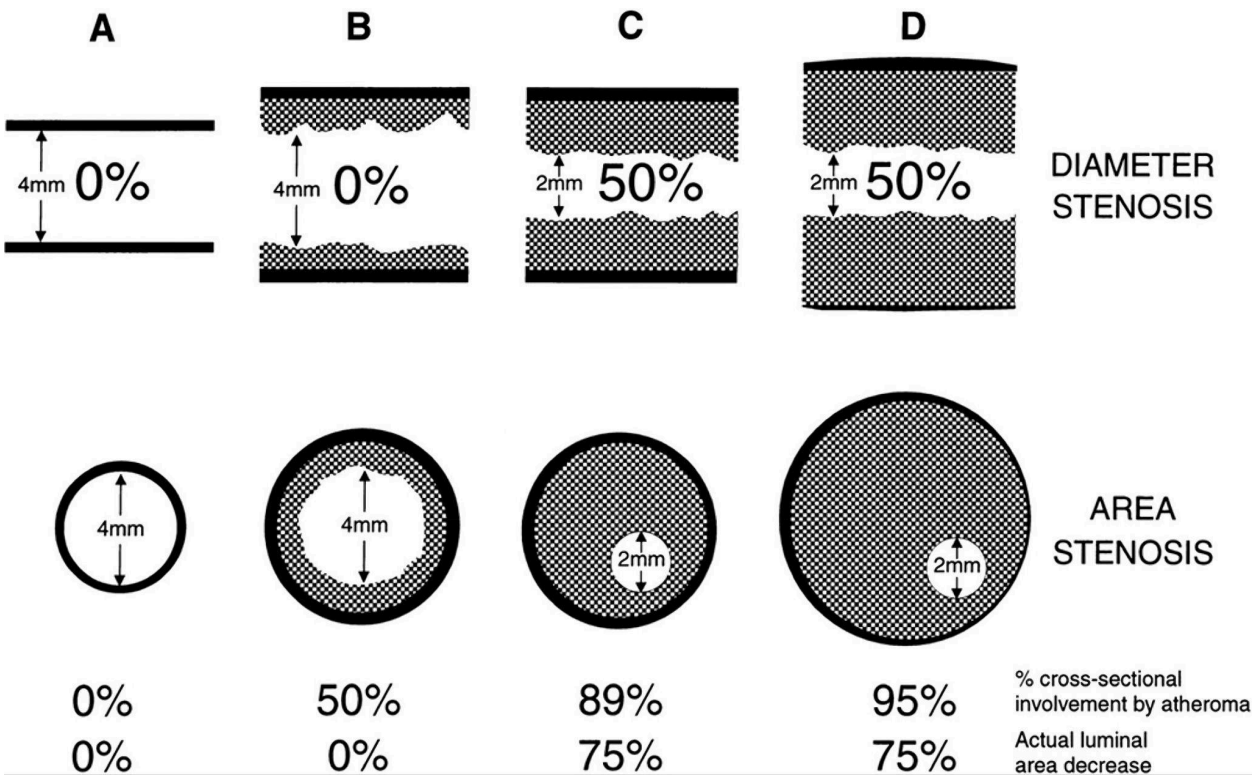

Image: Angiographic and cross-sectional evaluations of the arterial lumen. Top row, angiographic views. The examples (A– D) illustrate how angiography cannot be used to determine the presence or size of atherosclerotic plaques because of arterial remodeling. (Image credit: Fishbein 1996)

External examination

- Frank's Sign (earlobe crease): A diagonal crease in one or both earlobes. It has been suggested in some studies to correlate with CAD, although the specificity and sensitivity of this sign remain a matter of debate.
- Facial xanthomas: Yellowish, soft, raised lipid deposits that often appear on or around the eyelids. They can indicate underlying hyperlipidemia, a risk factor for CAD.
- Tendon Xanthomas: These are raised yellow nodules that appear on the tendons, especially the Achilles tendon. They can be indicative of certain types of inherited hyperlipidemias.
- Arcus Senilis: A gray or white opaque ring around the peripheral cornea. It can be an age-related change but in younger individuals might indicate hyperlipidemia.
- Obesity: While generalized obesity is a known risk factor for CAD, central obesity (increased abdominal girth) is particularly associated with metabolic syndrome and increased cardiovascular risk.

- Scars from previous surgical procedures: such as sternotomy for coronary artery bypass grafting, scars on medial lower extremities at sites of previous venous graft harvest, or the presence of a pacemaker.
- Stigmata of diabetes mellitus and/or peripheral vascular disease including amputated digits or legs.

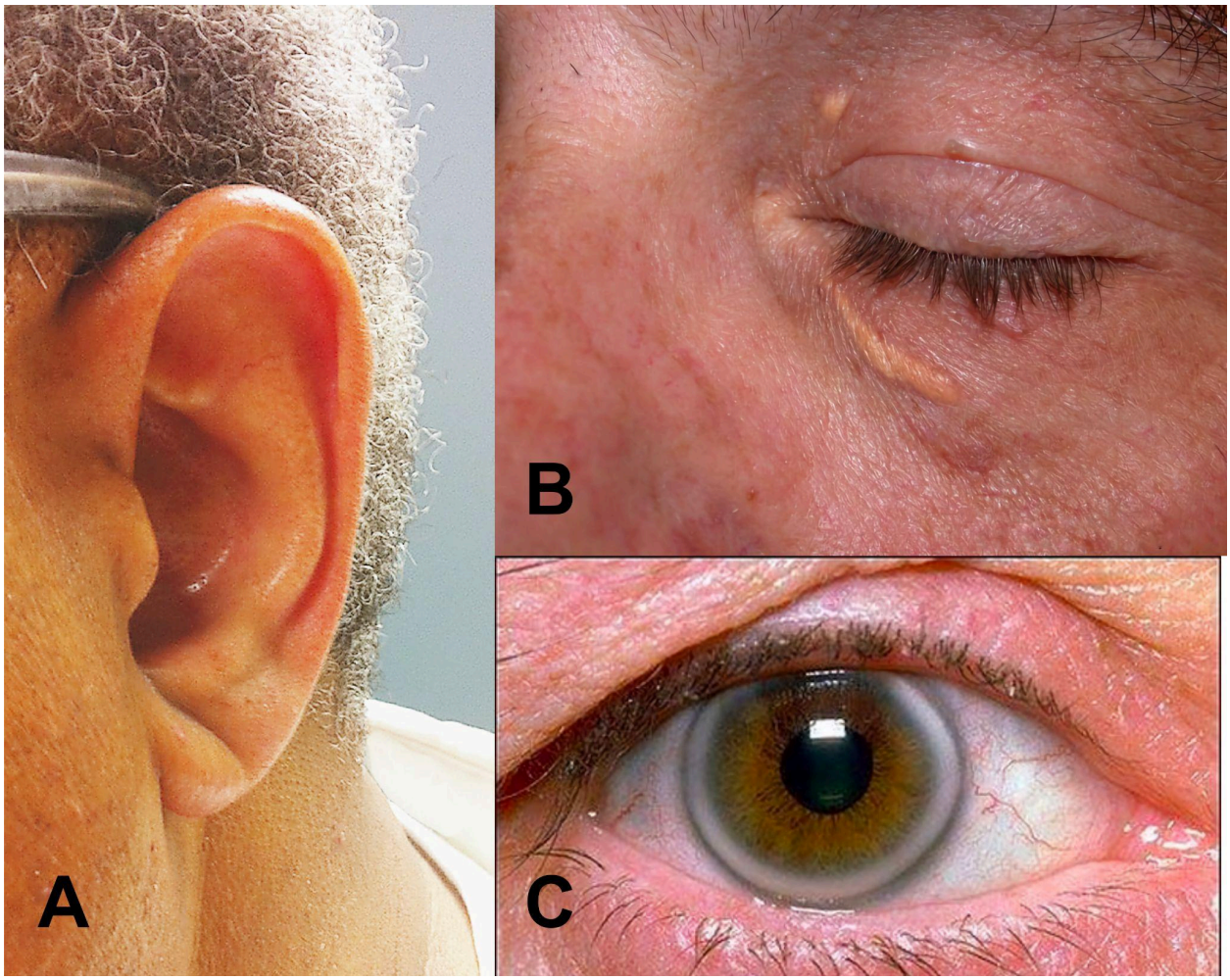

Image: Examples of findings on the gross examination of patients with CAD: Frank's sign (A), facial xanthomas (B), arcus senilis (C). (Image credit: A - George Griffing, B - AOCD, C - Howard).

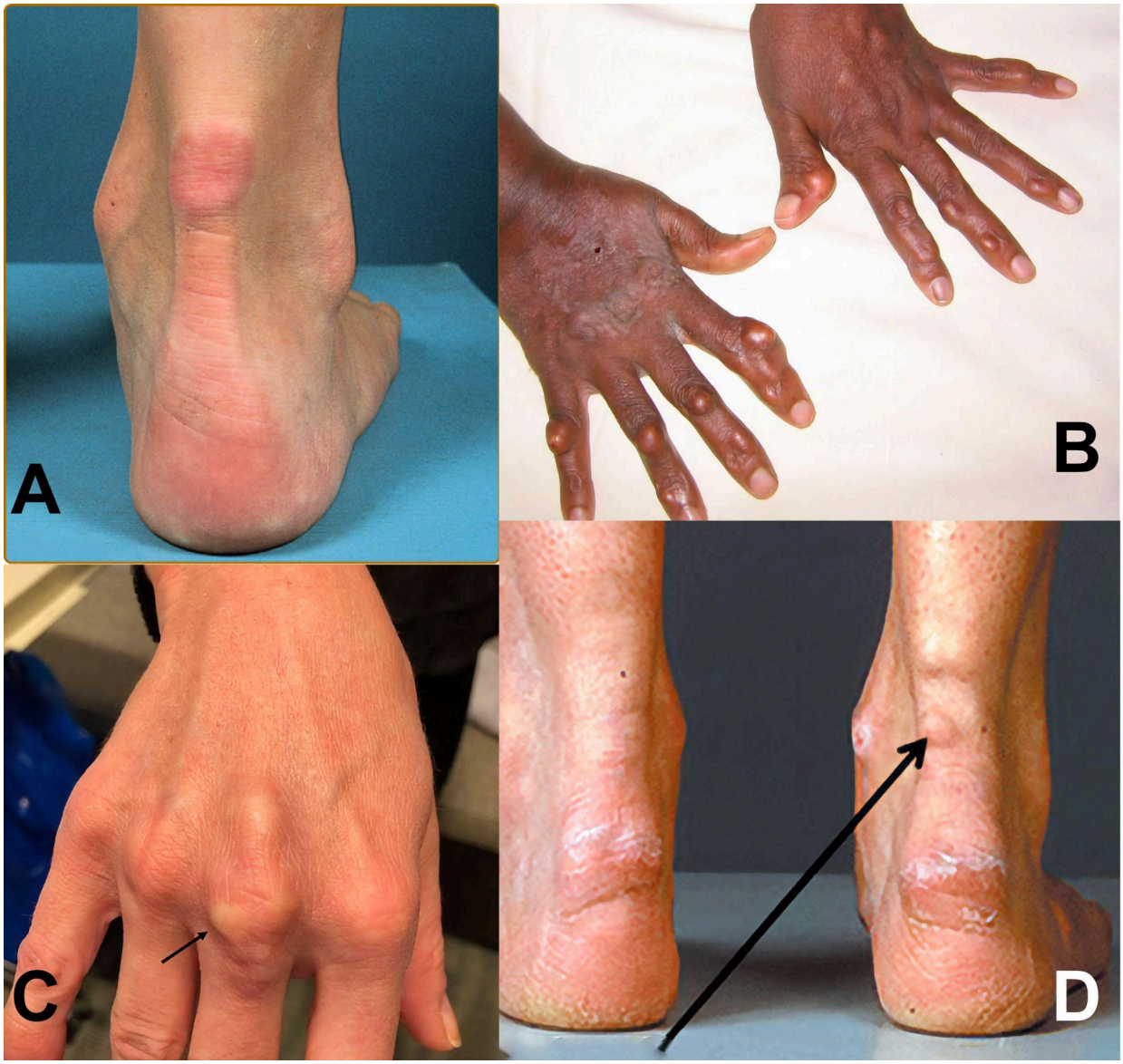

Image: examples of tendon xanthomas on the hands and ankles. They can be less yellow than the facial xanthomas and therefore easily overlooked. (Image credit: A - Goldsmith, B - PCDS, C - Davidson, D - Chicago Foot Clinic).

Gross examination

Heart

- The main epicardial coronary arteries (i.e. left anterior descending, left circumflex, right and posterior descending) should be transversely sectioned at approximately 3-5 mm intervals to identify degrees of atherosclerotic stenosis and/or thrombosis, which should be carefully documented.
- If the arteries are significantly calcified, they should be removed in their entirety from the surface of the heart, fixed in formalin, decalcified, and then sectioned as above with the most affected areas submitted for histology.

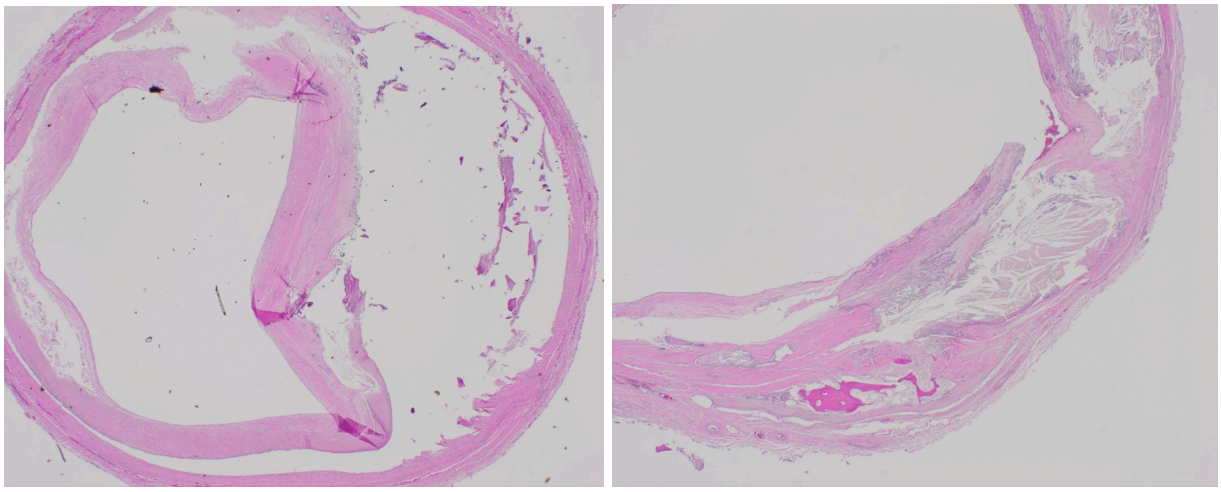

Image: If sections are submitted for histology they should be decalcified prior to sectioning. The artery on the left was not decalcified and the resulting slide over estimates the degree of stenosis as the top of the plaque has been artificially displaces into the lumen. The artery on the right after decal demonstrates appropriate estimates of plaque thickness and stenosis, as well as demonstrating the composition of the plaque (which here includes focal lamellar bone formation within the vessel wall!). (Image source: Meagan Chambers/University of Washington).

- In general, degrees of arterial stenosis can be semiquantitatively graded in the following manner;
    - Slight = <50% stenosis
    - Moderate = 50-75% stenosis
    - Marked = >75% stenosis
- Visual aids are available and should be easily accessible in the autopsy suite to help estimate degrees of stenosis:

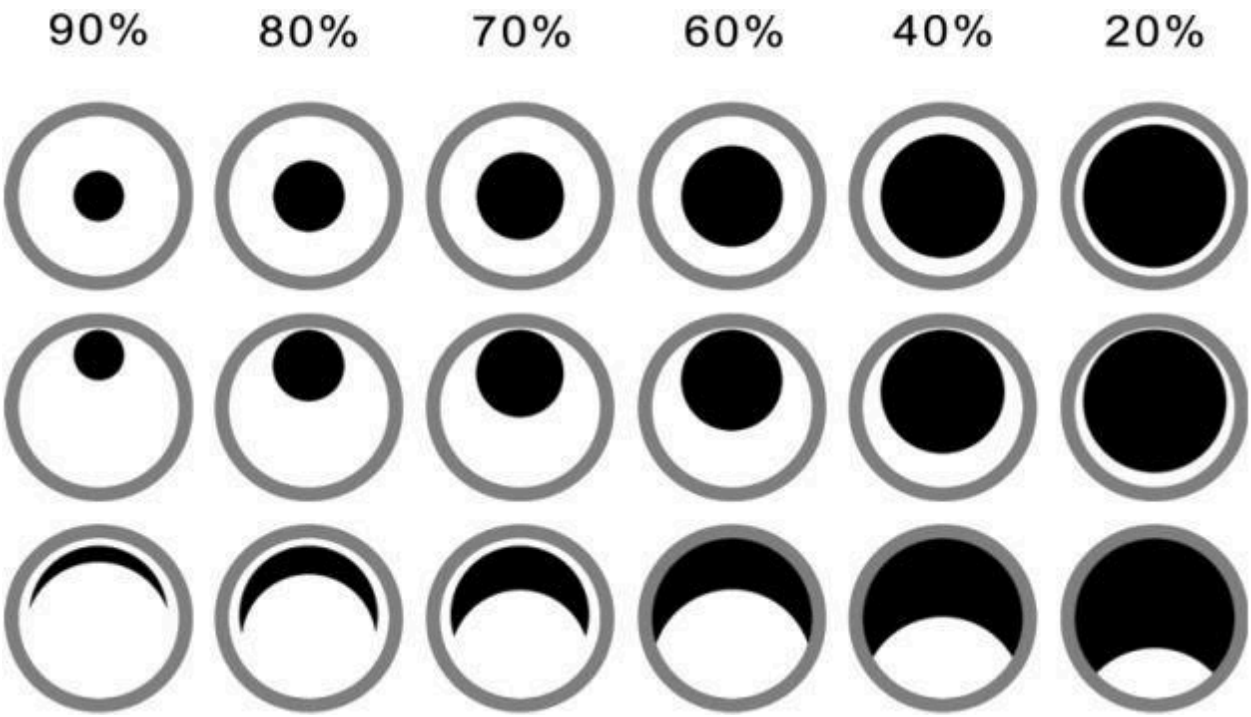

Image: diagram illustrates concentric stenosis (first row) and eccentric stenosis (second and third rows). (Image credit: Barth 2017)

- Patency of endovascular/coronary artery stents can be evaluated by looking from either end; if it does not appear patent (light seen on the other side) consider a stent thrombosis. DO NOT PROBE THE STENT; you may dislodge the thrombus.

Ancillary Testing

- When endovascular stents are present within an area of atherosclerosis, the stented coronary artery segment can be sent to a specialized reference laboratory that can section and histologically evaluate the specimen. Consider this in cases where there is cardiac death within 30 days after stent placement or when light does not travel through the lumen on inspection.

<u>Quick Tips at Time of Histology Evaluation</u>

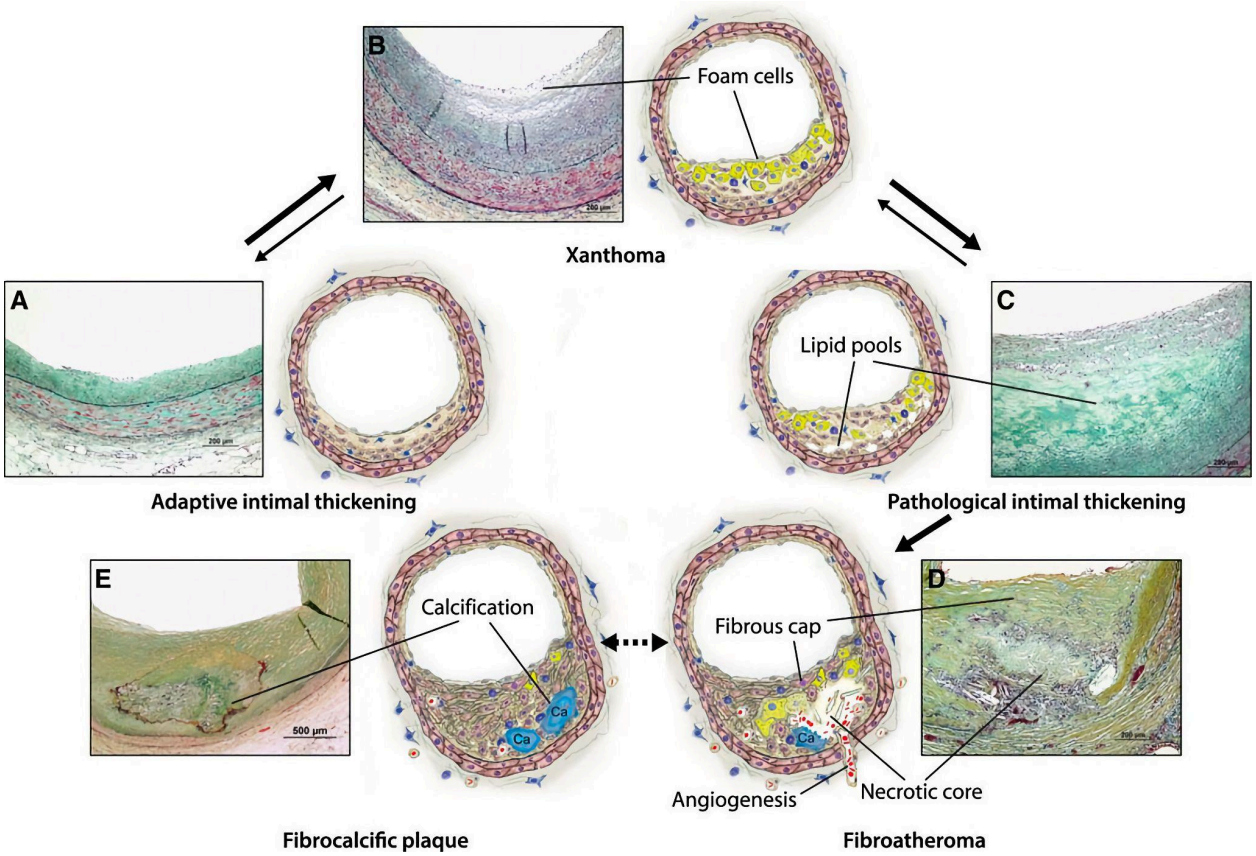

Image: Lesion types of atherosclerosis and a proposed sequence of their development. A, Adaptive intimal thickening characterized by smooth muscle cell accumulation within the intima. B, Intimal xanthoma corresponding to the accumulation of foam cell macrophages within the intima. Pathological intimal thickening in C denotes the accumulation of extracellular lipid pools in the absence of apparent necrosis. D, Fibroatheroma indicating the presence of a necrotic core. The necrotic core and surrounding tissue may eventually be calcified, which forms fibrocalcific plaque shown in E. Because some of the advanced lesion types (fibroatheromas and fibrocalcific plaques) evolve simultaneously in life, their interrelationships are difficult to resolve in autopsy studies. Movat pentachrome stain. (Image credit: Bentzon 2014).

- Macroscopic evaluation of stenosis usually suffices.
- Histologic correlation can
    - Refine and/or confirm the degree of stenosis
    - Clarify atherosclerotic pathology including plaque stability (see below table)
    - Reveal other non-atherosclerotic coronary artery disease (e.g. vasculitis, dissection)
    - Identify/confirm intraluminal thrombosis
- When estimating stenosis histologically, the internal elastic lamina is a good proxy for the original diameter of the non-pathologic artery.

Stable Plaque	**Unstable Plaque**
Thick fibrous cap	Thin fibrous cap (<65 microns)
Heavy calcification	Spotty calcification
Sparse inflammation	Increased inflammation
Lipid poor	Few smooth muscle cells
Proteoglycan*/ glycosaminoglycan rich *proteoglycans will be green on Movat Pentachrome	Large necrotic core (>30% of plaque)
Internal and external laminae and media are non-disrupted	Neovascularization

Table adapted from Revelo, Atherosclerosis - on ExpertPath (login required).

- Unstable plaques are more prone to rupture with or without subsequent thrombosis.

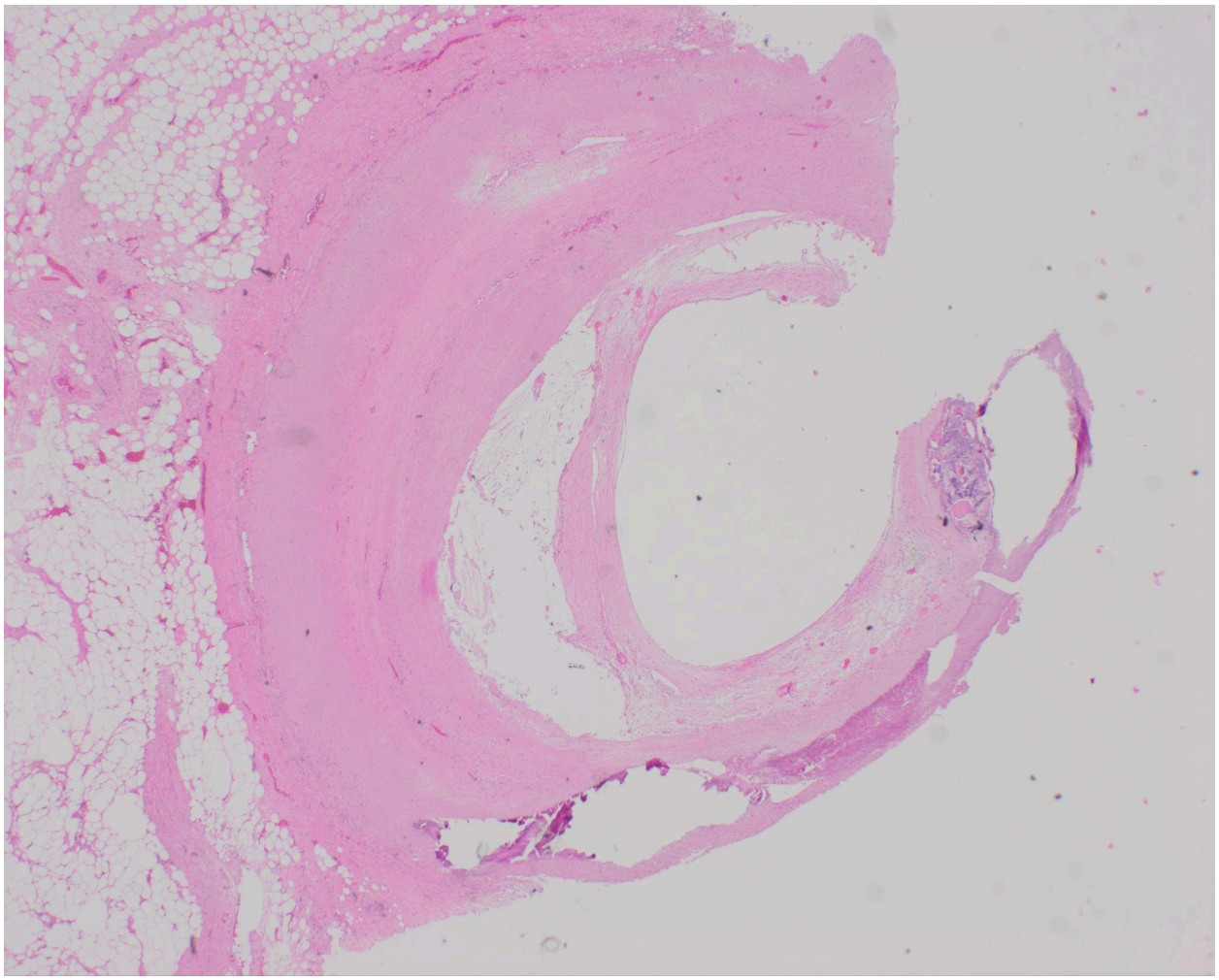

Image: An unstable plaque with thin fibrous cap and necrotic core. (Image credit: Meagan Chambers/University of Washington).

- Areas of suspected thrombosis should be histologically evaluated to confirm the diagnosis and provide a general timeframe of its formation.
    - Of note, the histologic findings do not always correlate with the onset of symptoms and it is possible to find histologic findings, such as necrosis, which necessitate the onset of pathology prior to the onset of clinical symptoms.

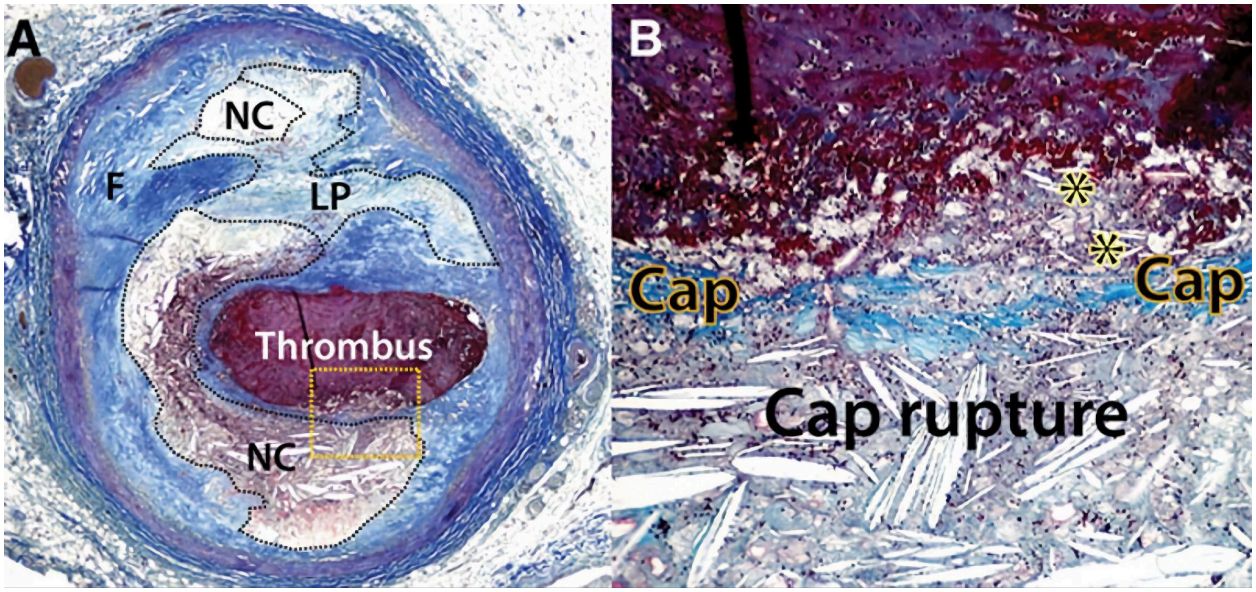

Image: A, Thrombosis caused by plaque rupture. The culprit plaque shown in A is a fibroatheroma consisting of fibrous tissue (F), areas dominated by extracellular lipid pools (LP), and fully developed necrotic cores (NC). B, Large magnification of the orange inset in A. The thin and inflamed fibrous cap covering the large necrotic core has ruptured and core material, including cholesterol crystals (*), has been propelled into the lumen where it can be found at the base of the thrombus. Elastin–trichrome stain (collagen blue). (Image credit: Bentzon 2014).

Quick Tips at Time of Reporting

- In cases of sudden death, acute coronary occlusion can explain arrhythmic death even in the absence of observable ischemic damage.
- The degree of coronary artery stenosis should be interpreted in the context of all autopsy findings, and in general
    - Marked stenosis (>75%) of one or more vessels can be considered lethal as it renders the myocardium ischemic even at rest.
    - Moderate stenosis (50-75%) involving more than one vessel usually requires additional pathology to explain death (e.g. cardiac hypertrophy, physical exertion, emphysema, and other scenarios with increased oxygen demand and decreased perfusion).
    - Slight stenosis (<50%) of one or more vessels is rarely fatal. However, in rare situations, such as significant myocardial tunneling or coronary artery vasospasm, it can contribute to death.
- Although not commonly used, there is an American Heart Association Consensus Criteria for the histological grading of atherosclerotic plaques.
- When composing cause of death statements, risk factors for coronary artery atherosclerosis should be included as contributing factors (as above in the clinical history: systemic hypertension, diabetes mellitus, tobacco smoking, hyperlipidemia, and/or obesity).

- Example cause of death: “Probable cardiac arrhythmia due to myocardial ischemia due to coronary artery atherosclerosis. Contributing factors include diabetes mellitus and obesity.”

Recommended References

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