Cardiac pathology III

Ischemic heart disease

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- IHD is a group of related syndromes resulting from myocardial *ischemia*-an imbalance between cardiac blood supply (perfusion) and myocardial oxygen demand.
- In the vast majority of cases, IHD is due to a reduction in coronary blood flow caused by obstructive atherosclerotic disease.
- Thus, IHD is also frequently called coronary artery disease (CAD).

There are four basic clinical syndromes of IHD

1. *Angina pectoris*
2. *Acute myocardial infarction (MI)*
3. *Chronic IHD*
4. *Sudden cardiac death (SCD)*

- *Angina pectoris* (literally *chest pain*), wherein the ischemia causes pain but is insufficient to lead to death of myocardium.
- angina may be

➢ *stable* (occurring reliably after certain levels of exertion),

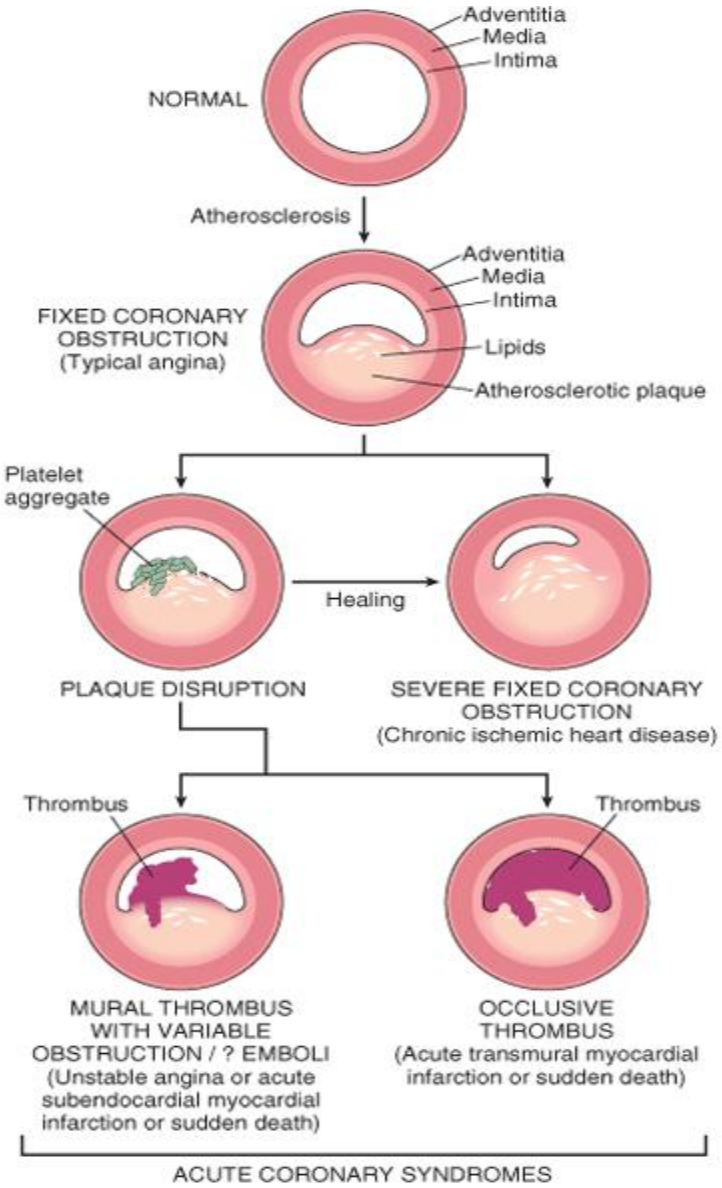
➢ due to vessel spasm *(variant angina or Prinzmetal angina),*

➢ *unstable* (occurring with progressively less exertion or even at rest).

- These syndromes are all relatively **late manifestations** of **coronary atherosclerosis** that **begins early in life** but manifests only after the vascular occlusions reach a critical stage.
- The term ***acute coronary syndrome*** is applied to three catastrophic manifestations of IHD: **unstable angina**, **acute MI**, and **SCD**.

Pathogenesis

- In most cases IHD occurs because of inadequate coronary perfusion relative to myocardial demand.
- This may result from a combination of pre-existing atherosclerotic occlusion of coronary arteries and new superimposed thrombosis and/or vasospasm.



- 70-75% (critical stenosis) causes angina only in the setting of increased demand.
- 90% stenosis can lead to inadequate coronary blood flow even at rest.
- If a coronary artery develops atherosclerotic occlusion at a sufficiently slow rate, it may be able to stimulate collateral blood flow from other major epicardial vessels; such *collateral perfusion* can then protect against MI even in the setting of a complete vascular occlusion.

- Acute coronary occlusions cannot spontaneously recruit collateral flow and will result in infarction.
- Atherosclerotic narrowing may affect one or more of major coronary arteries.
- Clinically significant plaques can be located anywhere but tend to predominate within the first several centimeters of the LAD and LCX, and along the entire length of the RCA.

- Sometimes, secondary branches are also involved (i.e., diagonal branches of the LAD, obtuse marginal branches of the LCX, or posterior descending branch of the RCA).
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- Symptom onset depends: on the extent and severity of fixed atherosclerotic disease and on dynamic changes in coronary plaque morphology.

- **<u>Role of Acute Plaque Change</u>**
- The initiating event is disruption of a plaque due to:
- *Rupture, fissuring, or ulceration* of plaques exposing highly thrombogenic plaque constituents or underlying subendothelial basement membrane.
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- *Hemorrhage into the core of plaques* with expansion of plaque volume and worsening of the luminal occlusion.
- plaque disruption??? (progressively enlarge)

- The events that trigger the abrupt plaque changes are:
- **Intrinsic:**
- large atheromatous
- Thin fibrous cap
- a paucity of smooth muscle cells or an increase in inflammatory cell activity in atherosclerotic lesions is associated with plaque vulnerability.???

- **Extrinsic:**
- Adrenergic stimulation

- Pathologic and clinical studies show that two-thirds of ruptured plaques are ≤50% stenotic before plaque rupture, and 85% have initial stenosis ≤70%.
- ????

Role of Inflammation

- atherosclerosis begins with the interaction of endothelial cells and circulating leukocytes, resulting in T-cell and macrophage recruitment and activation. These cells subsequently drive smooth muscle cell proliferation, with variable amounts of extracellular matrix (ECM) accumulating over an atheromatous core of lipid, cholesterol, calcification, and necrotic debris.
- At later stages, destabilization of atherosclerotic plaque occurs through metalloproteinase secretion.

Role of Thrombus

- Partial vascular occlusion by a newly formed thrombus can wax and wane with time and lead to unstable angina or sudden death.
- partial luminal occlusion by thrombus can compromise blood flow sufficiently to cause a small infarction of the innermost zone of the myocardium (subendocardial infarct).
- Mural thrombus in a coronary artery can also embolize causing distal microinfarcts.
- completely obstructive thrombus can cause a massive MI.
- organizing thrombi produce potent activators of smooth muscle proliferation, which can contribute to the growth of atherosclerotic lesions.

Role of Vasoconstriction

- Vasoconstriction directly compromises lumen diameter; and by increasing local mechanical shear forces, it can potentiate plaque disruption.

Vasoconstriction in atherosclerotic plaques can be stimulated by

1. circulating adrenergic agonists,
2. locally released platelet contents,
3. an imbalance between endothelial cell relaxing factors (e.g., nitric oxide) versus contracting factors (e.g., endothelin)
4. mediators released from perivascular inflammatory cells.

Other Pathologic Processes

- Rarely, processes other than atherosclerosis and superimposed thrombi can compromise coronary perfusion.
- These include
  - **emboli** originating from valve vegetations,
  - coronary **vasculitis**,
  - systemic **hypotension**.
  - Myocardial **hypertrophy** (e.g., hypertrophic cardiomyopathy, see below) can also increase myocardial demand beyond what even relatively normal coronaries can provide.


Thank
you