IHD, Angina & MI

Objectives:

(1) Understand the pathogenesis and clinical consequences of atherosclerosis.

(2) Be able to discuss pathology and complications of ischemic heart diseases with special emphasis on myocardial infarction.

(3) Know how lifestyle modifications can reduce the risk of ischemic heart diseases.

Editing file

Black: original content.
Red: Important.
Light Purple:From Robbin's.
Blue:only found in boys slides.

Green: Boy's doctor notes .
Dark orange: Girl's Doctor notes.
Grey: Explanation.
Pink: Only found in girls slides.

Reviewed by Razan AlRabah & Ibrahim AlDakhil

MED438 KING SAUD UNIVERSITY

Pathology Teamwork 438

Ischemic Heart diseases (IHD)

Definition

A group of closely related conditions/syndromes caused by an imbalance between the myocardial oxygen demand and blood supply.

Causes

"of the imbalance between myocardial oxygen demand and blood supply"

Usually:

decreased coronary artery blood flow (coronary artery disease)

Less common:

vasospasm and vasculitis

The most common cause of IHD is **coronary artery atherosclerosis** "in 90% of cases"

Epidemiology of IHD:

Peak incidence

Male

- 60 years
- Men are more affected than women

Female

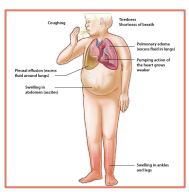
- 70 years[1]

Contributing factors

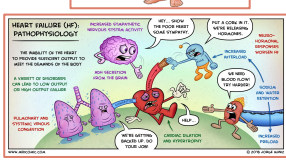
(Risk factors) (same as atherosclerosis)

- Diabetes mellitus
- Hypertension
- Smoking
- Genetic factors (direct or indirect)
- High level of LDL (low density lipoprotein)
- Lack of exercise

Four closely related conditions/syndromes that come under IHD are:



1. **Angina pectoris (chest pain)[2].**
2. **Acute myocardial infarction (MI).**
3. **Sudden cardiac death.**
4. **Chronic ischemic heart disease with congestive heart failure**



1: Estrogen protects females from cardiovascular diseases till 60.

2: reversible and no necrosis

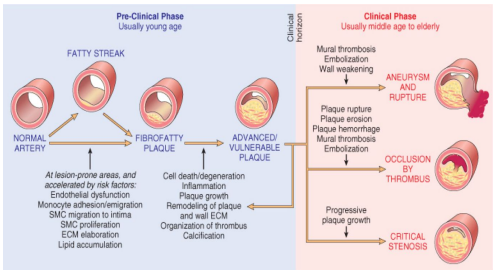
→ cardiac ischemia could also be the result of ***increased demand*** (e.g., with increased heart rate or hypertension); ***diminished blood volume*** (e.g., with hypotension or shock); ***diminished oxygenation*** (e.g., due to pneumonia or CHF); or ***diminished oxygen-carrying capacity*** (e.g., due to anemia or carbon monoxide poisoning).

Ischemic Heart diseases (IHD)

PATHOGENESIS OF IHD

1.Role of critical stenosis or obstruction:

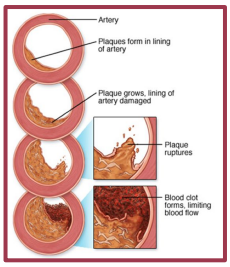
(>=70-75%) of the lumen of one or more coronary arteries by an atherosclerotic plaque)



2.Role of Acute Plaque Change:

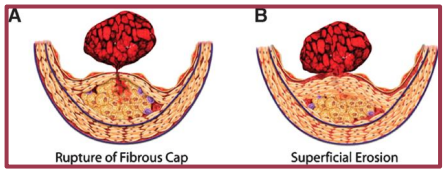
Acute plaque change can cause myocardial ischemia in the form of:

- Sudden cardiac death(in many cases).
- acute myocardial infarction
- unstable angina



Disruption of a mildly **stenosing plaque leading to rupture/ ulceration** which can lead to:

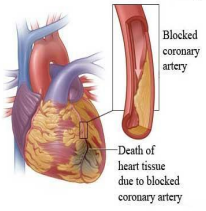
- hemorrhage into the atheroma which will expand in volume.
- exposure of the thrombogenic basement membrane just below the endothelial lining followed by thrombosis



3.Role of Coronary Thrombus:

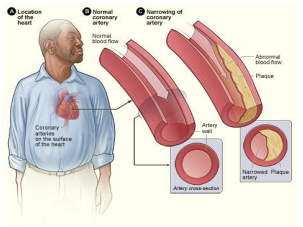
The thrombus superimposed on a disrupted partially occluding plaque can embolize or convert the plaque to either:

A **total occlusion** leading to: **acute transmural MI or sudden death.**



Or a **partial/incomplete/ subtotal occlusion** leading to:

- unstable angina
- acute subendocardial infarction
- sudden cardiac death



4.Role of Vasoconstriction:

Vasoconstriction reduces lumen size and can therefore potentiate plaque disruption

5.Role of Inflammation:

Inflammatory processes play important roles at all stages of atherosclerosis

➔ Pre-clinical phase shows no symptoms

Extra information (Robbins)

Role of acute plaque change	Role of coronary thrombus
➔ Plaques that contain large atheromatous cores or have thin overlying fibrous caps are more likely to rupture and are therefore termed *vulnerable*. ➔ Influences extrinsic to the plaque are also important. Adrenergic stimulation can put physical stress on the plaque by causing hypertension or local vasospasm.	➔ An atheromatous plaque is eroded or suddenly disrupted by endothelial injury, intraplaque hemorrhage, or mechanical forces, exposing subendothelial collagen and necrotic plaque contents to the blood. ➔ Platelets adhere, aggregate, and are activated, releasing thromboxane A2, adenosine diphosphate (ADP), and serotonin—causing further platelet aggregation and vasospasm. ➔ Activation of coagulation by exposure of tissue factor and other mechanisms adds to the growing thrombus. ➔ Within minutes, the thrombus can evolve to completely occlude the coronary artery lumen.
Role of vasoconstriction	**Role of Inflammation**
Stimulated by the following: ➔ Circulating adrenergic agonists. ➔ Locally released platelet contents. ➔ Imbalance between endothelial cell–relaxing factors e.g., nitric oxide), and the contracting factors (e.g., endothelin) due to endothelial dysfunction. ➔ Mediators released from perivascular inflammatory cells.	➔ It begins with the interaction of endothelial cells and circulating leukocytes, resulting in T-cell and macrophage recruitment and activation. ➔ These cells drive subsequent smooth muscle cell accumulation and proliferation, with associated matrix production, superimposed on an atheromatous core of lipid, cholesterol, calcification, and necrotic debris. ➔ At later stages, destabilization of atherosclerotic plaque can occur through macrophage metalloproteinase (enzyme that contributes to plaque rupture, atherothrombosis & MI) secretion.

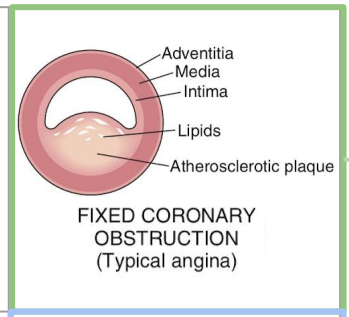
Ischemic Heart diseases (IHD)

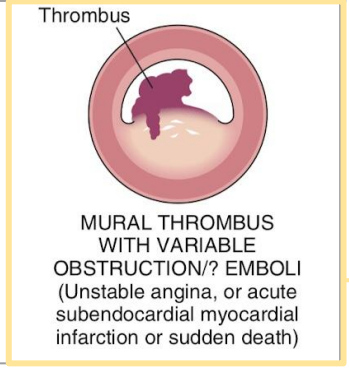
Summary of the pathogenesis of IHD:

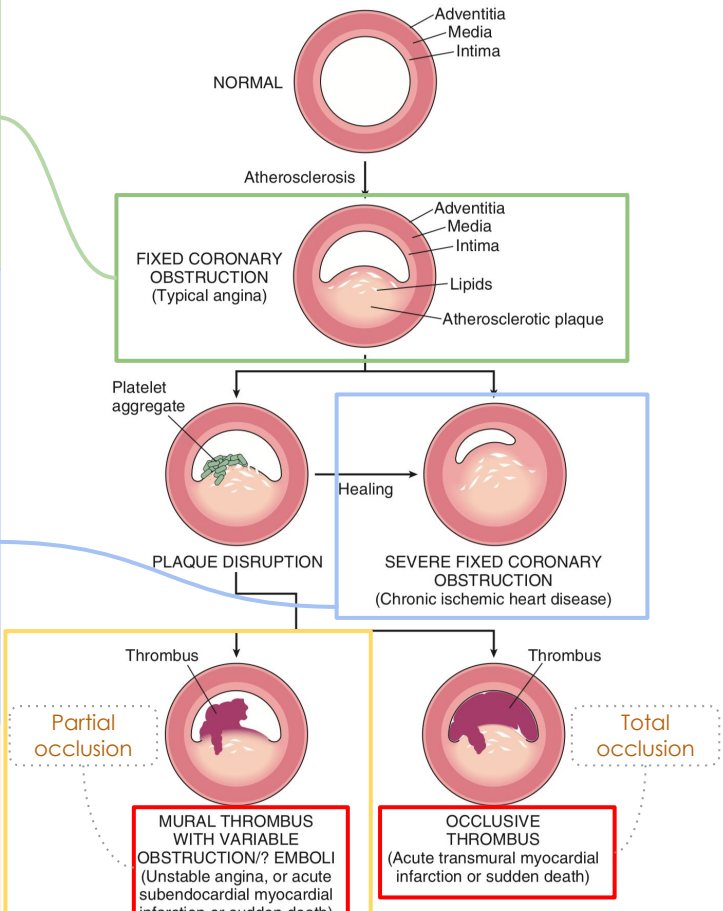
Fixed obstructions that occlude **less than 70%** of a coronary vessel lumen typically are asymptomatic, even with exertion

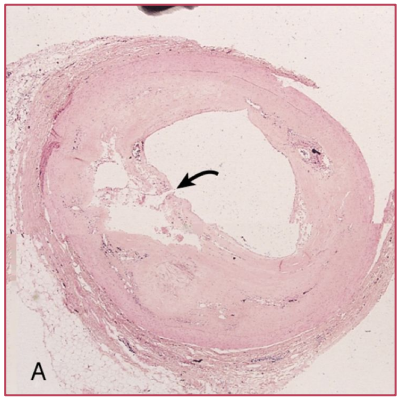
Lesions that occlude **more than 70%** of a vessel lumen—resulting in so-called "critical stenosis" generally cause symptoms in the setting of increased demand; with critical stenosis, certain levels of exertion predictably cause chest pain, and the patient is said to have stable angina.

A fixed stenosis that occludes **90% or more** of a vascular lumen can lead to inadequate coronary blood low with symptoms even at rest—one of the forms of unstable angina

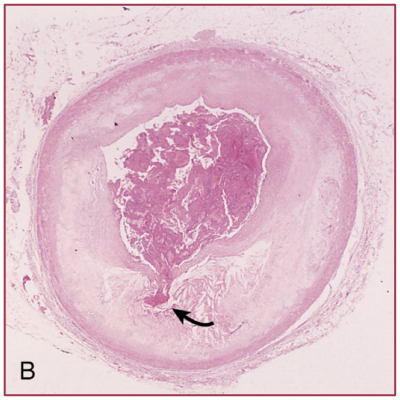




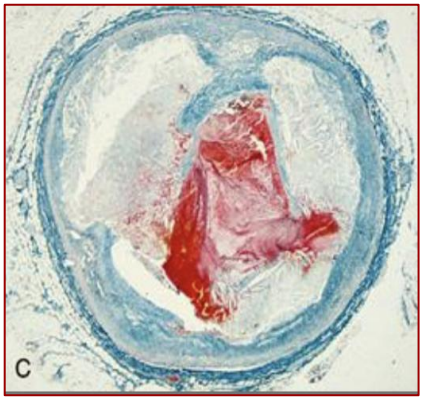




A. Plaque rupture without superimposed thrombus in a patient who died suddenly.



B. Acute coronary thrombosis superimposed on an atherosclerotic plaque with focal disruption of the fibrous cap, triggering fatal myocardial infarction.



C. Massive plaque rupture with superimposed thrombus, also triggering a fatal myocardial infarction(special stain highlighting fibrin in red)

Angina pectoris

Helpful video

Definition

A type of IHD characterized by paroxysmal[1] (intermittent) and usually recurrent attacks of substernal or precordial chest discomfort, described as constricting, crushing, squeezing, choking, or knifelike pain. The pain may radiate down the left arm or to the left jaw (called as referred pain).

Etiology

Angina pectoris is due to inadequate perfusion, and is caused by transient (**15 seconds to 15 minutes**) and reversible myocardial ischemia that falls short of inducing the cellular necrosis that defines myocardial infarction i.e. duration and severity is not sufficient for infarction.

Types of Angina pectoris

Stable or typical angina[2]

- the **most common** form of angina.
- It is **caused by atherosclerotic disease** with usually 70% to 75% narrowing of the lumen i.e. (critical stenosis or fixed chronic stable stenosis).
- This reduction (70 to 75% stenosis) of coronary vessels makes the heart vulnerable, so whenever there is increased demand, e.g. physical activity, emotional excitement, or any other cause of increased cardiac workload, there is angina pain.
- The chest pain is episodic and associated with exertion or some other form of stress.
- It is usually **relieved by rest** (thereby decreasing demand) or with a strong vasodilator like nitroglycerin[3].

Unstable or crescendo[4] angina

- It is an unstable and **progressive** condition.
- Pain occurs with progressively increasing frequency, and is precipitated with progressively less exertion, even at rest, and tends to have a more prolonged duration.
- It is induced by disruption or rupture of an atheroma plaque with superimposed partial thrombosis.
- Unstable angina is often the **precursor of subsequent acute MI.** Thus also called as **preinfarction angina**.

Prinzmetal or variant angina

- is an uncommon pattern of episodic angina that occurs at rest and is **due to coronary artery spasm.**
- Prinzmetal angina generally responds promptly to vasodilators, such as nitroglycerin and calcium channel blockers..
- **Not related** to atherosclerotic disease.
- The etiology is not clear.

1: episodic
2: can be controlled by the change of lifestyle
3: given sublingual for faster delivery
4: it means something progressive

Myocardial infarction

Helpful video

Definition

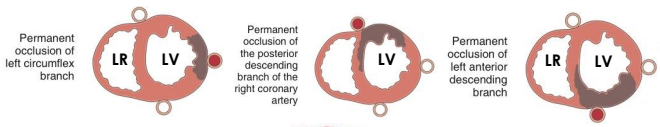
Also known as "heart attack", is the death of cardiac muscle[1] (coagulative necrosis) resulting from ischemia.

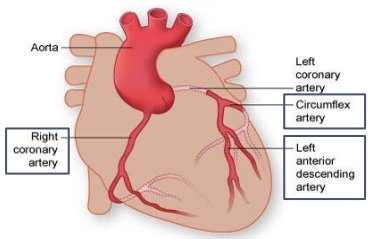
risk factors
(same as atherosclerosis)

- major
  - NON MODIFIABLE
    - Increasing age
    - Male gender[2]
    - Family history
    - Genetic
  - MODIFIABLE
    - Hyperlipidemia
    - Hypertension
    - Smoking
    - Diabetes
- minor
  - Obesity
  - Physical inactivity
  - Alcohol

people with dominant coronary artery (90% of ppl) the affected vessels are

Left circumflex artery (about 20%)	Right coronary artery (30-40%)	Left anterior descending artery (40-50%)





factors that the infarct will depend on

- The location, severity, and rate of development of coronary atherosclerotic obstructions
- The size of the area supplied by the obstructed vessels
- The duration of the occlusion
- The oxygen needs of the myocardium at risk
- The extent of collateral blood vessels
- Other factors, such as blood vessel spasm, alterations in blood pressure, heart rate, and cardiac rhythm

reperfusion may limit the size of the infarct[3]

1: when the severity or duration of ischemia is sufficient to cause cardiomyocyte death
2: the gap progressively narrows with age. Because women were protected by estrogen & after menopause (declining estrogen production) women are equally compromised
3: restoration of tissue perfusion as quickly as possible (hence the adage "time is myocardium")

Myocardial infarction

pathogenesis:

Most common cause is **thrombosis on a preexisting disrupted atherosclerotic plaque**. In the typical case of MI, the following sequence of events usually occur

Acute plaque change (sudden change in the structure of an atheromatous plaque e.g. disruption, ulceration, rupture or intraplaque hemorrhage)

Exposure of the thrombogenic subendothelial basement membrane resulting in **thrombus formation**.

Frequently within minutes, the thrombus evolves to **completely occlude** the lumen of the coronary vessel

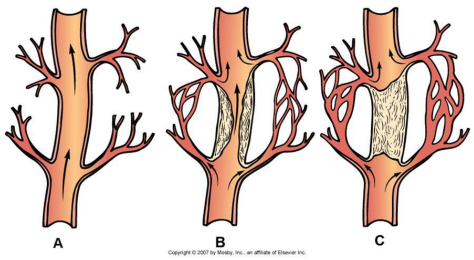
Severe ischemia lasting at least 20 to 40 minutes causes ***irreversible*** **injury**, and myocardial necrosis on the ultrastructural level (on electron microscopy).

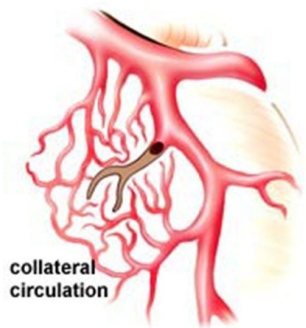
Myocardial necrosis mostly starts in the sub-endocardial region (20-30 minutes) because it is less perfused[1] and has high intramural pressure[2]

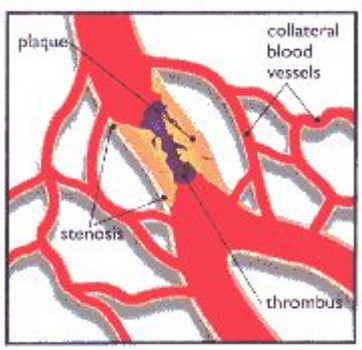
The full size of the infarct is usually determined **within 3-6 hours** of the onset of severe myocardial ischemia. During this period, lysis of the thrombus by treatment with streptokinase or tissue plasminogen activator, may limit the size of the infarct. Which will limit the final extent of necrosis

Collateral circulation[3]:

if an atherosclerotic lesion progressively occludes a coronary artery at a sufficiently slow rate over years, other coronary vessels may undergo remodeling and **provide compensatory blood flow to the area at risk**. Such ***collateral perfusion*** can subsequently protect against MI, even if the original vessel becomes completely occluded. Unfortunately, with **acute coronary blockage**, there is no time for collateral flow to develop and infarction results.





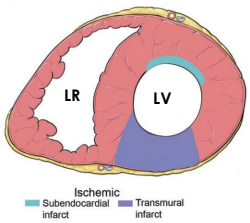


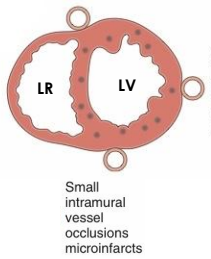
1: it is the last area to receive blood delivered by the epicardial vessels.
2: which act to impede the inflow of blood.
3: If a coronary artery in fully blocked then the blood will be backed up through the collateral circulation as a result the ischemia won't be as severe.

Myocardial infarction

MI types

- **Transmural** Full thickness (>50% of the wall)
- **Subendocardial** Inner 1/3 of myocardium
- **Microscopic infarcts** small-vessel occlusions

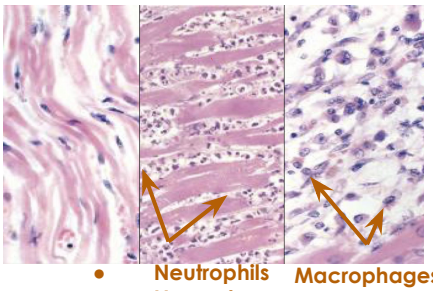




Morphology of MI

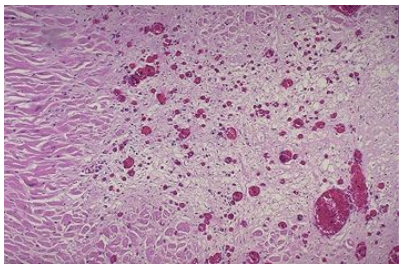
Begins with coagulative necrosis and inflammation (initially mainly neutrophils and later macrophages) → **Followed by formation of granulation tissue** → **Heals by formation of a fibrous scar**

Day 1 Day 3 Day 7

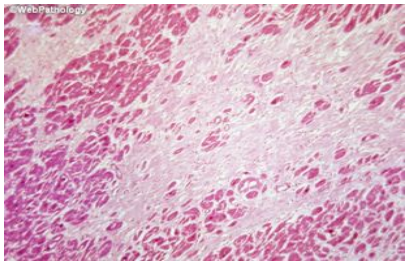


- Neutrophils
- No nucleus
- Ghost outlines of the cell

Macrophages



Granulation tissue approximately 3 weeks post MI



Healed MI with replacement of the necrotic fibers by dense collagenous scar. Residual cardiac muscle cells are present

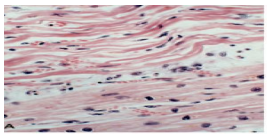
Time	Gross changes	Microscopic changes
0-4 hours	None	None
4-12 hours	Mottling "تبقع"	Coagulation necrosis
12-24 hours	Mottling	More coagulation necrosis, neutrophils come in
1-7 days	Yellow infarct center	Neutrophils die, macrophages come(after 3-7 days) to eat dead cells
1-2 weeks	Yellow center, red borders	Granulation tissue
2 to 8 weeks	Scar[1]	Collagen

1: Once an MI is completely healed, it is impossible to distinguish its age: whether present for 8 weeks or 10 years, fibrous scars look the same.

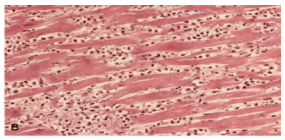
→ **Myocardial infarction stages:** coagulative necrosis (in the first couple of hours cells look normal under light microscope but under the electron microscope you will see features of necrosis "nucleus disappear, ghost outlines of the cell, inflammatory cells") → acute inflammation (neutrophils) → Chronic inflammation (macrophages) → granulation tissue → fibrosis

Myocardial infarction

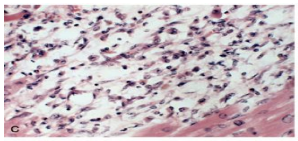
Morphology of MI (cont.)



One-day-old infarct showing coagulative necrosis with few neutrophils, wavy fibers with elongation, and narrowing, compared with adjacent normal fibers (lower right).



Dense neutrophilic infiltrate in an area of acute myocardial infarction of 3 to 4 days' duration.



Nearly complete removal of necrotic myocytes by phagocytosis (approximately 7 to 10 days).

Clinical features

Rapid & weak pulse.

Dyspnea

Diaphoresis(sweating).

ECG abnormalities

- shows typical findings of ischemia.

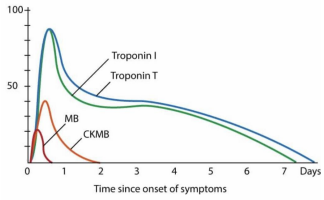
Pain

- Severe crushing substernal chest pain, which may radiate to the neck, jaw, epigastrium, shoulder or left arm.
- Pain lasts for hours to days and is not relieved by nitroglycerin.
- No pain[1] in 20-30% of patients (diabetics, hypertensive, or elderly).

Cardiogenic shock

- can be seen in massive MI (when >40% of left ventricle is affected).

Laboratory evaluation[2]



Troponins
(TnT,TnI more specific)
"Best marker"

TnI and TnT are not normally detectable in the circulation

After acute MI both troponins:

- **Are detectable after 2 to 4 hours.**
- **Peak at 48 hours.**
- **Remain elevated for 7 to 10 days.**

CK-MB
"Second best marker"

- **Begins to rise within 2 to 4 hours of MI.**
- **Peaks at 24 hours.**
- **Returns to normal within approximately 72 hours.**

Lactate dehydrogenase (LD)

- **Rise 24 hrs**
- **Peaks 72 hrs**
- **Gradually disappears in 5 to 14 days.**

1: Silent MI is when the patient stops feeling pain. They could have MI without them knowing
2: Of macromolecules that leak out of injured myocardial cells through damaged cell membranes

Myocardial infarction

Complications

- **There are no complications in 10-20% of patients.**
- **80-90% experience one or more of the following complications:**

Cardiac arrhythmia[1] (75-90%):
Patients have conduction disturbances and myocardial irritability which can lead to sudden death especially in ventricular arrhythmia .

Left ventricular failure (60%):
with mild to severe pulmonary edema.

Cardiogenic shock (10%).

Myocardial rupture
Rupture of:
- Free wall and septum
- papillary muscle (leading to papillary muscle and associated valve incompetence/dysfunction)

Thromboembolism[2] (15-49%):
the combination of myocardial abnormality in contractility (causing stasis) and endocardial damage can lead to cardiac thrombosis and embolism[3].

Pericarditis

Infarct extension & expansion

Ventricular aneurysm:
in which the ventricle is dilated and the wall is thinned out.

External rupture of the infarct
with associated bleeding into the pericardial space (hemopericardium).

Progressive late heart failure in the form of **chronic IHD**

Other Cardiac conditions

Chronic ischemic heart disease	Sudden cardiac death
• **Progressive** heart failure due to ischemic injury, either from: - prior infarction(s) (most common) - Or chronic low-grade ischemia	• **Unexpected** death from cardiac causes either without symptoms or within 1 to 24 hours of symptom onset. • Results from a fatal arrhythmia, most commonly in patients with severe coronary artery disease

1: When there's fibrosis (end stage of MI) the heart muscles are dead → disruption of the conduction → no contraction → ARRHYTHMIA.
2: It's scary because it can be sent to the rest of the body through the continuous contraction of the heart.
3: Due to exposure of underlying thrombogenic basement membrane.

Summary

Ischemic Heart Disease (IHD) syndromes:
imbalance between the myocardial oxygen demand and blood supply

- Angina pectoris (chest pain)
- Sudden cardiac death
- Acute myocardial infarction
- Chronic ischemic heart disease (with congestive heart failure)

causes

Coronary artery atherosclerosis — common — less common — **Vasospasm and vasculitis**

pathogenesis of IHD

1- Role of critical stenosis or obstruction

Pre-clinical phase: Normal artery → Fatty streak → Fibro-fatty plaque → Advanced/ vulnerable plaque

or

Clinical phase: Aneurysm and rupture / Occlusion by thrombus / Critical stenosis

2- Role of acute plaque change: plaque with fibrous cap → cap ruptures → blood clot forms → blocked coronary artery → death of heart tissue

3- Role of coronary thrombus
- **Total occlusion**
- **Partial occlusion**

4- Role of vasoconstriction

5- Role of inflammation

Common IHD syndromes

Angina pectoris

most common
- **Typical (stable) angina**: - Pain on exertion; - Fixed narrowing of coronary artery; - Usually relieved by rest
- **Unstable (pre-infarction) angina**: - Increasing pain with less exertion; - Plaque disruption and thrombosis; - Precursor of acute MI

uncommon
- **Prinzmetal (variant) angina**: - Pain at rest; - Coronary artery spasm of unknown etiology

Acute myocardial infarction

Necrosis of heart muscle caused by ischemia, mostly due to acute coronary artery thrombosis

- **Types**: **Transmural**: Full thickness; **Subendocardial**: Inner 1/3 of myocardium
- **Morphology**: coagulative necrosis & inflammation → granulation tissue → fibrous scar
- **Clinical features**: severe chest pain, not relieved by nitroglycerin and rest
- **Laboratory evaluations**: Increase in Troponins & CK-MB
- **Complications**: Myocardial rupture, arrhythmias, chronic progressive heart failure

Quiz

Answer key: Answers Explanation File

1) A 44-year-old man presents to the emergency room with acute chest pain. The ECG is normal. Analysis of which pair of serum markers given below would be most helpful in excluding a diagnosis of acute myocardial infarction in this patient?

A) Cardiac troponin-I and myoglobin.

B) CK-BB and myoglobin.

C) CK-MB and cardiac troponin-I.

D) CK-MM and lactate dehydrogenase (LDH)-1.

E) Myoglobin and CK-BB .

2) A 65-year-old man with a 2-year history of angina pectoris is admitted to the hospital with excruciating substernal chest pain that is not relieved by rest or medication. Physical examination shows diaphoresis and dyspnea. Results of laboratory studies include WBC of 13,000/µL, CK-MB of 6.8 ng/mL, and troponin-I of 3.0 ng/mL. An ECG shows ST segment elevation. The patient expires 1 hour after admission. At autopsy, the heart is found to be enlarged but otherwise anatomically normal. Which of the following is the most likely cause of death?

A)Cardiac tamponade.

B) Postmyocardial infarction syndrome.

C) Ruptured myocardial infarct.

D) Septal perforation.

E) Ventricular fibrillation.

3) A 48-year-old man complains of chest pain upon exertion. He had been well until 4 months previously, when he first developed a chest discomfort while jogging. His symptoms have progressed to the point that he now develops chest pain after climbing a single flight of stairs. He has a history of diabetes controlled by diet and of 25 pack-years of cigarette smoking. His father and maternal grandfather both died of heart disease before the age of 60. On the 5th hospital day, the patient develops chest pain during periods of mild activity, which is minimally responsive to sublingual nitroglycerin. Results of laboratory studies include WBC of 8,100/µL, CK-MB of 4.5 ng/mL, and troponin-I of 0.5 ng/mL. Which of the following is the most likely diagnosis?

A) Acute myocardial infarction.

B) Cardiac arrhythmia.

C) Dressler syndrome.

D) Pulmonary thromboembolism.

E) Unstable angina.

4) A 56-year-old man presents to the emergency room with 1 hour of chest pain. Laboratory studies show an increased leukocyte count and increased serum levels of cardiac enzymes. ECG confirms a massive transmural myocardial infarction of the left ventricle. The patient dies 2 days later. Examination of injured heart muscle would be expected to show which of the following pathologic changes by light microscopy?

A) Collagen-rich scar tissue

B) Extensive infiltration of myocardium with mononuclear cells

C) Necrosis of cardiac myocytes and infiltrates of neutrophils

D) No obvious changes evident by light microscopy

E) Proliferation of fibroblasts and capillary endothelial cells

5) A 68-year-old obese woman (BMI = 32 kg/m2) presents with substernal chest pain and a history of recurrent angina pectoris and intermittent claudication. The following day, she develops a fever of 38°C (101°F). Results of laboratory studies include an elevated WBC count (13,000/µL), CK-MB of 6.6 ng/mL, and troponin-I of 2.5 ng/mL. ECG confirms a myocardial infarction of the left ventricular wall. Which of the following mechanisms is most likely responsible for the myocardial infarction in this patient?

A) Coronary artery thrombosis.

B) Coronary artery vasospasm.

C) Decreased collateral blood flow.

D) Deep venous thrombosis.

E) Paradoxical embolism.

6) A 66-year-old woman collapses while shopping and expires suddenly of cardiac arrest. Her past medical history is significant for long-standing type 2 diabetes mellitus. Her relatives note that she had complained of chest heaviness and shortness of breath for the past 2 weeks. Sterile fibrinous pericarditis and pericardial effusion are observed at autopsy. What additional finding would be expected during autopsy of this patient?

A) Endocardial fibroelastosis.

B) Marantic endocarditis.

C) Mitral valve prolapse.

D) Myocardial infarct.

E) Right ventricular hypertrophy.

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THANK YOU