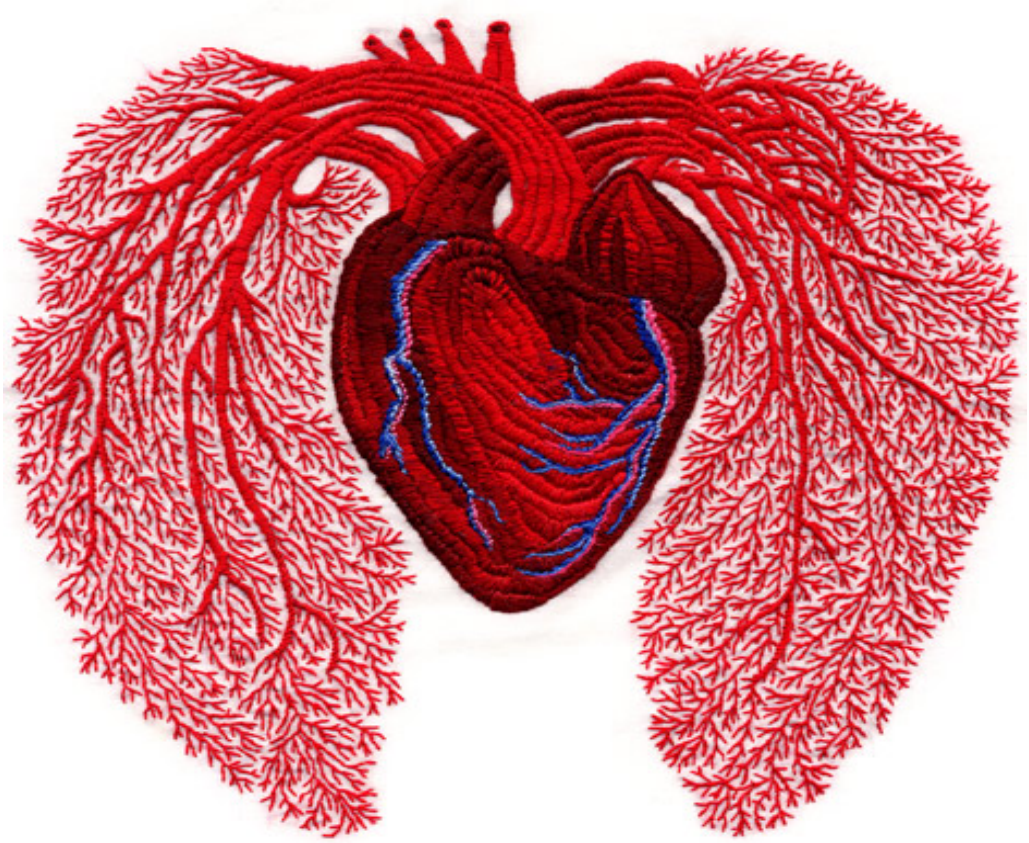
Ischemic Heart Diseases

Robbins page (376, 377, 384)



Objectives:

- Understand the pathogenesis and clinical consequences of atherosclerosis.
- Be able to discuss pathology and complications of ischaemic heart diseases with special emphasis on myocardial infarction.
- Know how lifestyle modifications can reduce the risk of ischaemic heart disease.

Important note: During the previous blocks, we noticed some mistakes just before the exam and we didn't have the time to edit the files. To make sure that all students are aware of any changes, please check out this link before viewing the file to know if there are any additions or changes. The same link will be used for all of our work: Pathology Edit

Ischemic Heart Disease (IHD) - (Coronary Heart Disease).

Overview of Coronary Artery Disease + Coronary Heart Disease

IHD are group of closely related conditions (syndromes) caused by an imbalance between the myocardial oxygen demand and blood supply. it occurs when the myocardium need oxygen and there is no enough blood supply. Usually caused by decreased coronary artery blood flow, so it's called also (**coronary artery disease**).

IHD can cause these four conditions/syndromes:

1. **Angina pectoris** (chest pain).
2. **Acute myocardial infarction** (MI) = heart attack.
3. **Sudden cardiac death**. due to ventricular arrhythmia.
4. **Chronic ischemic heart disease** (IHD) with **congestive heart failure** (CHF). It is the reduction in heart power to pump blood to the body. It usually happen after MI. Because some of the heart muscle dies after a heart attack (MI), its power to squeeze out blood is reduced and heart failure develops.

Epidemiology.

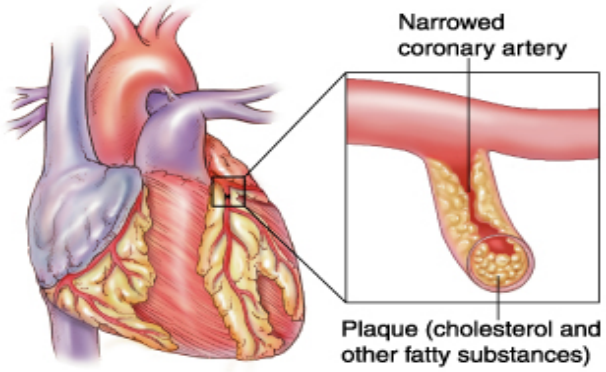
Peak incidence: 60y for males and 70y for females, Men are more affected than women.
The *main cause* of Ischemic heart disease is **(coronary atherosclerosis[1])** → 90% of cases**.**

Contributing factors :are same as that of atherosclerosis e.g.

- **Hypertension** because it's results in a thickening and inelasticity of arterial walls and hypertrophy of the left heart ventricle,also because high blood pressure put added forced against arterial walls.
- **Diabetes mellitus** the hyperglycemia itself increases lipId and lipoprotein,the excessive glucose in the blood act with protein to form advanced glycation end product[AGE],this AGE cause inflammation in the vessels which lead to IHD.

Other factors: Smoking, High levels of LDL, Genetic factors (direct or indirect), Lack of exercise.

Less commonly: due to **vasospasm:** it is blood vessel reducing its (diameter) and blood flow. & **vasculitis:** it is inflammation of a blood or lymph vessel—called also *angiitis.*



[1] abnormal fatty (LDL cholesterol) deposit in forming plaque and fibrosis of the inner layer of the arteries (atheroma).

Pathogenesis of Ischemic Heart Disease.

1) Role of Critical stenosis or obstruction: 70% of the lumen of one or more coronary arteries by atherosclerotic plaque.

2) Role of Acute Plaque Change: Disruption of a mildly stenosing plaque leading to rupture/ ulceration. This 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

Acute plaque change can cause myocardial ischemia in the form of **unstable angina**, **acute myocardial infarction** and (in many cases) **sudden cardiac death.**

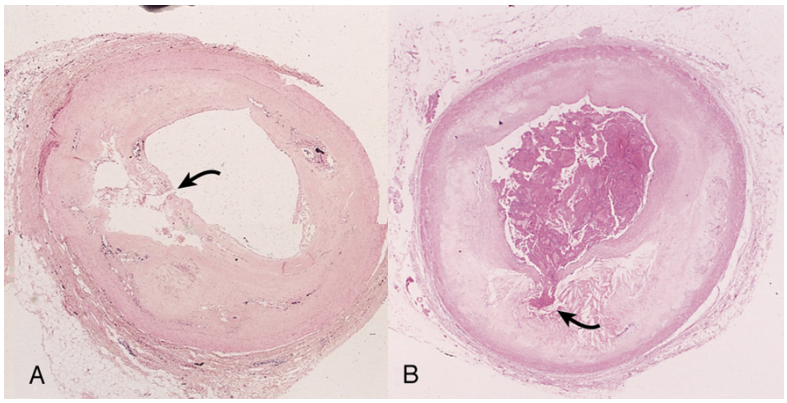
3) Role of Coronary Thrombus:
thrombus superimposed on a disrupted but previously only partially stenotic plaque converts it to either:

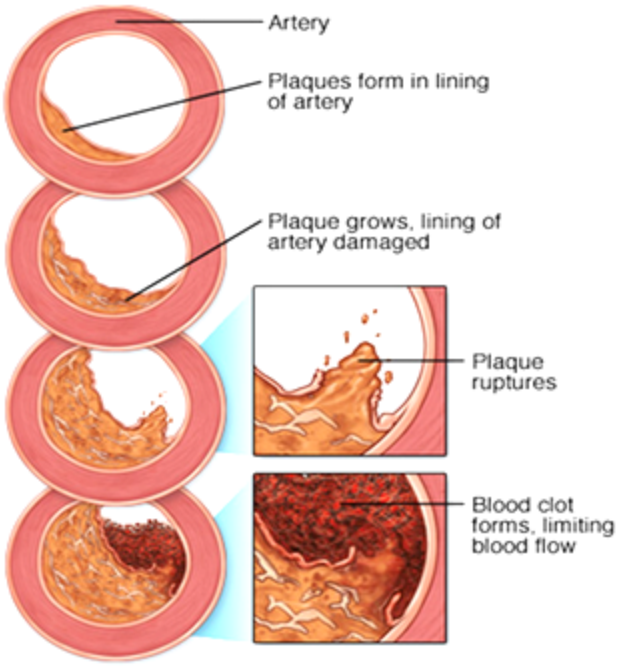
- A total occlusion leading to acute transmural MI **OR..**
- partial (incomplete/subtotal) occlusion leading to unstable angina, acute subendocardial infarction, or sudden cardiac death.

- **Thrombosis in coronary artery can also embolize.**

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.

- the augmented coronary flow because of vasodilatation is insufficient to meet the increase in myocardial demand of O2.



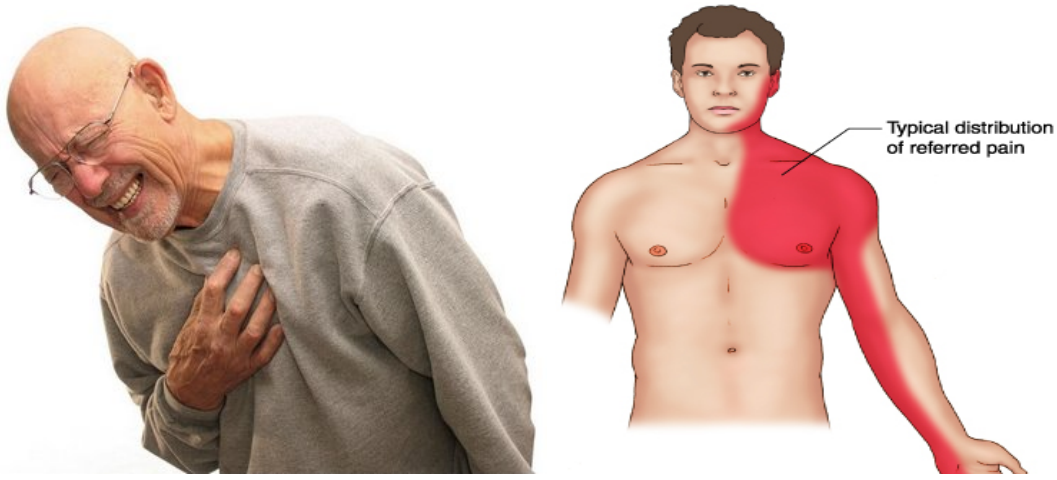


A. Plaque rupture without superimposed thrombus in a patient who died suddenly.
B. Acute coronary thrombosis superimposed on an atherosclerotic plaque with focal disruption of the fibrous cap, triggering fatal myocardial infarction.

Angina pectoris.

Angina pectoris is a type of IHD characterized by paroxysmal 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) .

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



There are three types of angina pectoris:

1- Stable or typical angina.
2- Prinzmetal's or variant angina.
3- Unstable or crescendo angina.

1- Angina pectoris: Stable angina/ typical angina pectoris:

Stable angina (typical angina) is the most common form of angina. It is caused by atherosclerotic disease with usually ≥70% to 75% narrowing of 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, Is usually relieved by rest (thereby decreasing demand) or with a strong vasodilator like **nitroglycerin**.

2- Angina Pectoris: Unstable or crescendo angina:

It is an unstable and progressive condition (90% narrowing (fixed) of lumen).

Pain occurs with progressively increasing frequency, and is precipitated with progressively less exertion, even at **rest, and tends to be of 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.

3- Angina Pectoris: Prinzmetal's 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.**
It is Not related to atherosclerotic disease.

- **The etiology is not clear.**

Myocardial Infarction (MI).

MI, also known as "heart attack," **is the death of cardiac muscle** (coagulative necrosis) resulting from ischemia.

MI: commonly affected coronary vessel in persons with **right dominant coronary artery heart (90% of population).**

Left anterior descending artery (40-50%): it supplies the anterior left ventricle, apex and anterior two thirds of interventricular septum.

Right coronary artery (30-40%): it supplies the posterior wall of the left ventricle, posterior one third of interventricular septum.

Left circumflex artery (about 20%): it supplies the lateral wall of left ventricle.

Pathogenesis of MI.

- Most common cause is thrombosis on a preexisting disrupted atherosclerotic plaque.
- if an atherosclerotic lesion progressively occlude a coronary artery at a slow rate over years, remodeling of other coronary vessels may provide compensatory blood flow to the area at risk, but, unfortunately in acute coronary blockage there is no time for collateral flow to develop and infraction occur.

- in most patient it occurs because of abrupt plaque change followed by thrombosis, more than one mechanism of injury may involve: rupture , fissuring or ulceration. Frequently within **minutes**, the thrombus evolves to completely occlude the lumen of the coronary vessel.

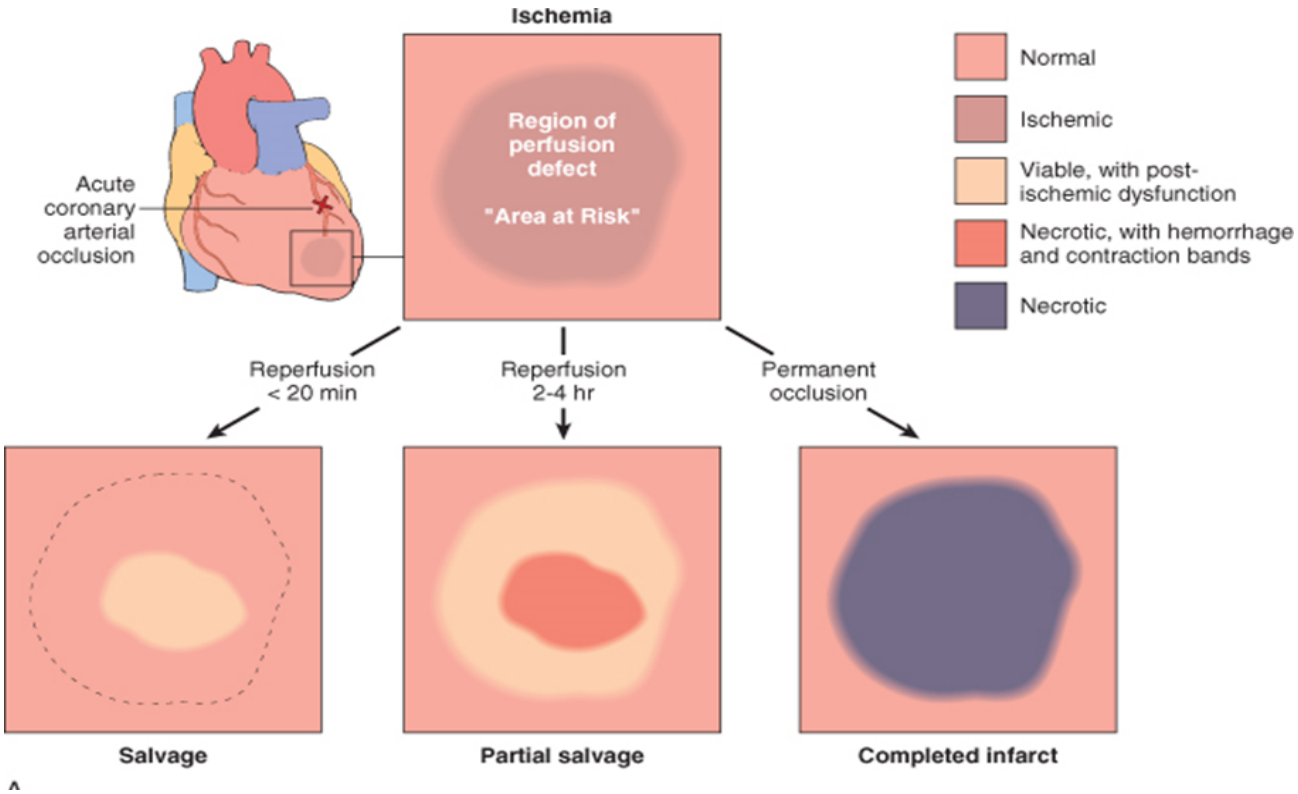
- factors that trigger acute plaque injury is believed to act by increasing the lesion's susceptibility to disruption by mechanical stress

- **Myocardial necrosis begins within 20-30 minutes**, mostly starting at the subendocardial region (less perfused, high intramural pressure).
- **Infarct reaches its full size within 3-6 hrs**, during this period, lysis of the thrombus by streptokinase or tissue plasminogen activator, may limit the size of the infarct.
  Irreversible cell injury: **20-40 min**
- If patient survive, thrombi may lyse spontaneously **OR** vasospasm relief , reestablish the flow of reperfusion injury that can incite greater local damage than might have otherwise occurred without rapid restoration of blood flow. reperfusion injury is mediated in part by oxygen free radicals generated by the increased number of infiltrating leukocytes facilitated by reperfusion. Reperfusion-induced microvascular injury causes not only hemorrhage but also endothelial swelling that occludes capillaries and may prevent local blood flow (called no-reflow).

A reperfused infarct usually has **hemorrhage** because the vasculature injured during the period of ischemia is leaky after flow is restored.

The precise location, size, and specific morphologic features of an acute myocardial infarct depend on:
1-The location, severity, and rate of development of coronary atherosclerotic obstructions.
2-The size of the area supplied by the obstructed vessels.
3-The duration of the occlusion.
4-The oxygen needs of the myocardium at risk.
5-The extent of collateral blood vessels.
Other factors, such as blood vessel spasm, alterations in blood pressure, heart rate, and cardiac rhythm.

In addition reperfusion may limit the size of the infarct.



MI types and morphology.

TYPES:

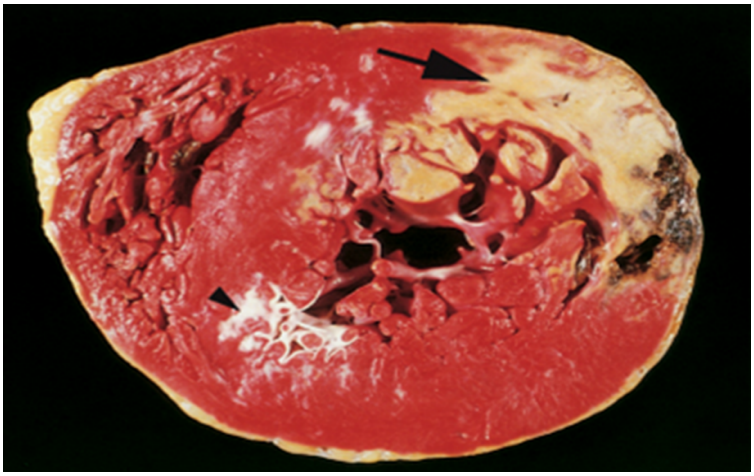
1. **Transmural:** Full thickness (>50% of the ventricle wall) caused by epicardial vessel occlusion through a combination of **chronic atherosclerosis and acute thrombosis** such transmural MIs typically yield **ST** segment elevations on the electrocardiogram (ECG) and can have a negative **Q** waves with loss of **R** wave amplitude. These infarcts are also called ST elevated MIs.
2. **Subendocardial: Inner 1/3 of myocardium**[2] , no effect he on ECG.
3. **Microscopic infarcts:** occur in the setting of small vessel occlusions and may not show any diagnostic ECG changes.

[2] الجهة الأبعد لمكان الcoronary artery

MORPHOLOGY:

Begins with coagulative necrosis and inflammation (initially mainly neutrophils and later macrophages).

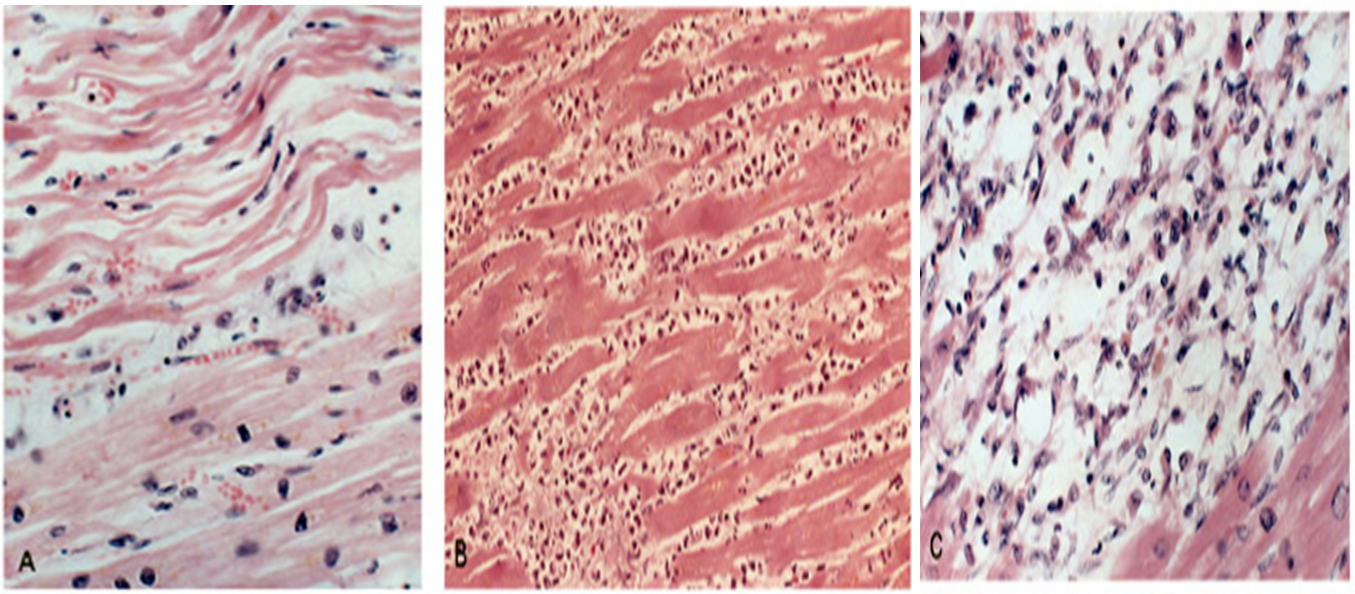
- Followed by formation of granulation tissue.
- Heals by formation of a fibrous scar.



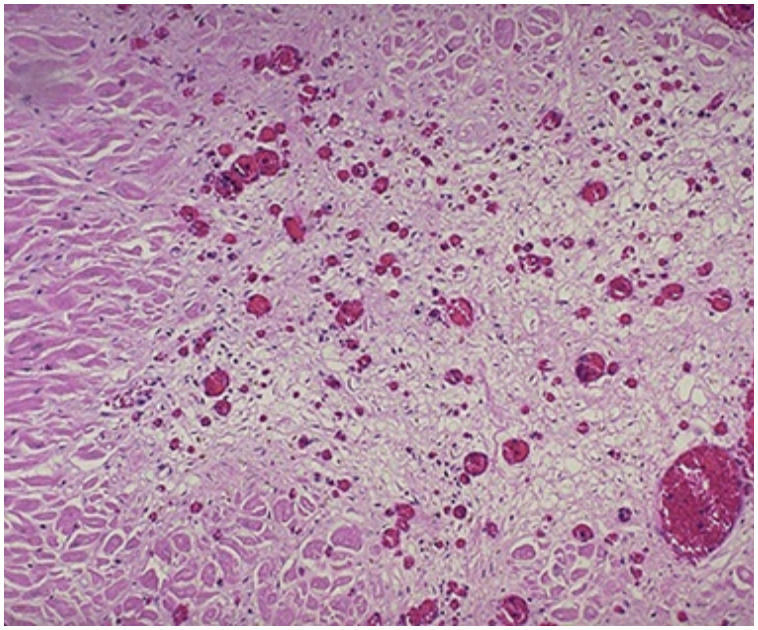
Morphologic Changes in Myocardial Infarction.

Time	Gross changes	Microscopic changes
0-4 h	None	None
4-12h	Mottling	Coagulation necrosis
12-24h	Mottling	More coagulation necrosis; neutrophils come in
1-7 d	Yellow infarct center	Neutrophils die, macrophages come to eat dead cells
1-2 w	Yellow center, red borders	Granulation tissue
2-8 w	Scar	Collagen

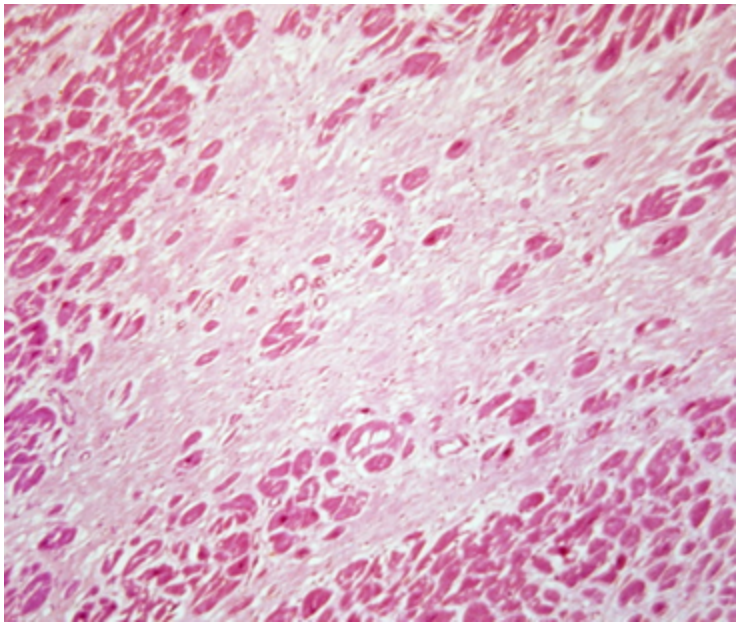
Microscopic features of myocardial infarction.



A.One-day-old infarct showing coagulative necrosis with few neutrophils, wavy fibers with elongation, and narrowing, compared with adjacent normal fibers (lower right).
B.Dense neutrophilic infiltrate in an area of acute myocardial infarction of 3 to 4 days' duration.
C. Nearly complete removal of necrotic myocytes by phagocytosis (approximately 7 to 10 days).



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

Myocardial Infarction: Clinical Features

Pain:

- Severe crushing sub-sternal chest pain, which may radiate to the neck, jaw, epigastrium, shoulder or left arm.
  - lasts for hours to days and is not relieved by nitroglycerin or rest.
  - In 10% to 15% of patients (diabetics, hypertensive, elderly) MIs can be asymptomatic. (no pain)
  (Diabetic patients have autonomic neuropathies that may prevent perception of pain.)

Pulse is rapid and weak.

Diaphoresis (excessive sweating)

Dyspnea

ECG shows typical findings of ischemia :

- Q waves (indicating transmural infarcts)
  - ST-segment abnormalities
  - T-wave inversion

Arrhythmias

Laboratory evaluation

The laboratory evaluation of MI is based on measuring blood levels of macromolecules that leak out of injured myocardial cells through damaged cell membranes .

- Cardiac troponins T and I (TnT, TnI)
- Creatine kinase (the myocardial-specific isoform, CK-MB)
- Lactate dehydrogenase
- Myoglobin

Troponins and CK-MB have high specificity and sensitivity for myocardial damage

Cardiac troponins	CK-MB
- best marker -not normally detectable in the circulation – detectable after 2 to 4 hours – Peak at 48 hours – Their levels remain elevated for 7 to 10 days	- the second best marker – detectable within 2 to 4 hours – Peaks at 24 to 48 hours – Returns to normal within approximately 72 hours

Outcomes or complications OF MI

- No complications in 10-20%.
- 80-90% experience one or more of the following complications:
  - **Cardiac arrhythmia (75-90%):** Patients have conduction disturbances and myocardial irritability → sudden death (especially in ventricular arrhythmia).
  - **Left ventricular failure with mild to severe pulmonary edema (60%).**
  - **Cardiogenic shock (10%).**
  - **Myocardial rupture:** Rupture of free wall, septum, rupture of papillary muscle (leading to papillary muscle and associated valve incompetence/dysfunction)
  - **Thromboembolism (15-49%):** the combination of myocardial abnormality in contractility (causing stasis[3]) with endocardial damage (exposure of underlying thrombogenic basement membrane) → cardiac/mural thrombosis and thromboembolism
  - **Pericarditis**
  - **Infarct[4] extension and expansion**
  - **Ventricular aneurysm:** They usually arise from a patch of weakened tissue in a ventricular wall, which swells into a bubble filled with blood.
  - **External rupture of the infarct** with associated bleeding into the pericardial space (hemopericardium).
  - **Progressive late heart failure in the form of chronic IHD.**

- 10% of the rest will die within a month.
- Overall 30% die in the 1st year.

Chronic ischemic heart disease & Sudden cardiac death.

- **Chronic ischemic heart disease:** Progressive heart failure due to ischemic injury, either from prior infarction (most common) **or chronic low-grade ischemia.**

- **Sudden cardiac death:** Unexpected death from cardiac causes either without symptoms or within 1 to 24 hours of symptom onset. Results from a fatal arrhythmia (Ventricular arrhythmia), most commonly in patients with **acute coronary artery disease**.

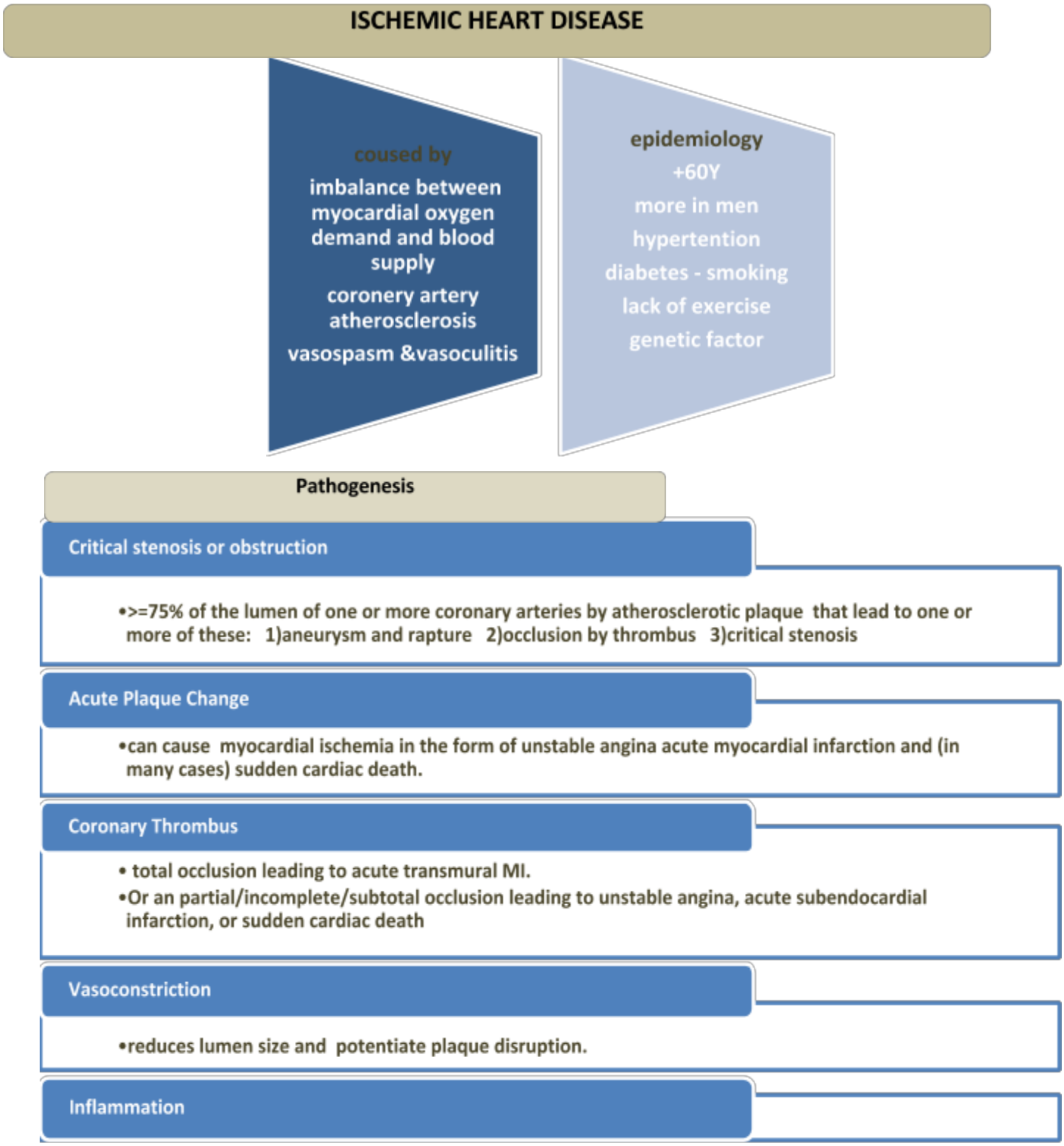
[3] a diminution of flow, as of blood or other body fluid.
[4] a small localized area of dead tissue resulting from failure of blood supply.

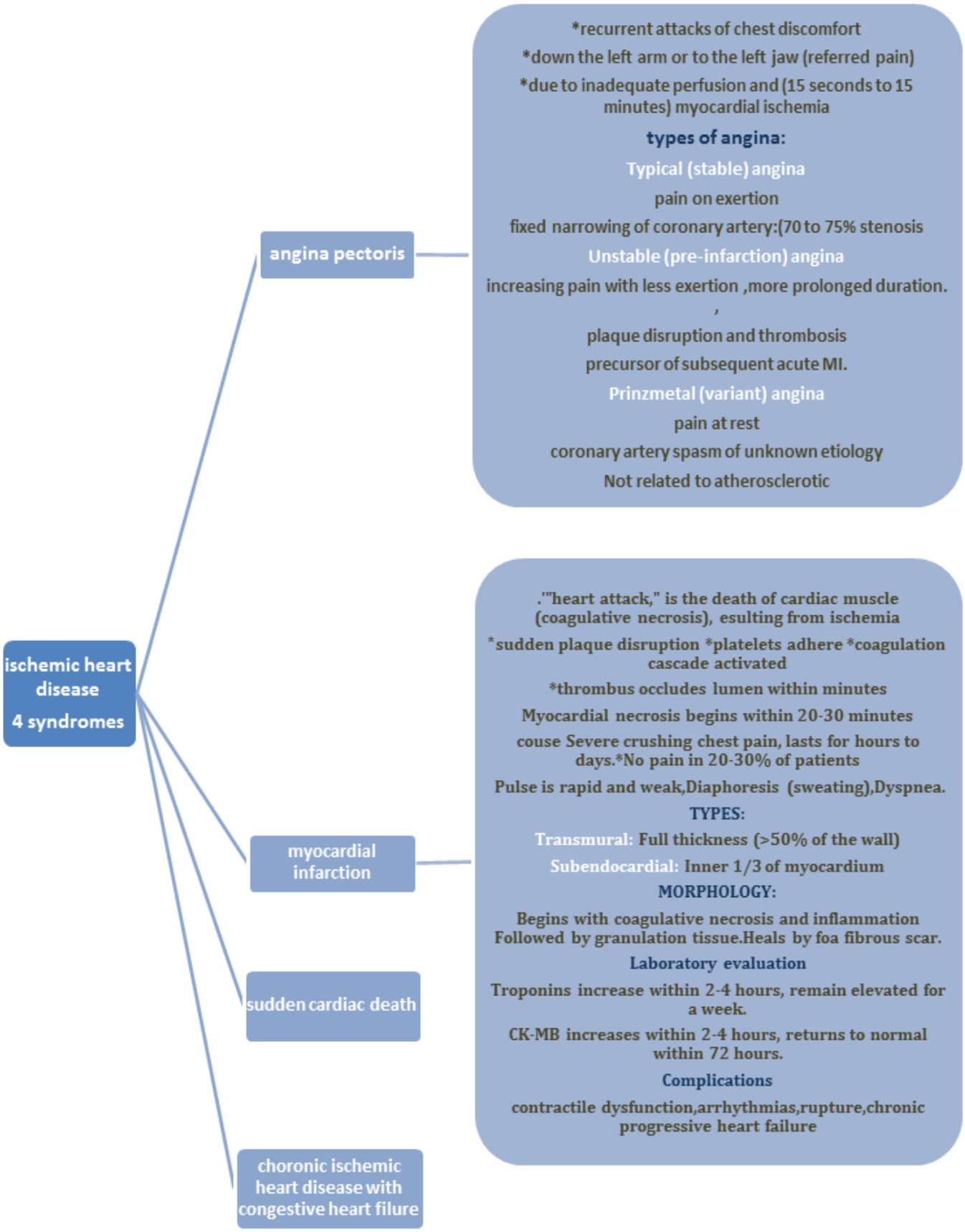
SUMMARY

Ischemic Heart Disease

- In the vast majority of cases, cardiac ischemia is due to coronary artery atherosclerosis; vasospasm, vasculitis, and embolism are less common causes.
- Cardiac ischemia results from a mismatch between coronary supply and myocardial demand and manifests as different, albeit overlapping syndromes:
  - *Angina pectoris* is exertional chest pain due to inadequate perfusion, and is typically due to atherosclerotic disease causing greater than 70% fixed stenosis (so-called critical stenosis).
  - *Unstable angina* results from a small fissure or rupture of atherosclerotic plaque triggering platelet aggregation, vasoconstriction, and formation of a mural thrombus that need not necessarily be occlusive.
  - *Acute myocardial infarction* typically results from acute thrombosis after plaque disruption; a majority occur in plaques that did not previously exhibit critical stenosis.
  - *Sudden cardiac death* usually results from a fatal arrhythmia, typically without significant acute myocardial damage.
  - *Ischemic cardiomyopathy* is progressive heart failure due to ischemic injury, either from previous infarction(s) or chronic ischemia.
- Myocardial ischemia leads to loss of myocyte function within 1 to 2 minutes but causes necrosis only after 20 to 40 minutes. Myocardial infarction is diagnosed on the basis of symptoms, electrocardiographic changes, and measurement of serum CK-MB and troponins. Gross and histologic changes of infarction require hours to days to develop.
- Infarction can be modified by therapeutic intervention (e.g., thrombolysis or stenting), which salvages myocardium at risk but may also induce reperfusion-related injury.
- Complications of infarction include ventricular rupture, papillary muscle rupture, aneurysm formation, mural thrombus, arrhythmia, pericarditis, and CHF.

Summary.


ISCHEMIC HEART DISEASE
coused by
imbalance between myocardial oxygen demand and blood supply
coronery artery atherosclerosis
vasospasm &vasoculitis
epidemiology
+60Y
more in men
hypertention
diabetes - smoking
lack of exercise
genetic factor
Pathogenesis
Critical stenosis or obstruction
•>=75% of the lumen of one or more coronary arteries by atherosclerotic plaque that lead to one or more of these: 1)aneurysm and rapture 2)occlusion by thrombus 3)critical stenosis
Acute Plaque Change
•can cause myocardial ischemia in the form of unstable angina acute myocardial infarction and (in many cases) sudden cardiac death.
Coronary Thrombus
• total occlusion leading to acute transmural MI.
•Or an partial/incomplete/subtotal occlusion leading to unstable angina, acute subendocardial infarction, or sudden cardiac death
Vasoconstriction
•reduces lumen size and potentiate plaque disruption.
Inflammation


ischemic heart disease
4 syndromes
angina pectoris
*recurrent attacks of chest discomfort
*down the left arm or to the left jaw (referred pain)
*due to inadequate perfusion and (15 seconds to 15 minutes) myocardial ischemia
types of angina:
Typical (stable) angina
pain on exertion
fixed narrowing of coronary artery:(70 to 75% stenosis
Unstable (pre-infarction) angina
increasing pain with less exertion ,more prolonged duration.
,
plaque disruption and thrombosis
precursor of subsequent acute MI.
Prinzmetal (variant) angina
pain at rest
coronary artery spasm of unknown etiology
Not related to atherosclerotic
myocardial infarction
."heart attack," is the death of cardiac muscle (coagulative necrosis), esulting from ischemia
*sudden plaque disruption *platelets adhere *coagulation cascade activated
*thrombus occludes lumen within minutes
Myocardial necrosis begins within 20-30 minutes
couse Severe crushing chest pain, lasts for hours to days.*No pain in 20-30% of patients
Pulse is rapid and weak,Diaphoresis (sweating),Dyspnea.
TYPES:
Transmural: Full thickness (>50% of the wall)
Subendocardial: Inner 1/3 of myocardium
MORPHOLOGY:
Begins with coagulative necrosis and inflammation Followed by granulation tissue.Heals by foa fibrous scar.
Laboratory evaluation
Troponins increase within 2-4 hours, remain elevated for a week.
CK-MB increases within 2-4 hours, returns to normal within 72 hours.
Complications
contractile dysfunction,arrhythmias,rupture,chronic progressive heart failure
sudden cardiac death
choronic ischemic heart disease with congestive heart filure

MCQ's.

A 60-year-old man has experienced angina on exertion for the past 6 years. A coronary angiogram performed 2 years ago showed 75% stenosis of the left anterior descending coronary artery and 50% stenosis of the right coronary artery. For the past 3 weeks, the frequency and severity of the anginal attacks have increased, and pain sometimes occurs even when he is lying in bed. Which of the following is most likely to explain these findings?

A. Hypertrophy of ischemic myocardium with increased oxygen demands
B. Increasing stenosis of right coronary artery
C. Fissuring of plaque in left coronary artery with superimposed mural (partial) thrombosis

C) This patient has 75% stenosis of the left anterior descending branch of the coronary artery. This degree of stenosis prevents adequate perfusion of the heart when myocardial demand is increased, which occurs during exertion.(Unstable angina).

A study of ischemic heart disease analyzes cases of individuals hospitalized with acute chest pain in which myocardial infarction was documented at autopsy. The gross and microscopic appearances of the hearts are correlated with the degree of coronary atherosclerosis and its complications, clinical symptoms, and therapies given before death. Hemorrhage and contraction bands in necrotic myocardial fibers are most likely to be seen with infarction in which of the
following settings?

A. Acute vasculitis
B. Coronary thrombosis
C. Pericarditis

(B) Reperfusion of an ischemic myocardium by spontaneous or therapeutic thrombolysis changes the morphologic features of the affected area. Reflow of blood into vasculature injured during the period of ischemia leads to leakage of blood into the tissues (hemorrhage).

A 48-year-old woman has had increasing dyspnea for the past 2 days. She experiences sudden cardiac arrest and cannot be resuscitated. The light microscopic appearance of the left ventricular free wall at autopsy is shown in the figure. Which of the following is the most likely diagnosis?

A. Viral myocarditis
B. Myocardial infarction
C. Acute rheumatic myocarditis

B) The figure shows myocardial fibers with loss of nuclei, indicative of coagulative necrosis. Myocardial fibers are between neutrophils. This pattern is most likely caused by a myocardial infarction (MI) that is approximately 24 to 48 hours old.

The other name of myocardial infarction is:

A. Ischemic heart disease
B. Non Infectious myocarditis

C. Heart attack

C)

When myocardial necrosis involves the entire ventricular wall is called:

A. Transmural
B. Caseous necrosis necrosis
C. Subendocardial

A)

2nd best marker of MI is:

A. Troponin
B. Lactate dehydrogenase
C. CK-MB

C)

The other name of ischemic heart disease is:

A. Atherosclerosis
B. Coronary artery disease
C. Congestive Heart failure

B) Atherosclerosis is one of its causes, isn't another name of it.

Most site of MI:

A. left circumflex
B. right coronary artery
C. left anterior descending

C)

Contact us on: Pathology434@gmail.com

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Good Luck!

عمر الرهيبني
عبدالرحمن بري

مها الربيعة
ريما الرشيد
نجلاء الدريويش
فتون سالم
هيفاء المحسن
أمل سعد