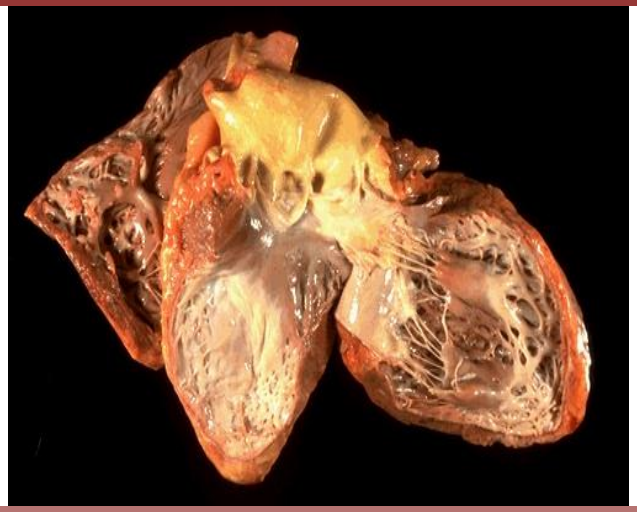
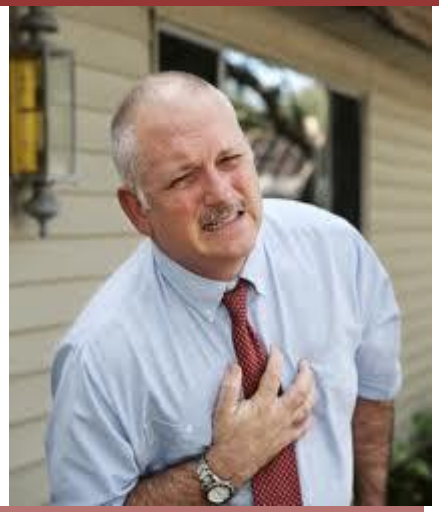




Third Lecture

Ischemic Heart Disease

432 Pathology Team

Done By: Alaa Baghazal Nada Alouda

Reviewed by: Abdulrahman Alaqeel

Ischemic Heart Disease (IHD): A group of related syndromes resulting from myocardial *ischemia & it's also called Coronary Artery Disease (CAD)*

-Ischemia: decrease O2 to a certain tissue (e.g. restriction in blood supply to tissues)

-Infarction: tissue death (necrosis) caused by an obstruction of the tissue's blood supply

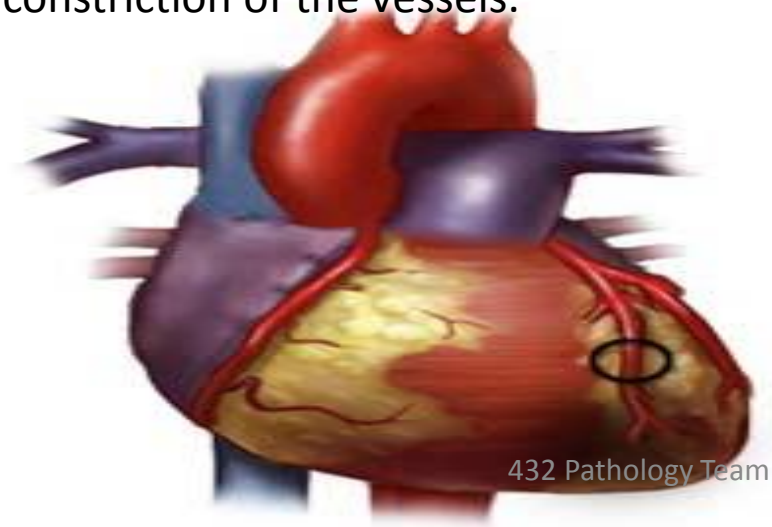
Ischemia → Injury → Infarction

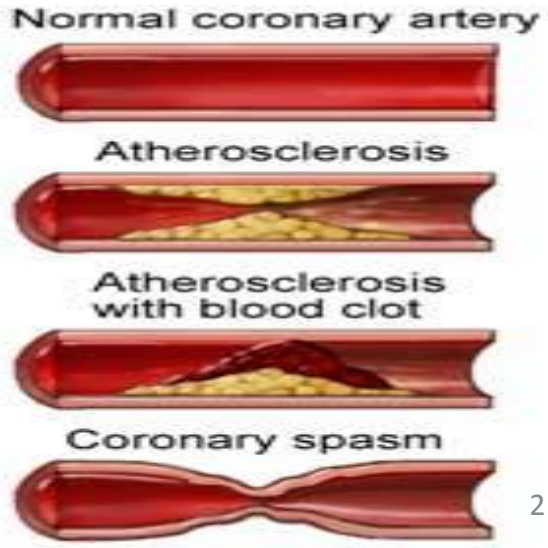
Atherosclerosis of coronaries is the most common cause of myocardial infarction BUT atherosclerosis is not usually the direct cause, the complications of it are, such as: thrombosis

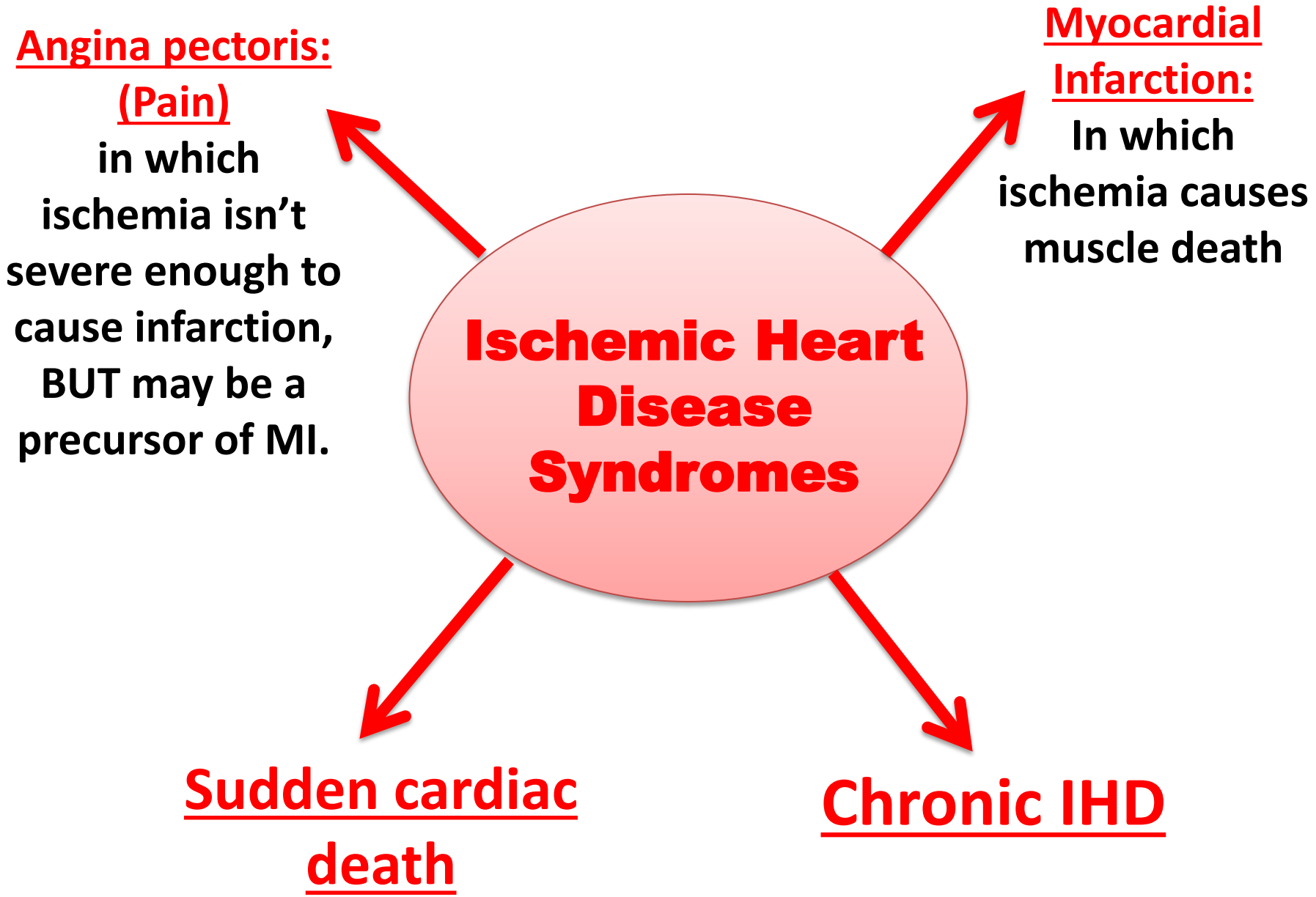
Uncommon causes:

Vasospasm: constriction of the vessels.

Vasculitis






Angina pectoris:
(Pain)
in which ischemia isn't severe enough to cause infarction, BUT may be a precursor of MI.
Myocardial Infarction:
In which ischemia causes muscle death
Ischemic Heart Disease Syndromes
Sudden cardiac death
Chronic IHD

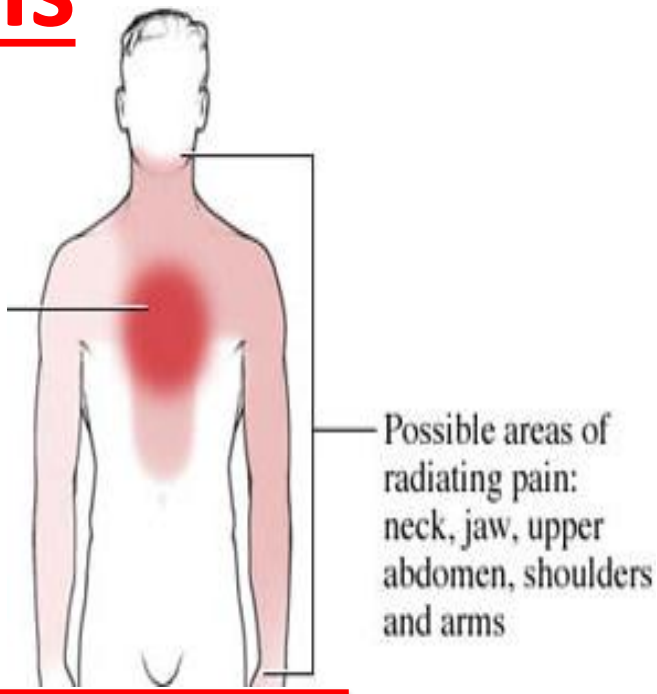
Angina Pectoris

Clinical presentation:

Chest Discomfort (Pain) can be **prolonged, recurrent and with different qualities.** Can radiate down the left arm or to the left jaw

"The patient usually survives angina pains"

Note that In angina pectoris there is no death of heart tissue.



Cause: TRANSIET **myocardial ischemia from seconds to minutes Due to inadequate perfusion then perfusion is restored**

PATTERNS

Stable

-75% vessel block
-Transient (<15 minutes)
-Aggravated by exertion, after certain levels of exertion.
-Relived by rest & Nitroglycerin *VD
*Vasodilator

Prinzmetal

-Also called Variant angina or Vessel spasm
-Occur at rest
-caused by coronary spasm
-Episodic
-Typical ECG change: ST elevation
-Relived by VD but not rest

Unstable

-90% vessel block or Acute plaque change (superimposed thrombus)
-It increases gradually with time; *crescendo*
-Prolonged (>15 min.)
-Not relived by rest and VD
-Pre-infarction Angina
"Can Cause infarction"

Myocardial Infarction "Heart attack"

Risk factors

Major modifiable- SMOKING, DM, hypertension, Hypercholesterolemia

- **Incidence:**

-Mainly in old age group (45% in 65 yrs), (10% in 40)

-Males>Females "It's believed that females' self secreted hormones like estrogen acts as a prophylaxis, BUT Hormone replacement therapy for Postmenopausal females will not protect the heart"

- Ischemic heart disease (myocardial infarction)

When the **severity** or **duration** of ischemia is enough to cause cardiac muscle death, typically results from acute thromboses that follow **plaque disruption**

-Note: In MI we should also think about increase in demand of the O_2, not only the occlusion.

TYPES

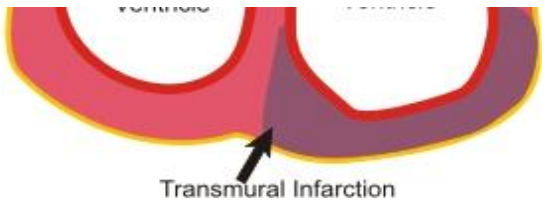
Transmural

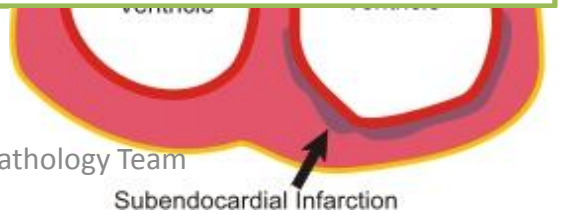
- Full thickness, (>50% of the wall)
- More severe
- Superimposed thrombus in atherosclerosis

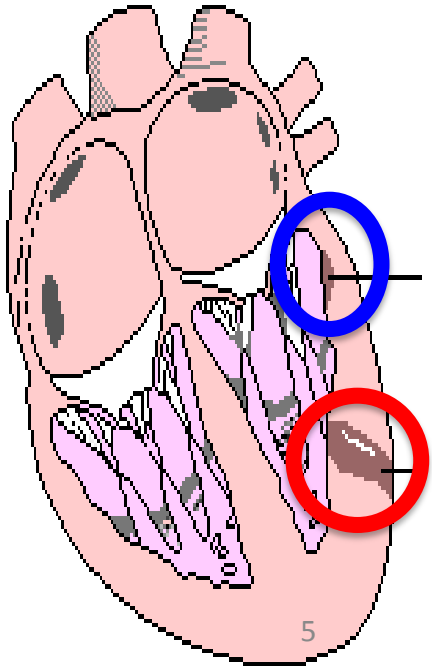
mural = wall

Sub-endocardial

- Inner 1/3 to half of ventricular wall
- Caused by small thrombus.
- Decreased circulating blood volume(shock, Hypotension, Lysed thrombus)







Pathogenesis of MI

Coronary occlusion "**Atherosclerosis with thrombosis** 90%, vasospasm 10%"

Most important mechanism:
dynamic changes in the plaque (rather than plaque size)

Hemodynamic changes: "Plaque rupture, surface is eroded" platelets aggregation "Plaque rupture is the most common cause of heart attacks"

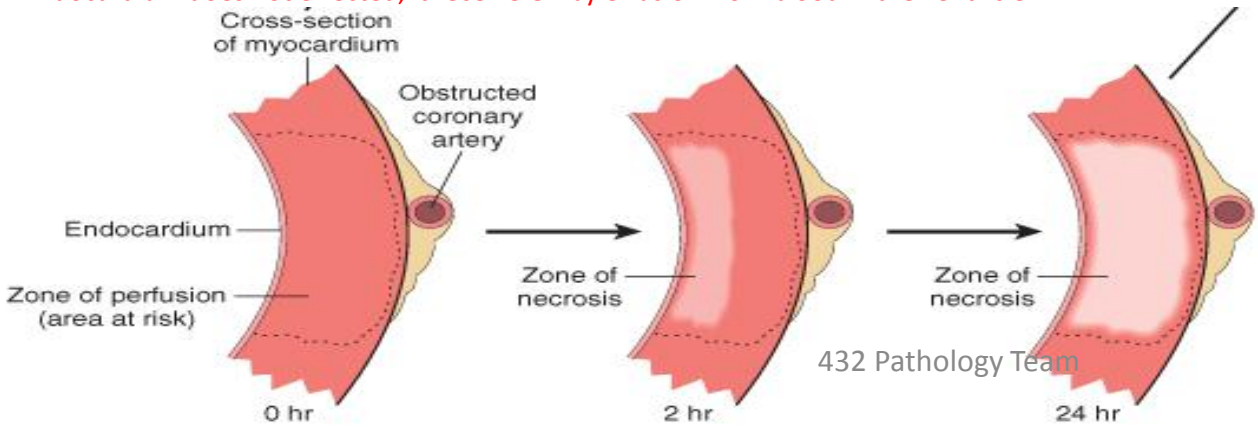
→ thrombus and vasoconstriction (happens in minutes; fast)

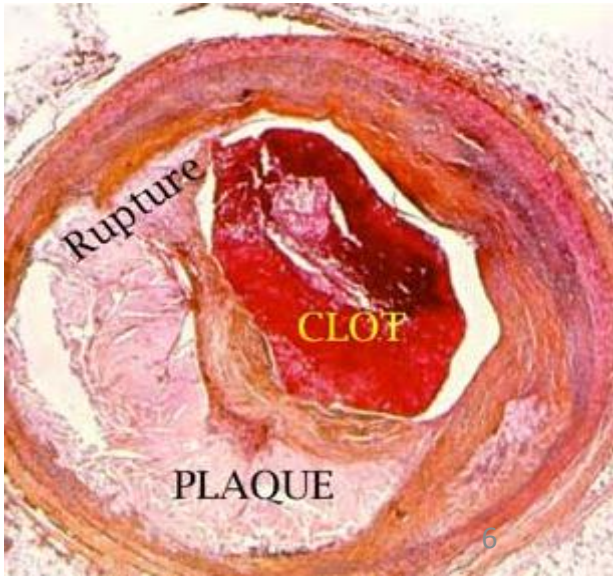
Irreversible changes happens **after 30 minutes** "It's clinically important because **re-perfusion should be started within this 30 minutes (reversible)**, for example: give Nitroglycerin

Mechanism of Cell death = "coagulative necrosis"

Progression of myocardial necrosis after coronary artery occlusion. Necrosis begins in a small zone of the myocardium beneath the endocardial surface in the center of ischemic zone. The area that depends on the occluded vessel for perfusion is the "at risk".

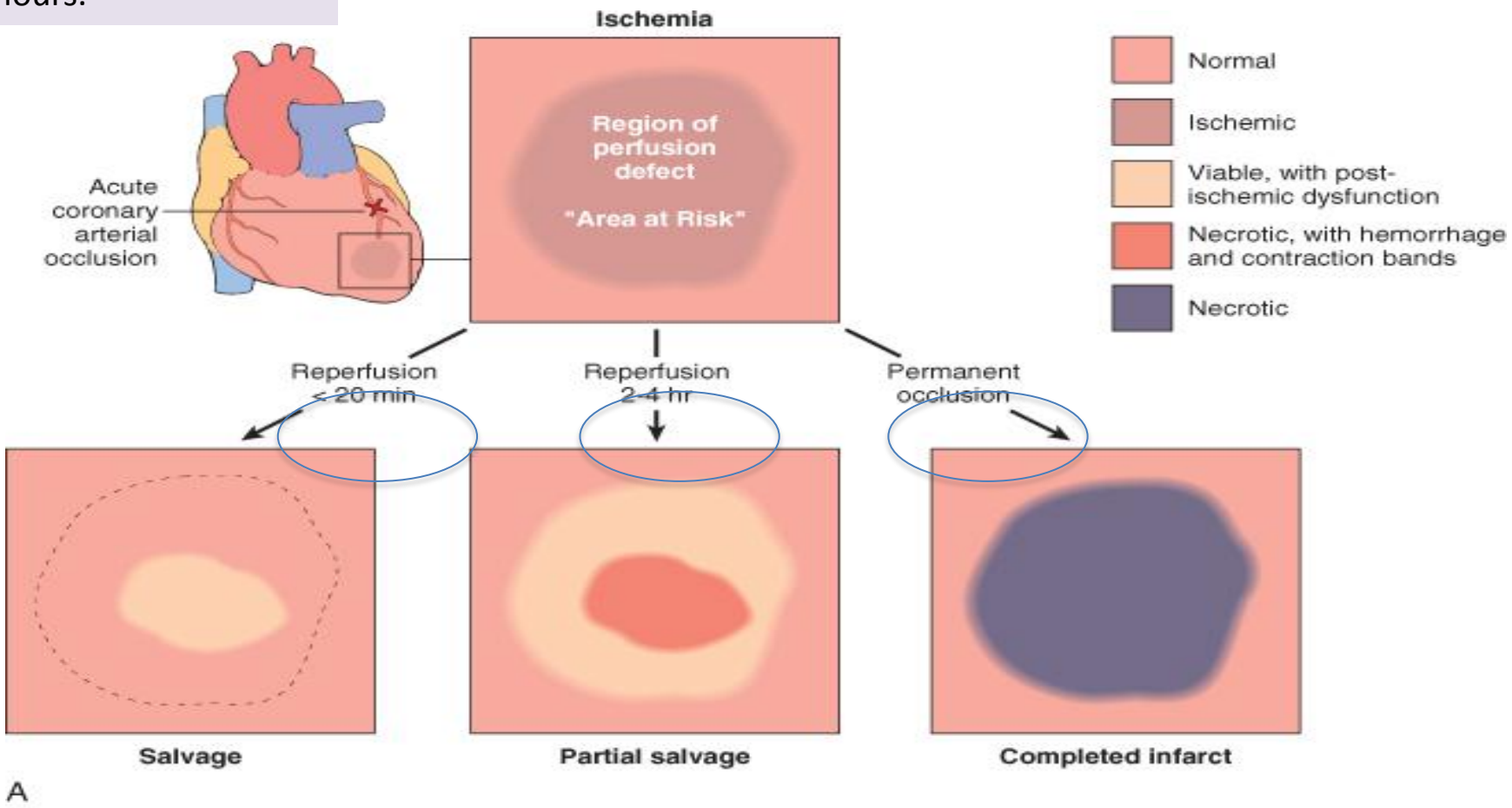
-Endocardium does not effected, it receive O2 by effusion from blood in the ventricle.





Consequences of myocardial ischemia followed by reperfusion

Note that: progressive loss of viability occurs that is completed by 6 to 12 hours.



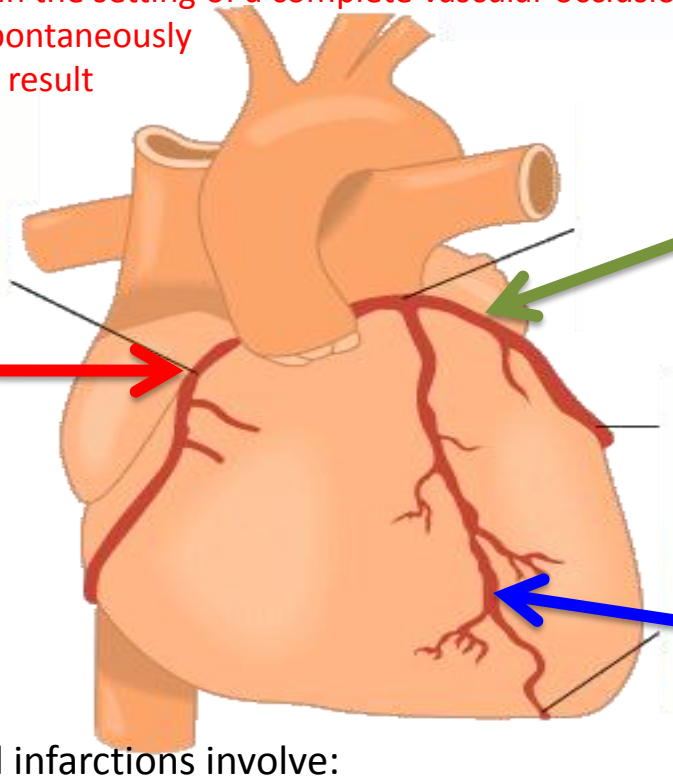
Salvage: Saving; returned back

Coronary blood supply

Depending on which coronary vessel is affected → so the heart tissue that is supplied by it is affected

-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. Unfortunately, acute coronary occlusions cannot spontaneously recruit collateral flow and will result in infarction.

The right coronary artery provides blood mainly to the right atria, right ventricles, and inter ventricular septum



The left circumflex artery provides blood to the left atrium and the posterior and lateral walls of the left ventricle

The left anterior descending artery anterior left ventricular wall

-Nearly **50%** of all myocardial infarctions involve:

1- **The left anterior descending artery** that supplies blood to the main pumping mass of the left ventricle.

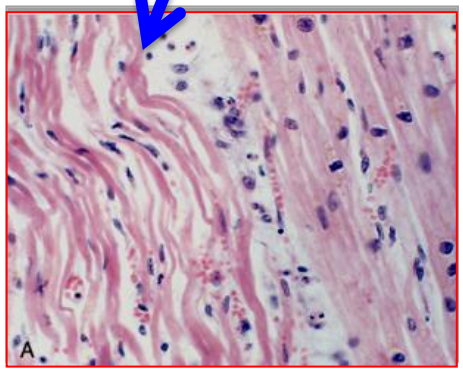
2- **The next** most common site for myocardial infarction is **the right coronary artery**,

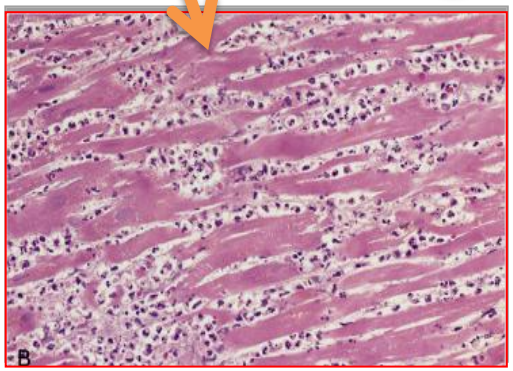
3- followed by **the left circumflex**.

Morphology

1 **Light Microscopy**

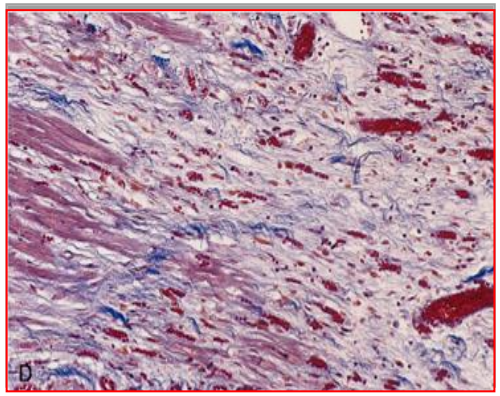
First 12 hrs (no changes)
From 12 hours up to 3 days:
Coagilative necrosis + neutrophils infiltrate

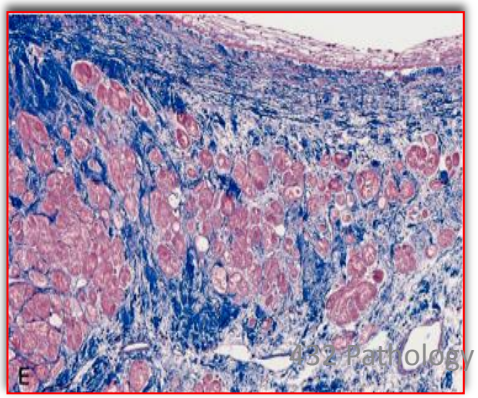




1 to 2 weeks, granulation tissue

>3 weeks, fine scar
>2 months, dense scar





Why these changes are important?
For forensic medicine, to know the cause of death.

2 **EM:**
membrane disruption and Mitochondrial densities

3 **Special stain:**

TTC (Triphenyl Tetrazolium chloride)

It's used grossly to see the infarcted area by taking a section → stain
It binds to Lactate dehydrogenase enzyme "LD"

-Detects and stains Mahogany brown with Lactate dehydrogenase in normal heart
-Unstained area = infarction (No LD)
-White, glistening= scar

Note: period of time between disintegration of dead tissue and formation of good tissue, between 3-10 days, is dangerous because of rupture may happen.

Clinical Features

- **Typical features:**

Severe, crushing substernal chest pain or discomfort that can radiate to the neck, jaw, epigastrium, or left arm

Rapid, weak pulse and sweating profusely (diaphoretic), Dyspnea, chest pain.

Diaphoresis is excessive sweating commonly associated with shock and other medical emergency conditions.

- **Silent MI (no pain)**:

DM (due to peripheral neuropathy), elderly, cardiac transplantation recipients,

Lab Investigations

1- Diagnostic (biochemical markers)

Most IMPORTANT

- **Troponins (T & I),**
  - **Best markers.**
  - **They are both sensitive and cardio – specific.**
- **CK-MB (Creatinine Kinase)**
  - **Next best.**
  - Total CK activity is not a reliable marker of cardiac injury (i.e., it could come from skeletal muscle injury).
- **Lactate dehydrogenase**
- **Myoglobin**

2- Predictive

- **CRP- >3mg/l – highest risk**

Laboratory Evaluation

- **Troponin T and I** are **not normally** detectable in the circulation
- After acute MI both troponins (T & I):
  - Become detectable after **2 to 4 hours**
  - **Peak at 48 hours**
  - Their levels remain elevated for **7 to 10 days**

Investigations should be done immediately because these enzymes raise then return to normal level

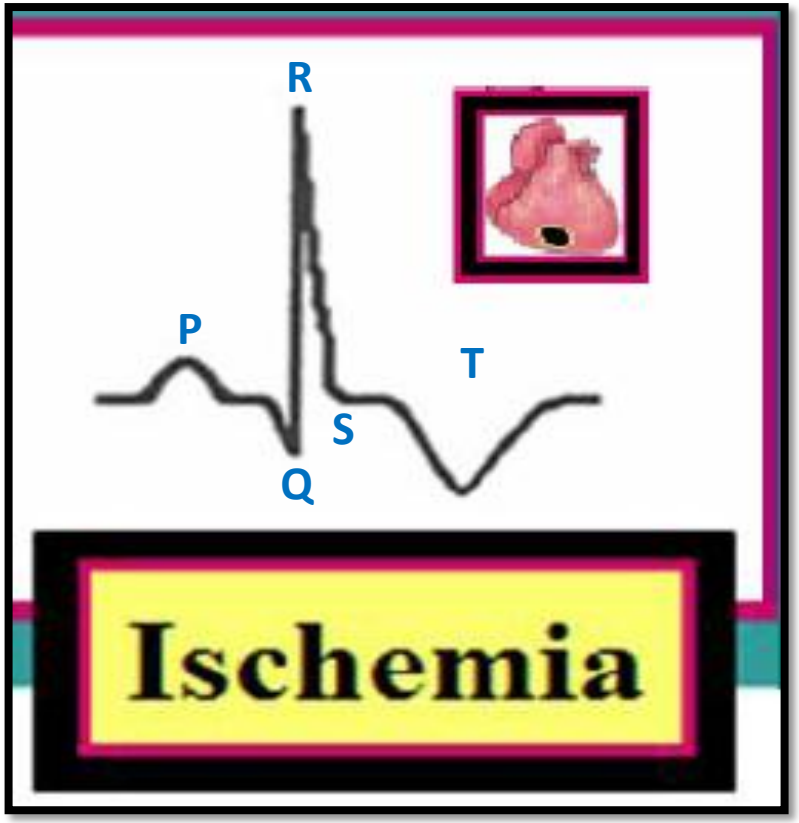
- **CK-MB** is the second best marker
- CK-MB activity:
  - Begins to rise within **2 to 4 hours** of MI
  - **Peaks at 24 to 48 hours**
  - **Returns to normal** within approximately **72 hours**
  - Although cardiac troponin and CK-MB are equally sensitive at early stages of an MI, persistence of elevated troponin levels for approximately 10 days allows the diagnosis of an acute MI long after CK-MB levels have returned to normal

ECG changes

Changes such as:

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

- Arrhythmias



(MI)–Complications

- In 75% of Patients with MI
- Poor prognosis in elderly, females, DM, old case of MI, Anterior wall infarct (LV)– worst, posterior –worse, Inferior wall – best.
- **Arrhythmia responsible for many deaths**
- **Rupture will lead to cardiac tamponade,**
- Aneurysm lead to failure, thrombosis ,arrhythmia and no rupture
- Mural thrombus, potentially source of emboli

Complications	
Arrhythmia	Ventricular Fibrillation – **arrhythmia leads to sudden death in MI patients, before they reach hospital**
Ventricular aneurysm (abnormal dilatation)	**Rupture** is very rare but can occur leading to blood accumulation in the pericardium
Pump failure	Left ventricular failure (LVF), cardiogenic shock, if >LV wall infarcts, lead to death (70% of hospitalized MI patients)
Ventricular rupture	Free or lateral LV wall – MC site, later cause false aneurysm
Pericarditis	Dressler's syndrome (Late MI complication)
Recurrence	

Dressler's syndrome : It consists of a triad of features, fever, pleuritic pain and pericardial effusion.

Chronic IHD or Ischemic Cardiomyopathy

prior infarction(s) (most common)

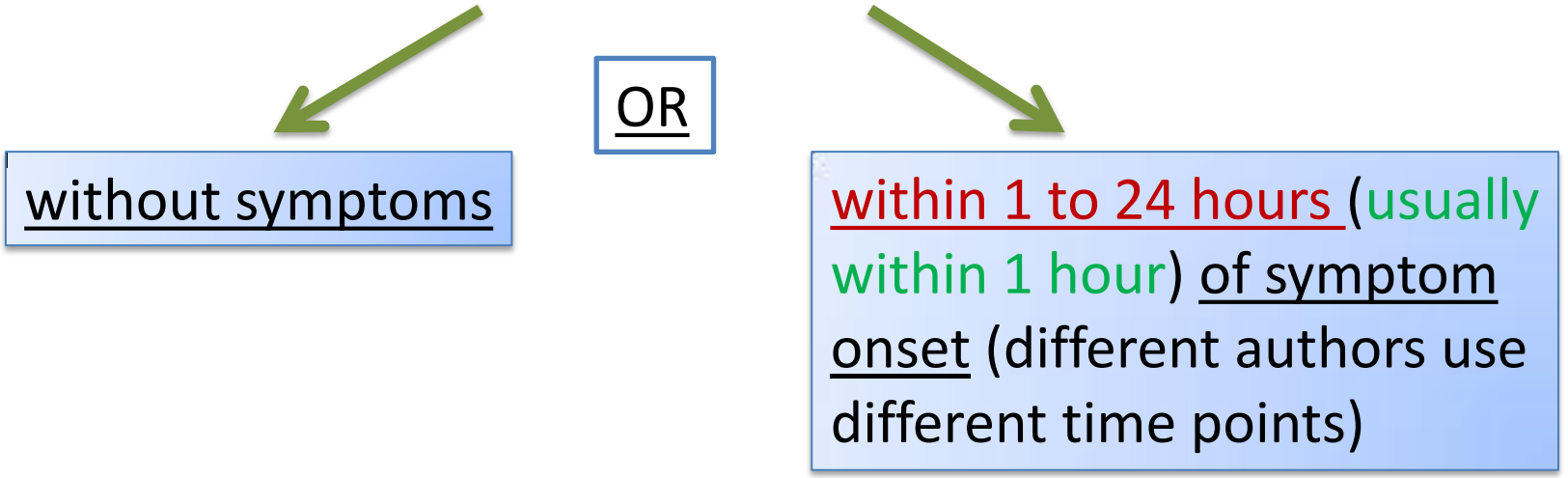
chronic low-grade ischemia

Progressive heart failure due to ischemic injury

- **Cause** =compromised ventricular function.
- **Morphology** =vacuoles, myocyte hypertrophy.
- **Diagnosis**= by exclusion

Sudden Cardiac Death

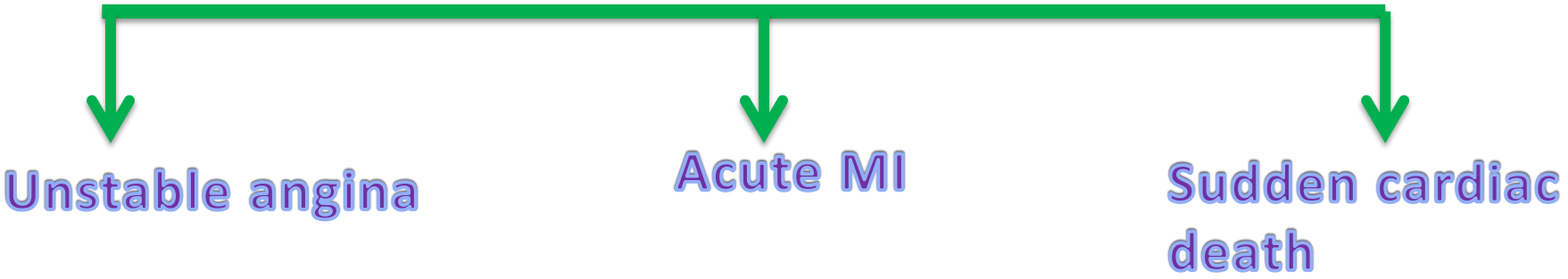
- **Unexpected** death from cardiac causes either:



- Results from a fatal arrhythmia, most commonly in patients with severe coronary artery disease (IHD).

Acute coronary syndrome

It is applied to three catastrophic (disastrous) manifestations of IHD:



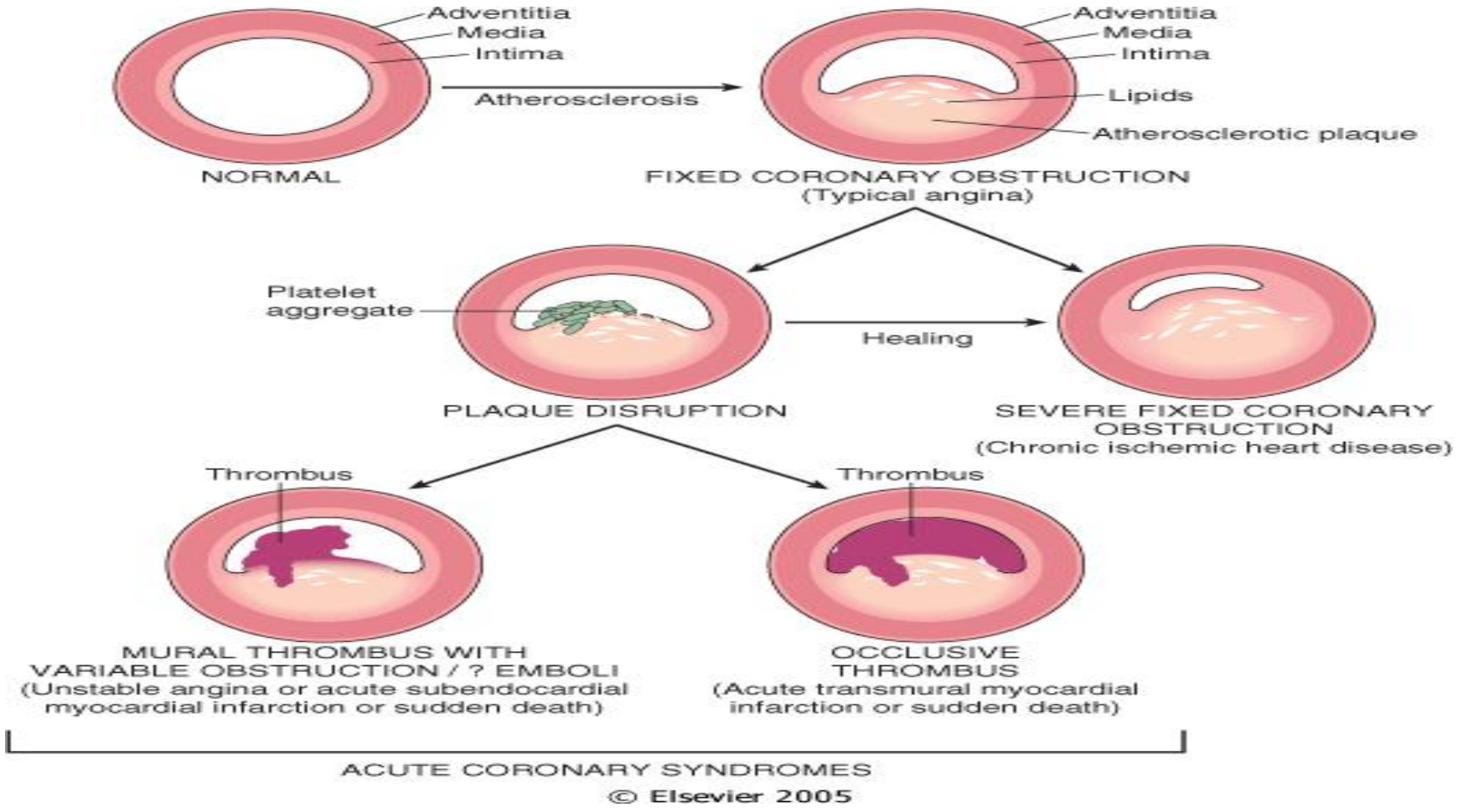
- **They usually lead to immediate death.**

They share common patho-physiologic basis in:

1- coronary atherosclerotic plaque disruption

2- associated intra-luminal platelet-fibrin thrombus formation

Frequently initiated by an unpredictable and abrupt conversion of stable atherosclerotic plaque to unstable plaque followed by thrombosis.



NOTES from Dr. Hisham:

- Ischemia to myocardium rapidly (minutes) leads to loss of function and causes necrosis after 20 to 40 minutes
- Size and volume of infarction depend on: location and duration of thrombosis.
- When we treat the heart of MI, it doesn't mean that the heart well return to its normal condition. Instead, sustain contraction may happen because of reperfusion injury.
- Reperfusion injury: is the tissue damage caused when blood supply returns to the tissue after a period of ischemia or lack of oxygen. Reperfusion injury is mediated in part by oxygen free radicals generated by the increased number of infiltrating leukocytes facilitated by reperfusion.

From Dr. slides:

- If patient survive thrombi may lyse spontaneous or by rx
- 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

Questions:

- What is the primary cause of ischemic heart disease?

Atherosclerosis

- What individuals may have “ silent” MI ?

Diabetes

- Tell what cardiac condition is indicated by ECG change (Q wave)

Transmural infarction

- Which type of angina pectoris is most worrisome?

Unstable angina

Thank You