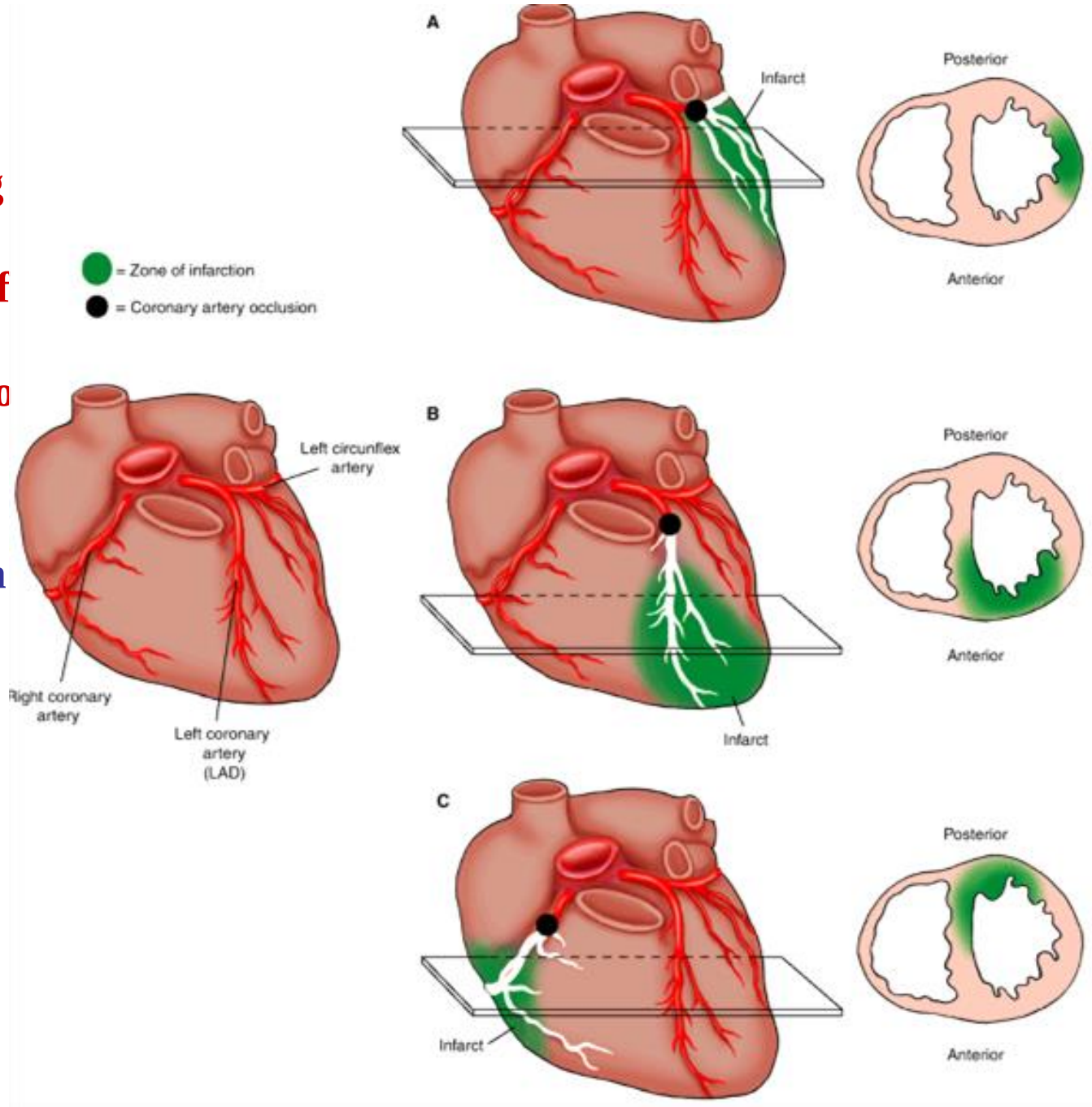
The Normal heart

- **Average weight of the heart in females is 250 - 300 g**
- **Average weight of the heart in males is 300 - 350 g.**
- **Normal Rt. ventricular wall thickness is 0.3 to 0.5 cm**
- **Normal left ventricular wall thickness is 1.2 to 1.5 cm.**
- **Higher weight or ventricular thickness signifies *hypertrophy*;**
- **Below normal weight signifies *atrophy*;**
- **Below normal thickness of the ventricular wall implies *dilatation*.**
- **A normal ventricular thickness may be found in a markedly heavy (hypertrophied) heart indicating ventricular dilatation.**

A:Posterolateral infarct, which follows occlusion of the LCX.

B. Occlusion of LAD result in MI involving the anterior LV wall, adjacent two-thirds of the septum and the entire circumference o the wall near apex.

C. A posterior infarct results from occlusion of the RCA and involves the posterior wall, including the posterior third of the interventricular septum and the posterior papillary muscle in the basal half of the ventricle.



Cardiac hypertrophy

- This is an **adaptive response to increased mechanical load on the heart** in which there is an increase in the rate of protein (myofilaments) synthesis within each cell. As a result there is an increase in cell size (hypertrophy).
- **Causes of hypertrophy include**

1. Pressure overload

a. systemic or pulmonary hypertension

b. aortic or pulmonary stenosis

2. Volume overload

a. aortic or pulmonary valve regurgitation

b. abnormal communications between the two sides of the heart, congenital or acquired

3. Excessive stimulation as of β-adrenergic receptors e.g. in hyperthyroidism leading to an increase in heart rate.

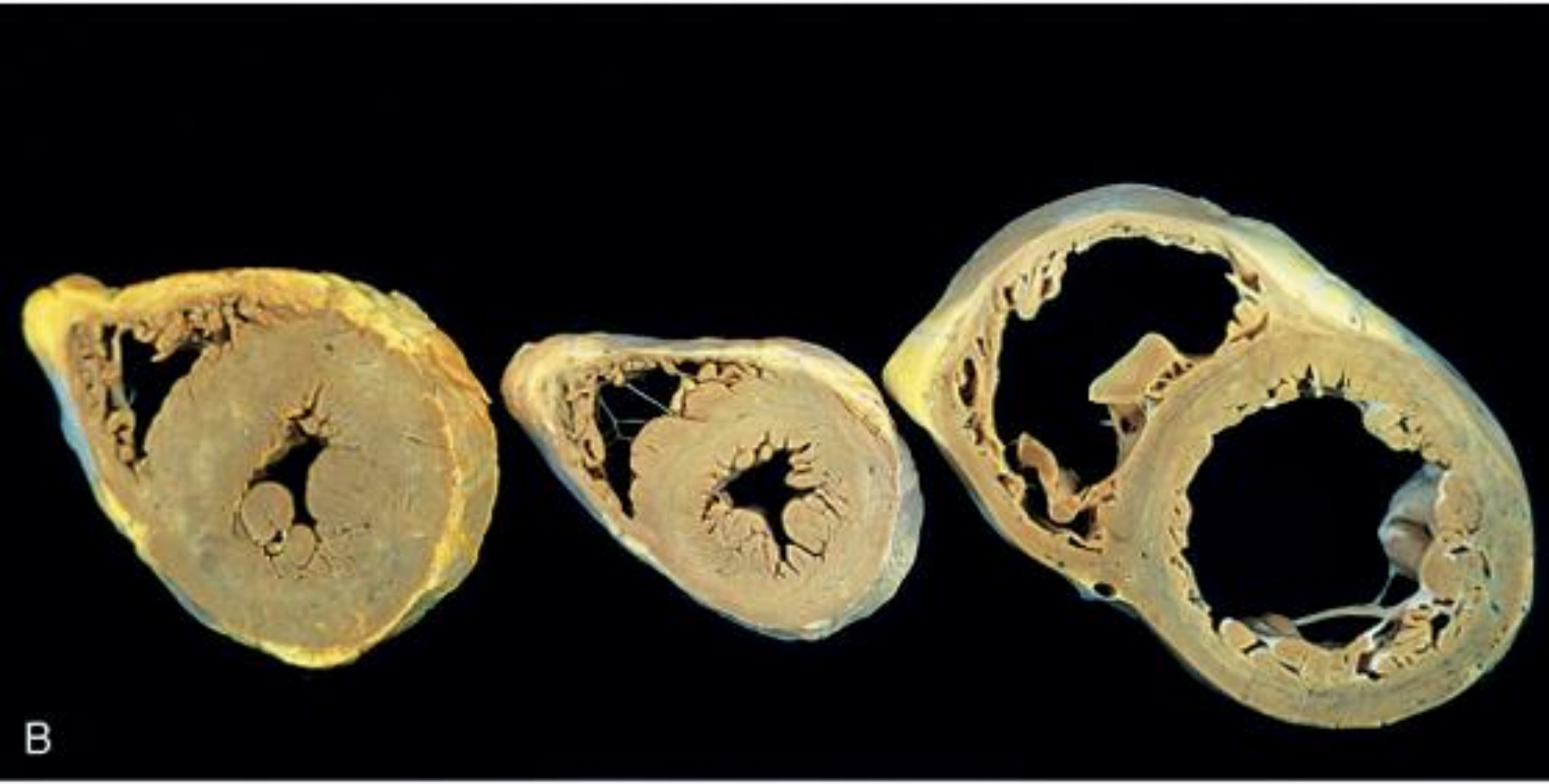
- ***The severity of hypertrophy depends on the underlying causes***

  1. Mild hypertrophy (up to 2X normal weight) as in ischemic heart disease

  2. Moderate hypertrophy (>2-3X normal) as in systemic hypertension & aortic stenosis

  3. Marked hypertrophy (> 3X normal; up to 1000 g heart weight) as in aortic regurgitation and hypertrophic cardiomyopathy.

Patterns of left ventricular hypertrophy compared to normal (middle)



The pattern of hypertrophy reflects the nature of the underlying cause

In pressure-overload hypertrophy there is ***concentric hypertrophy*** of the left ventricle. This hypertrophy may reduce the cavity diameter i.e. restrict diastolic filling**.**

In contrast, in volume-overload hypertrophy there is also **dilation** that increases the size of the ventricular cavity. Owing to the dilation, wall thickness of a heart in which both hypertrophy and dilation have occurred is not necessarily increased, and it may be normal or even less than normal i.e. the dilation masks hypertrophy. **Thus, wall thickness is not by itself an adequate measure of volume-overload hypertrophy.**

Hypertrophied heart shows increased oxygen consumption due to increased metabolic requirements and thus, hypertrophy constitutes a breakable balance of the adaptation-related changes (e.g. new myofilaments synthesis) versus those related to the injurious agent e.g. **decrease in capillary density** due to the pressure effect of the enlarged myocyte and this stimulates deposition of fibrous tissue. Thus ***sustained cardiac hypertrophy often progresses to cardiac failure***.

In contrast to the pathologic hypertrophy, **physiologic hypertrophy** that is induced by regular tough exercise is rather an extension of normal growth and has minimal or no harmful effect.

- In heart failure there is usually a combination of forward & backward failures. Explain.

CONGESTIVE HEART FAILURE

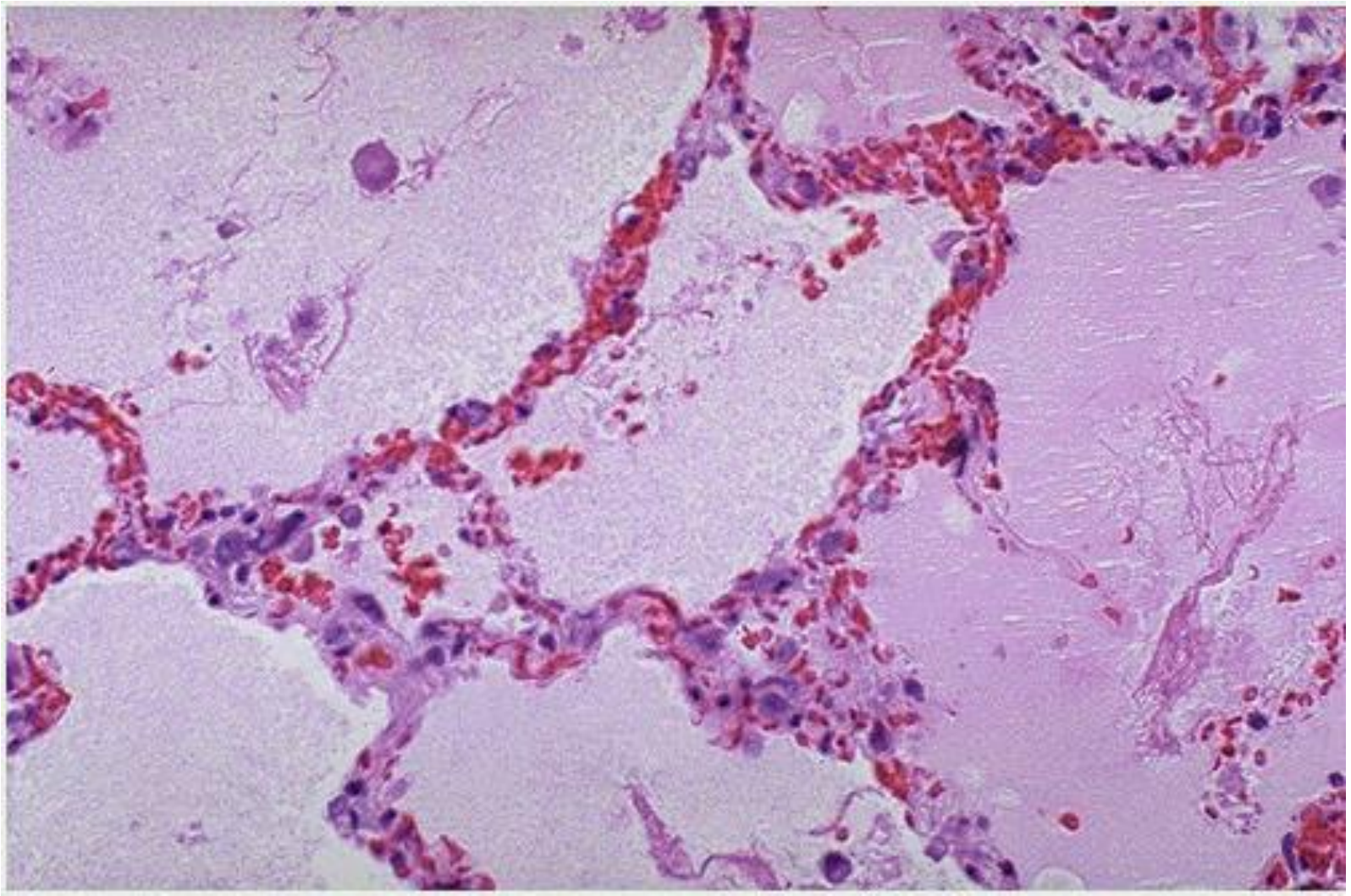
Congestive Heart Failure is the end point of many cardiac diseases.

The failing heart is unable to pump sufficient blood to meet the requirements of the body.

Inadequate cardiac output (***forward failure***) means that the failing ventricle can no longer pump the whole blood delivered to it by the venous circulation. Thus, there is an associated increase in venous pressure & congestion of the venous circulation (***backward failure***). In Congestive HF, other organs are eventually affected by some combination of forward and backward failure.

Excluded from HF definition are conditions in which inadequate cardiac output (COP) is not due to cardiac abnormality e.g. shock states including blood loss or conditions of impaired blood return to the heart (e.g. thrombosis of inferior vena cava).

A 60-year-old diabetic, hypertensive & heavy smoker male. He developed sudden onset of vague epigastric pain with severe dyspnea . He rapidly deteriorated to his death. This is a section of his lung



Heart failure is a common eventual outcome of many forms of heart disease.

Left-sided and right-sided failure can occur independently. Nevertheless, because the CVS is a closed circuit, failure of one side (particularly the left side) often produces excessive strain on the other side, terminating in global heart failure.

Causes of left-sided cardiac failure include

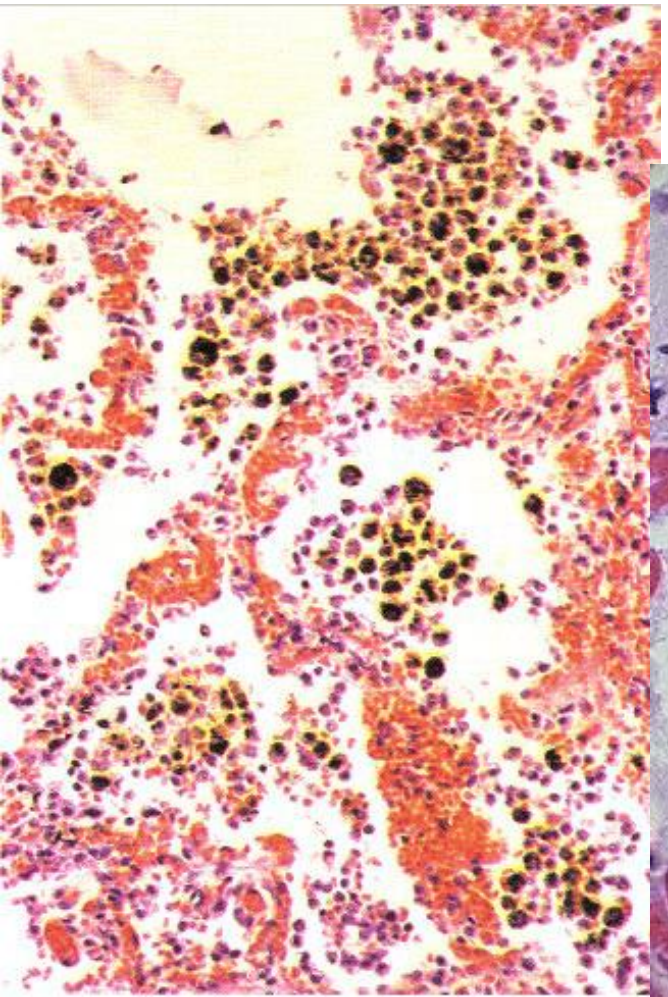
1. IHD (the most common)
2. Systemic hypertension (the next most common)
3. Mitral or aortic valve disease
4. Primary diseases of the myocardium (cardiomyopathies)

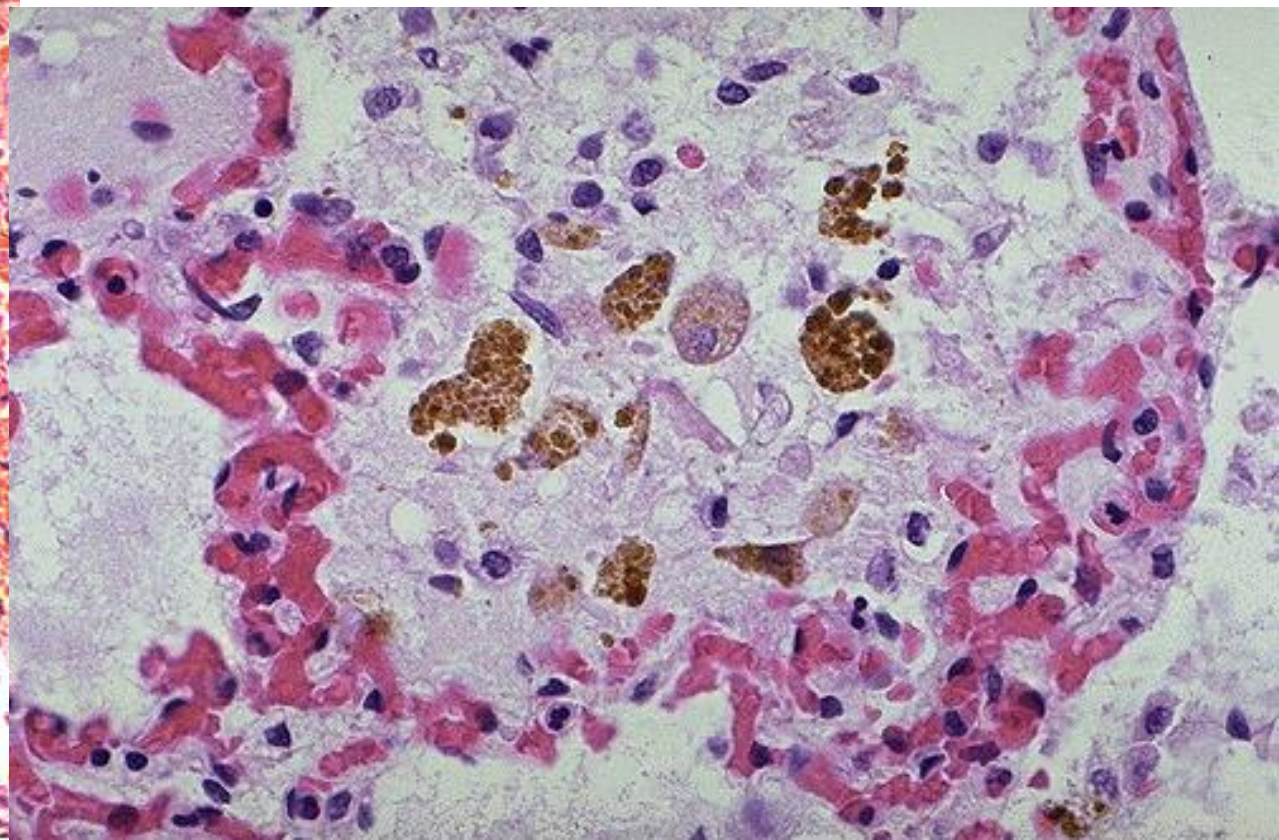
Causes of right-sided heart failure include

1. **Left ventricular failure** (the most common); it is due to its associated pulmonary congestion with elevation of pulmonary arterial pressure.
2. **Intrinsic diseases of the lung parenchyma** and/or pulmonary vasculature (cor pulmonale)
3. **Right sided valve diseases**
4. **Congenital heart diseases, associated with left → right shunts**

• ***The changes in the lungs*** are a conseuence of chronic venous congestion which manifests grossly as (Brown induration). Microscopically there is congestion of venules and capillaries, edematous widening of alveolar septa, accumulation of edema fluid in the alveolar spaces, heart failure cells and later increased interstitial fibrosis.

CVC lung

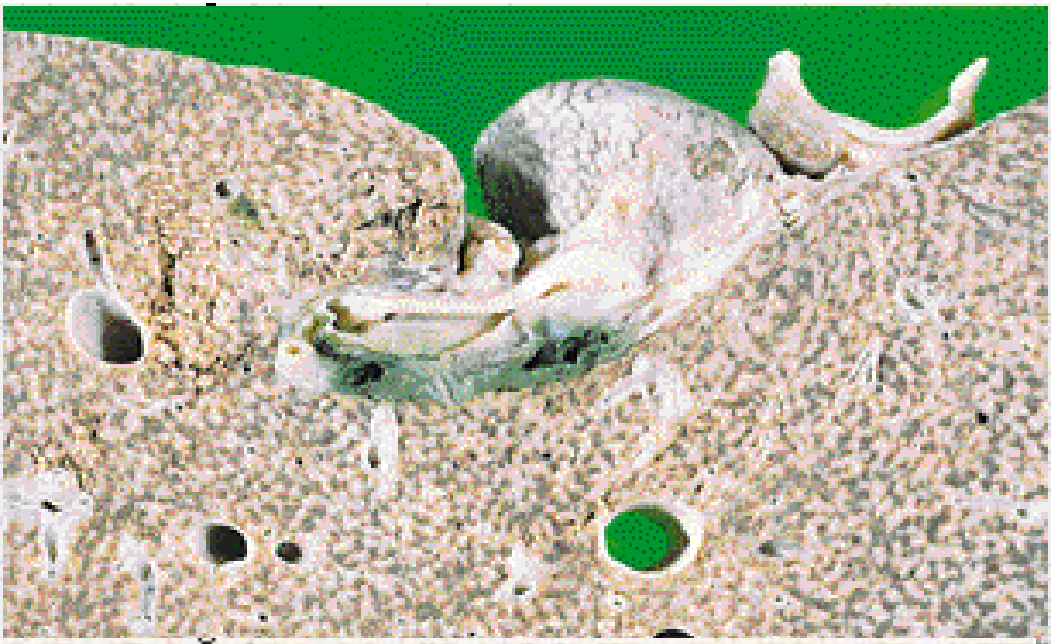




- ***The Kidneys*** suffer a reduction in perfusion due to reduced cardiac output, which activates the renin-angiotensin-aldosterone system, inducing retention of salt and water with consequent expansion of the interstitial fluid and blood volumes. This can contribute to the pulmonary edema in LHF. If the perfusion deficit of the kidney becomes severe, impaired excretion of nitrogenous products may cause azotemia.
- ***Hypoxic encephalopathy*** may occur in far-advanced LHF, causing irritability and restlessness, which may progress to coma.

- **Right-sided heart failure (RHF)**
- Chronic pulmonary hypertension (secondary to LHF, or pulmonary disease) predispose to RVH and often dilation which are confined to the right ventricle and atrium in pure RHF. The major morphologic and clinical effects of pure right-sided heart failure differ from those of left-sided heart failure in that
- Pulmonary congestion is minimal
- Engorgement of the systemic and portal venous systems is prominent.

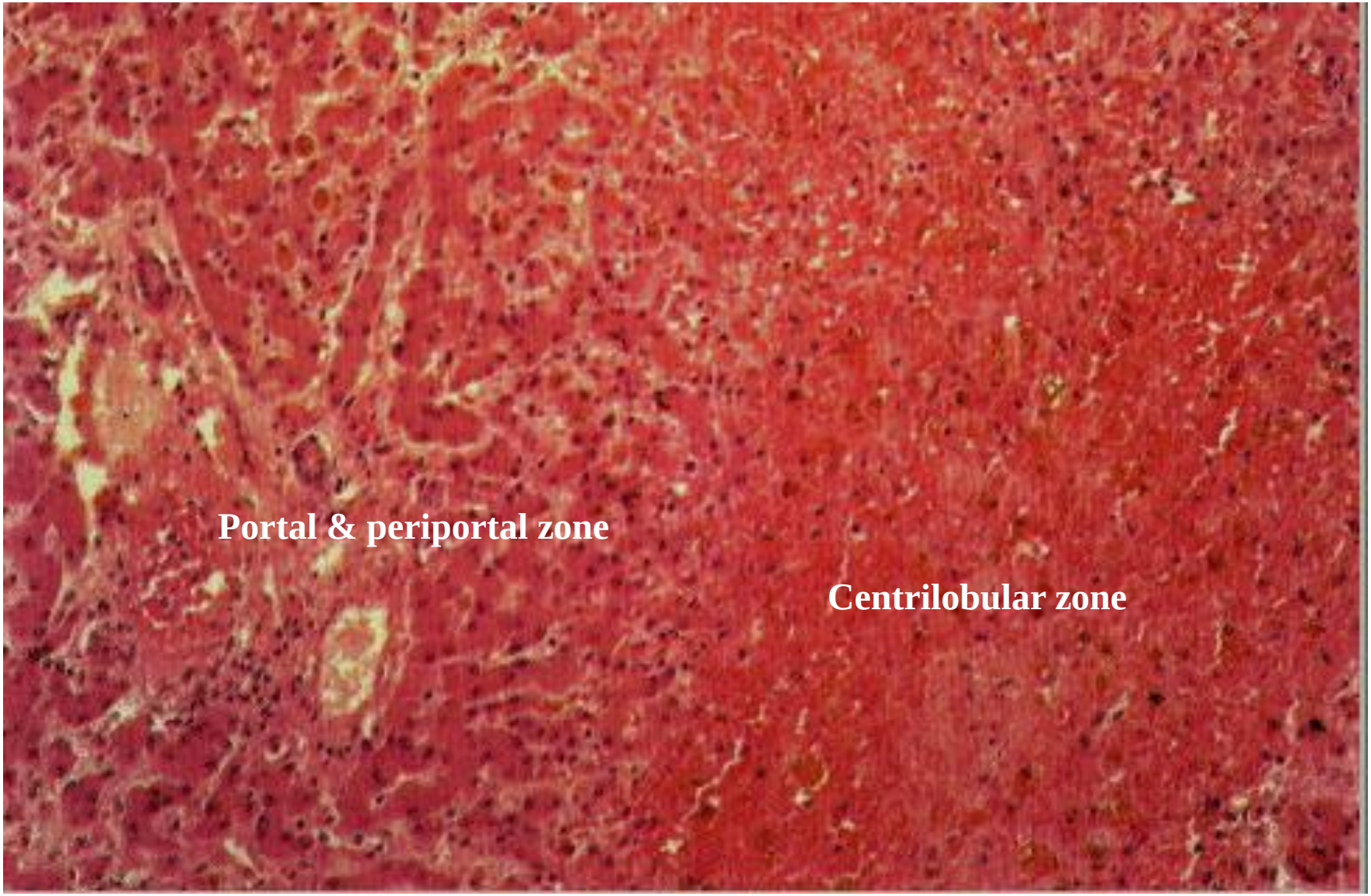
CVC-LIVER (Nutmeg liver)



Morphological changes of RHF In addition to cardiac changes, the result of RHF, systemic and portal venous congestion include:

The Liver is usually increased in size and weight (congestive hepatomegaly), with a cut section that displays nutmeg appearance. Sometimes when LHF is also present, the severe central hypoxia produces centrilobular necrosis (*central hemorrhagic necrosis*). With long-standing severe RHF, the central areas can become fibrotic, creating *cardiac fibrosis*.

CVC liver



DISEASES OF THE HEART

- *Heart disease, especially ischemic, is the predominant cause of disability and death. It accounts for about **40% of all postnatal deaths**; this is twice the number of deaths caused by all forms of cancer combined.*
- ***Five categories of disease account for nearly all cardiac mortality***
- *Congenital heart disease*
- *Ischemic heart disease (IHD) (coronary heart disease)*
- *Hypertensive heart disease (systemic and pulmonary)*
- *Valvular heart disease (Rheumatic, etc.)*
- *Cardiomyopathies (non-ischemic-primary myocardial disease)*

ISCHEMIC HEART DISEASE

- IHD includes a group of closely related syndromes resulting from **an *imbalance between the supply and demand*** *of the heart for oxygenated blood*.
- Depending on the **rate** of development and **severity of arterial narrowing(s), *four ischemic syndromes may result***

1- Angina pectoris

2- Myocardial infarction

3- Chronic ischemic heart disease

4- Sudden cardiac death, which may be superimposed on any of the above three.

- **The occurrence of any one of the above depends largely on the relative contributions of four events**

a. Stenosis b. thrombosis

c. platelet aggregation d. coronary artery spasm

The heart may suffer a deficiency of oxygen supply in the following circumstances

1. Reduction in coronary blood flow (90% of the cases)

- Atherosclerosis (the main cause)
- Coronary artery spasm
- Hemodynamic derangement (as in shock and HF)
- Non-atherosclerotic coronary diseases (e.g. arteritis)

2. Increased demand

as in tachycardia, ventricular hypertrophy

3. Reduced oxygen carrying capacity of the blood

a- Anemia

b-Advanced lung diseases

c-Carbon monoxide poisoning

d- Cigarette smoking

e- Cyanotic congenital heart diseases

The role of coronary atherosclerosis:

Over **90%** of patients with IHD have advanced coronary atherosclerosis**.** This is defined as having *one or more stenotic lesions causing at least **75%** reduction of the cross sectional area of at least one of the major (epicardial) coronary arteries*. The stenosing plaques tend to occur within the first 2 cm of the LAD and LCX & proximal and distal thirds of the RC.

***The role of platelets*:**

Rupture of an atheromatous plaque exposes subendothelial collagen, which is thrombogenic causing platelet adherence, activation, release reactions resulting in the production of a large pool of activated platelets within the coronary system.

The aggregated platelets may lead to

- Occlusive thrombosis
- Micro-emboli that aggravate the perfusion deficit
- The activated platelets liberate vasoactive products that include thromboxane A2, histamine, and serotonin, which contribute to a possible coronary vasospasm.

- ***The results of long-term use of small doses of aspirin*** *have resulted in a reduction in death from IHD due* to inhibition of synthesis of thromboxane A2, a potent aggregator of platelets and a vasoconstrictor.

- ***Diets rich in fish with their polyunsaturated omega-3 fatty acids*** substantially lower the incidence of mortality from IHD due to reduced platelet aggregation.

The role of vasospasm:

- Vasospasm of large atheromatous epicardial arteries has been **documented angiographically** in some patients with angina or MI.
- This may contribute to rupture or fissuring of plaques leading to thrombosis and platelet aggregation.
- Platelets activation could initiate or aggravate coronary artery spasm through their products e.g. thromboxane A2.
- In rare cases, coronary artery spasm has been associated with acute MI in patients having no atheromatous coronary narrowing.

The role of nonatheromatous lesions of the coronaries

The following disorders, when involving the coronaries, have been associated with one or more of the IHD syndromes:

- Emboli to the coronaries
- Arteritis (e.g., Takayasu's disease, SLE, Kawasaki's syndrome, PAN and others)
- Cocaine abuse through triggering arrhythmias and vasospasm
- Trauma to the coronaries.

The acute ischemic coronary syndromes include

- Unstable angina
- Acute MI (transmural or subendocardial)
- Sudden cardiac death

An acute coronary syndrome usually result from disruption of a stable atherosclerotic plaque, causing rapid progression of coronary obstruction, and initiated by

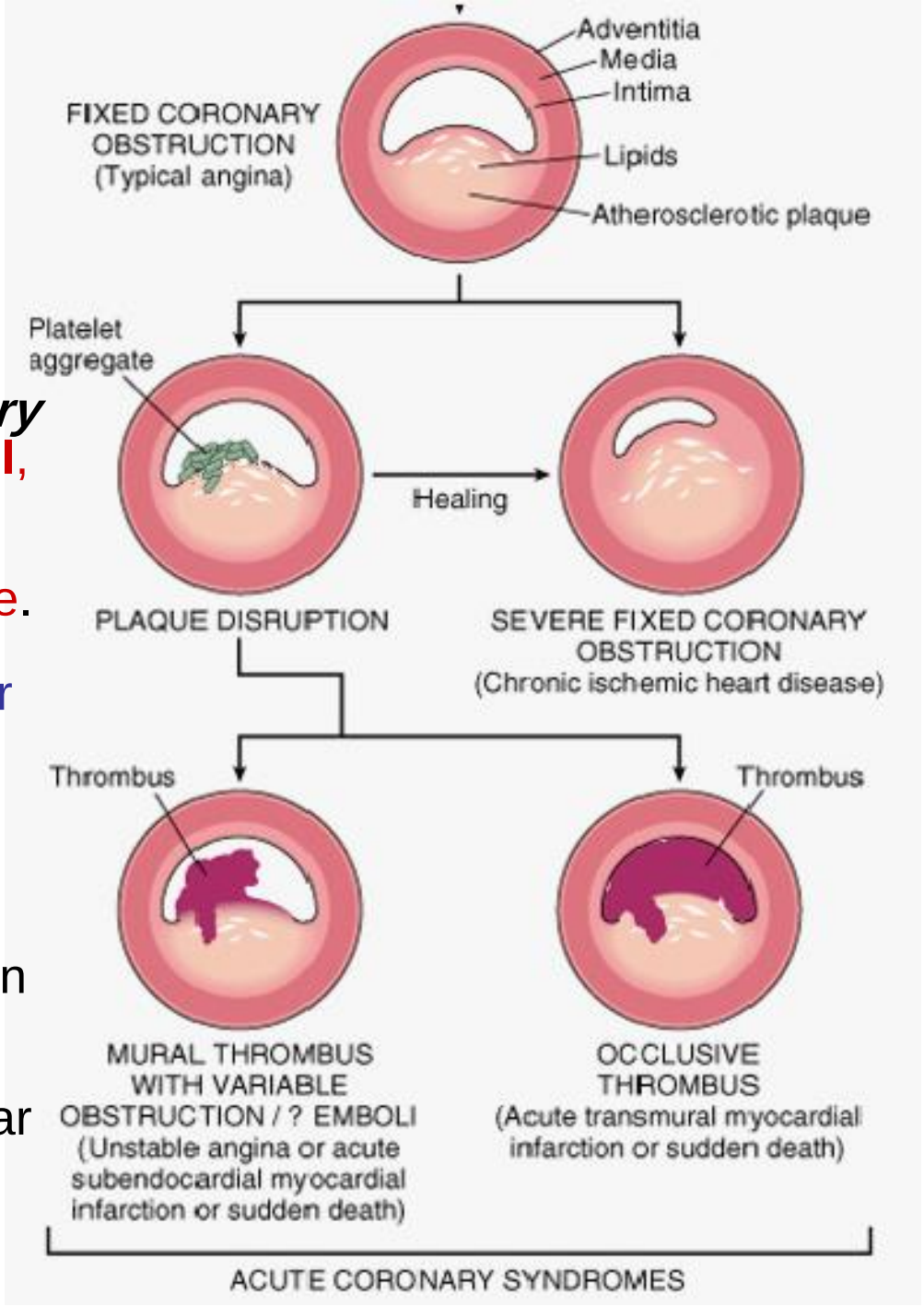
1- Erosion, ulceration, fissuring or rupture; these are complicated by superimposed thrombosis.

2- Hemorrhage into the plaque, expanding its volume and thus aggravates the already present stenosis.

- **Slowly developing occlusions may stimulate collateral vessels over time**, which protect against myocardial ischemia and infarction even with an eventual high-grade stenosis. Although only a single major coronary artery may be affected by the stenosis, two or all three coronaries (LAD, LCX, and RCA) are often involved.

Sequencial progression of Coronary artery lesion

Disruption of the atheromatous plaque is decisive to the pathogenesis of the acute coronary syndromes. In **acute transmural MI**, the usual event is an **occlusive thrombus** superimposed on a disrupted but partially stenotic plaque. In contrast, with **unstable angina**, acute **subendocardial infarction**, or **sudden cardiac death**, the luminal obstruction by thrombosis is usually incomplete. Mural thrombus in a coronary artery can **embolize** to the smaller distal intramyocardial circulation. Sudden cardiac death can be the result of regional myocardial ischemia that induces a fatal ventricular arrhythmia (e.g. ventricular fibrillation).



Angina pectoris is characterized by ***paroxysmal, usually recurrent attacks of substernal or precordial chest discomfort or pain caused by transient myocardial ischemia***. This ischemia is not sufficient enough to cause infarction. There are three overlapping patterns of angina that are caused by varying combinations of increased myocardial demand and decreased myocardial perfusion.

1- Stable (typical) angina is the most common form that is caused by reduction of coronary perfusion to a critical level by chronic **fixed stenosing atherosclerosis of 75% or greater of the original lumen**. This generally causes symptomatic ischemia whenever there is increased cardiac workload, such as that produced by physical activity, emotional excitement, etc. It is usually relieved by rest or nitroglycerin.

2- Prinzmetal (variant) angina is uncommon form that occurs at rest and is due to **episodic occlusive coronary artery spasm of normal or minimally diseased coronary artery.**

3- Unstable angina is one of the acute coronary syndromes characterized by progressively increased frequency and more prolonged attacks of angina. **It is induced by disruption of an atherosclerotic plaque with superimposed thrombosis and possibly embolization to a more distal vessels and/or vasospasm**. These changes generally cause a severe reduction of the arterial lumen by 90%. Unstable angina lies intermediate between stable angina on the one hand and MI on the other.

Myocardial infarction *is the leading cause of death in many countries.* Over 50% of these fatalities occur before the patient reaches the hospital, mainly due to fatal arrhythmias as ventricular fibrillation.

Morphologically MI are divided into two types; **Transmural infarct,** which is the most common and more serious, and **Subendocardial infarct**.

Pathogenesis of MI

- ***Transmural infarction:*** the vast majority of these **(90%)** are caused by an *occlusive coronary thrombus* overlying an ulcerated or fissured stenotic atheroma.
- Increased myocardial demand, as with tachycardia or hemodynamic disturbances, may constitute the final blow in an already unstable situation.
- It seems that behind every acute MI a dynamic interaction has occurred among several or all of the following:
  - severe coronary atherosclerosis
  - acute atheromatous change (fissuring, ulceration, etc.)
  - Platelet activation
  - superimposed thrombosis
  - vasospasm

- ***Subendocardial myocardial infarction***
- The subendocardium is most vulnerable region to any reduction in coronary blood flow.
- Almost always there is advanced, but often not severe, coronary atherosclerosis.
- Thrombosis has been demonstrated in only 25% of the cases and ***total occlusion of a major coronary artery or branch is uncommon*** (autopsy studies). There is a suspicion that a thrombus often initiates the process, but is then spontaneously lysed. In support of this hypothesis is the beneficial effect of ***fibrinolytic treatment*** of patients with recently developed subendocardial infarcts.
- It has been proposed that diffuse atherosclerosis with global reduction of coronary flow (increased demand, vasospasm, or platelet aggregation) transform the situation into critical insufficiency that eventuates in this form of infarction

Gross features of MI

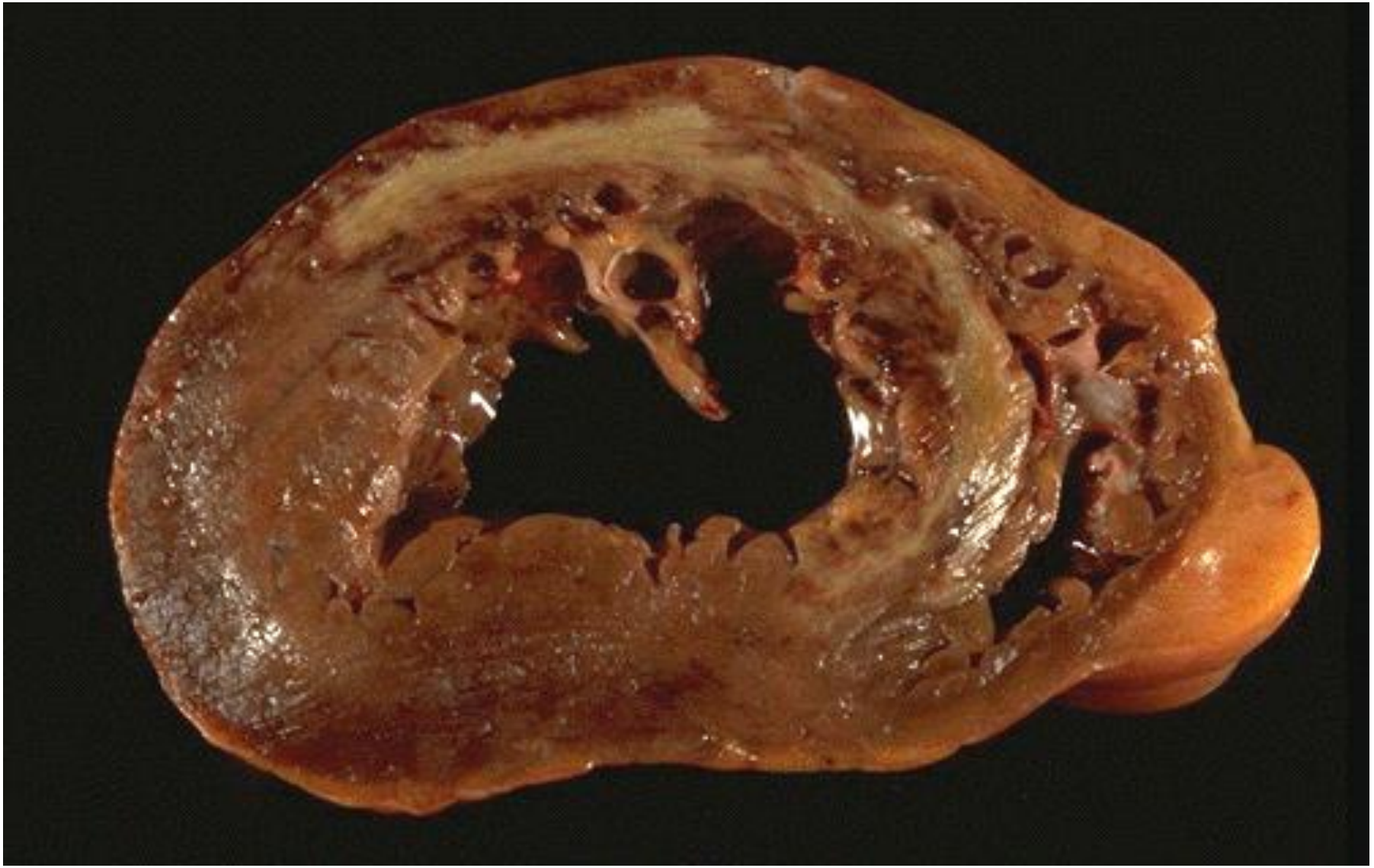
- ***Transmural infarcts***
- Virtually all tranasmural infarcts involve the Lt ventricle (including the interventricular septum).
- When they affect the posterior free wall and posterior portion of interventicular septum, they extend into the adjacent Rt ventricular wall in up to 30% of the cases.
- Isolated infraction of the Rt ventricle is distinctly uncommon (1-3%).
- The transmural infarct is usually 4 to 10 cm in the longest dimension, but may involve the entire circumference of the Lt Ventricle. The efficiency of the collaterals may modify the extent and distribution of the infarct.
- Severe stenosing coronary atheroma is generally present but occlusive thrombus may or may not be identified at the time of postmortem examination.

- **Left anterior descending coronary artery (40% to 50%): infarct involves anterior wall of left ventricle near apex; anterior portion of ventricular septum; apex circumferentially**
- **Right coronary artery (30% to 40%): infarct involves inferior/posterior wall of left ventricle; posterior portion of ventricular septum; inferior/posterior right ventricular free wall in some cases.**
- **Left circumflex coronary artery (15% to 20%): infarct involves lateral wall of left ventricle except at apex**

Depending on the length of patient's survival, the area of necrosis undergoes a progressive sequence of gross changes.

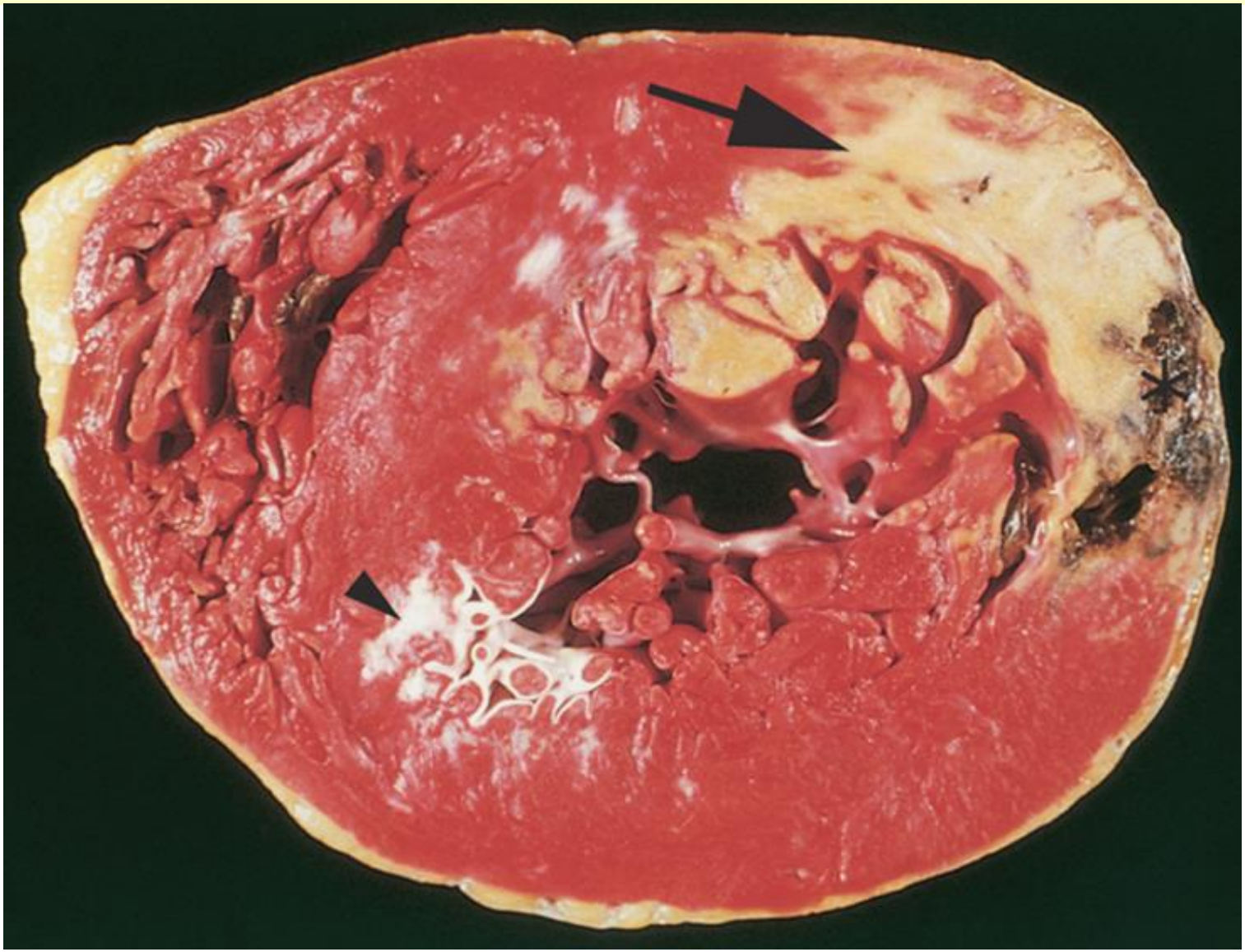
- Myocardial infarcts less than12 hours old are usually inapparent on gross examination.
- By **18-24 hours**, the lesion displays pallor or red-blue cyanotic discoloration (due to stagnated, trapped blood)
- Thereafter the infarct becomes progressively a more sharply defined, yellow, softened area
- By the end of the first week it is rimmed by a hyperemic, narrow zone of highly vascularized connective tissue (line of demarcation)
- Over the succeeding weeks, the necrotic muscles are progressively replaced by the ingrowth of granulation tissue.
- In most instances, scarring is well advanced by the end of six weeks, but the time required for total replacement depends on the size of the original infarct.

MI involving LV anterior free wall and septum



A cross section of a post-mortem heart; posterior wall above. Describe

To what diseased coronary artery does the large lesion is possibly related



The following are features of subendocarial infarction EXCEPT

A. Associated coronary atherosclerosis is often severe

B. Coronary thrombosis is demonstrated in one fourth the of the cases

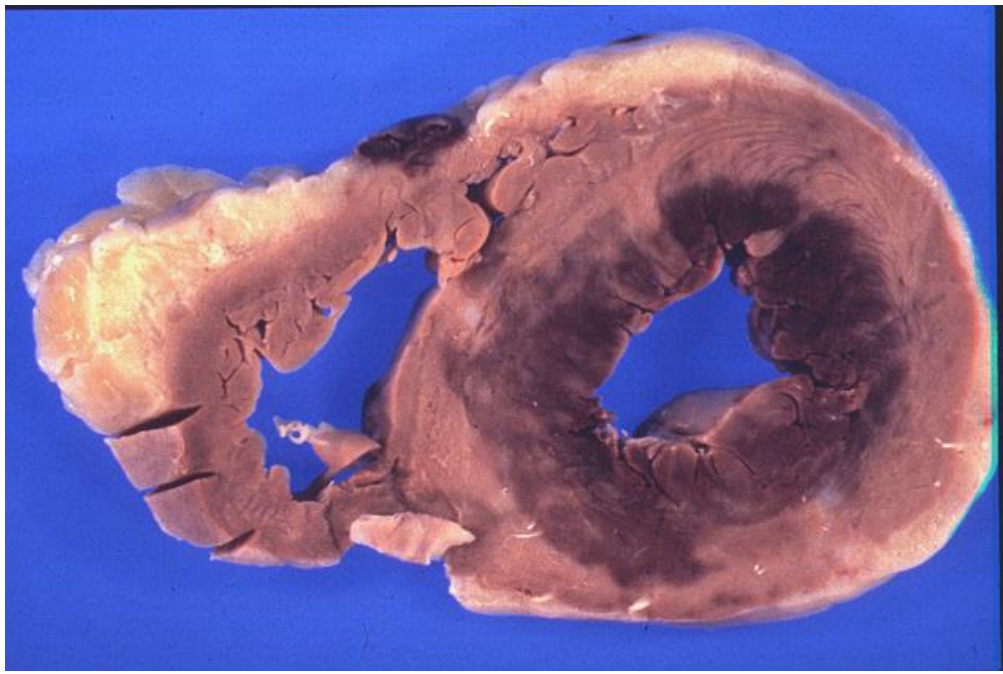
C. Total occlusion of a major coronary artery is uncommon

D. Early treatment by fibrinolytic agents *is* beneficial

E. Global reduction of coronary flow is the precipitating factor.

Subendocardial myocardial infarction

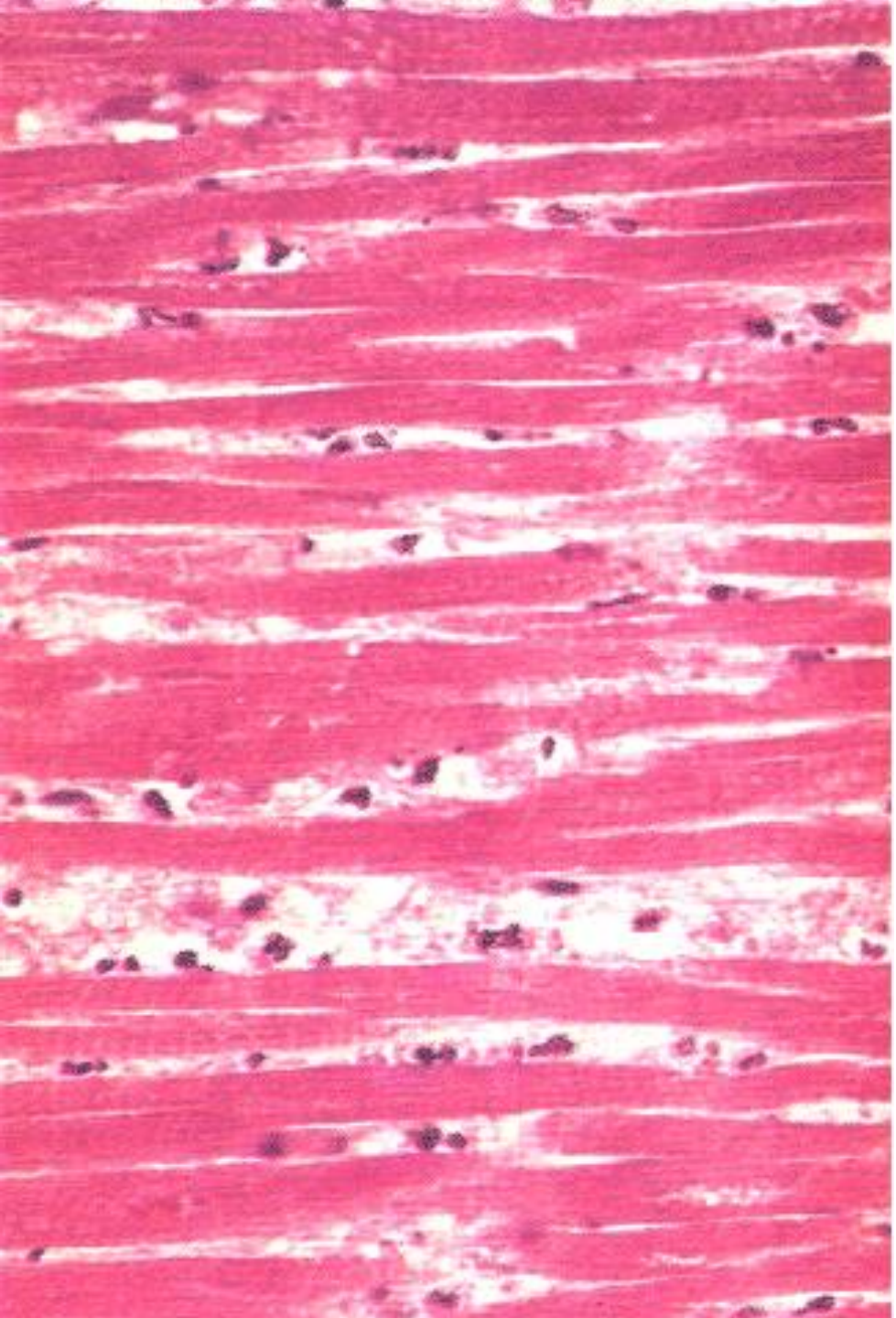
Subendocardial infarct is is ***limited to the inner third of the LV wall***. The lesion may be multifocal, cover an arc of the circumference of the LV, or sometimes totally encircle it. Although mural thrombi may complicate the picture, pericarditis, ventricular aneurysms and rupture rarely follow.

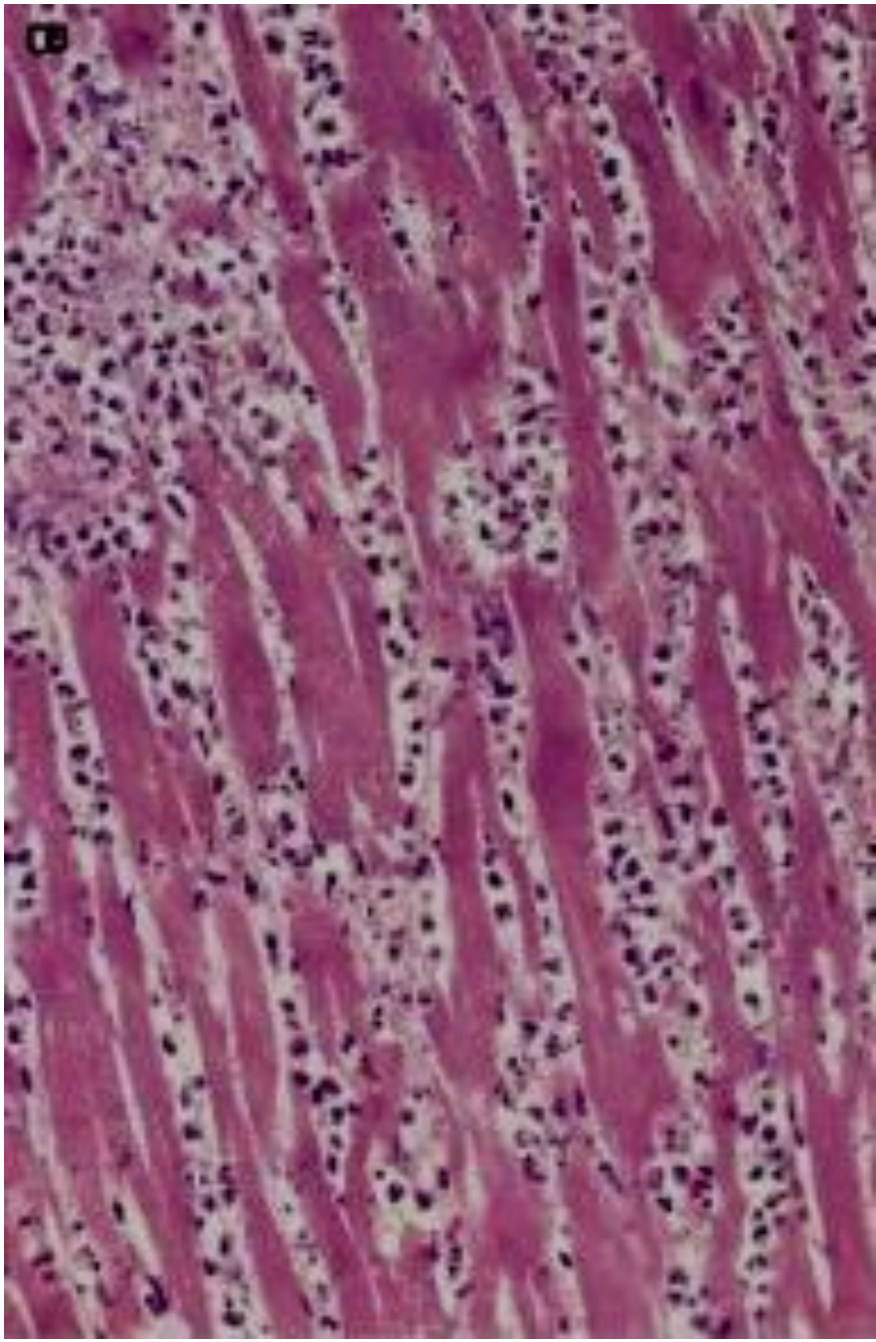


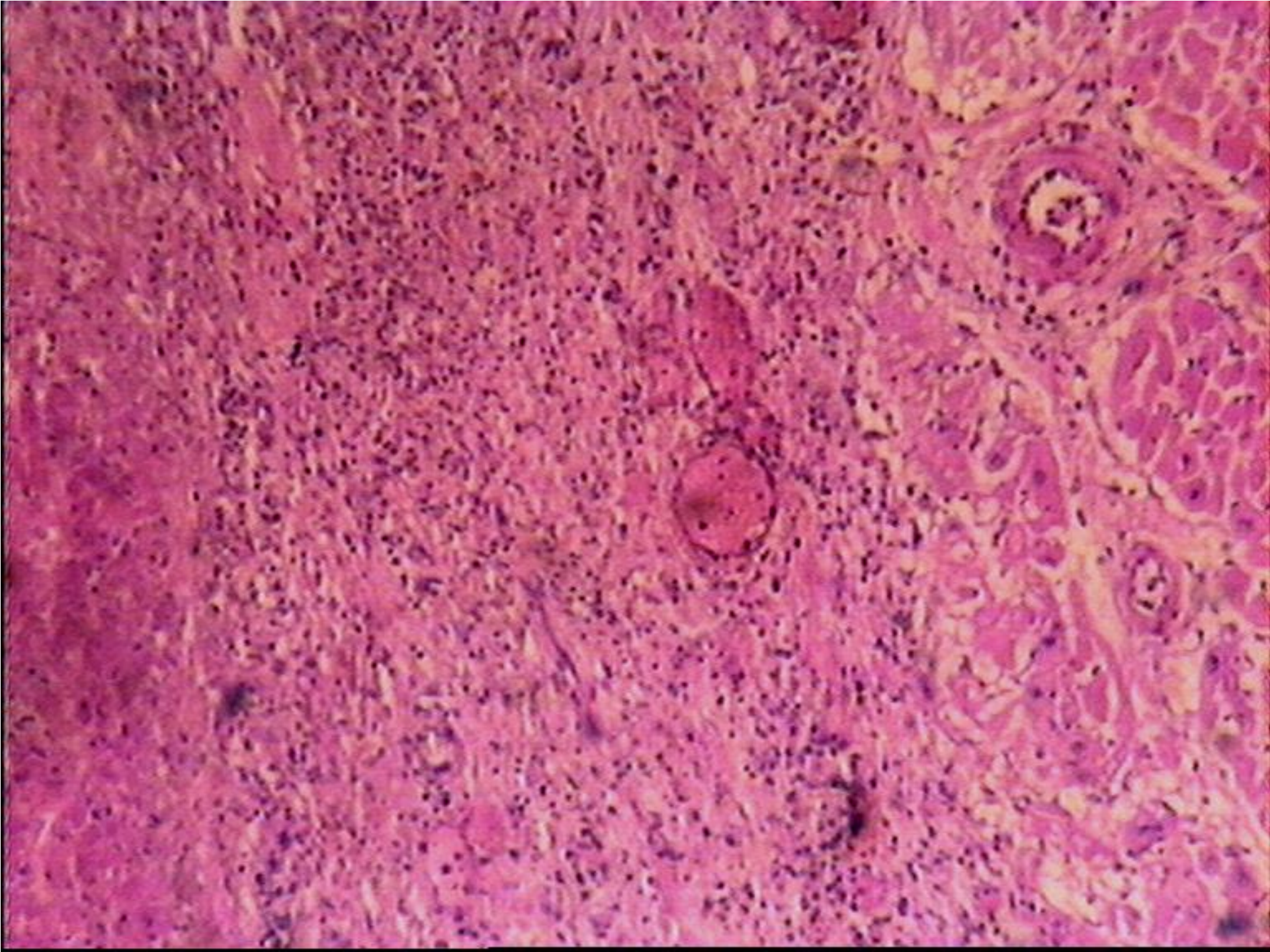
This infarct is limited to the inner third to one half of the LV wall. The red-blue cyanotic discoloration is totally encircling the Lt V inner wall.

MICROSCOPIC CHANGES IN MYOCARDIAL INFARCTION

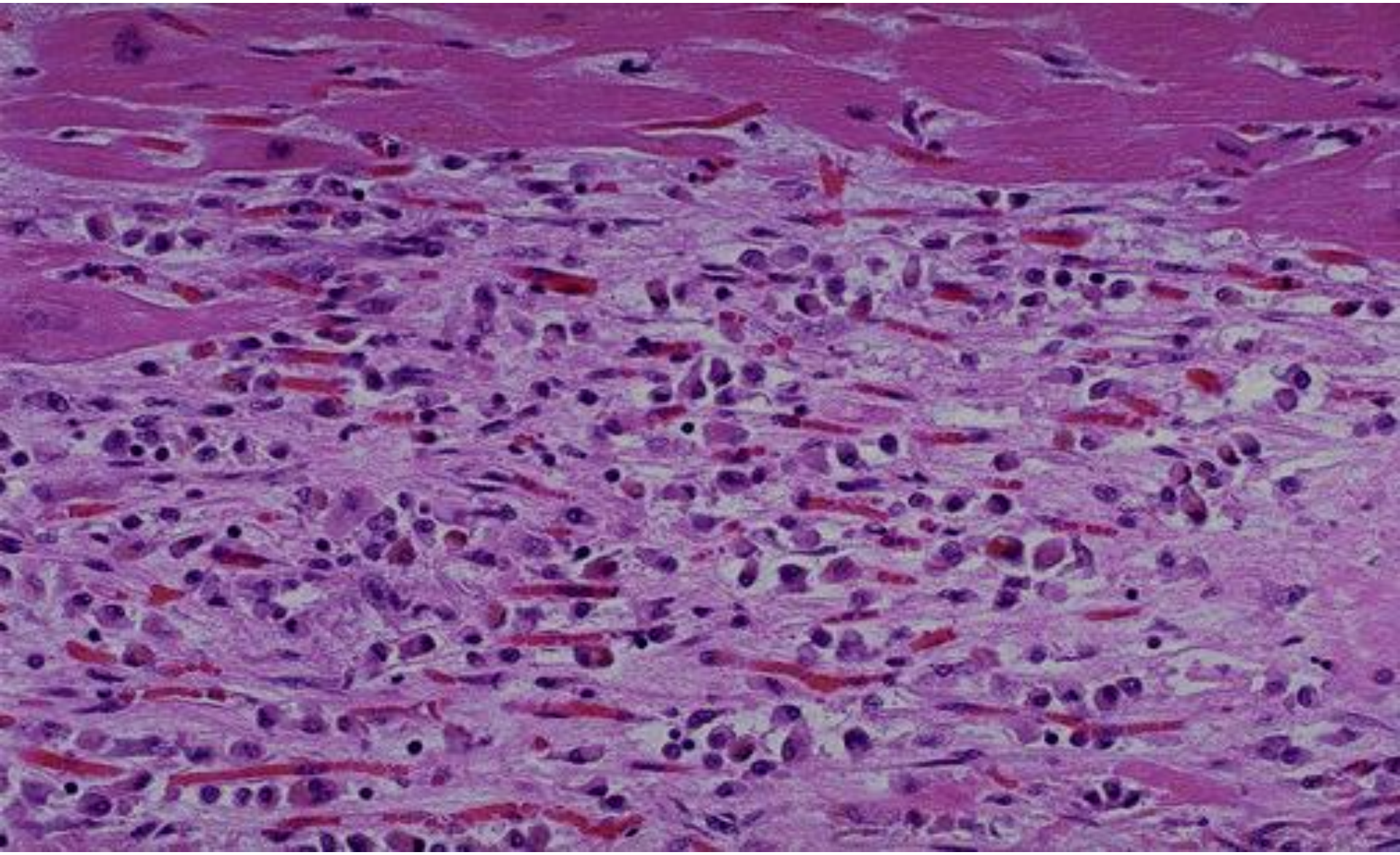
- Typically the myocardial cells show coagulative necrosis. This is not detectable for the first 4 to 8 hours.
- The necrotic area is invaded by acute inflammatory cells & later by macrophages.
- Gradual replacement of the infarct by granulation tissue froms a line of demarcation.
- The eventual event is healing by fibrosis.
- Once an MI is completely healed, it is impossible to distinguish its age.







MI



Complications of Myocardial Infarction

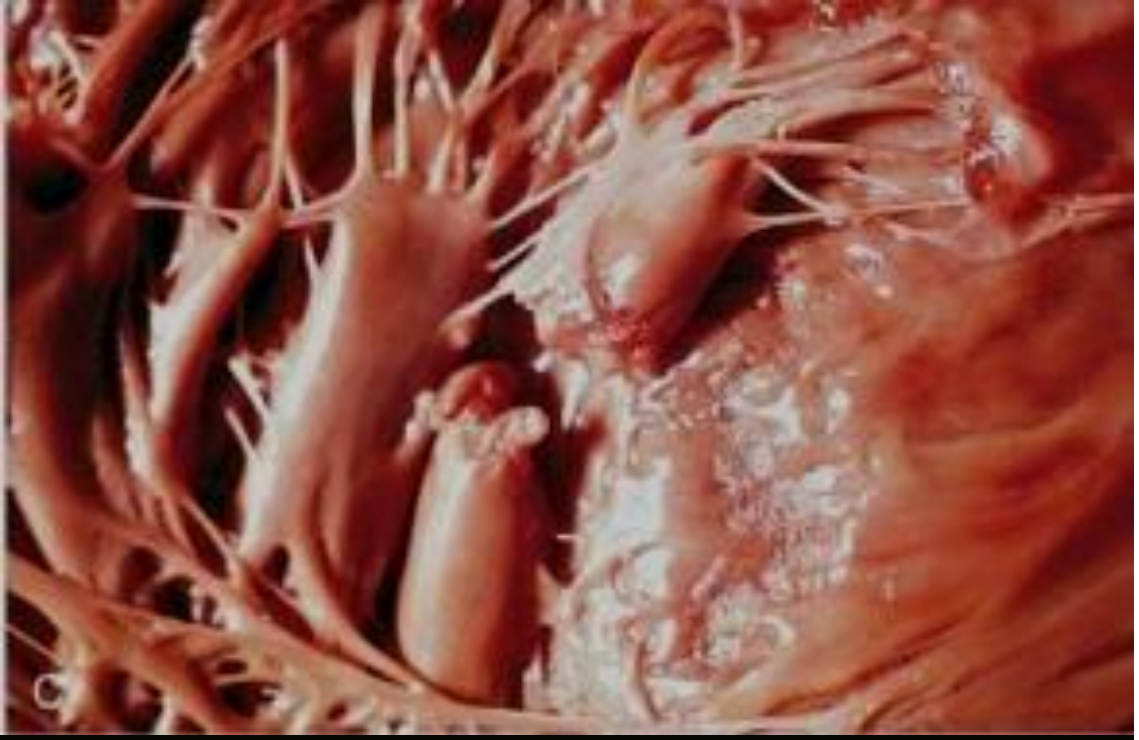
75% of patients with acute MI sustain one or more of the following complications

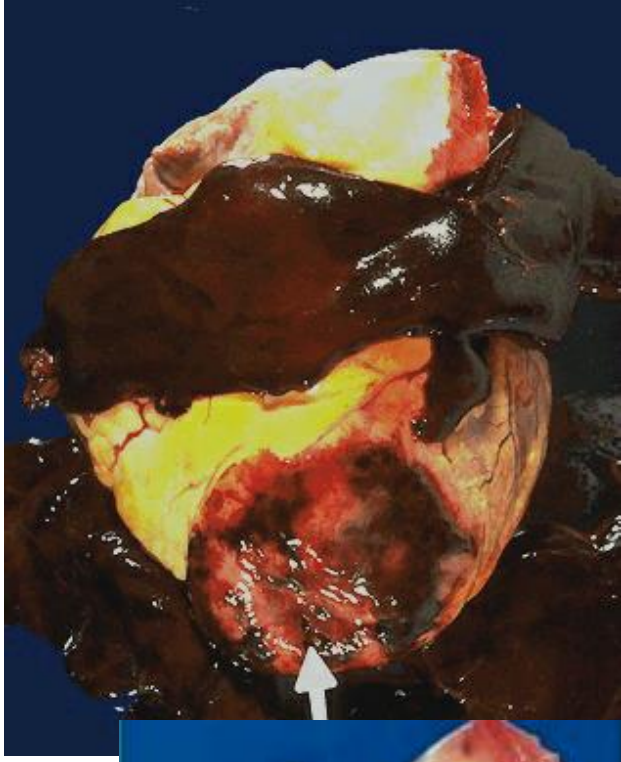
1. Heart failure, which is proportional to the size of the infarct. ***Cardiogenic shock*** complicates severe HF in extensive infarcts involving more than 40% of the left LV.

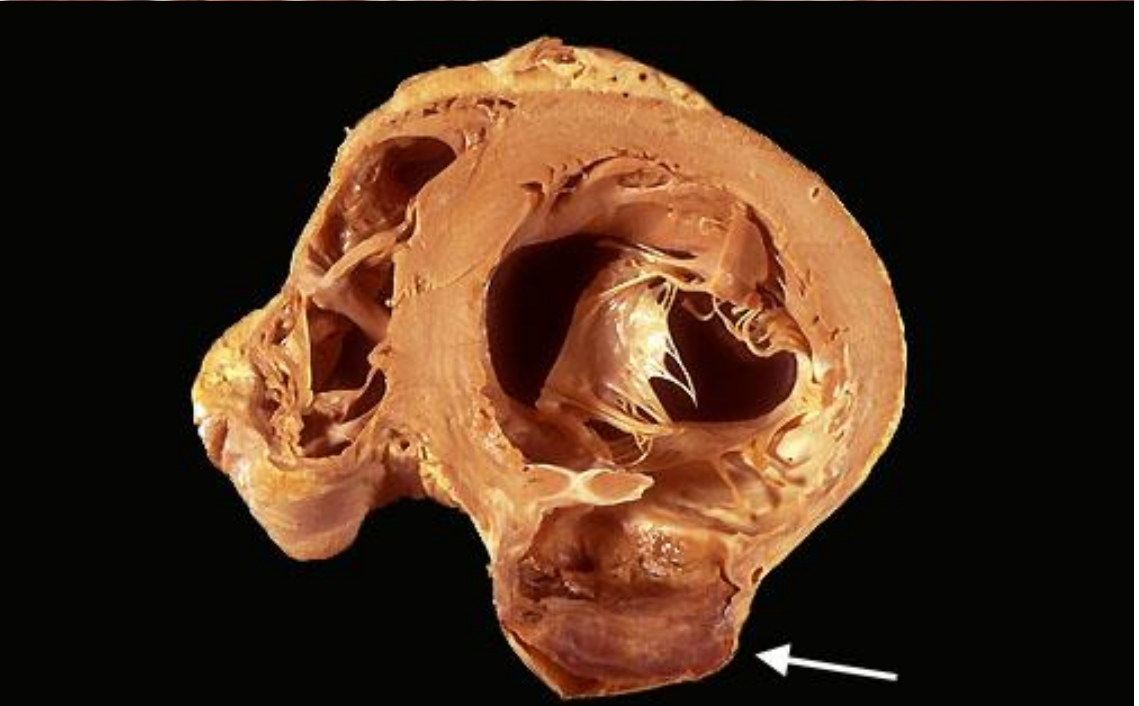
2. Arrhythmias; due to conduction disturbances and myocardial irritability following MI. Responsible for up to 50% of deaths that occur within 1 hr of onset of MI;

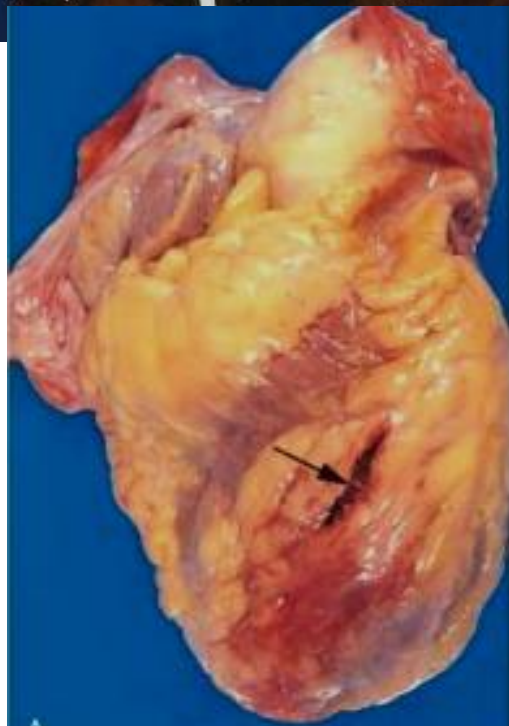
3. Myocardial rupture occurs in up to 5% of patients and is the result of weakening of necrotic and subsequently inflamed myocardium and include

- **a. Rupture of the ventricular free wall**, with hemopericardium and cardiac tamponade;
- **b. Rupture of the ventricular septum,** leading to a L→R shunt
- **c. Rupture of the papillary muscles,** resulting in acute severe mitral regurgitation.









4. Pericarditis: a fibrinous or fibrohemorrhagic pericarditis can occur but usually resolve

5. Right ventricular infarction; often accompanies ischemic injury of the adjacent posterior LV and ventricular septum. A RV infarct can yield serious functional impairment.

6. Infarct extension: new necrosis may occur adjacent to an existing infarct.

7. Infarct expansion: owing to the weakening of necrotic muscle, there may be disproportionate stretching, thinning, and dilation of the infarct region (especially with anteroseptal infarcts), which is often associated with mural thrombus.

8. Mural thrombus;occurs due to:

locally deficient contractility (causing stasis) and ***endocardial damage*** that exposes the subendocardial thrombogenic zone with eventual thrombus formation that could act as a potential embolus.

9. DVT and pulmonary embolism

10. Mitral regurgitation (insuffiency) The ***early onset insufficiency*** is either due to ischemic dysfunction of a papillary muscle and underlying myocardium or rupture of a necrotic papillary muscle. ***Late onset insufficiency*** is due to papillary muscle fibrosis and shortening &/or ventricular dilation

11. Progressive late heart failure.

12- Ventricular aneurysm of the ventricular wall that is bounded by a healed fibrotic myocardium, which paradoxically bulges during systole. Complications of aneurysms include mural thrombosis, arrhythmias, and HF. *Rupture , however, does not occur.*

Chronic ischemic heart disease (ischemic cardiomyopathy)

- By definition this is a "***progressive heart failure that complicates ischemic myocardial damage***".
- CIHD usually represents a post-infarction cardiac decompensation but may be present without acute or healed infarction due to diffuse myocardial dysfunction.
- CIHD is characterized by the development of severe, progressive heart failure, sometimes punctuated by **episodes of angina** or **MI**. **Arrhythmias** are common.
- The diagnosis rests largely on the exclusion of other forms of cardiac diseases. Such patients make up nearly half of cardiac transplant recipients.

Sudden cardiac death

Sudden cardiac death is defined as "***unexpected death from cardiac causes early after symptom onset (usually within 1 hour) or without the onset of symptoms***".

- In many adults, SCD is a complication and often the first clinical manifestation of IHD.

With decreasing age of the victim, the following nonatherosclerotic causes of SCD become increasingly probable:

- Congenital structural coronary arterial abnormalities
- Aortic valve stenosis
- Mitral valve prolapse
- Myocarditis and Cardiomyopathy

The following are features of Systemic HHD

A. May be a cause of sudden cardiac death

B. Even when of mild degree, it induces left ventricular hypertrophy

C. The hypertrophy is concentric (symmetrical)

D. May be manifested clinically by the onset of atrial fibrillation

E. All of the above

HYPERTENSIVE HEART DISEASE

This refers to the ***adaptive response on the part of the heart to the increased pressure overload induced by hypertension.***

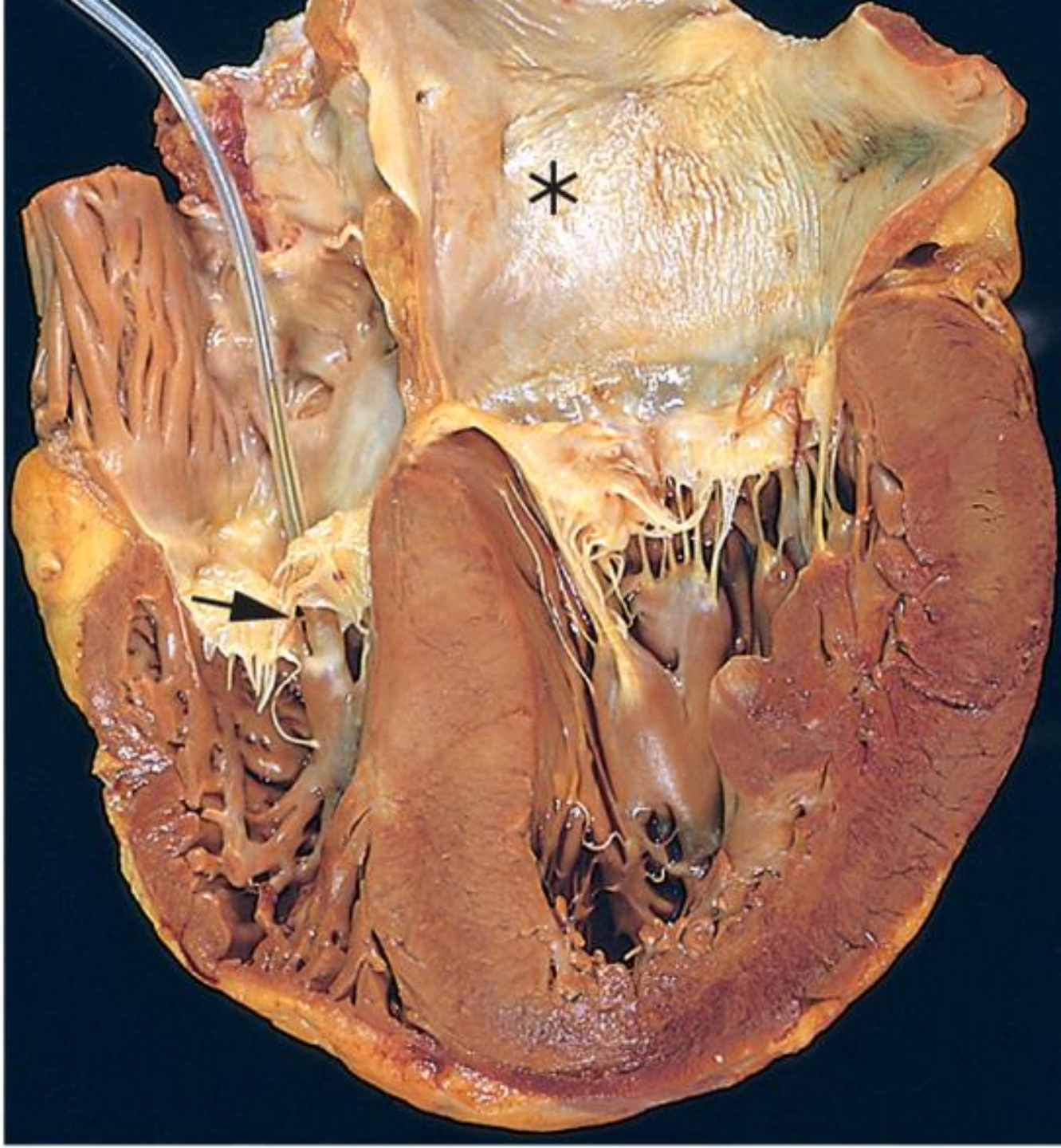
The left-sided (Systemic) HHD

Even mild hypertension if sufficiently prolonged can lead to LVH. Systemic hypertension, can lead to cardiac dilation, congestive heart failure or sudden death.

Systemic HHD may be indirectly manifested clinically by either the onset of atrial fibrillation (owing to left atrial enlargement).

Effective control of hypertension can prevent or lead to regression of cardiac hypertrophy and its associated risks.

Left ventricular
Hypertrophy And
left atrial dilation in
Systemic hypertension



The following are features of Cor pulmonale EXCEPT

A.Pulmonary hypertension is complicated by RVH, dilation and eventually Rt sided heart failure

B. Causes include congenital heart diseases

C. The acute form can follow massive pulmonary embolism

D. In the acute form, there is marked dilation of the right ventricle without hypertrophy.

E. In chronic form the right ventricular wall thickens may approximate that of the left ventricle

Right-sided (pulmonary) HHD (Cor pulmonale)

Pulmonary hypertension leads to RVH, dilation and eventually RHF.

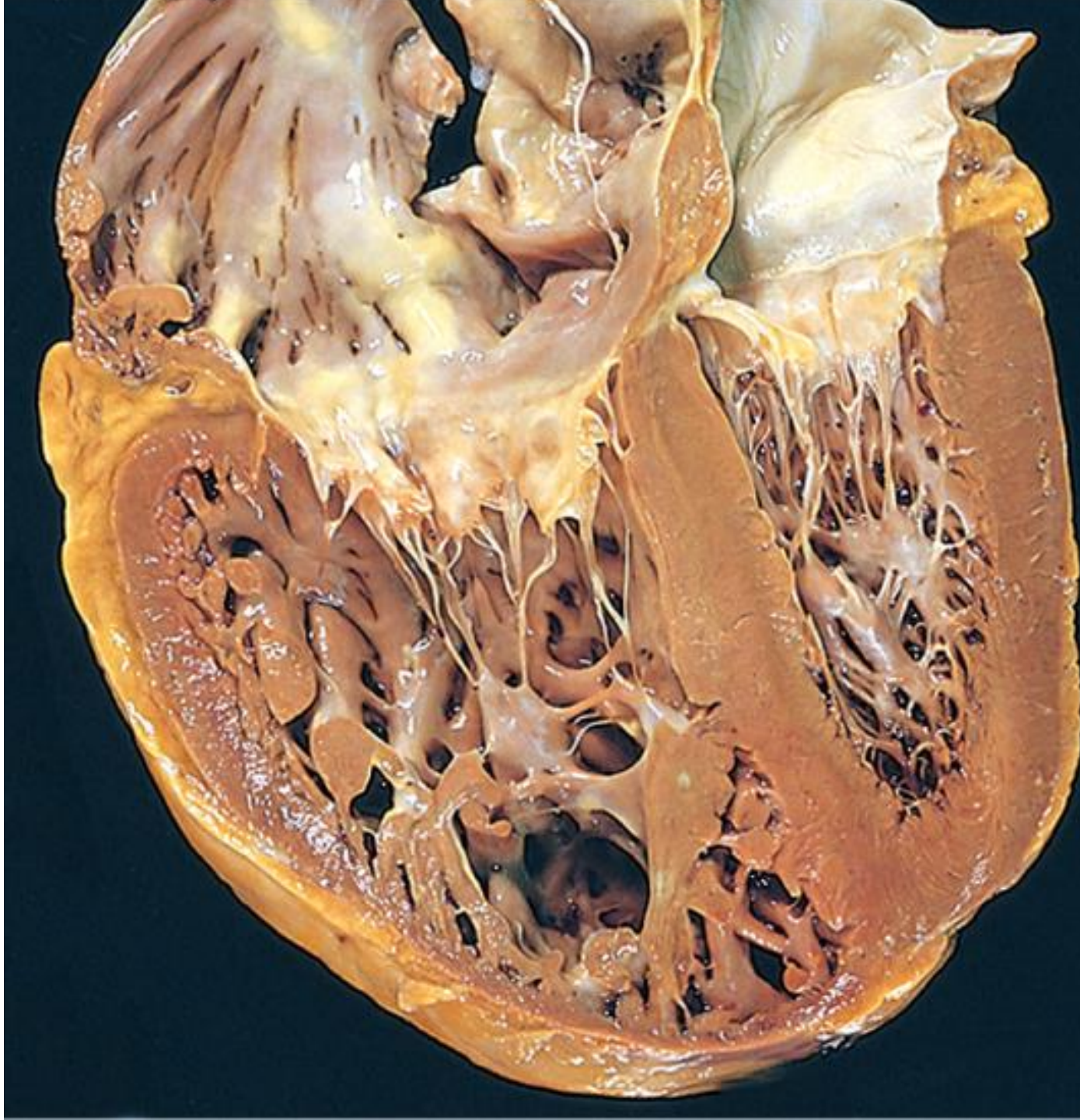
Pulmonary hypertension is caused by disorders of the lungs or pulmonary vasculature. Not included under this heading is RVH & dilation secondary to diseases of the left side of the heart or congenital heart diseases.

Cor pulmonale may be acute or chronic.

Acute cor pulmonale can follow massive pulmonary embolism. There is usually marked dilation of the right ventricle without hypertrophy.

Chronic cor pulmonale usually implies right ventricular hypertrophy (and dilatation) secondary to prolonged pressure overload caused by **obstruction of the pulmonary arteries or arterioles or compression or obliteration of septal capillaries (e.g., owing to primary pulmonary hypertension or emphysema).** In chronic cor pulmonale, the right ventricular wall thickens, sometimes up to 1.0 cm or more (N: 0.3 to 0.5 cm), and may even come to approximate that of the left ventricle.

RVH and Right Atrial dilation in right sided HHD

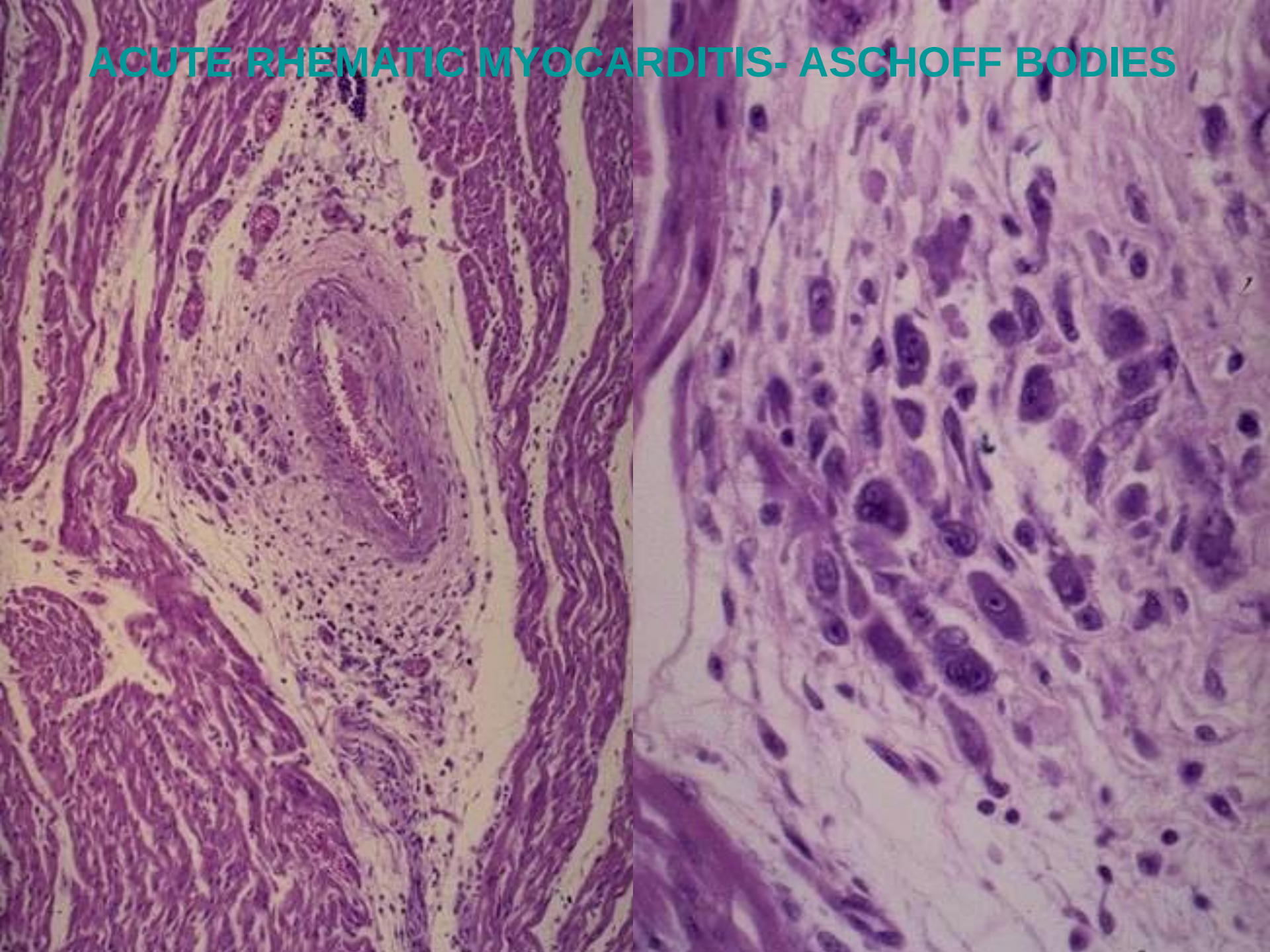


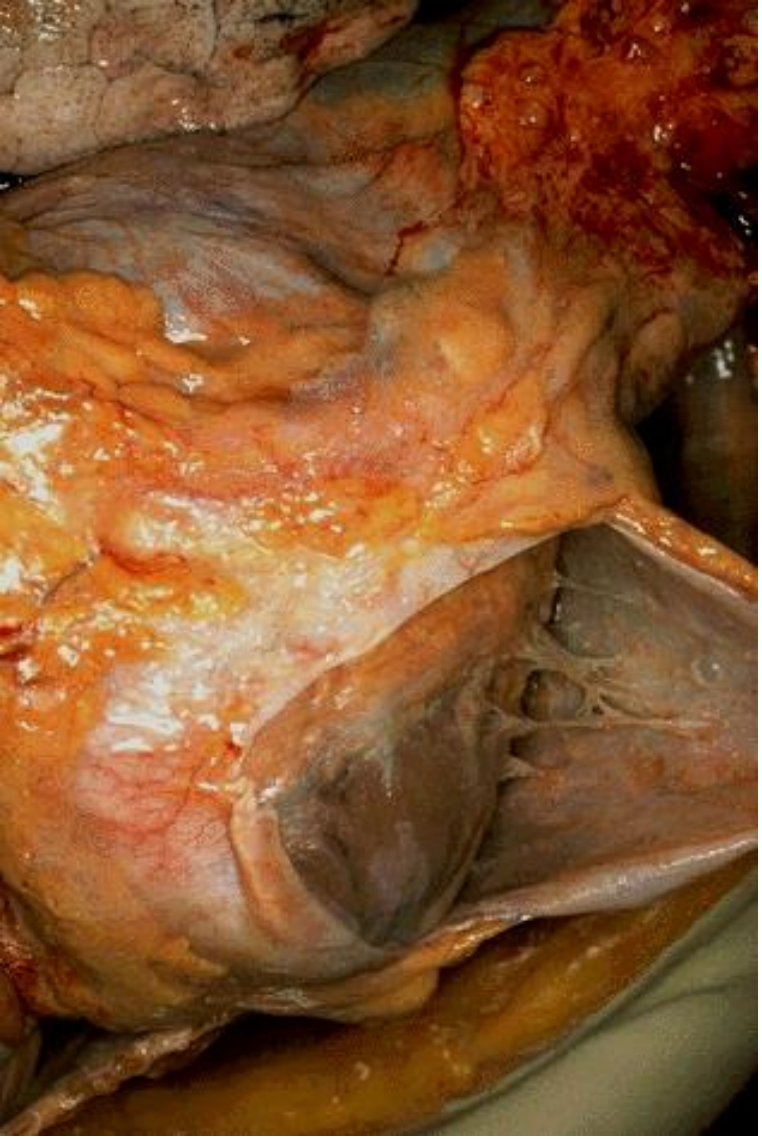
RHEUMATIC FEVER AND RHEUMATIC HEART DISEASE

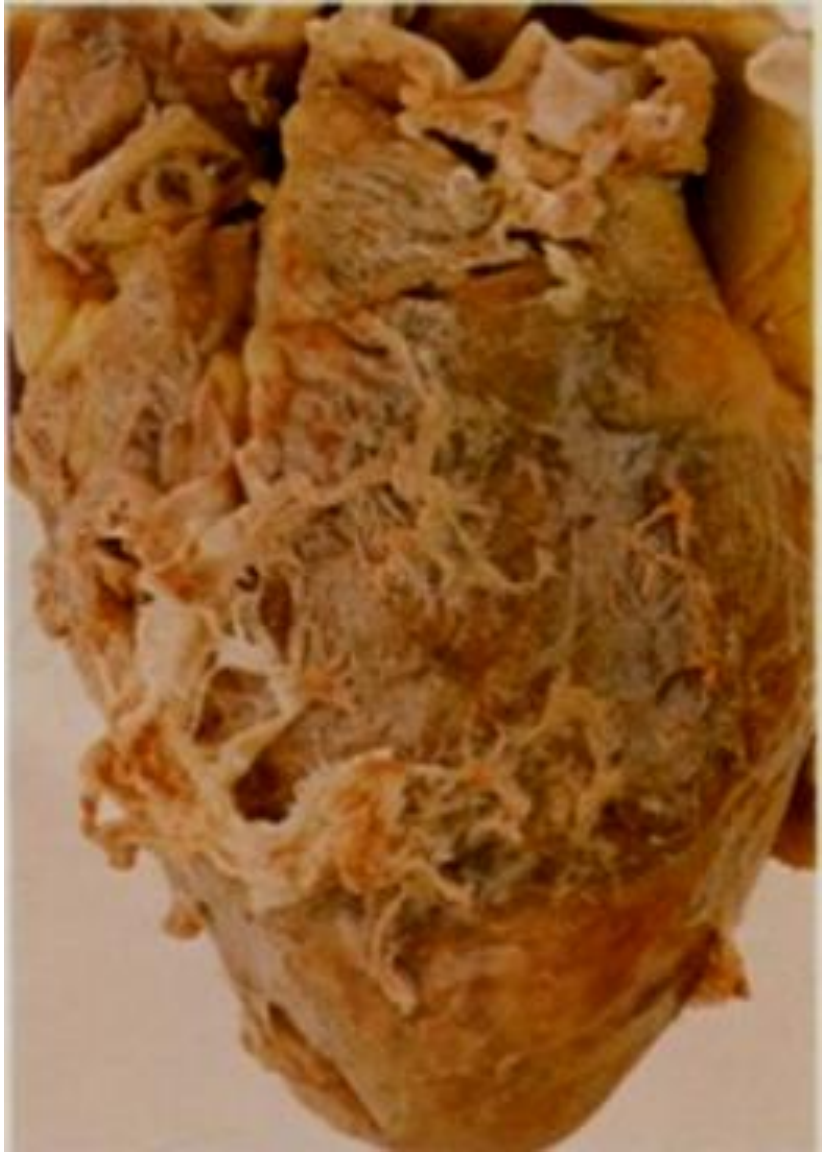
- **Rheumatic fever is an immunologically mediated acute inflammatory systemic disease occurring a few weeks after an episode of group A streptococcal pharyngitis.**
- **Acute RF appears most often in children between ages 5-15 yrs.**
- **The incidence of RF has declined remarkably in many parts of the world over the past 40 yrs.**
- **In acute RF, focal inflammatory lesions are found in various tissues of the body but most distinctively within the heart.**
- **Diffuse inflammation and Aschoff bodies may be found in any of the three layers of the heart, pericardium, myocardium, or endocardium- hence the designation *rheumatic pancarditis.***

- ***Aschoff bodies*** **consist of foci of swollen collagen surrounded by lymphocytes, some plasma cells, and distinctive (pathognomonic) plump macrophages called *Anitschkow cells* which have abundant cytoplasm and central round-ovoid nuclei in which the chromatin is disposed in a central, slender, wavy ribbon (hence called "*caterpillar cells*"). Some of these macrophages become multinucleated to form *Aschoff giant cells*.**

ACUTE RHEMATIC MYOCARDITIS- ASCHOFF BODIES

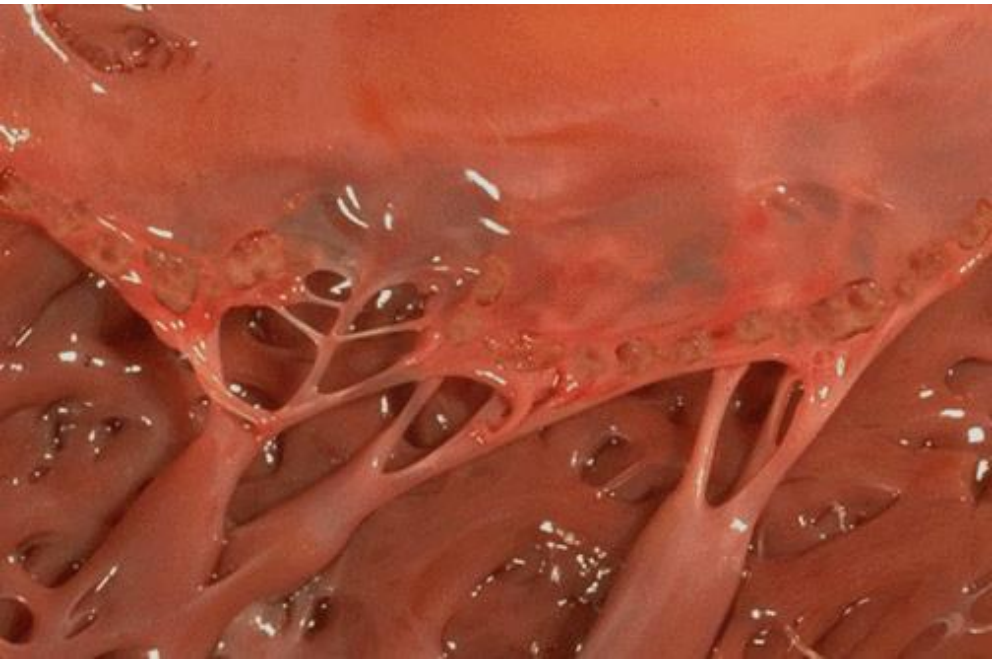


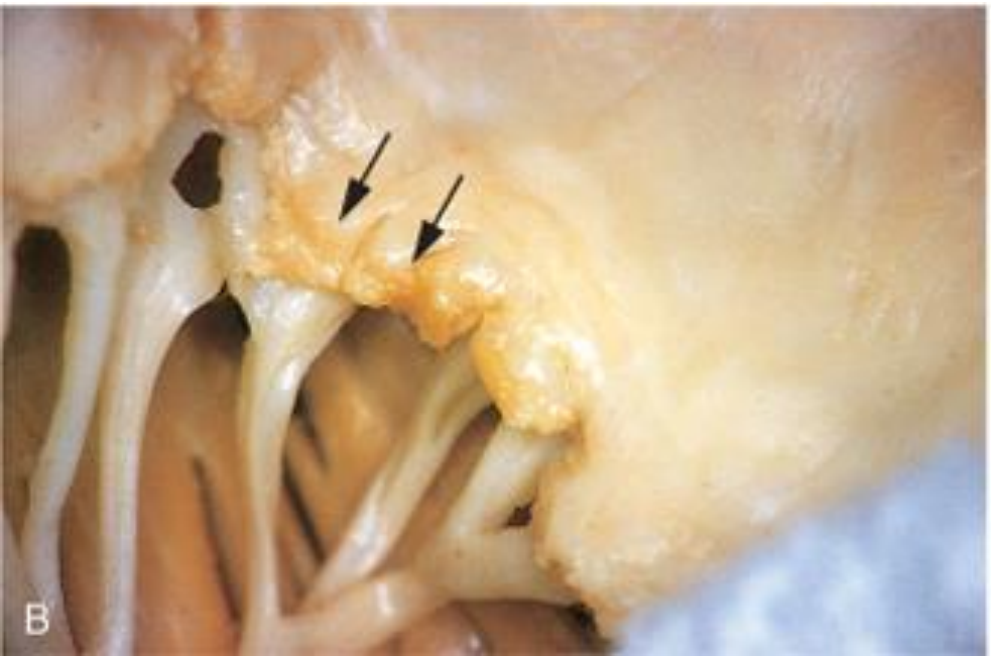




In the pericardium, the inflammation is accompanied by a fibrinous or serofibrinous pericardial exudate, described as a "***bread-and-butter" pericarditis.***

ACUTE RHEUMATIC VALVULITIS





Concomitant involvement of the endocardium and the left-sided valves by inflammatory foci typically results in **fibrinoid** necrosis of **collagen** within the cusps (and along the tendinous cords) on which sit small (1- to 2-mm) vegetations (verrucae) along the lines of closure.These vegetations probably arise from the deposition of fibrin at sites of erosion, but cause little disturbance in cardiac function. Subendocardial lesions, perhaps exacerbated by regurgitant jets, may induce irregular thickenings called ***MacCallum patches***, usually in the left atrium.

Chronic Rheumatic heart disease

- **is the result of organization of the acute inflammation and subsequent fibrosis.**
- **In particular, the valvular leaflets become thickened and retracted, causing permanent deformity.**
- ***In chronic disease*, the mitral valve is virtually always abnormal*; alone (70% of the cases) or together with the aortic valve (25%).**
- ***RHD is the most frequent cause of mitral stenosis (99% of cases)*.**
- **The cardinal anatomic changes of the mitral valve are**

1. Leaflet thickening

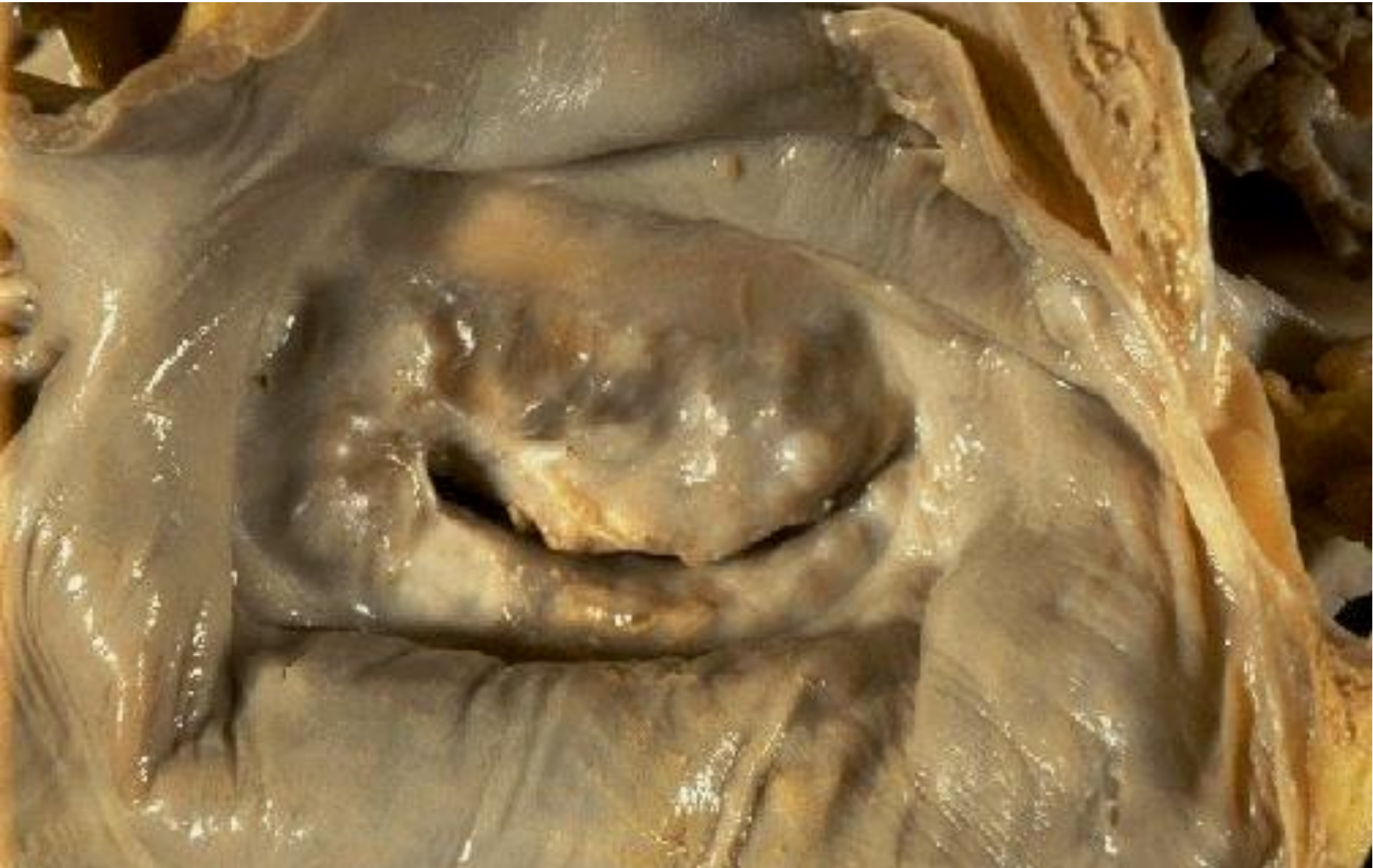
2. Commissural fusion

3. Shortening, thickening and fusion of the tendinous cords.

- **Fibrous fusion at the valvular commissures and calcification create "*fish mouth" or "buttonhole" stenoses*.**

- **Microscopically diffuse fibrosis with vascularization is noted in valvular leaflets.**
- **Thrombotic vegetations on the surface and calcifications may be seen.**
- **Aschoff bodies are rarely seen being replaced by fibrosis.**
- **With tight mitral stenosis, the left atrium progressively dilates and may harbor mural thrombus.**
- **The chronic pulmonary venous congestion can induce pulmonary hypertension and RVH.**
- **The left ventricle is generally normal with isolated pure mitral stenosis.**

MITRAL VALVE- CHRONIC RHEUMATIC VALVULITIS
Fish mouth (Button hole) appearance



Pathogenesis of RF & RHD

- It is assumed that RF is due to a hypersensitivity reaction induced by group A streptococci. It is thought that ***antibodies that are originally developed and directed against the M protein of the offending streptococci also cross-react with glycoprotein antigens in the heart, joints, and other tissues***. In support of this is the absence of the bacteria in RF lesions of various tissues.
- A ***genetic predisposition*** to the disease appears operating as well, because only a minority of infected patients (3%) develop RF.
- Although pharyngeal cultures for streptococci are negative by the time the illness begins, antibodies to one or more streptococcal enzymes, such as ***streptolysin O and DNAse B***, are present and can be detected in the sera of most patients.
- After an initial attack, there is an increased tendency of having further insults of the disease with subsequent pharyngeal infections.

COMPLICATIONS OF CRHD

- 1. The chronic sequelae result from progressive fibrosis due to both healing of the acute inflammatory lesions and the turbulence of blood flow induced by the valvular deformities.

  With recurrent attacks of RF, the chronic valvulitis is likely to worsen and damage is cumulative.
- 2. Arrhythmia
- 3. Embolization primarily from atrial thrombi
- 4. Infective endocarditis superimposed on deformed valves.

- The manifestations of chronic rheumatic carditis usually occur years or even decades after the initial episode of acute RF.

INFECTIVE ENDOCARDITIS

- This serious condition signifies "***colonization of the heart valves or the endocardium by microbes with eventual formation of bulky, friable vegetations that often results in destruction of the underlying cardiac structures***".
- Bacteria are the most common offenders (bacterial endocarditis) but other microorganisms are occasionally the causative agents e.g. fungi, rickettsiae of Q fever, and chlamydiae.
- Clinically classified into:

1- Acute infective endocarditis which signifies an infection that is

- Destructive
- Involving frequently a normal heart valve
- Caused by virulent organism
- Have a rapid clinical course leading to death within days-weeks of more than 50% of patients despite antibiotics and surgery;
- It is difficult to cure by antibiotics and usually require surgery.

2- Subacute endocarditis which signifies an infection that is

- Less destructive
- Affect previously abnormal heart, particularly deformed valves
- Caused by organisms of low virulence
- Has insidious and protracted clinical course (weeks to months).
- It recovers after appropriate antibiotic therapy

Etiology and Pathogenesis of infective endocarditis

Two sets of factors predispose to IE

1. ***Structural abnormalities of the heart valves***;

IE may develop on previously normal valves, but a variety of cardiac and vascular abnormalities predispose to this form of infection.

a. Rheumatic heart disease

b. Myxomatous (floppy) mitral valve

c. Degenerative calcific aortic stenosis

d. Bicuspid aortic valve (calcified or not)

e. Artificial (prosthetic) valves

2. ***Host factors*** particularly those that interfere with defenses; such as

a. neutropenia

b. immunodeficiency e.g. associated with malignancy & therapeutic immunosuppression.

c. diabetes mellitus

d. alcoholism

e. intravenous drug abuse.

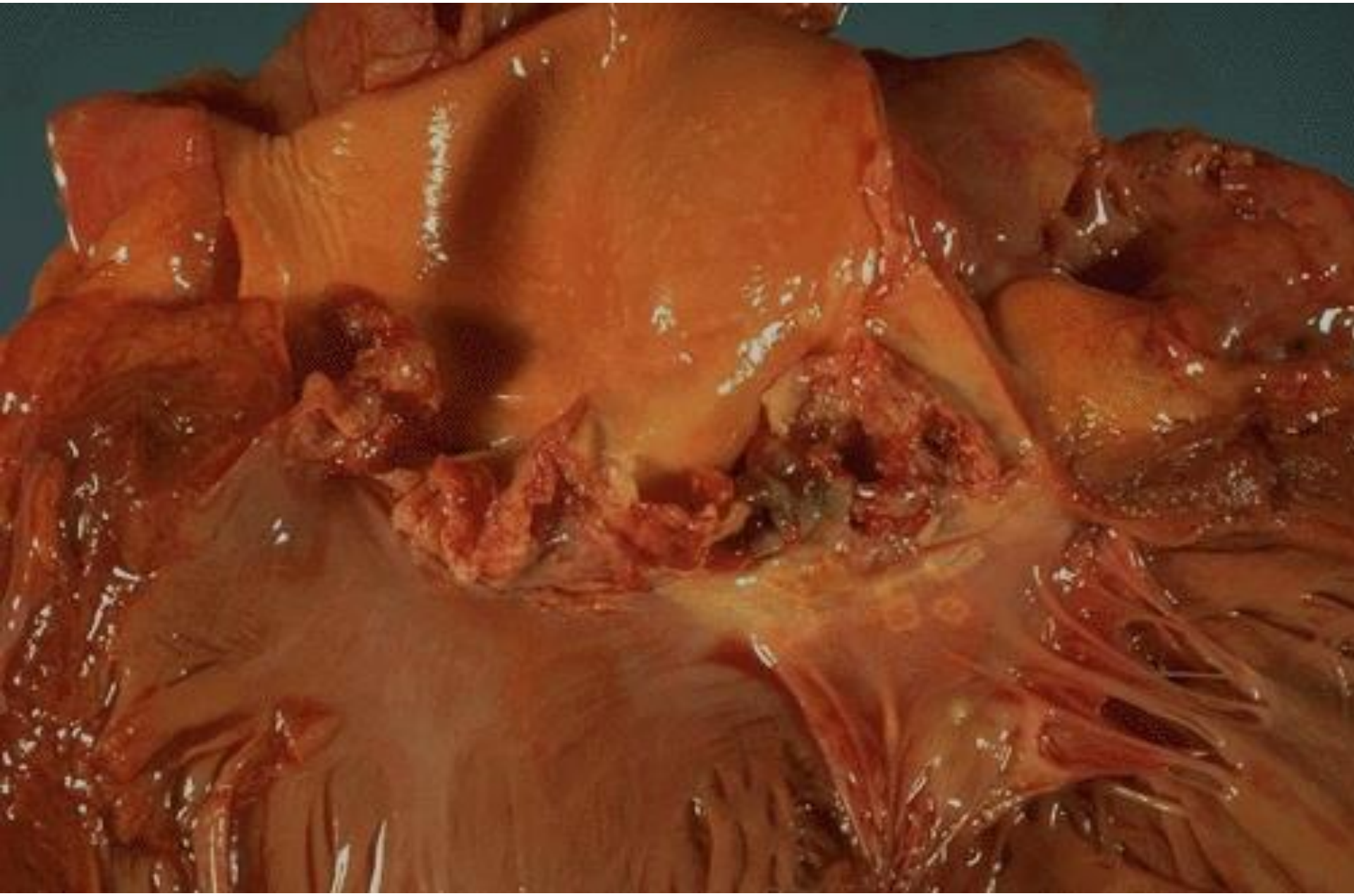
- IE of previously damaged or abnormal valves is caused most commonly (60% of cases) by ***Streptococcus viridans*** (oral commensal)
- In contrast, the more virulent ***Staph. aureus*** can attack either healthy or deformed valves and are responsible for 10%-20% of IE cases. Staph. aureus is also a major offender in intravenous drug abusers.
- Prosthetic valve endocarditis is caused most commonly by coagulase-negative staphylococci (e.g., **Staph. epidermidis).**
- *In about 10% of all cases of IE, no organism can be isolated* from the blood ***(culture-negative***).
- **The portal of entry of the agent into the bloodstream** may be

a. Obvious infection elsewhere
b. Dental or surgical procedure causing a transient bacteremia
c. injection of contaminated material into the bloodstream by IV drug users
d. Occult source

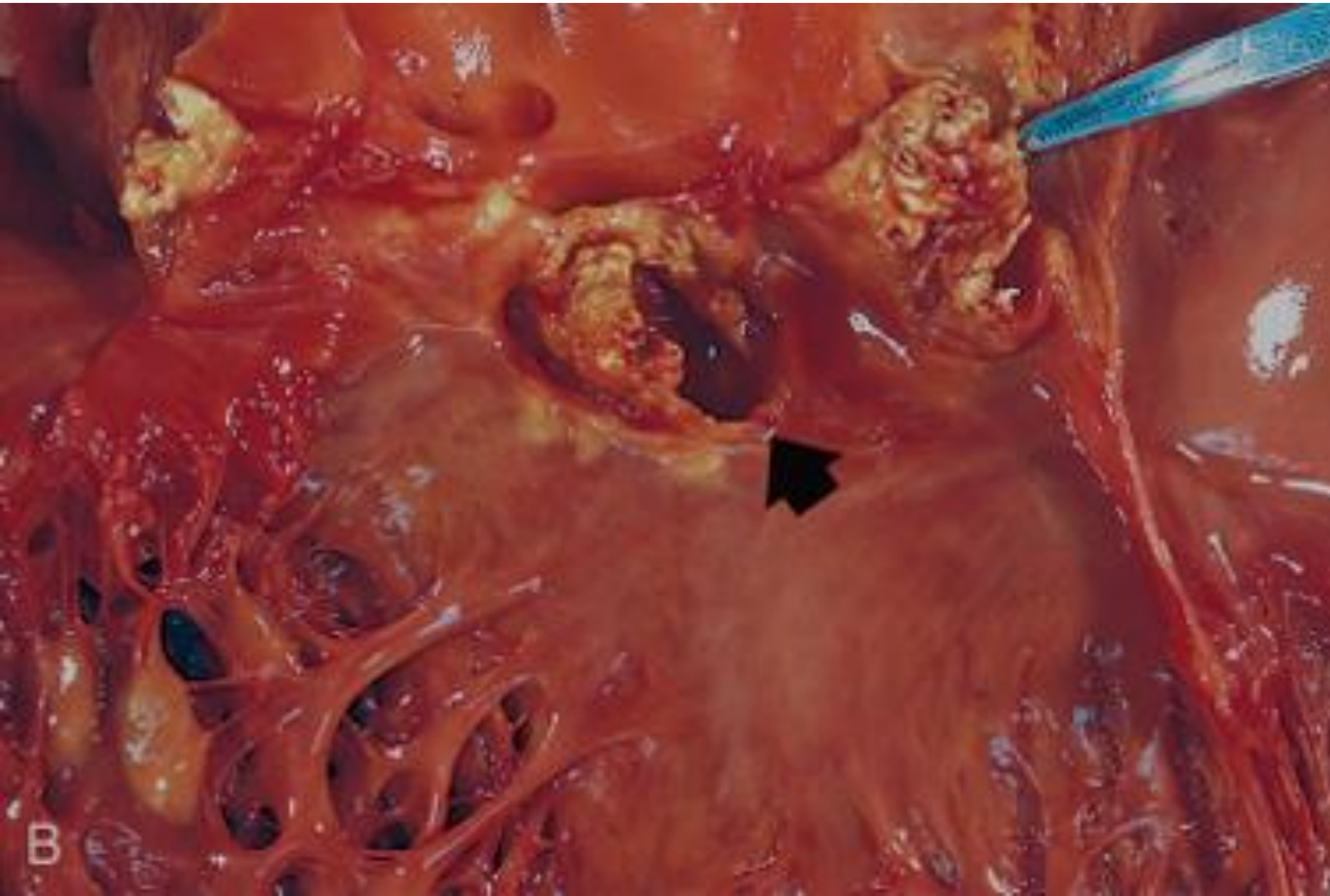
Gross features of infective endocarditis

- In both the subacute and acute forms of the disease there are ***friable, bulky, and potentially destructive vegetations***.
- **The mitral and aortic valves** are the most common sites of infection, although the valves of the right heart may also be involved, particularly in intravenous drug abusers.
- The vegetations may be single or multiple and may involve more than one valve.
- Vegetations sometimes erode into the underlying myocardium to produce an abscess cavity.
- The vegetations of subacute endocarditis are associated with less valvular destruction than those of acute form, although the distinction between the two forms may be difficult.

Acute bacterial endocarditis



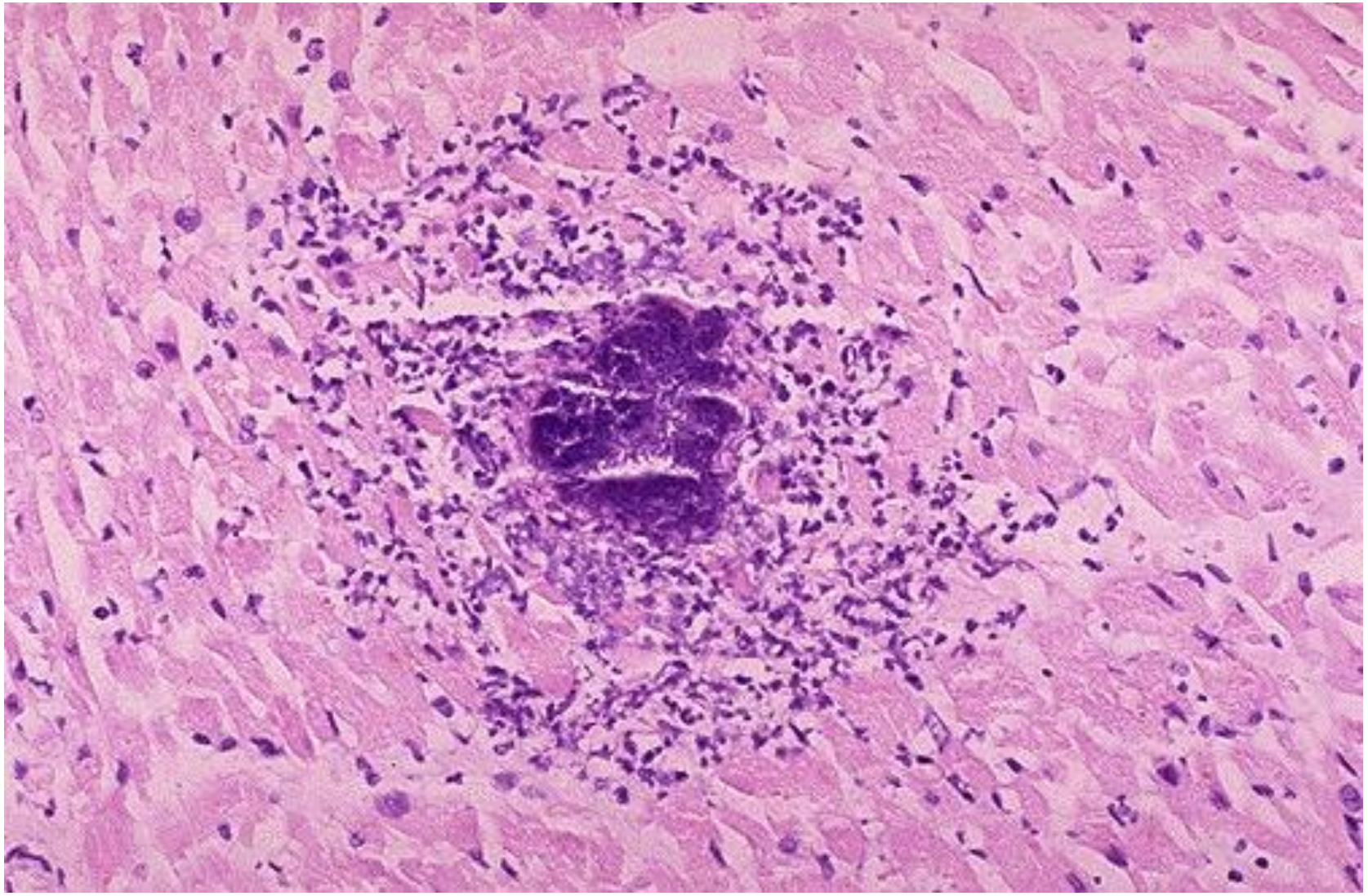
Acute endocarditis of congenitally bicuspid aortic valve



Microscopic features of infective endocarditis

- The vegetations in general contain fibrin, inflammatory cells, and bacteria (or other organisms)
- The vegetations of typical subacute IE often have granulation tissue at their bases (suggesting chronicity).
- With the passage of time, fibrosis, calcification, and a chronic inflammatory infiltrate may develop.

Bacterial endocarditis: myocardial microabscess



The center consists of blue bacterial colonies and is surrounded by acute inflammatory cells.

Complications of Infective endocarditis (whether acute or subacute)

A. Cardiac

1. *Valvular dysfunction (insufficiency or stenosis) that eventuates in heart failure*
2. *Myocardial abscesses that eventuates in perforation of IV septum or free wall*
3. *Suppurative pericarditis*
4. *Dehiscence of artificial valve*

B. Embolic with infarctions

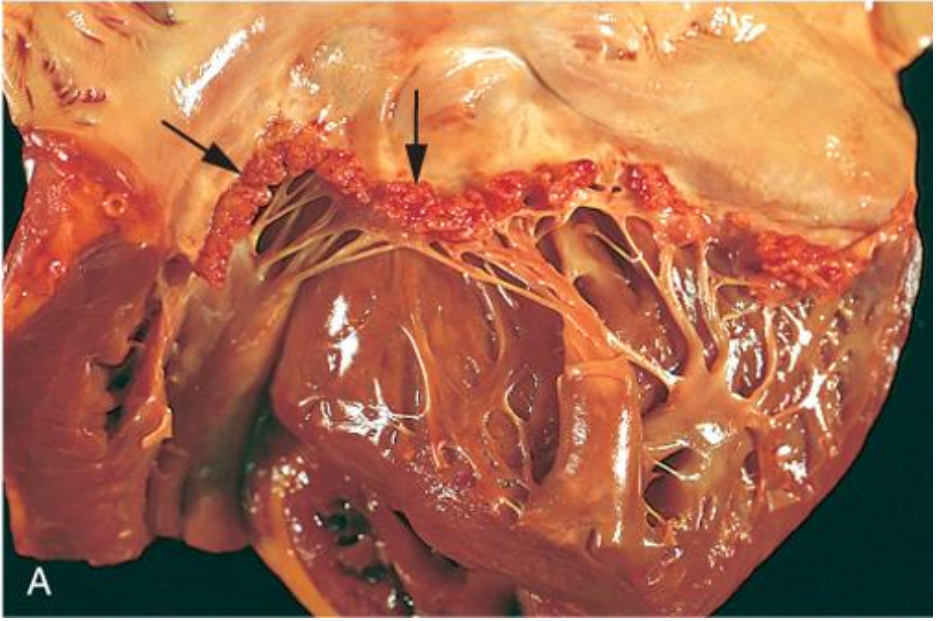
1. *Lt sided: brain, spleen, kidneys,*
2. *Rt sided: lungs*

C. Metastatic infections *(including septic infarcts) esp. in acute IE e.g. brain and renal abscesses, meningitis.*

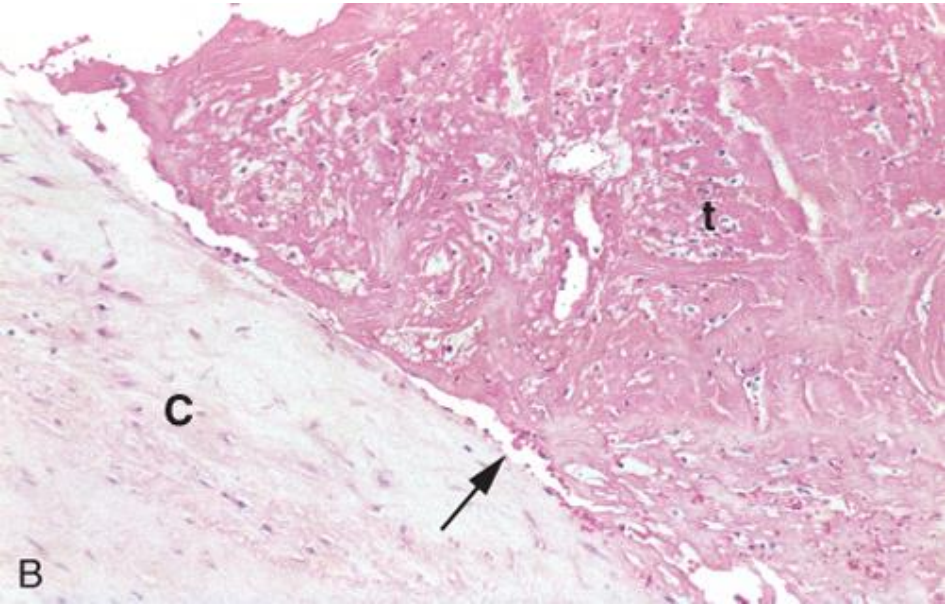
D. Renal complications

1-Embolic infarction that may be multiple and septic

2-Immunologically mediated Glomerulonephritis; owing to trapping of antigen-antibody complexes, which can cause hematuria, albuminuria, or renal failure.



NON-INFECTED VEGETATIONS



1. Nonbacterial thrombotic endocarditis (NBTE)

This is characterized by the deposition of small sterile thrombotic vegetations (fibrin, platelets, etc.) on the leaflets of the cardiac valves that may be a source of emboli resulting in infarcts of the brain, heart, etc. Because of its frequent association with venous thromboses (and pulmonary embolism), a common origin of the two has been suggested i.e. a hypercoagulable state with systemic activation of the coagulation system .

Conditions associated with NBTE include

A. Hypercoagulability states

1. Cancer (especially, mucinous adenocarcinomas of the pancreas) 2. Hyperestrogenic states. 3. Extensive burns. 4. Sepsis

B. Endocardial trauma, *as from an indwelling catheter.*

2- Libman-Sacks endocarditis

In some SLE patients, there is mitral and tricuspid valvulitis complicated by presence of small, sterile vegetations.

Subsequent fibrosis can lead to serious valvular deformities that resemble chronic Rheumatic heart disease

Flat, pale tan, spreading vegetations over the mitral valve surface and even on the chordae tendinae. This patient has SLE and Libman-Sacks endocarditis).