Reference: ROBBINS BASIC PATHOLOGY, By Kumar et al. 9th Edition (2013), 81W+51F= 132 Slides @ 21/2/2021.
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♥ THE HEART ♥

♥ Despite dramatic improvement over the past 4 decades, heart disease remains the 1st leading cause of morbidity & mortality in industrialized nations.
☠ **IHD** in its 4 forms, **still** represents the **1st cause of death** in the US & other nations, causing **40%of all deaths in the US, (42%in Jordanians),** totaling **3/4 million** Americans annually {**nearly double the whole number of all cancer deaths}, (cancer is the 2nd & CVA is the 3rd commonest** causes of death in Americans}.

♥ We will discus the major categories of heart disease including

★ IHD/hypertensive HD/cor pulmonale,

★ Rheumatic HD/infective endocarditis,

★ Myocarditis/ cardiomyopathy/ pericardial disease/cardiac neoplasms .

ISCHEMIC HEART DISEASE (IHD)

☹ IHD is a group of related syndromes resulting from myocardial ***ischemia*** - an imbalance between cardiac blood supply (perfusion) & myocardial oxygen demand.

Although ischemia can result from
(1) ↑ **demand** (e.g.,↑ heart rate or hypertension), or
(2) ↓ **Diminished oxygen-carrying capacity** (e.g., anemia, carbon monoxide poisoning), But,

(3) **In the vast majority of cases, IHD is due to a reduction in coronary artery (CA) blood flow caused by obstructive atherosclerotic (A) disease.** Thus, IHD is also frequently called coronary artery disease (CAD).

☹ The clinical manifestations of IHD are a direct consequence of insufficient blood supply to the heart.

★ **There are four basic clinical syndromes of IHD**

(1) ***Angina pectoris*** (*chest pain*), wherein the ischemia causes **pain** but insufficient to lead to death of myocardium. Angina may be ***stable*** (occurring reliably after certain levels of exertion), may be due to vessel spasm *(**variant** angina or Prinzmetal angina),* or may be ***unstable*** (occurring with progressively less exertion or even at rest).

(2) ***Acute MI,*** wherein the severity or duration of ischemia, is enough to cause cardiac muscle **death (necrosis)**.

(3) ***Chronic IHD*** refers to progressive cardiac heart failure following MI.

(4) ***Sudden cardiac death (SCD)*** can result (among other causes of SCD) from a lethal arrhythmia following myocardial ischemia.

►These syndromes are all relatively **late manifestations** of coronary atherosclerosis (CA) that begins early in life,

☹ ***Acute coronary syndrome,*** term is applied to the three catastrophic manifestations of IHD: unstable angina, acute MI, & SCD.

Epidemiology of IHD

▼ After peaking in 1963, the overall death rate from IHD has fallen in the US by approximately 50% in the year 2000.
Why?

☺ The decline can be attributed largely to the recognition of cardiac risk factors leading to atherosclerosis & their interventions such as;
(I) **stopping smoking, (II) treating hypertension, diabetes, & lowering cholesterol**.

☺ To a lesser extent, ***diagnostic & therapeutic advances*** are also contributory; these include:
Aspirin prophylaxis, **statins,** better arrhythmia control, coronary care units, **coronary angiography**, **angioplasty** & endovascular **stents**, **thrombolysis for MI, & coronary artery bypass surgery.**

Pathogenesis of IHD

IHD occurs because of inadequate coronary perfusion relative to myocardial demand. This may result from **a combination of:** (F11-7).

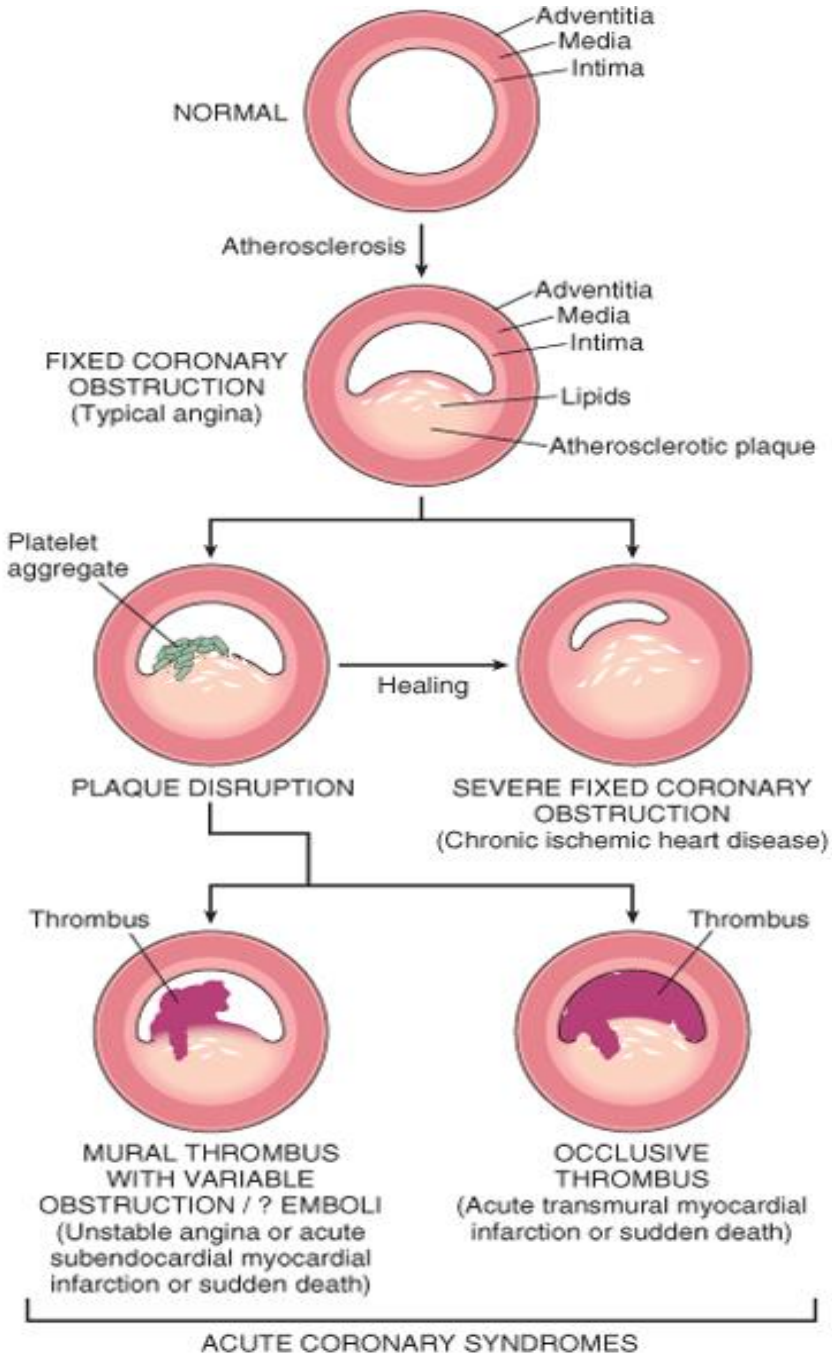
(1) pre-existing ("fixed") A occlusion of coronary arteries + (2) new superimposed thrombosis &/or vasospasm.

☹ **Critical stenosis -** is a lesion **obstructing 70% to 75% or more** of a single vessel lumen, generally causes (angina) only in the setting of ↑ demand.

☹ **A fixed 90% stenosis** can lead to inadequate coronary blood flow even **at rest**.

☺ **Importantly**, ***chronic*** CA occlusion, occuring at a sufficiently ***slow rate,*** may be able to **stimulate collateral blood flow** from other major coronaries; 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 & will result in infarction.



F11-7:
Sequential progression of coronary artery lesion morphology,

➔ beginning with stable chronic plaque, responsible for typical angina, &

➔ leading to the various acute coronary syndromes.

☹ **Although only a** single **major coronary artery may be affected** by A narrowing, **2 or ALL 3** arteries:

►Left anterior descending (LAD),

►Left circumflex (LCX), &

►Right coronary artery (RCA), can be **concurrently** involved.

★ Clinically significant plaques can be **located anywhere,** but tend to predominate *within the first several centimeters of the LAD & LCX*, & along the entire length of the RCA. Sometimes, secondary branches are also involved.

★ Symptom onset depends:
(I) on the extent & severity of **fixed** A disease, &

(II) **more critically**, on dynamic changes in coronary plaque morphology, so-called ***Acute Plaque Change*** (see below).

(I) Role of Acute Plaque Change

Acute coronary syndrome includes unstable angina, MI, & SCD, all occur because of **sudden plaque change** followed by thrombosis (F11-7), The initiating event is typically, disruption of a plaque, :

►**Commonly** due to ***Fissuring, ulceration***, or ***rupture*** of plaques, exposing highly thrombogenic plaque constituents (lipid) or underlying subendothelial BM*, or **rarely** due to:*

►***Hemorrhage into the core of plaques,*** with expansion of plaque volume & worsening of the luminal occlusion.

Basically, rupture reflects the inability of a plaque to withstand mechanical stresses.

☹ Plaques that contain: (1) a **large** lipid core, or (2) those with **thin** overlying **fibrous caps,** are more likely to **rupture** & are therefore denoted as "vulnerable."

Fissures frequently occur at the **A shoulder,** i.e., junction of the fibrous cap & the adjacent normal plaque-free arterial segment, a location at which the mechanical stresses are highest & the fibrous cap is thinnest.

☺ ☹ Fibrous caps are also continuously remodeling; the balance of **collagen synthesis & degradation** determines its mechanical strength & thus plaque stability.
Collagen is **produced** by SMCs & **degraded** by the action of **metalloproteinases** (MMPs), elaborated by macrophages in the A plaque. Consequently,
(1) A paucity of SMCs or
(2) An ↑ in inflammatory cell activity in A lesions is associated with plaque vulnerability. ☺ Interestingly, **statins** may reduce clinical events associated with IHD by their lipid-lowering effect, as well as by reducing plaque inflammation.

Influences **extrinsic to the plaque** are also important

☹ **Adrenergic stimulation** can elevate physical stresses on the A plaque through systemic hypertension or local vasospasm. Indeed, the adrenergic stimulation associated with awakening & rising may underlie the known peak incidence (between 6 AM & 12 noon) of acute MIs.
☹ **Intense emotional stress** can also contribute to plaque disruption.

☹ Acute plaque changes often develop in A plaques **not initially critically stenotic or even symptomatic before rupture.**

☹ Pathologic & clinical studies show that 2/3 of ruptured plaques are ≤50% stenotic before plaque rupture, & 85% have initial stenosis ≤70%.

☹ Thus, the **worrisome conclusion** is that a rather large number of now **asymptomatic** adults in the industrial world, have a significant, but unpredictable risk of a catastrophic coronary event.

☹ **Regrettably**, **it is presently impossible** to reliably predict plaque rupture in any given patient!!!

►Plaque disruption with ensuing platelet aggregation & **thrombosis are common, repetitive, & often clinically silent** complications of A.

☹ Moreover, **healing** of subclinical plaque disruptions & overlying thrombosis are an important mechanism by which atherosclerotic lesions **progressively enlarge!**

(II) Role of Thrombus

Thrombosis, associated with a disrupted plaque **is critical** to the pathogenesis of acute coronary syndromes.

(I) → **Partial (Mural)** vascular occlusion by a newly formed thrombus on a disrupted plaque can lead to **unstable angina, SCD or a small subendocardial MI.** # Mural thrombus in a coronary artery can also **embolize** to smaller, down-stream branches;

(II) → **Completely obstructive** thrombus, over a disrupted plaque can cause **SCD or a massive MI**

☹ Since blood flow is suddenly blocked by thrombosis, collateral circulation cannot develop.

☹ Finally, **organizing thrombi** → produce potent activators of SMC proliferation, which can contribute to the **growth** of **A** lesions!

(III) Role of Inflammation

A plaque begins with the interaction of EC & circulating WBC, resulting in → T-cell & macrophage recruitment & activation, → which **drive SMC proliferation**, with ECM accumulating over an **A** core of lipid & cholesterol.
At later stages, destabilization of plaque occurs through **metalloproteinase** secretion by macrophages.

(IV) Role of Vasoconstriction

☹ Vasoconstriction directly ↓ **lumen diameter**; & by ↑ local mechanical shear forces, it can potentiate plaque disruption.
Vasoconstriction in plaques can be **stimulated by** (1) circulating adrenergic agonists, (2) locally released platelet contents, (3) an imbalance between EC relaxing factors (e.g., nitric oxide) versus contracting factors (e.g., endothelin), & (4) mediators released from perivascular inflammatory cells.

Other Pathologic Processes

Rarely, other processes can ↓ coronary perfusion. including: **emboli** originating from valve vegetations, **vasculitis**, **systemic hypotension, & myocardial hypertrophy.**

Angina Pectoris

Is **intermittent chest pain** caused by transient, reversible myocardial ischemia. There are 3 variants:

►***Typical* or *stable angina*** is episodic **chest pain associated with → exertion** or other form of ↑ myocardial oxygen demand (e.g., tachycardia or hypertension due to fever, anxiety, fear). Pain is classically → **crushing or squeezing substernal sensation,** which can → **radiate** down the left arm or to the left jaw.

☺ The pain is usually **relieved by → rest** or → by administering agents such as **nitroglycerin**; which cause peripheral vasodilation, & thus reduce venous blood return to the heart , in larger doses, nitroglycerin also ↑ blood supply to the myocardium by direct coronary vasodilation

►Stable angina pectoris is usually **associated with a fixed A narrowing (≥75%) of one or more coronary arteries**. With this degree, the myocardial oxygen supply may be sufficient under resting conditions, but cannot be adequately ↑ to meet any ↑ requirements.

►►***Prinzmetal or variant angina*** is angina occurring **at rest** due to **coronary artery spasm.** typically occur either on or near an existing **A plaque**, or in completely normal coronary.
😐**The etiology is not clear**.
☺ Prinzmetal angina **typically responds promptly** to the administration of vasodilators such as nitroglycerin or calcium channel blockers.

▼ ▼ ***Unstable angina = crescendo angina,*** is characterized by ↑ **frequency of pain**, precipitated by **progressively less exertion;** the episodes tend to be **more intense & longer** lasting than stable angina.

☹ Unstable angina is associated with plaque **disruption** with superimposed **partial thrombosis**, distal **embolization** of the thrombus, and/or **vasospasm**. It is the harbinger of more serious, potentially irreversible ischemia (due to complete luminal occlusion by thrombus) & is therefore sometimes called ***pre-infarction angina.***

Myocardial Infarction (MI)

MI, popularly known as ***heart attack***, *is* ***death*** *&* ***necrosis*** *of heart muscle resulting from ischemia*.

- Roughly **1.5 million people in the US suffer an MI every year**; of these, 1/3 die, of which half die even before reaching the hospital!!
- The major underlying **cause of IHD** is **A**, & therefore *the frequency* of MIs *rises progressively with ↑* ***age,*** **diabetes hypertension,** ***hypercholesterolemia, &*** **smoking.**
- Approximately, **10%** of MIs occur in people **younger than 40** years, & **45%** occur in people **younger than age 65**. Blacks & whites are equally affected.

☹ Men are at significantly greater risk than women, although the gap progressively narrows with age.

Pathogenesis of MI

Most* MIs are caused by acute coronary artery *thrombosis, following disruption of A plaque; but…

? Sometimes, particularly with infarcts limited to the innermost myocardium (**subendocardial MI**), **thrombi may be absent.**

In these cases, **severe & diffuse A** significantly limits coronary BV perfusion, & a prolonged period of ↑ demand due to **tachycardia or hypertension** may be sufficient to cause necrosis of myocytes most distal to the epicardial vessels, i.e., **subendocardial area.**

Coronary Artery Occlusion

► **In a *typical MI,*** the following sequence of events transpires:

1 → There is a sudden disruption of an A plaque- by **fissuring, ulceration, or rupture -** exposing subendothelial collagen & necrotic plaque lipid contents.

2 → **Platelets adhere**, aggregate, become activated, & release potent secondary platelet aggregators, including **thromboxane A2, adenosine diphosphate, & serotonin.**

3 → **Vasospasm is stimulated** by platelet aggregation & mediator release.

Other mediators activate the extrinsic pathway of coagulation, adding to the bulk of the thrombus.

4 → **Within minutes, the thrombus completely occlude the coronary lumen.**

The evidence for this series of events derives from:
(1) Autopsy studies of patients dying with acute MI,
(2) Angiographic studies demonstrating a high frequency of thrombotic occlusion early after MI, **(3)**
The high **success rate** of therapeutic thrombolysis & primary angioplasty, & **(4)**
The demonstration of **residual** disrupted A plaque lesions by angiography **after thrombolysis**.

♥ Interestingly, coronary angiography performed within 4 hours of the onset of MI shows a thrombosed coronary artery in almost 90% of cases.

However, when angiography is delayed until 12 to 24 hours after onset of symptoms, occlusions are observed in only 60% of patients, ***even without intervention.***

☺Thus, **at least some occlusions seem to clear spontaneously as a result of lysis of the thrombus and/or relaxation of spasm**.

☹ Any residual thrombus is likely to be incorporated into the growing A plaque.

Myocardial Response to Ischemia

☹ **Within seconds** of vascular obstruction, cardiac myocyte aerobic glycolysis ceases, leading to inadequate production of ATP & accumulation lactic acid.

☹ The *functional* consequence is a striking → **loss of contractility**, occurring **within a minute** of the onset of ischemia. EM changes, including

→ myofibrillar relaxation**,**

→ glycogen depletion, &

→ rapid cell & mitochondrial swelling.

However, these early 3 changes are potentially ***reversible,*** & myocardial cell death is not immediate.

☹ Only severe ischemia lasting at least **20 to 40 minutes causes *irreversible* coagulation necrosis.**

☹ With longer periods of ischemia, **microvasculature (blood vessel) injury** follows.

☺ **If myocardial blood flow is restored anywhere along this timeline (*reperfusion*), cell viability may be preserved.**

☺ That is why → early clinical detection of acute MI, & prompt intervention by **angioplasty** or thrombolysis, can restore blood flow to the at-risk areas, ischemic but still viable myocardium. However, reperfusion can also have some untoward effects…

☹ Myocardial ischemia may result in **arrhythmias, probably by causing *electrical instability (irritability)* of ischemic regions** of the heart, the commonest arrhythmia is **ventricular fibrillation (VF), which is the most common cause of sudden cardiac death in 80% to 90%** of myocardial ischemia cases.

☹ Less commonly, massive MI can clearly cause a fatal **acute HF**.

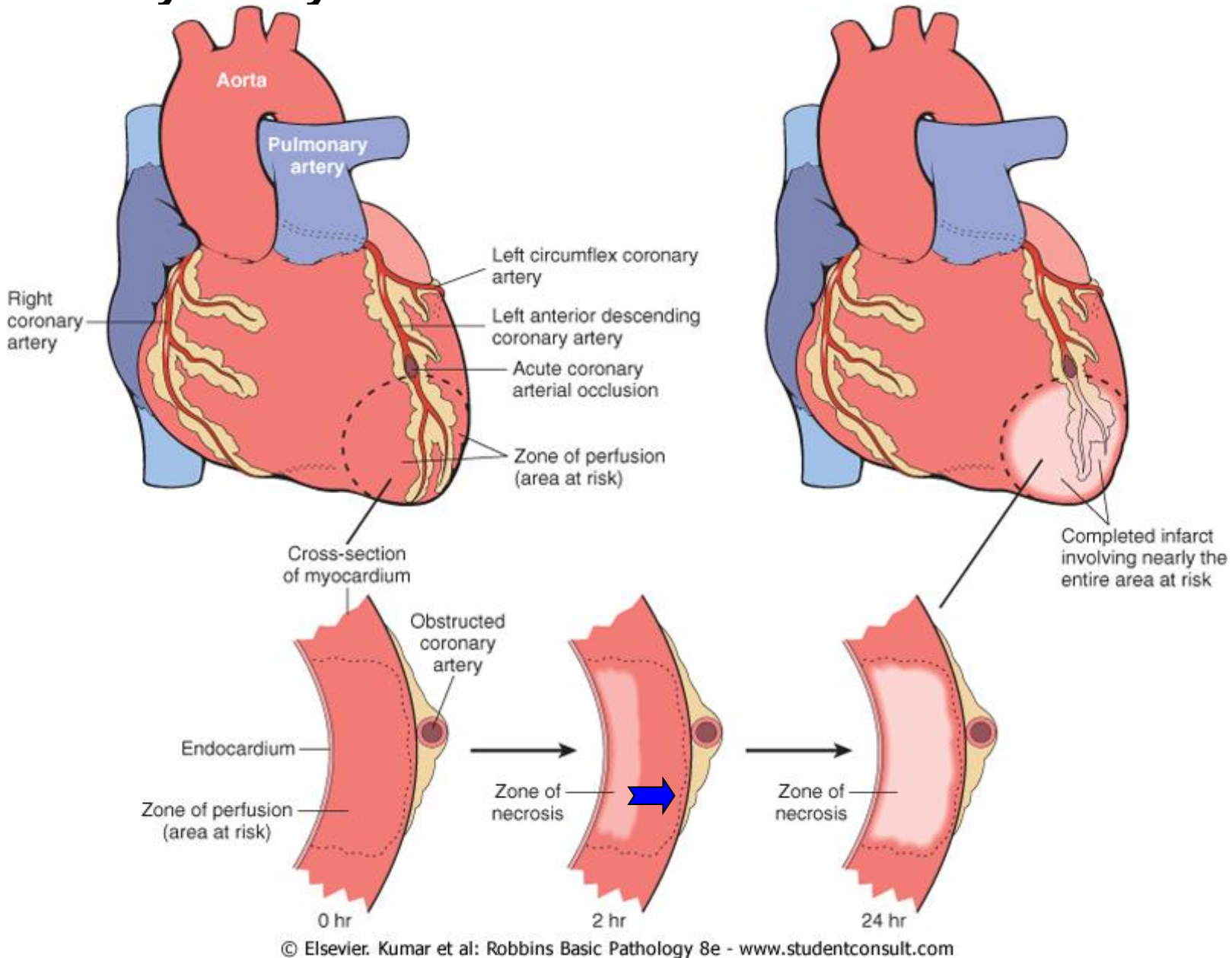
Ischemic necrosis of myocytes → first occurs in the subendocardial zone, why? Because…

☹ Not only is this region the last area to receive blood delivered by the epicardial vessels, the relatively higher intramural pressures there further compromise blood inflow.

► With **more prolonged ischemia**, a wavefront of cell death moves from the subendocardial area outwards, through the myocardium to involve progressively more of the transmural thickness of the ischemic zone **{ transmural infarcts defined as involving ≥50% of the myocardial wall thickness},** usually reaching MI **full size within 3 to 6 hours (F11-8**)

☺ Any intervention in this time, can potentially limit the final extent of necrosis. The site, size of an acute MI depend on the: **coronary occlusion** location, severity, & rate of development + **Size** of the vascular bed perfused by the obstructed vessels + **Duration** of the occlusion + **Metabolic demands** of the myocardium affected (e.g., by BP & HR) + Extent of **collateral** supply.

F11-8; **Progression of myocardial necrosis after coronary artery occlusion.**



Morphology of MI

➔Nearly, **all transmural MI** affect **LV** {which includes the interventricular septum (IVS)}. Roughly 15% to 30% of MIs affecting the posterior or posteroseptal wall, also extend into the adjacent right ventricular **(RV)** wall; BUT
→ **Isolated RV MI** occurs in only 1% to 3% of cases, **why?**
☺ Even in transmural infarcts, a narrow rim **(0.1 mm) of viable subendocardial myocardium is preserved, Why?**
→ because of the direct diffusion of oxygen & nutrients to this area from the ventricular lumen.

▼ 90% of people have dominant RCA, i.e., the posterior descending artery is supplied by the right CA. In these individuals the following, the **infarcts distribution** is seen:

→ Left anterior descending artery (**40% to 50**%): MI involves anterior LV, anterior IVS, & apex circumferentially.
→ Right coronary artery (**30% to 40%):** MI involves posterior LV, posterior IVS, & RV free wall in some cases.

→ Left circumflex artery (**15% to 20**%): MI involves lateral LV, except the apex.

Occasional coronary occlusions encountered in the (1) **left** main CA, or (2) in **CA secondary branches**.

☺ In contrast, significant atherosclerosis or thrombosis of **penetrating** intramyocardial branches of coronary artery **rarely occurs**.

☺ Severe CA occlusion without associated myocardial damage suggests the prior formation of **protective collaterals.**

The gross & microscopic appearance of an MI depends on the interval of time since the original injury (Table 11-2).

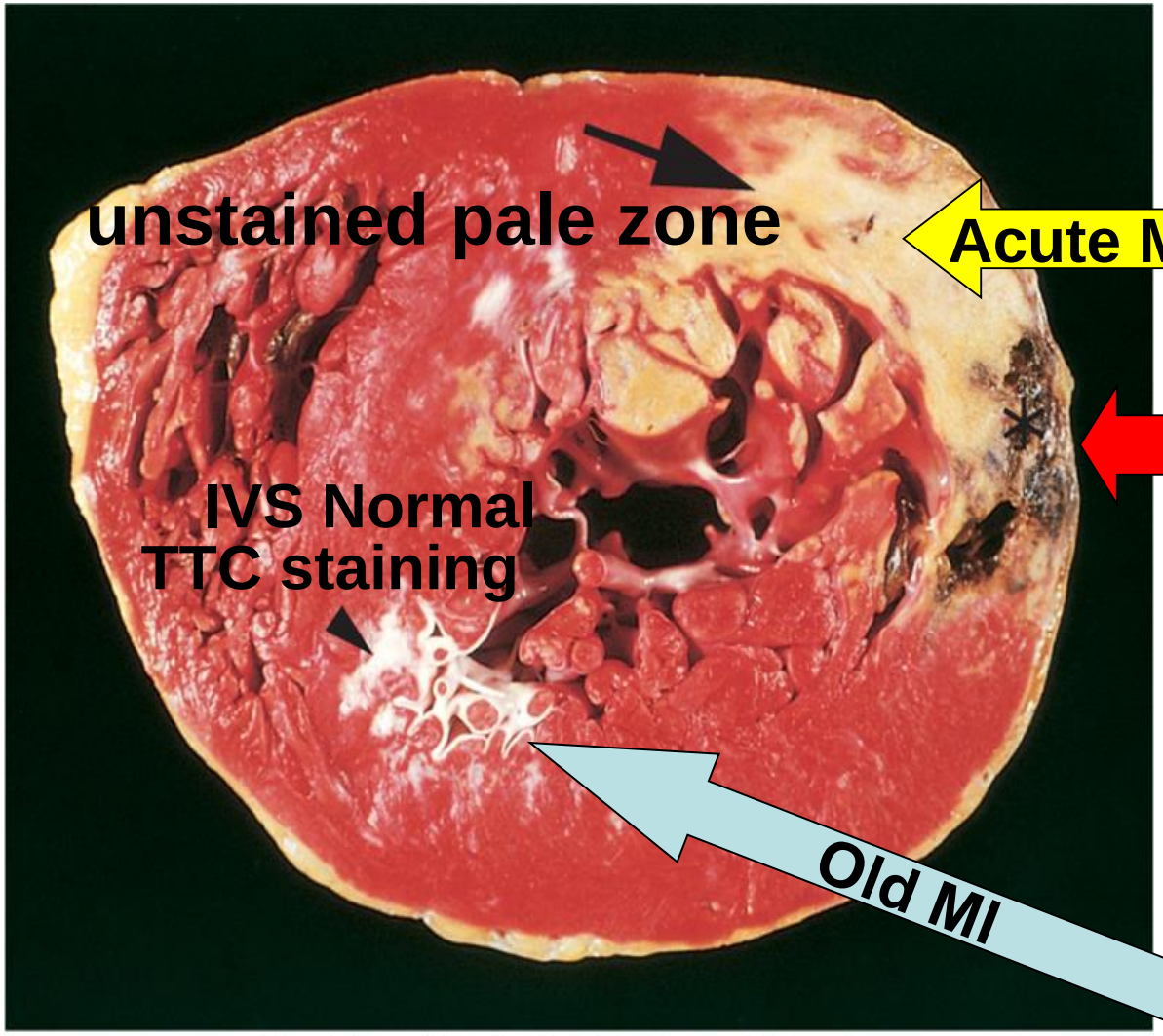
☹ ☹ Despite recent excitement about potential myocardial repopulation by **resident or circulating stem cells (SC**), **myocardial cell necrosis proceeds invariably to scar** formation without any significant regeneration.

► **MIs less than 12 hours old are usually not grossly apparent. & if death** occurs within a few hours after symptom onset, recognition of acute MIs can be difficult.
😐 However, **infarcts more than 3 hours old** can be visualized by → exposing heart slices to vital stains (e.g., **triphenyl tetrazolium chloride (TTC)**, a substrate for lactate dehyrogenase in viable heart).
Because → **dehydrogenases** are depleted in the area of MI as they leak through damaged cell membranes (this actually form the basis for detecting MI in peripheral blood samples); an **infarcted area** is revealed as an **unstained pale zone** (old scars appear white & glistening; **(F11-9**).

► **Grossly, 12 to 24 hours** infarction can be identified as a **reddish blue discoloration** caused by stagnant, trapped blood. Thereafter, an infarct becomes more sharply delineated as **a yellow-tan, softened area**;

►By **10 to 14 days** infarcts become rimmed by hyperemic (highly vascularized) **granulation tissue**.

Over the succeeding *weeks the MI evolves to a fibrous scar.*



F11-9:

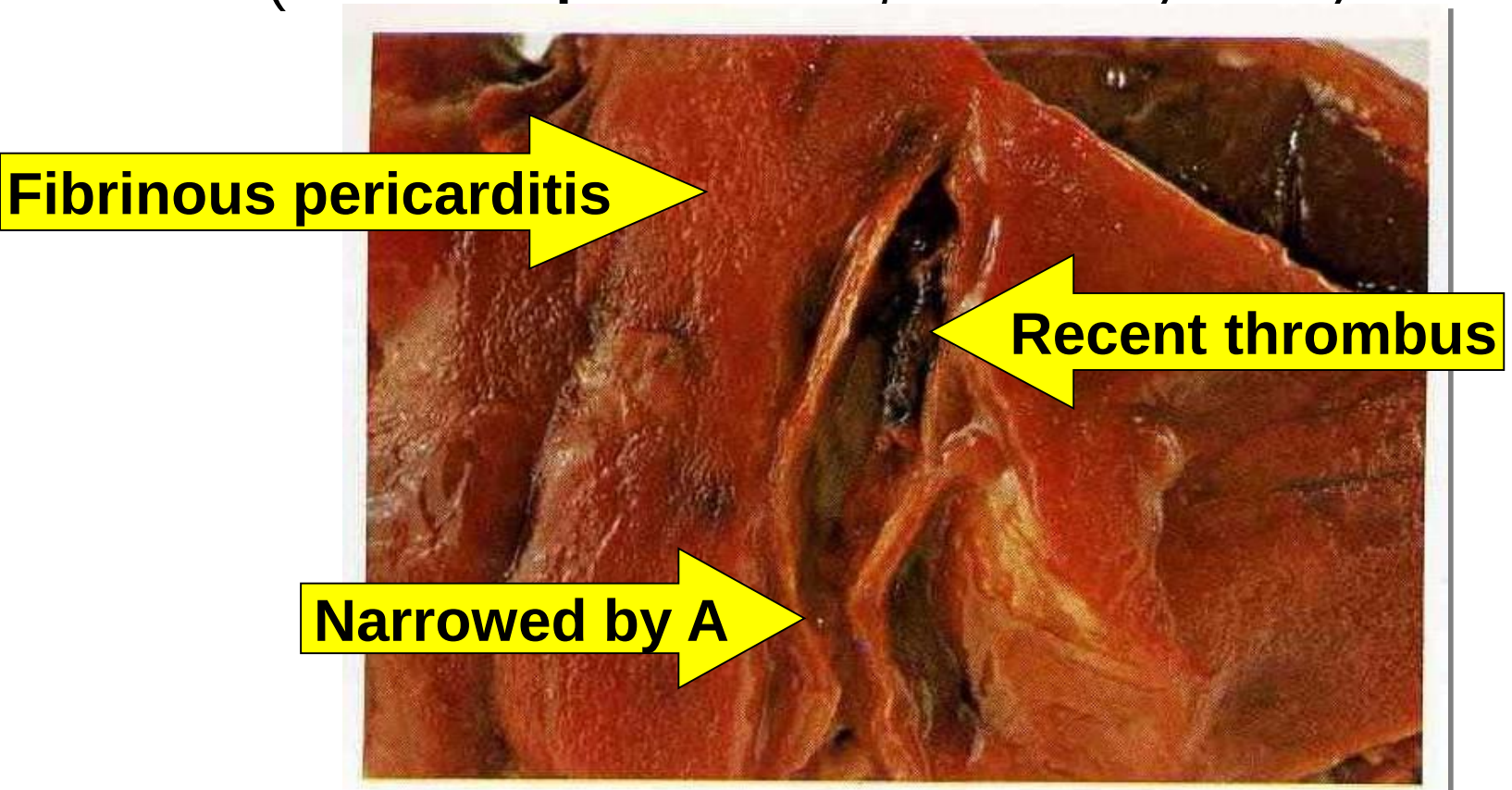
Acute posterolateral **MI of LV** demonstrated by a lack of TTC staining in areas of necrosis.

* Site of hemorrhage at the right edge of the MI is due to **ruptured MI**, which was the cause of ☠ death ☠.

Note **anterior old MI scar.**

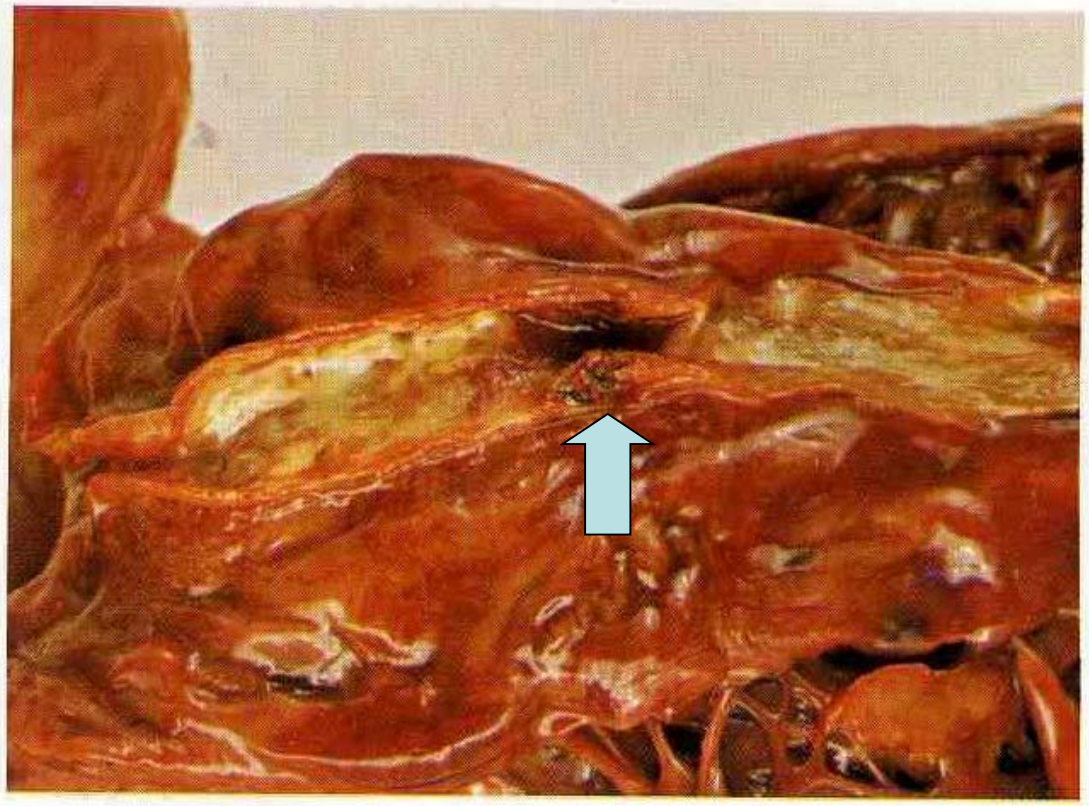
F6.67: The left anterior descending artery contains a recent <u>thrombus</u> (center) & the vessel distal to the thrombus (below it) <u>is narrowed by</u> <u>atherosclerosis</u>.

☠ The patient had a recent extensive MI of the anterior IVS, with the epical surface of the LV covered by a granular fibrinous exudate (**fibrinous pericarditis,** secondary to MI).



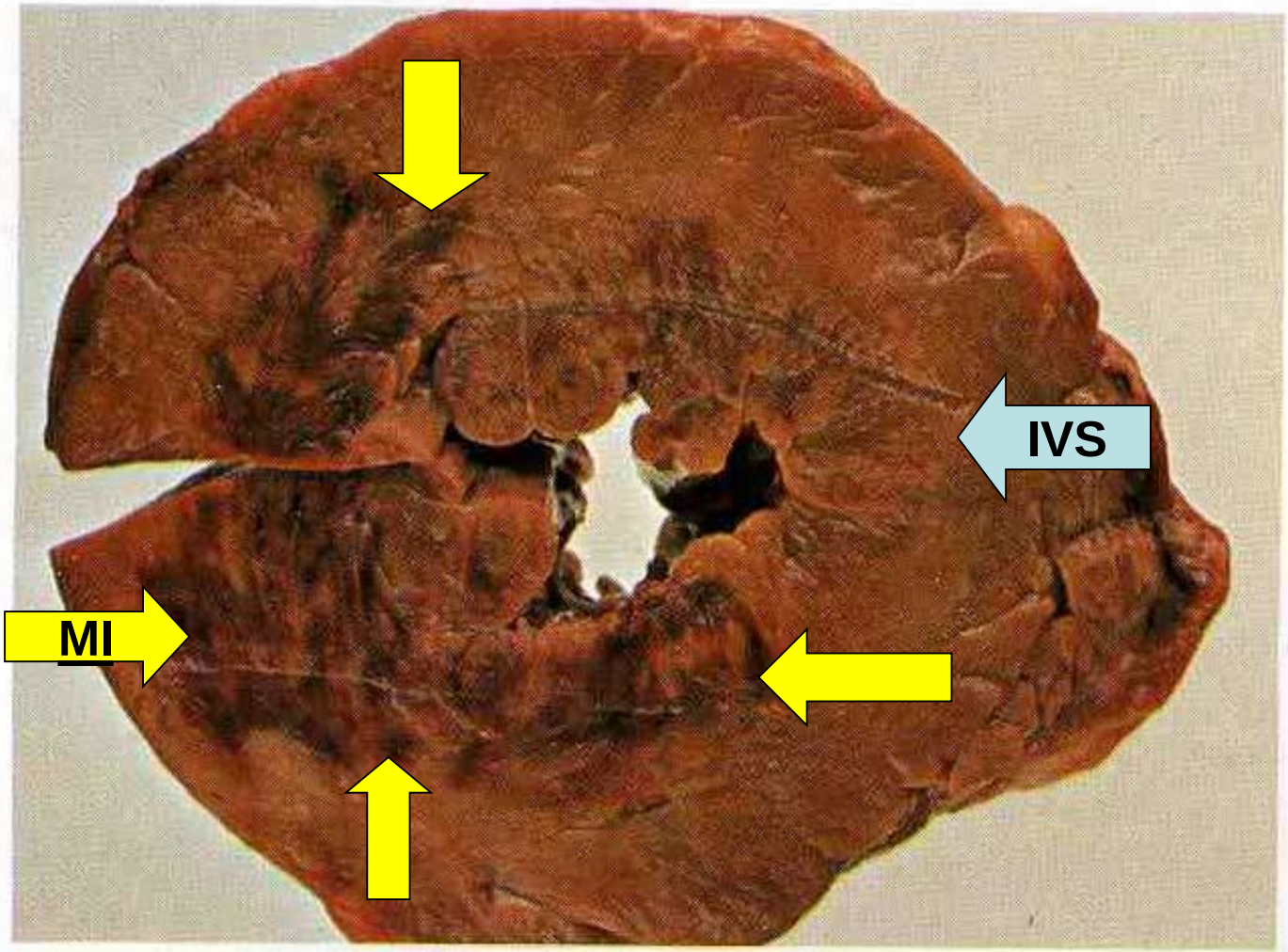
6.67 Coronary artery: thrombosis

F6.68: The Rt coronary artery (top) is widely patent but a calcified **atherosclerotic plaque** has produced a stenosed segment (top centre). Stenosis has been greatly increased by **hemorrhage into the plaque (arrow)**, which accordingly is red in color, causing → **<u>coronary occlusion</u>** , even in the absence of thrombus formation on the plaque!!



6.68 Coronary artery: atherosclerosis

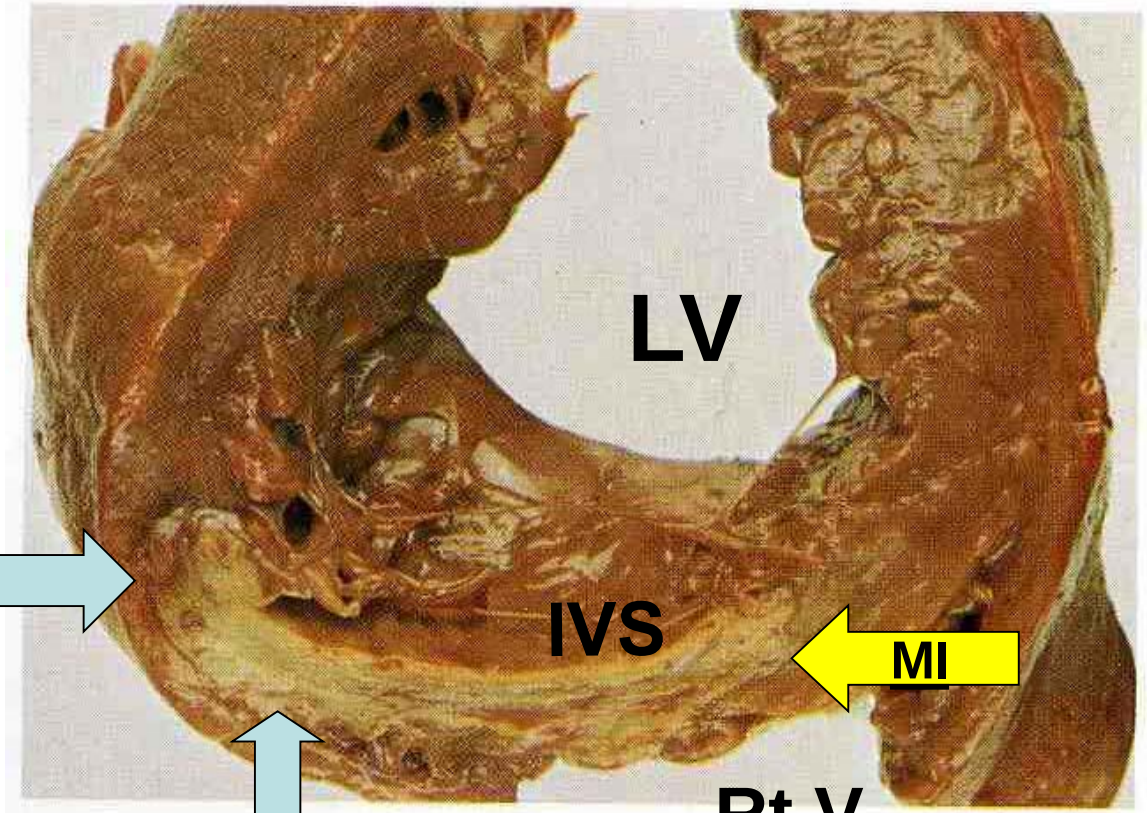
F6.69: Coronal section of the LV, with the IVS at the right, close to the apex. ☠ Fatal **massive recent (2-3 days old)** **hemorrhagic** MI is present in the posterolateral wall of LV.



6.69 Infarct of myocardium

F6.70: Coronal section of the LV from a 44y old female patient sustained clinical **<u>MI 8 days before her death</u>**, showing yellow-white MI of the anterior part of the IVS (bottom, arrows).

Between the 8th and 10th days a reddish-purple zone appears at the periphery of the necrotic muscle, & such a zone is just visible (lower left) around this lesion.



Reddish granulation tissue

6.70 Infarct of myocardium

The microscopic appearance also undergoes a characteristic sequence of changes (Table 11-2 & **F11-10**).

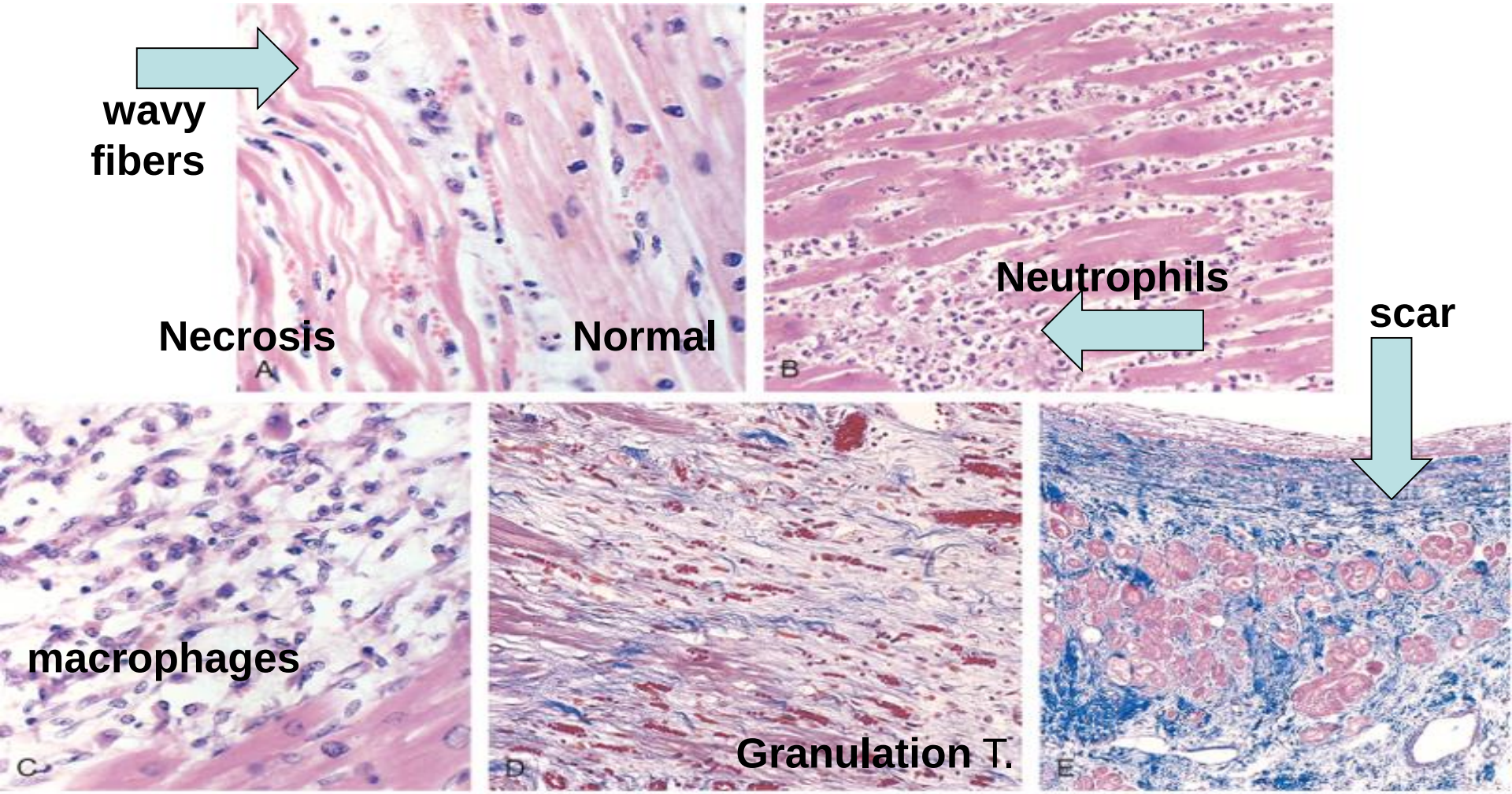
► **Within 4 to 12 hours of infarction,** typical features of **coagulative necrosis** become detectable.

"**Wavy fibers**" can also be present at the edges of an infarct; these reflect the stretching & buckling of **noncontractile dead fibers.**

"Myocyte vacuolization", with cleared intracellular spaces, probably containing water; are still alive but are poorly contractile myocytes.

► Necrotic myocardium elicits **acute inflammation** (typically most prominent **1-3 days after MI**); followed by a wave of **macrophages** to remove necrotic myocytes & neutrophil fragments (most pronounced **5-10 days after MI).**

F11-10: H of MI & its repair. **A**, 1-day old MI→ coagulative necrosis + wavy fibers on the left. **B**, 2-3 days: dense neutrophils infiltration. **C**, 7-10 days, complete removal of necrotic muscle by macrophages. **D**, Granulation tissue (angiogenesis + collagen). **E**, Healed MI, dense collagenous scar, with few residual myocytes. (Masson's trichrome stain collagen blue).



► The infarcted zone is progressively replaced by **granulation tissue** (**most prominent 2-3 weeks after MI**), which in turn forms the provisional scaffolding upon which dense **collagenous scar** is formed. In most instances scarring is well advanced by the end of the sixth week.
► ***Healing*** requires the migration of inflammatory cells & angiogenesis, that can access infarcts, from, **Where? only**, from the intact vasculature at the infarct **margins.** Thus, an **MI heals from its borders toward the center,** & a large MI may not heal as readily or as completely as a small one.

► **Once an MI is completely healed**, it is **impossible** to distinguish its age (i.e., the dense fibrous scars of 8-week-old and 8-year-old lesions look similar).

Changes in MI due to Reperfusion

☺ The current therapeutic goal in acute MI, is to salvage the maximal amount of ischemic viable (but not necrotic) myocardium, by restoration of tissue perfusion as quickly as possible. Such *reperfusion* is achieved by:

→ **Thrombolysis** (dissolution of thrombus by **streptokinase** or **tissue plasminogen activator, t-PA**),

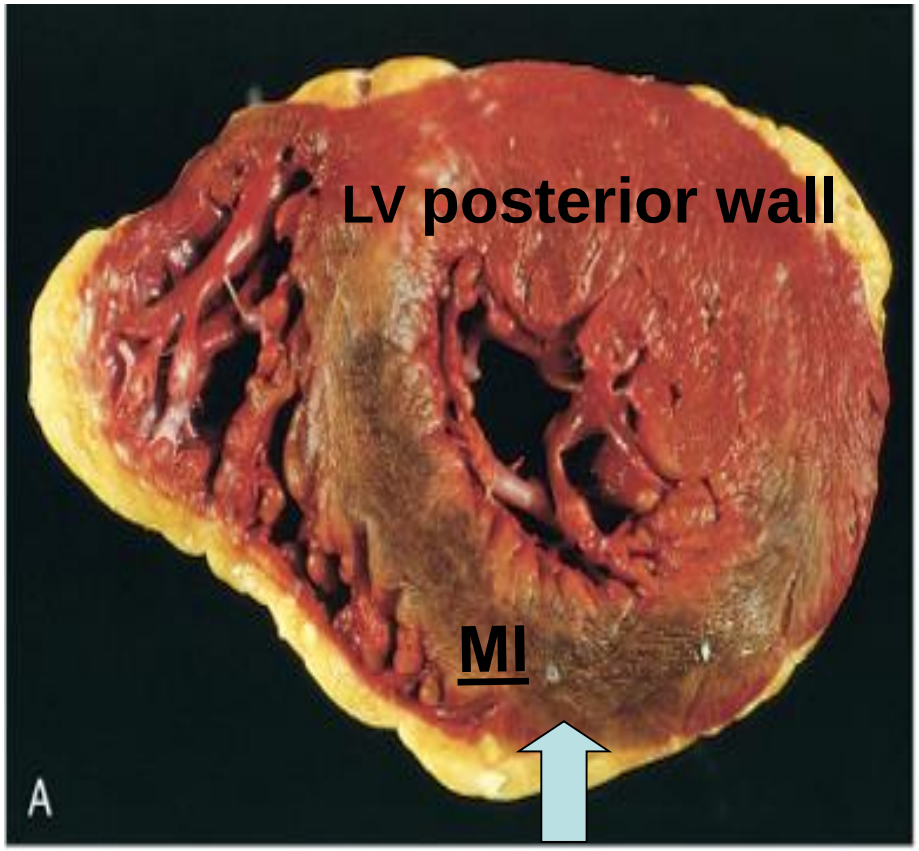
→ **Balloon** angioplasty (with or without stenting), or

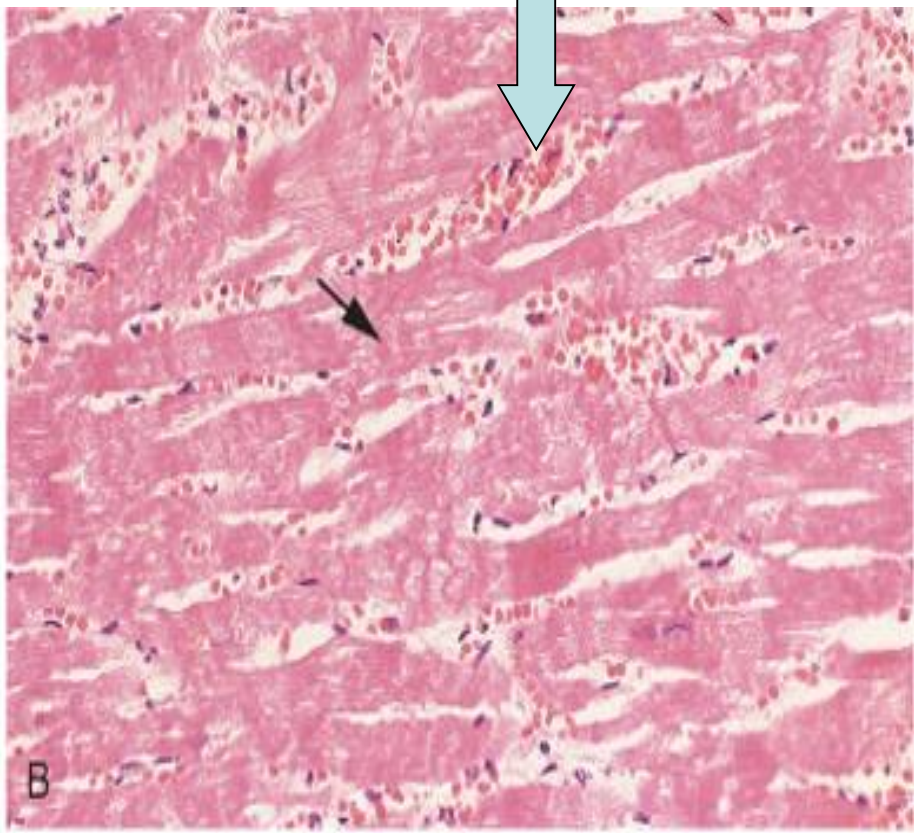
→ CA **bypass graft**. But…

☹ ***Reperfusion injury*** can incite *greater* local damage than might have otherwise occurred without **rapid** restoration of blood flow.

It is **mediated** by oxygen free radicals (**FR**) generated by the ↑ number of infiltrating WBC facilitated by reperfusion. Reperfusion-induced microvascular injury causes → **hemorrhage** & → **EC swelling** that occludes capillaries & may prevent local blood flow (called ***no-reflow*).** The typical appearance of ischemic & reperfused myocardium is shown in **F11-11A & B**.

F11-11: Consequences of myocardial ischemia followed by **reperfusion**. A, Large hemorrhagic **antero-septal MI** of a patient treated with streptokinase, (TTC -stained TS section; posterior wall at top).
B. Myocardial coagulation necrosis with (I) **hemorrhages** & (II) **contraction bands** spanning myofibers.





►Necrotic myocytes, subjected to reperfusion also show ***contraction band necrosis***, an intensely eosinophilic **transverse bands** composed of **hypercontracted**, tetanic state sarcomeres, due to high extracellular calcium (Ca ++) concentrations in the restored blood flow are able to cross damaged plasma membranes & drive actin-myosin interactions, in the absence of ATP which allow relaxation.

Ischemic (but viable) myocardium following perfusion, can show profound dysfunction. Most of this viable myocardium can ultimately recover normal function,

▼ but abnormalities in cellular biochemistry may persist for several days after ischemia & lead to a noncontractile state ***(stunned myocardium).***

Such stunning can produce a state of transient reversible cardiac failure that may require pump assistance to support the patient until cardiac function returns.

Consequences & Complications of MI

The *in-hospital death rate* has declined from approximately 30% to an overall rate of between 10% & 13% today (& to 7% for patients receiving aggressive reperfusion therapy).

☹ Unfortunately, **half of the deaths** associated with acute MI occur in individuals who **never reach the hospital**; such patients generally die within 1 hour of symptom onset-usually **as a result of serious arrhythmias (mostly VF)**.

☹ Advanced age, female gender, diabetes mellitus, & previous MI are associated with poor prognosis.

Complications after acute MI

Nearly three-fourths (3/4) of patients have one or more complications after acute MI **(F11-12 A to F**):

☹ ***Contractile dysfunction (LVF).*** An MI affects LV pump function approximately proportional to its size. Typically, there is **some degree of LV failure,** with hypotension + pulmonary congestion & edema, (fluid transudation into the pulmonary interstitial & alveolar spaces).

☹ ***Cardiogenic shock*** **= is severe "pump failure", occurs in 10% to 15% of** patients after acute MI, generally with a massive **large infarct (often > 40% of the LV)**, with nearly **70% mortality rate,** accounting for 2/3 of in-hospital deaths.

☹ ***Arrhythmias: are the most common*** **(80% to 90%)** ***cause of*** **sudden deaths following an MI**. It include the → most serious **ventricular fibrillation (VF) & heart block.**

In addition, other arrhythmias, such as sinus bradycardia, tachycardia, ventricular premature contractions or ventricular tachycardia may occurs.

☹ ***Pericarditis****.* A fibrinous or hemorrhagic pericarditis usually develops **within 2 to 3 days of a transmural MI** & typically spontaneously resolves with time **(**F11-12D); it is the epicardial manifestation of the underlying myocardial inflammation reaction to the infarction necrosis.

☺ ***Pericarditis is the*** **simplest complications of MI**.

☹ ☹ ☹ ***Myocardial rupture***: complicates 1% to 5% of MIs, but causes 7% to 25% of MI-associated deaths. It includes:
(1) rupture of the **ventricular free wall**, with fatal hemopericardium & cardiac tamponade (**F11-9 & 11-12A & 6-73 & 6- 74);**

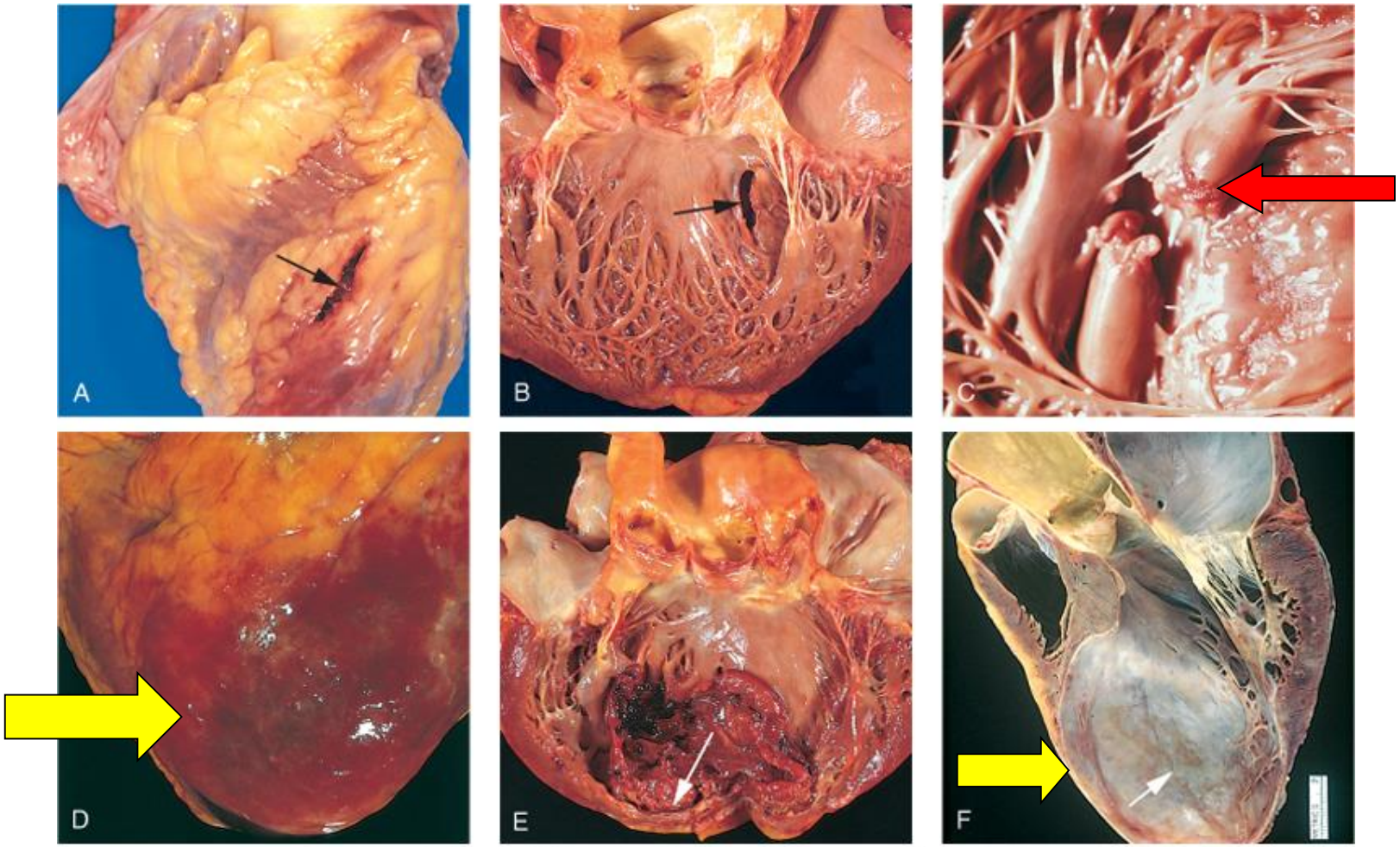
(2) rupture of the **infarcted IVS**, leading to a **new VSD** & left-to-right shunt **(F11-12B**); &

(3) rupture of **infarcted papillary muscle**, resulting in severe mitral regurgitation (**F11-12C**).

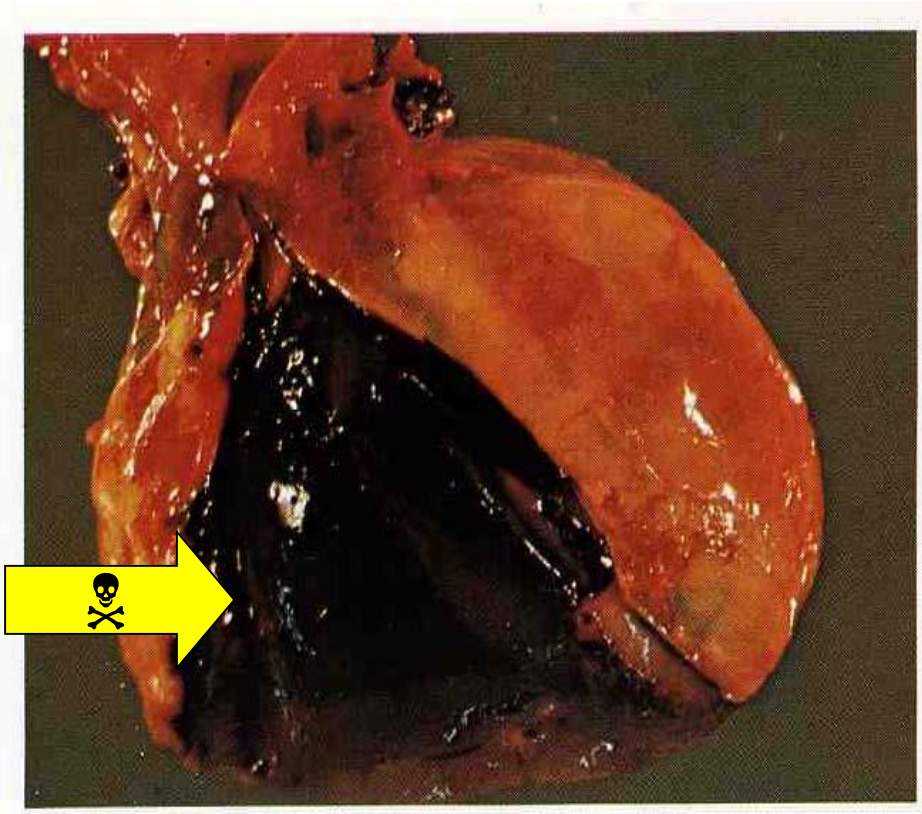
Rupture can occur at almost any time after MI, but is: **most common 3 to 7 days after infarction;** when:
▼ **lysis of** the myocardial connective tissue is **maximal** &
▲the **granulation tissue has not deposited sufficient collagenous matrix to buttress (repair) the wall**.

5 Risk factors for free-wall rupture include:
(1) age older than 60 years, (2) female gender, (3) pre-existing **hypertension**, & (4) **lack of LV hypertrophy**, &
(5) **no previous MI !!!**
(pre-existing scarring tends to prevent myocardial tearing!).

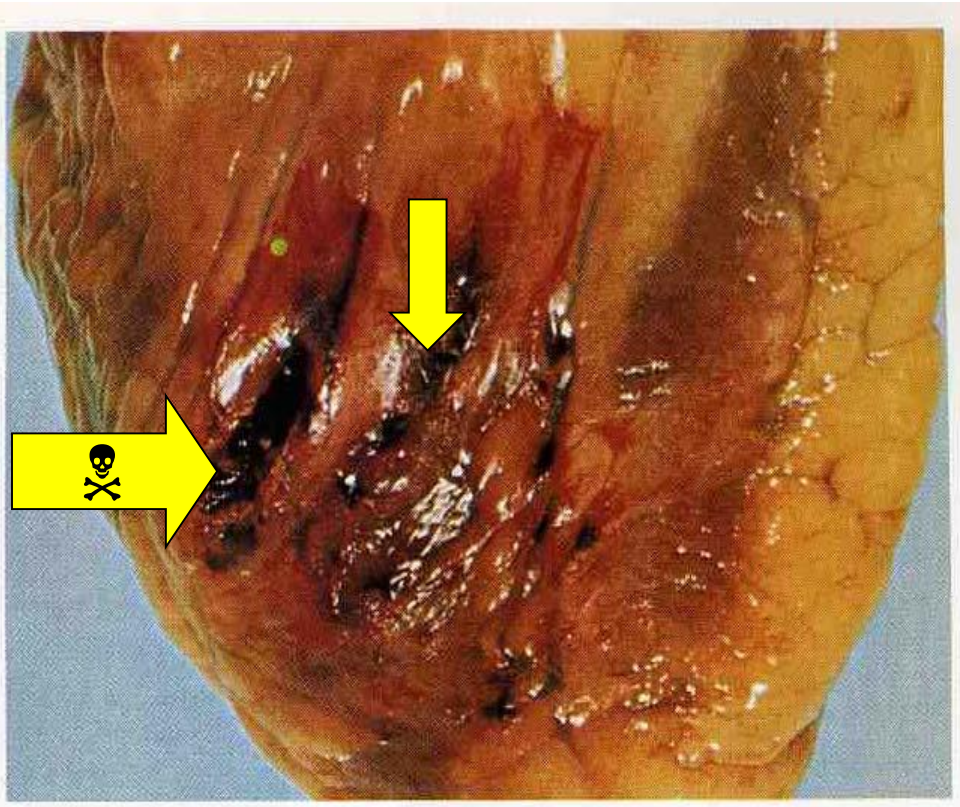
F11-12: **Complications of MI. A**, **Rupture** acute anterior MI. **B**, **Rupture** of IVS. **C**, Complete **rupture** of infarcted papillary muscle. **D,** Fibrinous **pericarditis** overlying acute MI. **E**, Early **expansion** of anteroseptal MI with wall thinning & mural thrombus. **F**, Large apical LV **aneurysm.**



F6-73: The pericardial sac is reflected to reveal a large hematoma distending the sac **(hemopericardium),** causing ☠ **fatal cardiac temponade**. After washing the pericardium, F6-74: the source of hemorrhage is shown, two slit- like tears in the heart wall, over **ruptured anterior MI of the LV**. The epicardial fat adjacent to the tear appears red & bruised.



6.73 Myomalacia cordis



6.74 Myomalacia cordis

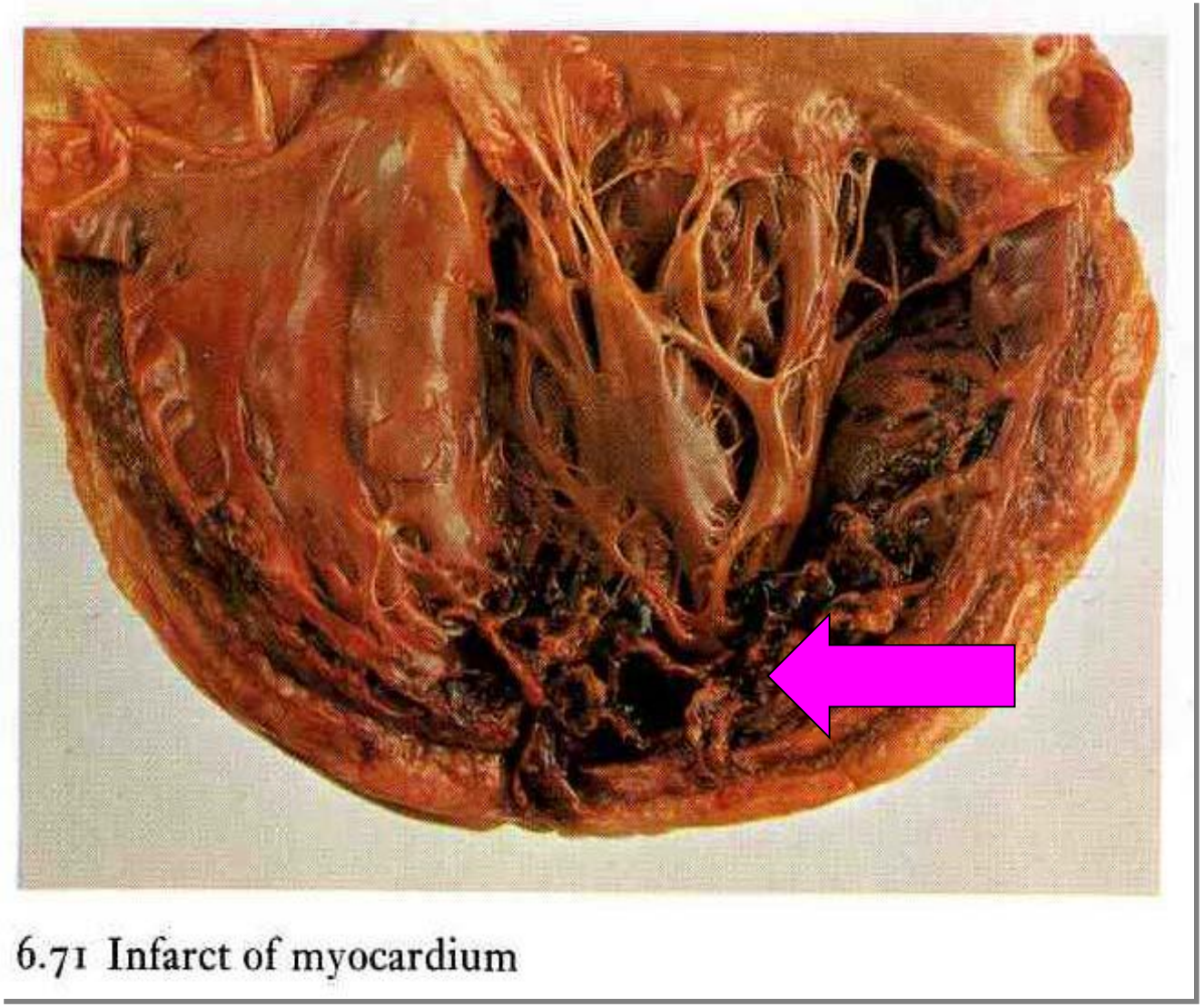
☹ ***Infarct expansion:*** weakening of necrotic muscle leads **stretching**, thinning, & dilation of the infarcted area, (especially in anteroseptal MI); this is often associated with **mural thrombus (F11-12E**).

☹ ***Mural thrombus:*** the combination of a local loss of contractility (causing stasis) + with endocardial (EC) damage (causing a thrombogenic surface) can result in ***mural thrombosis &***, **potentially, systemic *thromboembolism*** **(F**11-12E & 6-71)

☹ ***Ventricular aneurysm (AN)***. A late complication, aneurysms of the ventricular wall most commonly result from a large transmural anteroseptal MI that heals with the formation of thin scar tissue (**F11-12F & 6-75**).
Complications of ventricular aneurysms include mural **thrombus, arrhythmias & HF**,

☺ but **rupture of the fibrotic aneurysmal wall does not occur.**

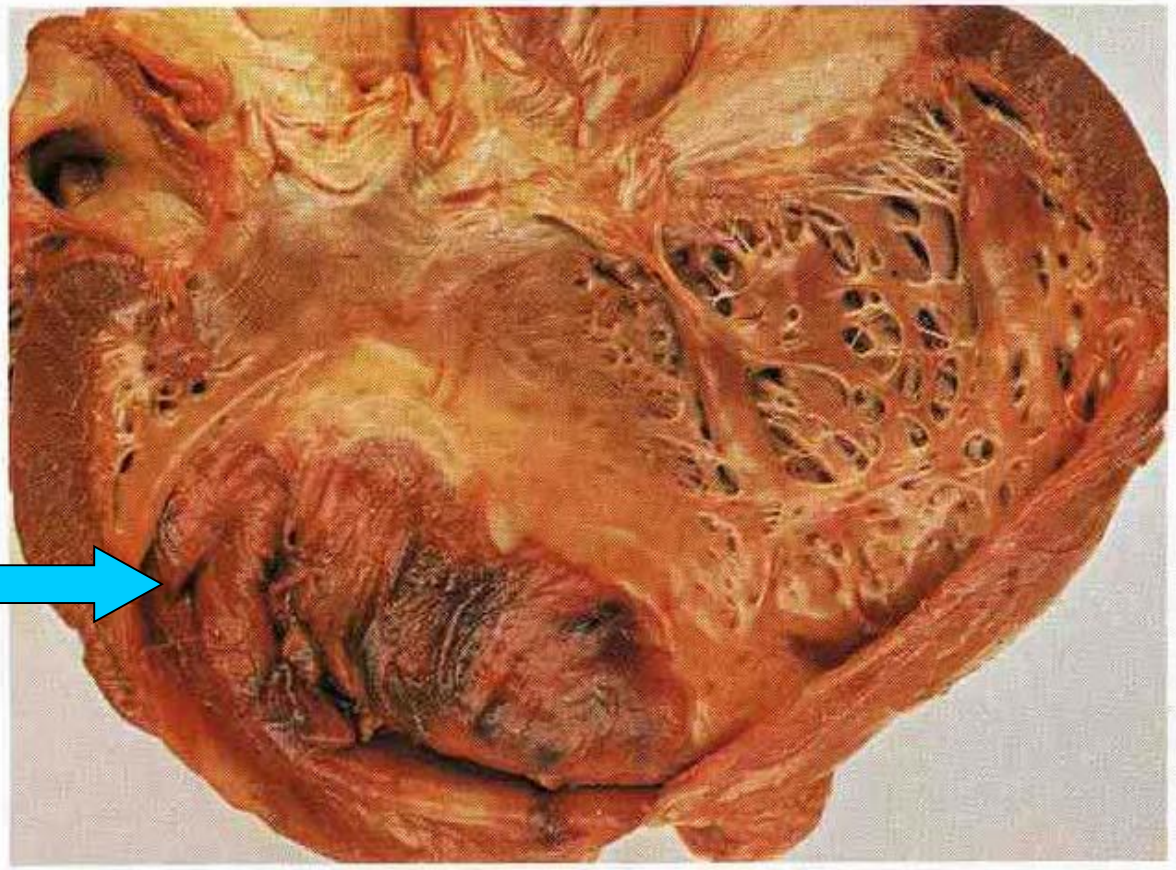
F6.71: There is an extensive recent, full-thickness antero-septal **MI** of the LV which involves the endocardial surface, causing **<u>mural</u> <u>thrombosis over the infarcted area, which is</u>** an important **source of ☹ systemic thromboembolism**.



6.71 Infarct of myocardium

F6.75: Large, thin-walled aneurysm at the apex of the LV {the most common site of cardiac aneurysm} contains laminated mural thrombus. The **aneurysm follows massive septal MI** which has become fibrosed, greyish-white in color, weak & has yielded → to produce the **cardiac aneurysm.**

Cardiac aneurysm



6.75 Aneurysm of the left ventricle

☹ ***Papillary muscle dysfunction;***

Dysfunction of a papillary muscle after MI (postinfarct mitral regurgitation) most frequently results from either :

- **early: from ischemic dysfunction** of a papillary muscle & the underlying myocardium, or
- Rarely because of **rupture** of the infarcted papillary muscle or
- **later:** from ► **papillary muscle fibrosis & shortening**, or
- **Ventricular dilation.**

All the above disorders result in valve incompetence!

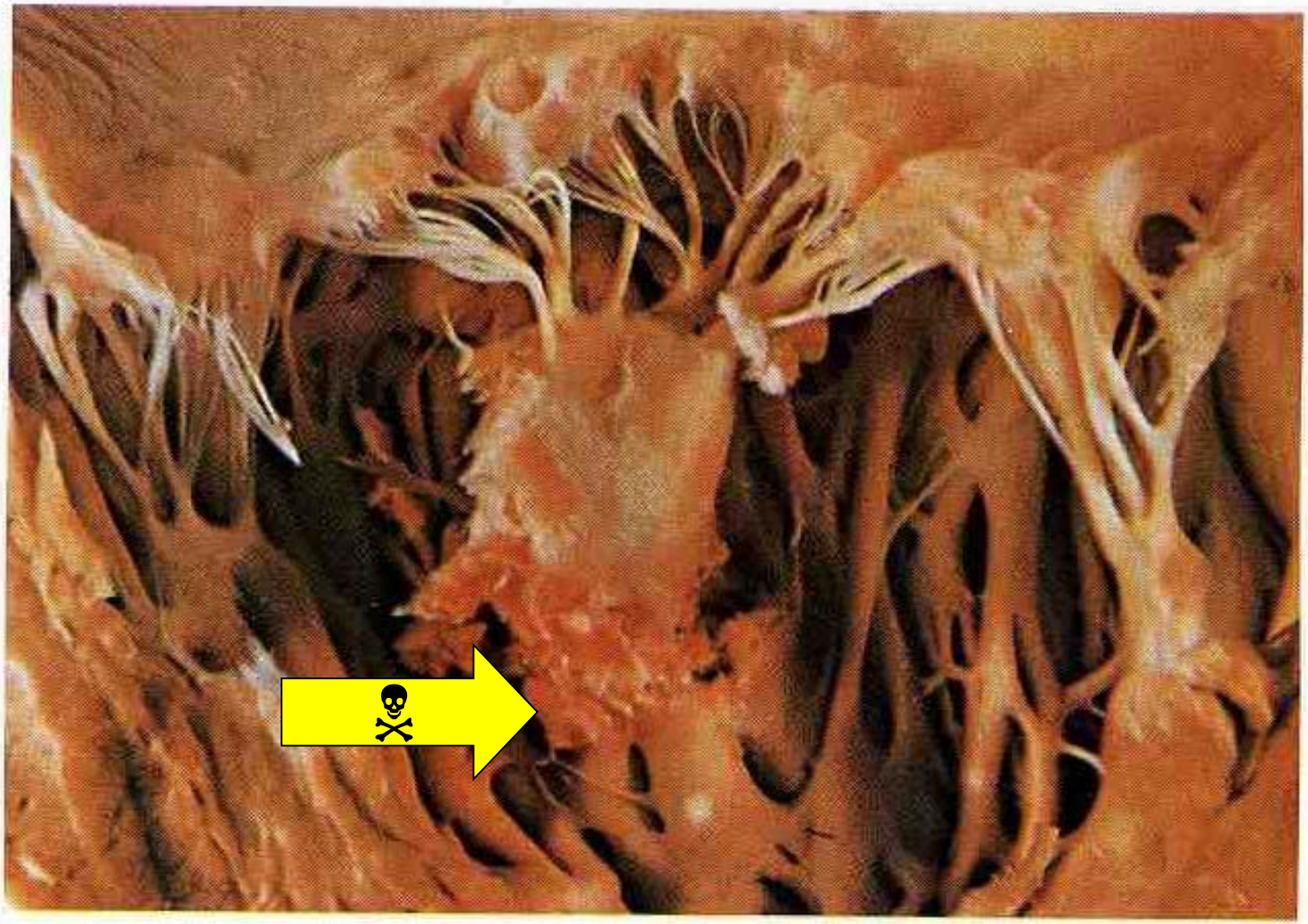
☹ ***Progressive HF:*** discussed as chronic IHD below.

➔**Long-term prognosis** after MI depends on:

(1) the LV function quality after the MI &
(2) the **obstructions** degree of remaining vascular in vessels that perfuse the remaining viable myocardium.

☠ **The overall total mortality within the first year is about 30%,** including those who die before reaching the hospital. Thereafter, there is a 3% to 4% per year mortality.

F6.72: Rupture of infarcted superior papillary muscle of the LV & **mitral valve**, leading to → acute mitral valve incompetence & ☠ fatal acute left heart failure.



6.72 Myomalacia cordis: papillary muscle

Chronic Ischemic Heart Disease

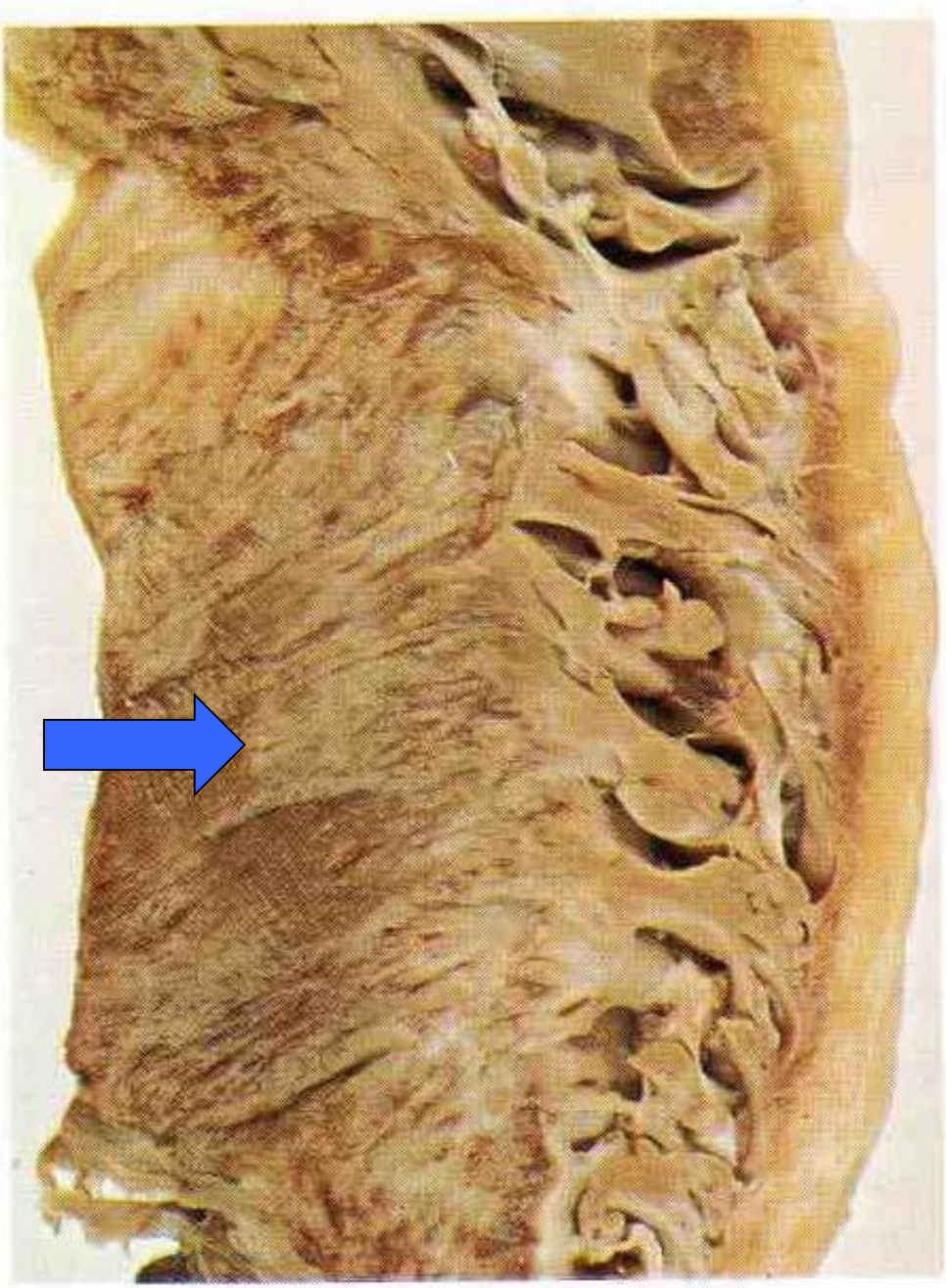
Chronic IHD is essentially progressive HF, as a consequence of ischemic myocardial damage.

1.→ **In most instances ,there is a history of MI** ➔ followed by **postinfarction** cardiac compensatory hypertrophy of the remaining viable myocardium ➔followed usually by **exhaustion and decompensation of it** ➔ chronic IHD

2. → In other cases severe obstructive CAD may be present, **without prior infarction**, but with diffuse myocardial dysfunction.

➔ Grossly, chronic IHD hearts are, usually, **enlarged & heavy** from **LV dilation & hypertrophy.**

Invariably (**in all cases**) there is **moderate to severe A** of the coronary arteries, sometimes with total occlusion. Discrete, gray-white **scars** of healed infarcts are usually present. The endocardium generally shows patchy, fibrous thickening, & mural thrombi may be present.



6.12 Fibrosis of myocardium

F6.12: Chronic ischemic heart disease with myocardial fibrosis.

Section of the LV wall, showing marked & **diffuse greyish-white fibrosis, resulted from chronic ischemia,** secondary to atherosclerotic narrowing of the coronaries.

◙ H, of chronic IHD reveals: **fibrosis** from previous infarcts + compensatory myocardial **hypertrophy** + diffuse subendocardial myocyte vacuolization.

Sudden Cardiac Death (SCD)

Affecting 300,000 to 400,000 individuals annually in the US. SCD is most commonly defined as:

► **Unexpected death from cardiac causes, either without symptoms, or within 1 to 24 hours of symptom onset.**

☹ **Coronary artery atheroma is the most common** underlying **cause**, & in many **adults** SCD is the first clinical manifestation of IHD; whoever,

♥ **with younger victims,** other non-atherosclerotic causes are more common, including:

●Congenital abnormalities of coronary arteries ● Aortic valve stenosis ● Mitral valve prolapse ● Cardiomyopathy (Dilated or hypertrophic) ● Myocarditis or sarcoidosis ● Pulmonary hypertension ● Hereditary or acquired abnormalities of the cardiac conduction system, of which the most important cause is the autosomal dominant long-QT syndrome, due to mutations in various cardiac ion channels.

Thus, some young individuals who die suddenly (including athletes) have unsuspected hypertrophic cardiomyopathy, myocarditis, or congenital abnormalities of coronary arteries.

☺ ***The ultimate mechanism of SCD is most often, a lethal arrhythmia,*** such as **VF**.

☺ The prognosis of patients vulnerable to SCD, especially those with chronic IHD, is markedly improved by **automatic cardioverter defibrillators,** which sense & electrically terminate episodes of ventricular fibrillation (VF).

Morphology

☹ I**n 80% to 90% of SCD** victims, severe CA with critical (≥75%) stenosis involving one or more of the 3 major vessels is **present**; acute plaque disruption is found in only 10% to 20% of these; and healed MI is present in about 40%, but in those who were successfully resuscitated from sudden cardiac arrest, new MI is found in only 25% or less. Subendocardial myocyte vacuolization indicative of severe chronic ischemia is common.

😐 Only a **minority** (10% to 20%) of cases of SCD are of **non-atherosclerotic origin.**

HYPERTENSIVE HEART DISEASE (HHD)

Chronic hypertension is a common disorder, affecting many organs, including heart.

The Pathophysiology of Cardiac Hypertrophy

myocardial hypertrophy, caused by many stressors, hypertension is one of them.

Cardiac myocytes cannot divide, & ***hyperplasia*** **cannot occur in response to exogenous stresses, & therefore,**

↑ work-resulting from **pressure** or **volume** overload, or from **hyperthyroidism** ➔ induces an ↑ myocyte mass & heart size ***(hypertrophy).*** The extent of hypertrophy varies with the underlying cause.

☺ Normal heart weight is 200g.

☹ Thus, heart weights usually range from 350 to 600 g in **pulmonary hypertension & IHD**,

☹ ☹ From 400 to 800 g in **systemic hypertension, aortic stenosis, mitral regurgitation, or dilated cardiomyopathy,**

☹ ☹ ☹ From 600 to 1000 g **(Cor-bovinum*)*** in **aortic regurgitation /or hypertrophic cardiomyopathy**.

The pattern of hypertrophy reflects the nature of the initiating stimulus (**F11-13**).

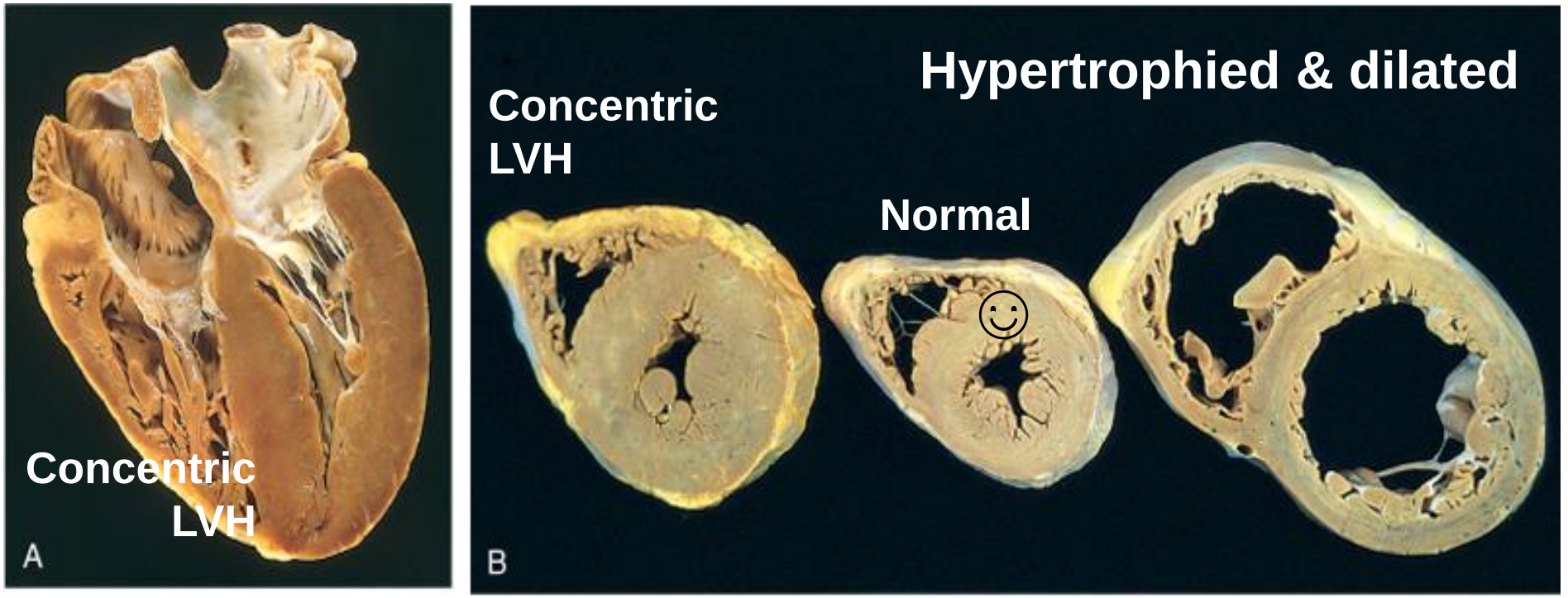
▲ ***Pressure-overloaded ventricles*** (e.g., in hypertension or aortic valve stenosis) develop ***concentric hypertrophy only,*** with an ↑ wall thickness; which can even reduce the cavity diameter in the LV and imparts a stiffness that impairs diastolic filling. in contrast… ▲ ***Volume overload*** (e.g., mitral or aortic regurgitation) is characterized by **hypertrophy & ventricular dilation.**
In volume overload, muscle mass ↑ roughly in proportion to chamber diameter; thus, in these severely dilated hearts there can actually be a substantial hypertrophy without ↑ wall thickness.

😐 Thus wall thickness is by itself not an adequate measure of hypertrophy due to volume overload.

F11-13:☺ **Normal** heart TS (center).

☹ **Pressure concentric LV hypertrophy** hearts in hypertension: with ↑ mass & a thick LV wall, with no dilation.

☹ ☹ **Hypertrophied & dilated** heart which has ↑ mass but a normal wall thickness (e.g., in Mitral incompetence)



While initially compensatory, prolonged or excessive hypertrophy can eventually result in myocyte contractile failure, ☹ **the** bases for this failure remain **obscure.**

▼What is known is that ⇨ cardiac hypertrophy is accompanied by numerous changes in gene expression, typically with patterns of protein synthesis recapitulating (Similar to the) fetal cardiac development, which may be **less functional** than the adult isoforms.

▼The ***hypertrophy & enlarged*** cardiac muscle mass has ↑ **metabolic requirements** with ↑ oxygen consumption;

▼ ***But*** the myocyte hypertrophy is usually **not accompanied by a concomitant ↑ in the vascular supply.**

☹ Thus, there is a relative ↓ in capillary density.
The resultant chronic ischemia **causes deposition of fibrous tissue, which limits diastolic relaxation.**

This sequence of events leads **eventually to cardiac failure**.

Systemic HHD

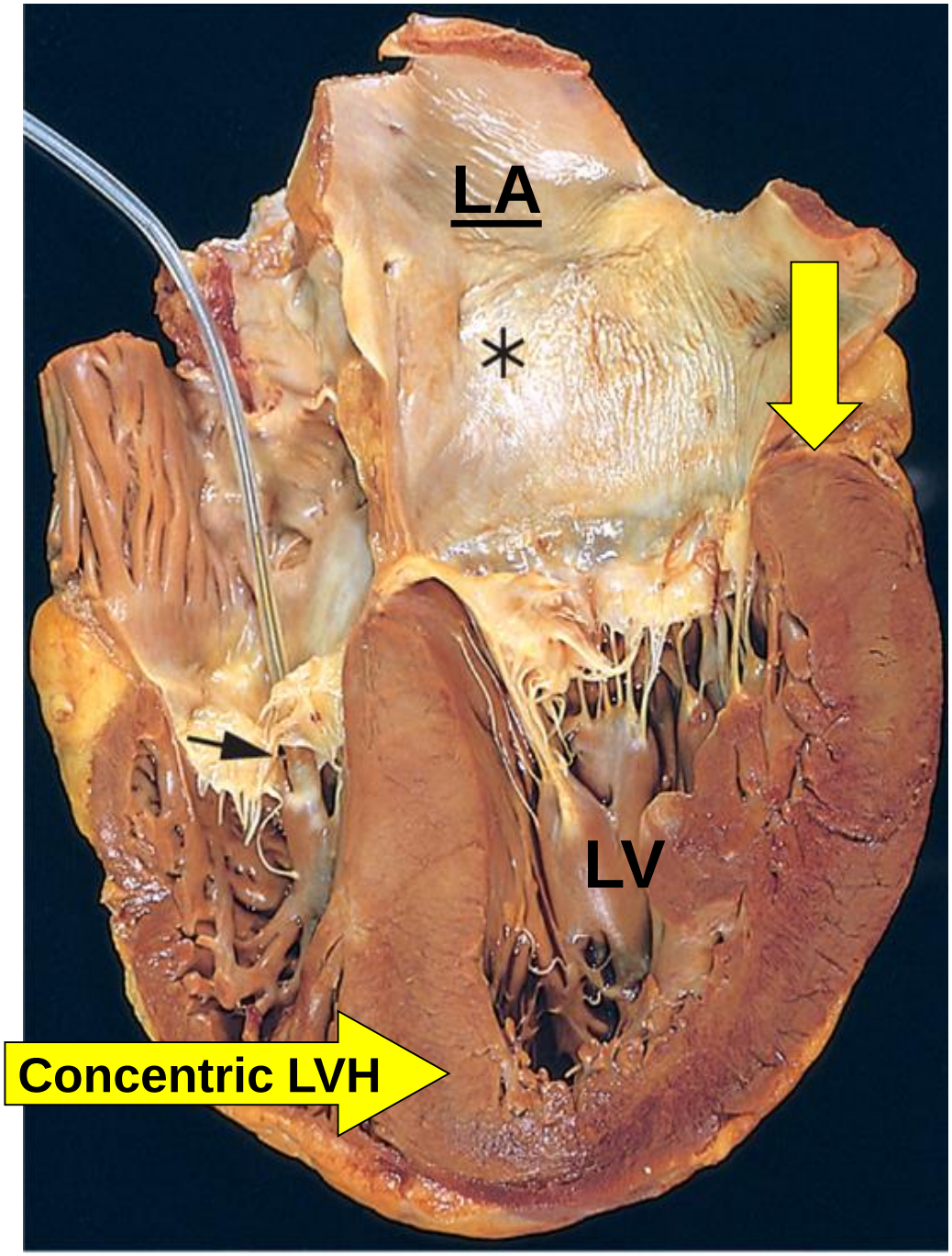
Systemic HHD is diagnosed when there is:
(1) a **history** of hypertension , and

(2) **LV hypertrophy** (usually concentric) in the absence of other causal cardiovascular pathology, like valvular stenosis
The Framingham Heart Study established unequivocally that even **mild hypertension** (levels only slightly above 140/90 mm Hg (roughly **25% of the US population suffers** from at least this degree of hypertension), if sufficiently prolonged, induces LV hypertrophy.

Morphology

There is **LV hypertrophy,** typically **without ventricular dilation (F11-14**). The LV wall thickness may exceed **2.0 cm** & the heart weight may exceed **500 gm**. In time, the ↑ thickness of the LV wall imparts a stiffness that impairs diastolic filling. ➔This often induces left atrial enlargement.

- H, there is ↑ myocyte diameter + ↑ interstitial fibrosis.

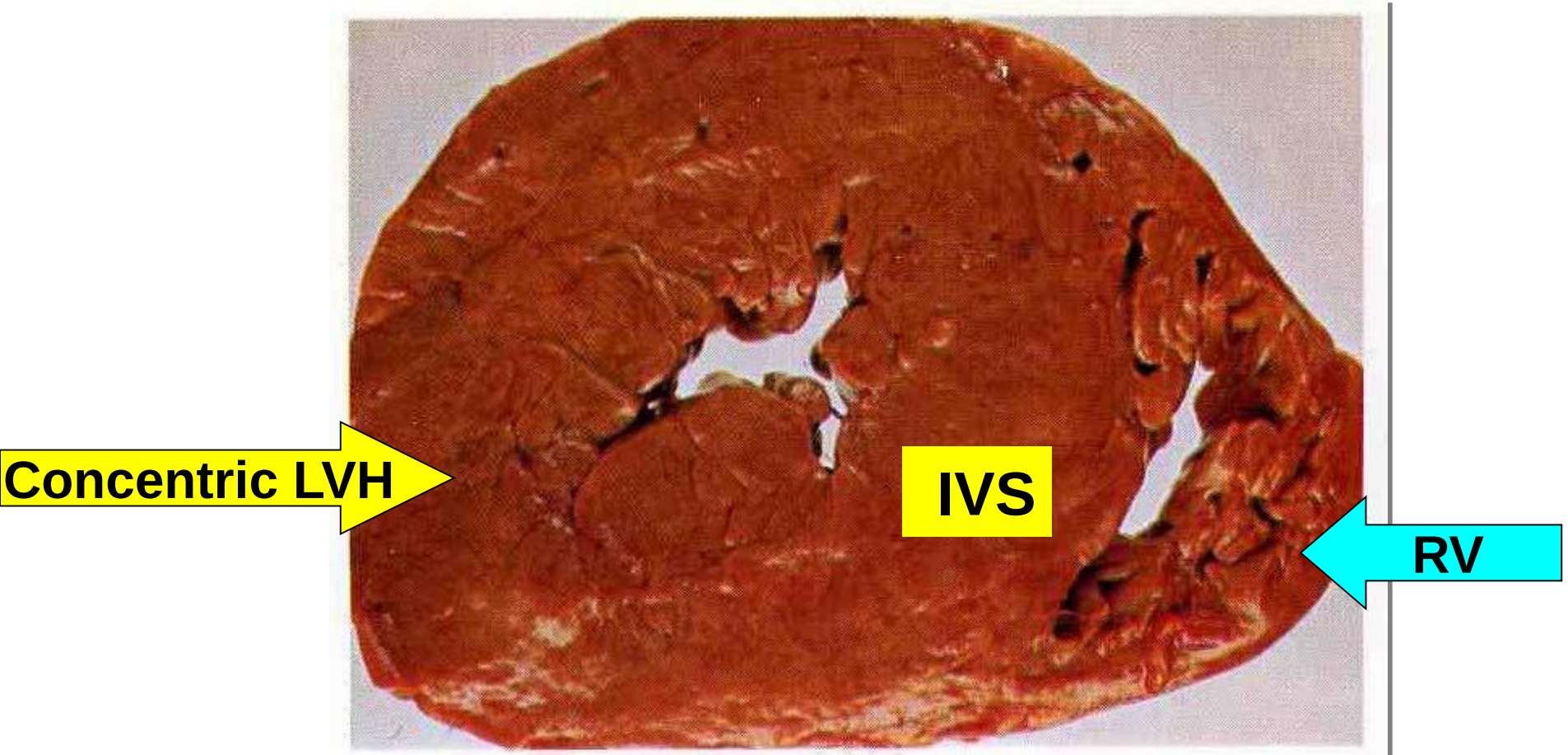


F11-14: HHD.
Marked concentric thickening of LV wall causing reduction in lumen size.

LA dilation (*asterisk) due to relative stiffening of the LV causing impaired diastolic relaxation & subsequent atrial volume overload.

A pacemaker is incidentally present in the RV (Black arrow).

F6.25: HHD: Chronic systemic hypertension causing → **massive concentric myocardial muscle hypertrophy** of the left ventricle, including the IVS (center).
The right ventricle (at right) shows secondary hypertrophy. The lumen of both ventricles appears smaller than normal.



6.25 Hypertensive cardiomegaly

Pulmonary HHD (Cor Pulmonale)

Cor pulmonale is **RV hypertrophy & dilation** due **to *pulmonary hypertension, caused by*** **primary *disorders of the lung parenchyma or pulmonary vasculature*** (Table 11-3).

★**Excluded by this definition** are RV dilation & hypertrophy caused by (I) **congenital** heart disease or by (II) **LV failure**.

Cor pulmonale may be **acute** or **chronic**, depending on the speed by which the pulmonary hypertension develops.

★ ***Acute cor pulmonale*** most commonly follows massive pulmonary embolism (PTE) with obstruction of >50% of the pulmonary vascular bed.

★***Chronic cor pulmonale*** occurs secondary to **prolonged pressure overload** caused by obstruction of the pulmonary vasculature from compression/obliteration of septal (alveolar wall) capillaries (resulting from **emphysema, interstitial pulmonary fibrosis, or primary pulmonary hypertension).**

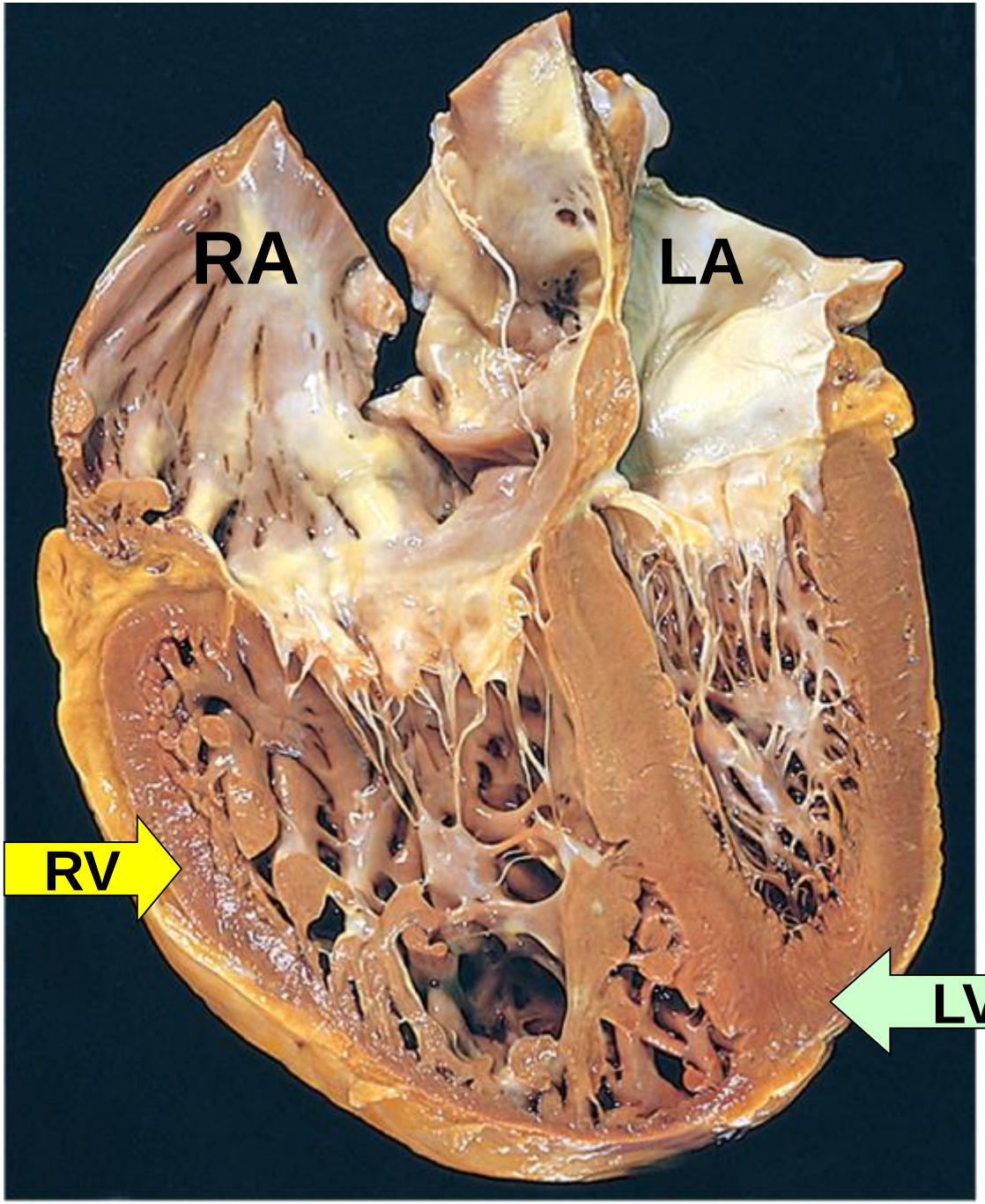
Morphology

► In **acute cor pulmonale, the RV is usually → dilated** but does not show hypertrophy; if an embolism causes **sudden death,** the heart may even be of normal size.

► **Chronic cor pulmonale** is characterized by RV (& often RA) → **hypertrophy, & in extreme cases the thickness of the RV** wall may be comparable to, or, even **exceed that of the LV (F11-15**).

+ When ventricular **failure** develops, both the RV & RA may also be **dilated.** Such dilation may mask RV hypertrophy.

► **In chronic pulmonary hypertension,** due to chronic cor pulmonale, the **pulmonary arteries** often contain atheromatous **plaques,** which are not seen usually (Why?).



F11-15: **Chronic cor-pulmonale, with hypertrophy & dilation of RV.**

The shape of the LV has been distorted by the RV enlargement.

Rheumatic fever (RF)

RF is an acute, immunologically mediated, multisystem inflammatory disease that occurs few weeks after an episode of group A, β-hemolytic streptococcal pharyngitis.

Acute rheumatic heart disease (RHD) is the cardiac manifestation of RF & is associated with inflammation of the endo-, myo-, peri-cardium, or all 3 layers (Pancarditis).

Chronic valvular deformities are the most important consequences of RHD; causing diffuse & dense scarring of valves, resulting in permanent dysfunction (the most common of which is **mitral stenosis).**

☺ The incidence of RF & thus RHD has declined in many parts of the west, this is due to a combination of:

→ improved socioeconomic conditions + rapid diagnosis & treatment of streptococcal pharyngitis + an unexplained decline in the virulence of group A streptococci.

☹ Nevertheless, in developing countries, RF & RHD remain important public health problems.

Morphology

▼ **Acute RF,** characterized by multiple, discrete inflammatory lesions found in various tissues throughout the body. Within the heart these lesions are called **Aschoff bodies,** & they are **pathognomonic for RF (F11-18A**).

Aschoff bodies consist of:

→ a central zone of degenerating hypereosinophilic ECM, infiltrated

→ by lymphocytes (primarily T cells), few plasma cells, &

→ plump activated macrophages called **Anitschkow cells**, with abundant cytoplasm & central nuclei, these **activated macrophages** can also fuse to form giant cells.

► Aschoff bodies can be found in any of the three layers, endocardium (including valves), myocardium, or pericardium or, in all three, so-called **pancarditis.**

The **pericardium** shows a fibrinous or serofibrinous exudate, which generally resolves without sequelae.

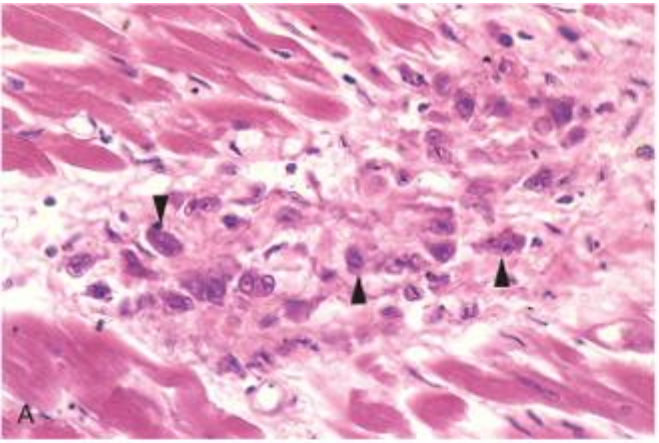
In **myocardial** involvement (myocarditis), there are scattered Aschoff bodies within the interstitial connective tissue.

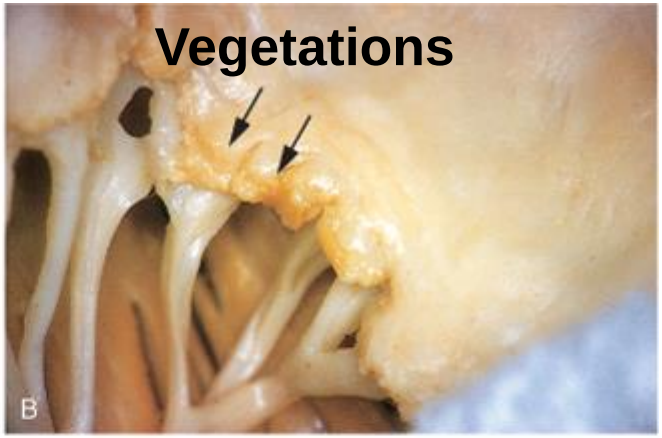
Acute valve involvement results in **rheumatic vegetations (F11-18B), consisting of fibrinoid necrosis along the lines of closure with erosion, followed by fibrin deposition, forming 1- to 2-mm in ∅ small thrombi, that have little effect on cardiac function in the form of valve incompetence.

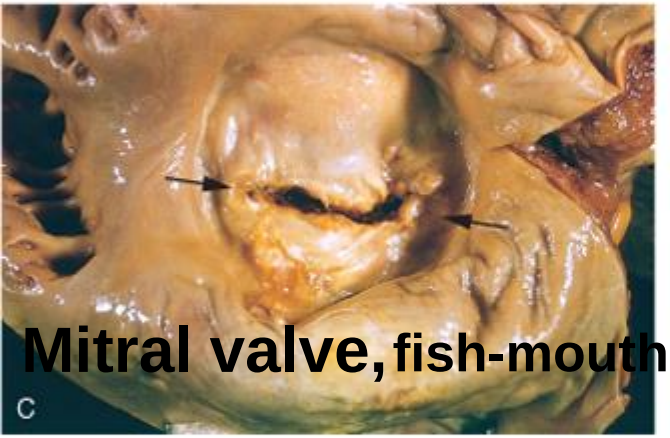
▼ **Chronic RHD** sequelae result from organization, fibrosis & progressive scarring of the acute inflammatory lesions.

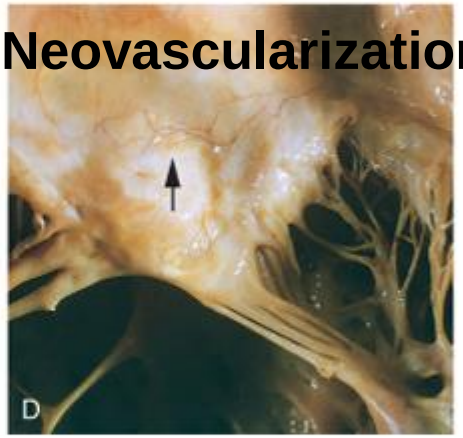
☹ The cardinal anatomic changes of the mitral (or tricuspid) valve include **leaflet thickening & commissural fusion, with** shortening, thickening & fusion of the chordae tendineae (**F11-18C-D**).

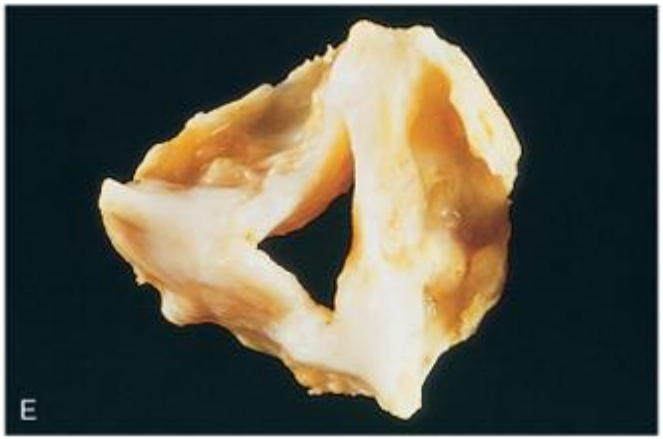
Fibrous bridging across the valvular commissures & calcification create **"fish mouth" or "buttonhole" stenoses (F11-18C**).











F11-16:
A. ◙ **Aschoff body**.
B. Acute RHD vegetations (arrows), superimposed on chronic RHD, with thickened & fused chordae tendineae.
C. Mitral valve leaflets fibrous thickening & distortion, with commissural fusion (arrows), causing **fish-mouth**, or **buttonhole stenosis**
D. mitral leaflet **Neovascularization**.
E. **Surgically** excised rheumatic aortic stenosis.

◙ H, there is → abnormal **neovascularization** (grossly evident in **F11-18D**); + with diffuse fibrosis that obliterates the normal leaflet architecture. Aschoff bodies are replaced by fibrous scar.

► The **functional** consequence of RHD is:

(1) valvular stenosis, ✱ {**RHD is the most frequent** cause, accounting for 99% of all cases of **mitral stenosis}** & less frequently

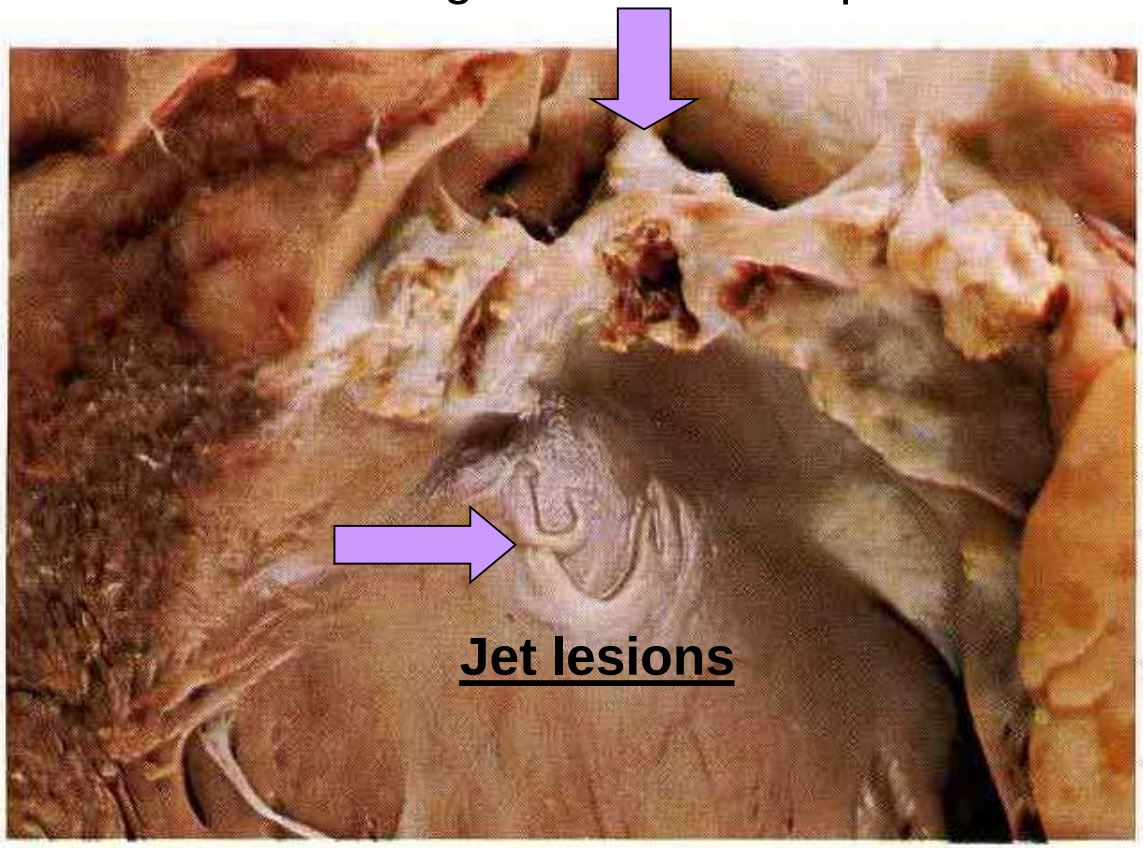
(2) valvular regurgitation.

The **mitral valve alone** is involved in **70%** of cases of RHD,

Combined *mitral & aortic* disease in another **25%;** tricuspid valve is less frequently & less severely involved, & the pulmonary valve almost always escapes injury.

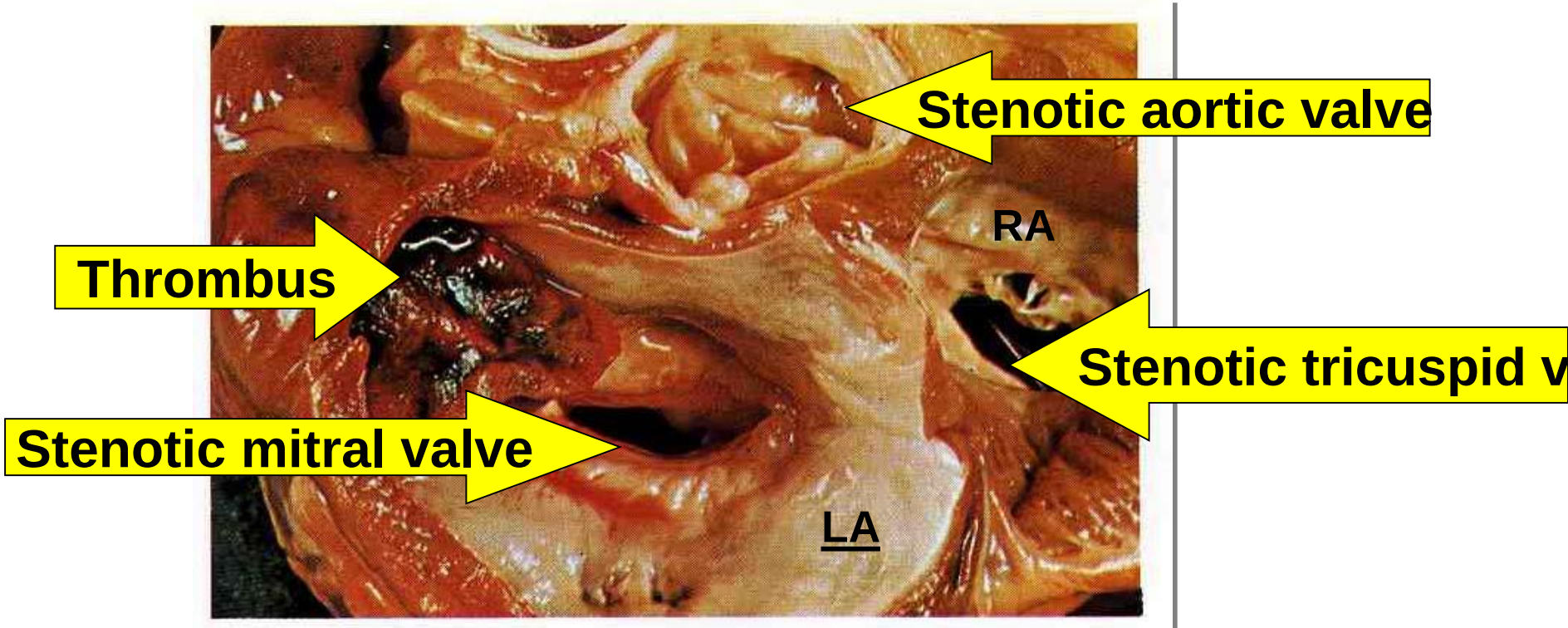
F6.42: Chronic RHD: The aortic valve cusps are greatly thickened, calcified & ulcerated, with extreme commissural fusion, producing **stenotic & incompetent aortic valve (at the same time).**

☹ **Jet lesions or endocardial pockets of Zhan**, i.e., crescentic bands of fibrous tissue, on the endocardium of the upper IVS, just beneath the incompetent aortic valve, with their openings directed upwards, formed by regurgitating jets of blood resulting from the incompetent valve.



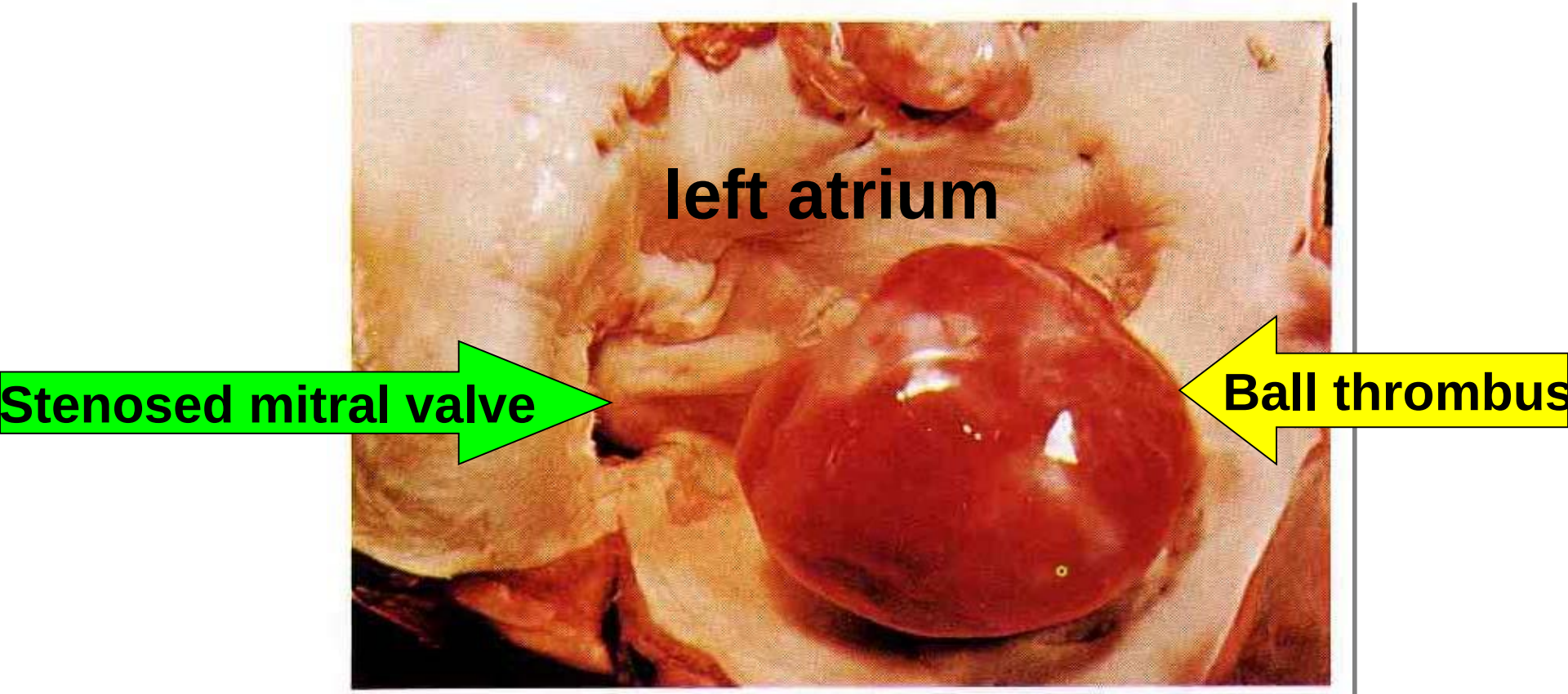
6.42 Chronic rheumatic endocarditis: left ventricle

F 6.44: Chronic RHD: Viewed from above, there are:
(1) thick walled, **dilated left atrium** with polypoid **thrombus** protruding from the left atrial appendage (the patient had atrial fibrillation). The **mitral valve** cusps show severe nodular thickening, with a **narrow** central opening.
(2) right atrium with **stenotic tricuspid** valve.
(3) the most severely **stenotic**, is the **aortic** valve.

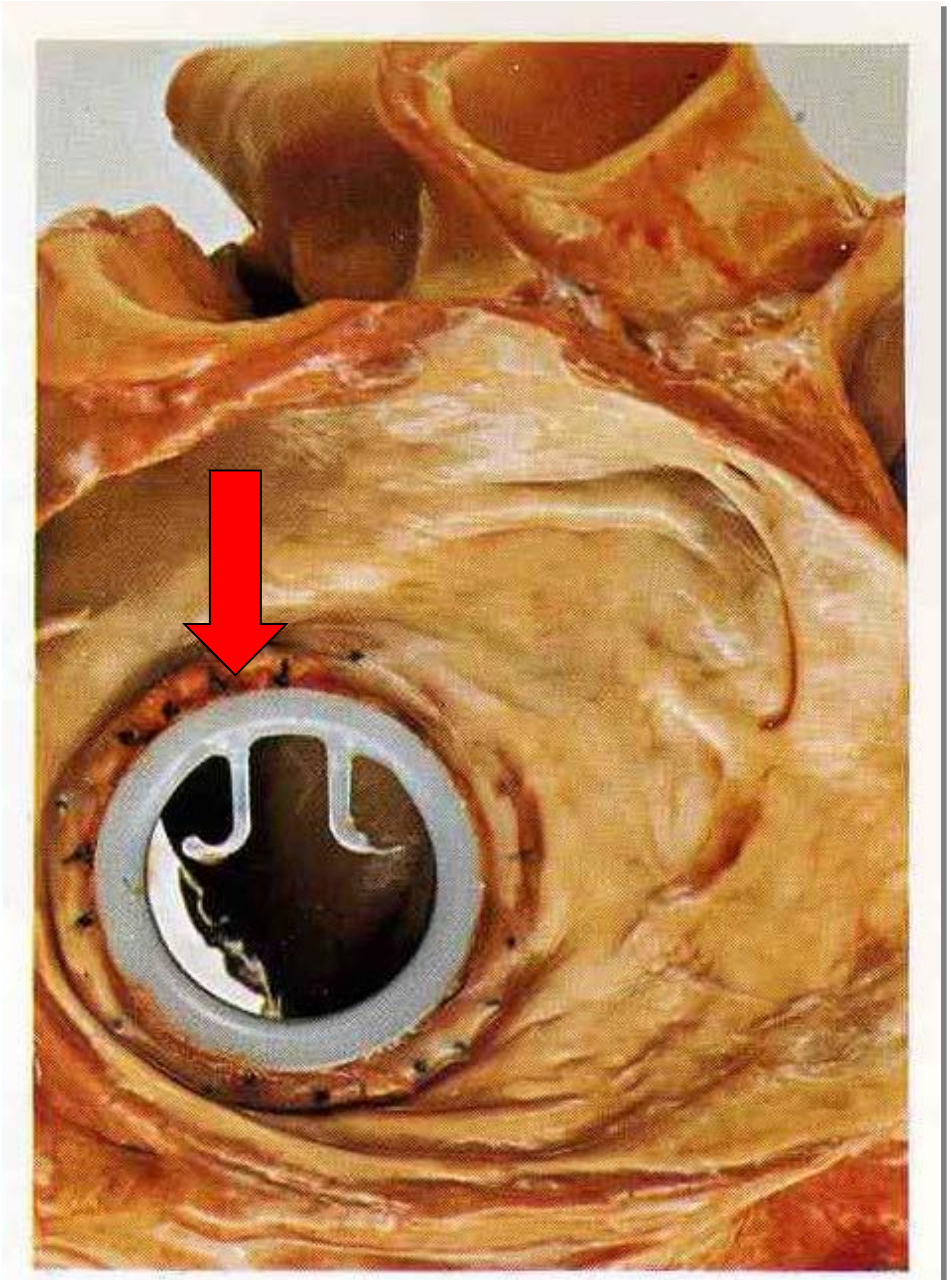


6.44 Chronic rheumatic endocarditis: left and right atria

F6.45: Ball thrombus: left atrium. The dilated, thick-walled left atrium is viewed from above, showing **stenosed mitral valve**. A globular red **"ball" thrombus lies free** within the atrial lumen, following detachment (as a mural thrombus) from the wall of the atrium, obstructing the mitral valve orifice intermittently, & **may cause sudden death**.



6.45 Ball thrombus: left atrium



6.51 Abrams-Lucas prosthesis: mitral valve

F6.51:☺ An **Abrams-Lucas prosthesis** has been used to replace a stenosed & incompetent mitral valve.

☹The hooks of the suspensory mechanism of the valve **disengaged** from the valve ring 6.5 years after insertion through mechanical wear-and-tear, resulting in ☠ **sudden death.**

In mitral stenosis, the **left atrium** progressively dilates & may harbor **mural thrombi.** Long-standing backpressure & congestive changes in the lungs may induce pulmonary vascular changes resulting in pulmonary hypertension & **RVH**

😐 **With pure mitral stenosis, the left ventricle is normal.**

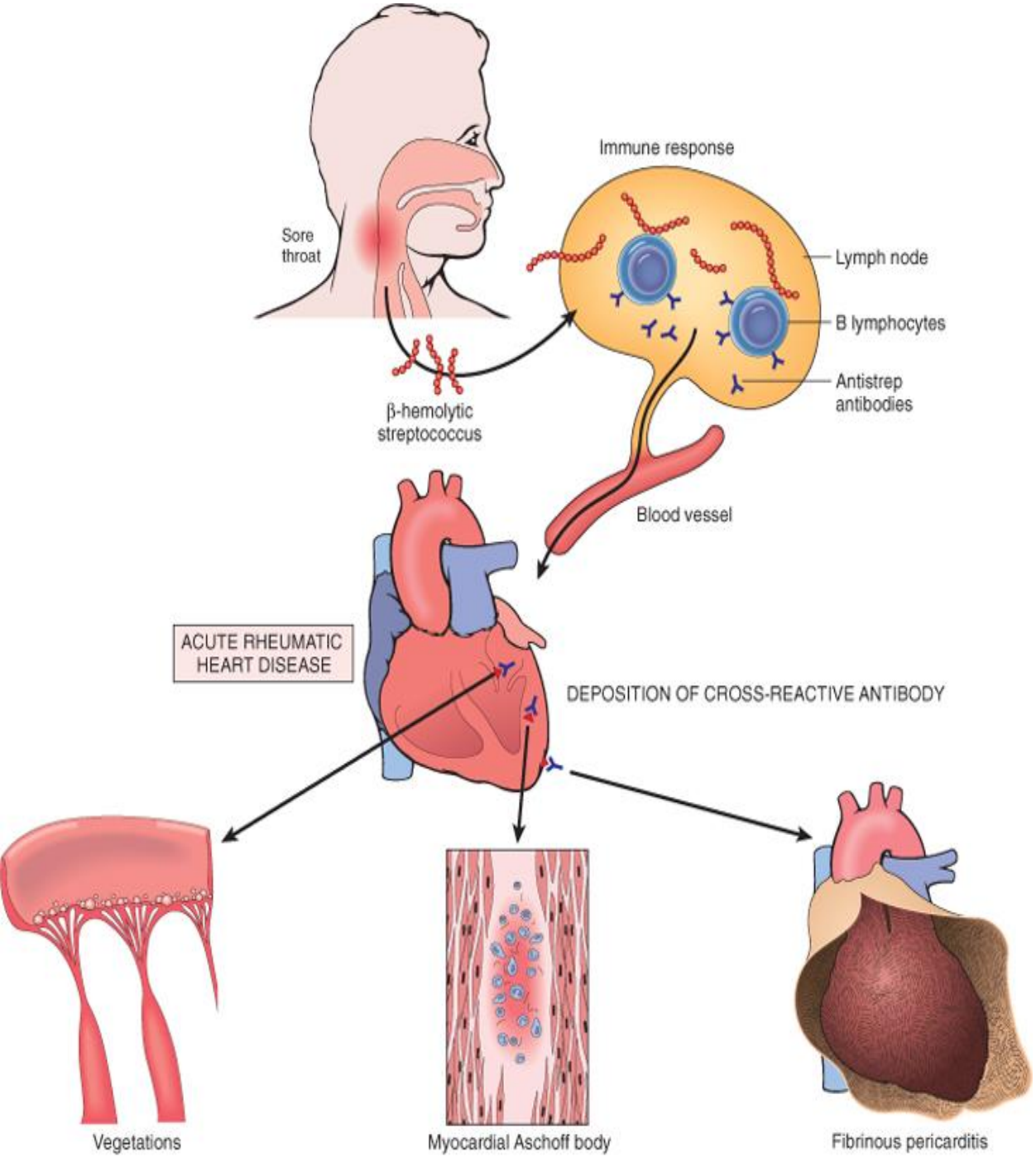
Pathogenesis (F11-19)

▼ *Although* the **pathogenesis remain uncertain up till now,** It appears that the M proteins of certain streptococcal strains infections → induce host antibodies that

►cross-react with glycoprotein Ags in the heart, joints & other tissues, inducing cytotoxic (type II *hypersensitivity reaction)* resulting in acute rheumatic fever.

This **explains** the typical 2 to 3 week delay in symptom onset after the original infection & absence of streptococci in the lesion.

☺ Since only a **small minority** (about **3%)** of patients infected by streptococci ever experience RF, therefore, a **genetic susceptibility is likely** to influence the development of the pathogenic Abs.



F11-19: Pathogenesis & key morphologic changes of:
(A) **Acute RHD**, causing changes in one or more of the: **endocardium, myocardium, or pericardium**.
(B) **Chronic RHD** is almost **always** caused by deformity of the heart valves, specially the **mitral & aortic valves.**

Infective Endocarditis (IE)

☠ Is a **serious** infection, caused by microbial invasion of heart valves or endocardium & results in bulky, friable **infective *vegetations*** composed of organisms, thrombus, & necrotic debris.

IE is classified into ***acute*** & ***subacute*** *forms*.

☹ ☹ ***Acute endocarditis*** is a **destructive** infection by a **highly virulent organism** attacking a previously **normal valve**, & causing **death** within days to weeks in more than 50% of patients despite antibiotics & surgery.

☹ ***Subacute endocarditis*** is infections by **low virulence** organisms**,** colonizing a previously **deformed heart valves** (congenitally, or by rheumatic heart disease).

In the subacute IE, the disease typically appears gradually & follows a long course of weeks to months with most patients recovering after appropriate antibiotic therapy.
☠ Without treatment, the disease is **fatal ☠.**

Morphology (F11-20)

In both acute & subacute forms of IE, there are:

Infective vegetations, a friable, bulky, & potentially **destructive,** containing microorganisms, fibrin, & inflammatory cells, are present on the heart valves. They can erode into the underlying myocardium producing an abscess **(ring abscess**) **(F11-20 B**).

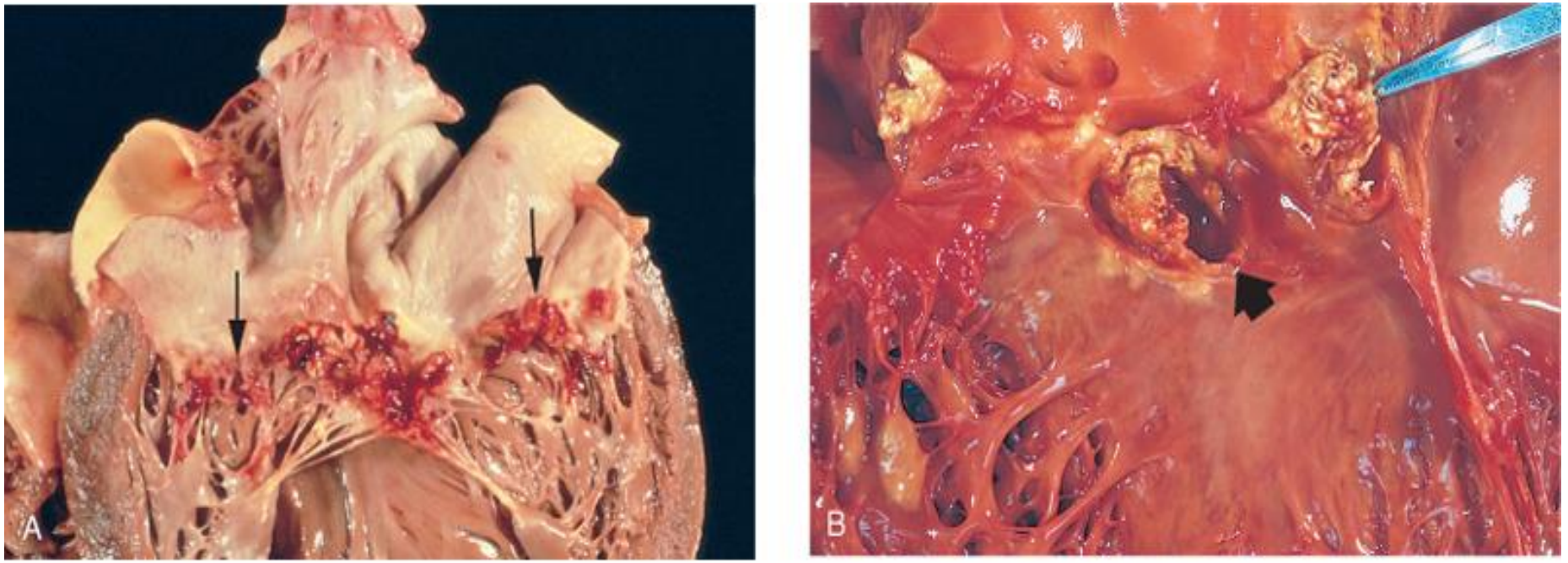
The vegetations may be **single or multiple,** & may involve **one or more valves**;

the **mitral & aortic valves** are the most common sites of infection,
the tricuspid valve is a frequent target in the setting of intravenous drug abuse.

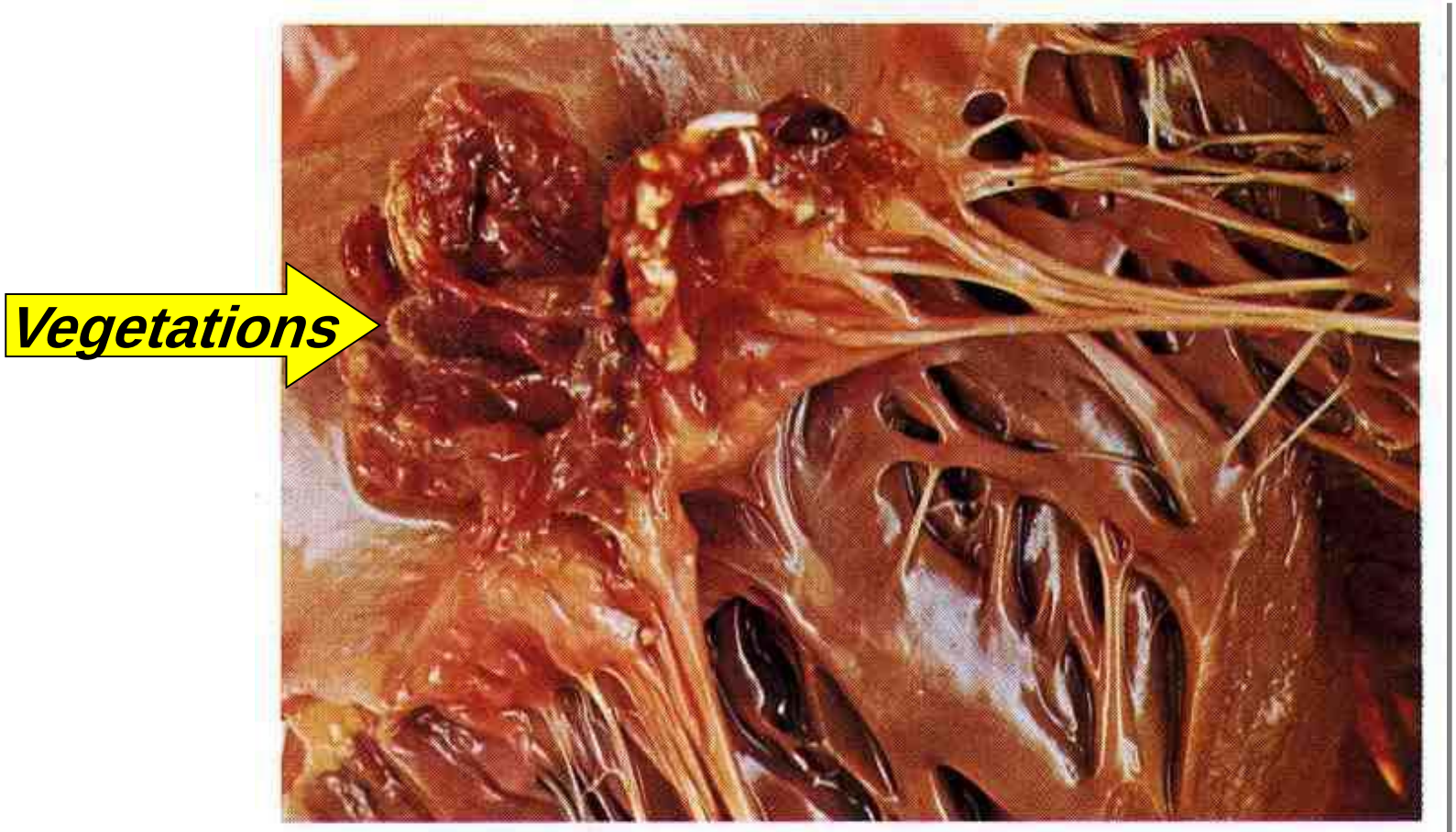
F11-20: Infective (Bacterial) endocarditis, IE.

A. <u>Subacute IE</u> (caused by *St. viridans*), of mitral valve with large , friable vegetations (arrows).

B. **<u>Acute IE</u>** <u>(caused by *Staph. Aureus*)</u> of a congenitally bicuspid aortic valve, with extensive cuspal destruction & ring abscess (arrow).



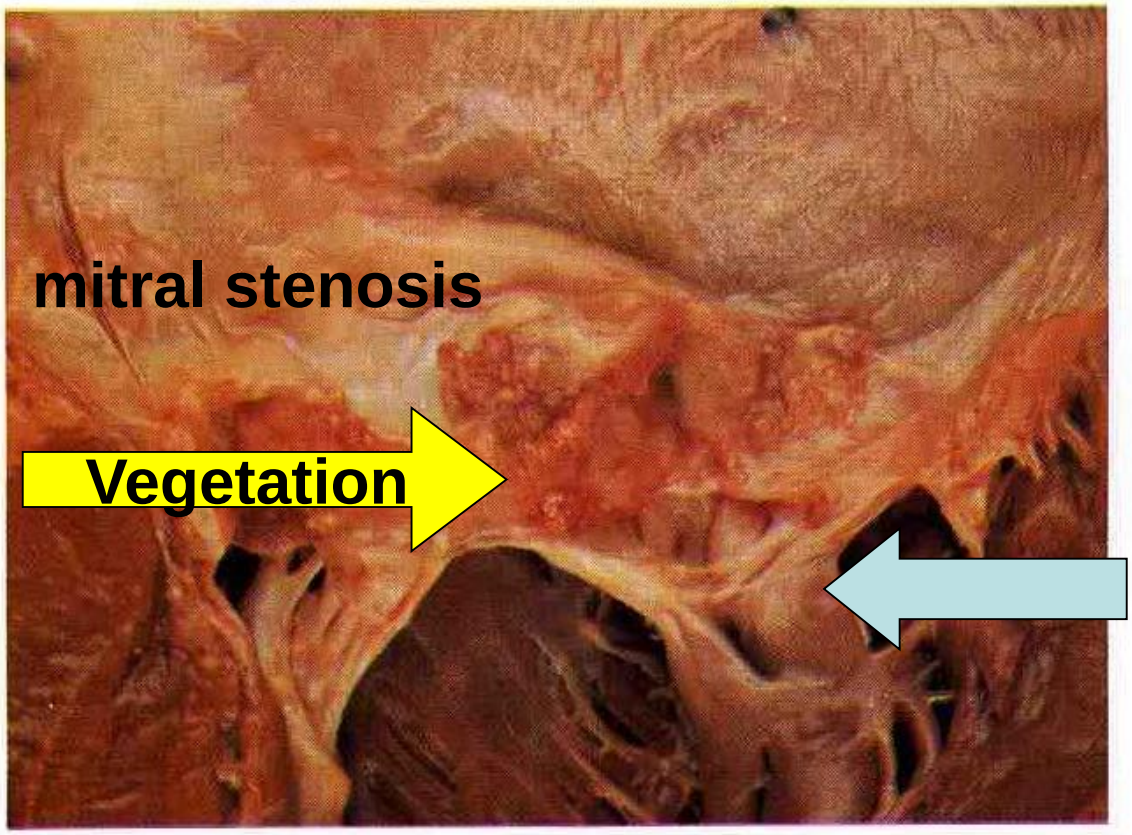
F6.46: Subacute bacterial endocarditis: mitral valve.
Large , globular, friable red-brown mass of vegetations on the superior surface of the mitral valve. **Streptococcus viridans** (the most common causative organism of this disease) was grown on blood culture from the patient, before his death.



6.46 Subacute bacterial endocarditis: mitral valve

F6.47: Chronic RHD with subacute bacterial endocarditis.

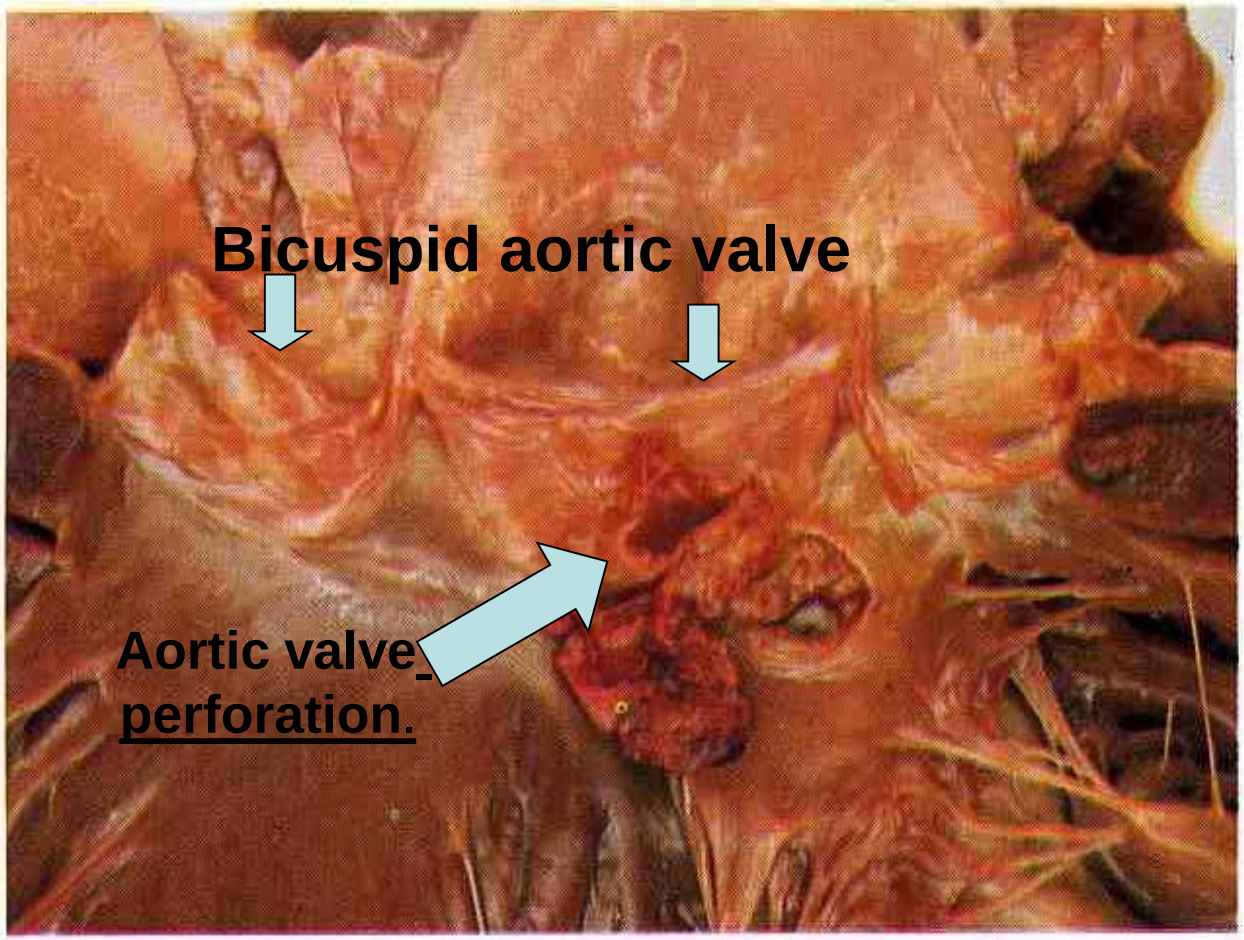
(1) Severe mitral stenosis, with wrinkled, thickened & fused valve cusps, & fusion & contraction of the chordae. The fibrosis extends into the papillary muscles (→). **(2)** Bulky red-brown **vegetation of infective endocarditis** has developed in the damaged valve cusps & covered it's surface.



6.47 Subacute bacterial endocarditis: mitral valve

Fusion &contraction of the chordae

F6.48: Congenital bicuspid aortic valve, with acute bacterial endocarditis, caused by Staphylococcus aureus. A large, friable (liable to release infective embolic fragments) globular vegetation is present with cusp necrosis , suppuration & perforation.



6.48 Acute bacterial endocarditis: aortic valve

Systemic emboli may occur at any time, to any site because of the friable nature of the vegetations. Because the embolic fragments contain large numbers of virulent organisms, **abscesses** often develop at the sites of such infarcts (**septic infarcts**).

Subacute endocarditis is typically associated with less valvular destruction than is acute endocarditis.

◙ H, in the subacute IE vegetations, there is

→ **granulation tissue at their bases**, suggesting chronicity, & as time passes…

→ chronic inflammatory infiltrate, fibrosis, & calcification may develop, resulting in valve incompetence.

Pathogenesis: Three important factors predisposes to IE:

☹ (I) IE can develop on **previously normal valves (50%)**,

But, **cardiac abnormalities** predispose to the other **50%:**

► **Mitral valve prolapse**

► **Bicuspid aortic valves (F11-20B & 6-48)**

►**Calcific valvular stenosis**

► **Indwelling vascular catheters** are important sites for IE

► **Prosthetic heart valves,** with their increasing use, are account for 10% to 20% of all cases of IE **now**,

►**RHD (F 6- 47)** was previously the major abnormality.

☹ (II) **Immunodeficiency increase the risk of IE,** such as in **malignancy, immunosuppressive treatment, neutropenia, DM, & alcohol or intravenous drug abuse.**

☹ (III) **Bacteremia**, with seeding of the blood with microbes predisposing to endocarditis, e.g.,
(1) a dental or surgical procedure that causes a **transient bacteremia**; (2) injection of contaminated material directly into the bloodstream by **IV drug users**; or (3) an **occult source** of **infection** from the gut, oral cavity, or trivial injuries.

Recognition of predisposing cardiac abnormalities & clinical conditions causing bacteremia allows appropriate **antibiotic prophylaxis.**

Endocarditis of previously damaged or otherwise abnormal valves is caused most commonly (50% to 60% of cases) by *viridans Streptococci,* a relatively banal group of **normal oral flora**.

☹ In contrast, the more virulent ***S. aureus*** (common to skin) can attack *deformed & healthy* valves & is responsible for 10% to 20% of overall IE cases; it is also the major offender in **intravenous drug abusers.**

★ Additional bacterial agents include enterococci & the so-called HACEK group (*Haemophilus, Actinobacillus, Cardiobacterium, Eikenella, & Kingella*), all commensals in the oral cavity. More rarely, gram-negative bacilli & fungi are
involved.

😐 **In about 10% of cases, no organism can be isolated from the blood** ("culture-negative" endocarditis).
This is attributed to

1. previous **antibiotic therapy,**
2. difficulties in isolating the offending agent, or
3. because **deeply embedded organisms** within the enlarging vegetation are not released into the blood

Non-infected Vegetations

(I) Nonbacterial Thrombotic Endocarditis (NBTE)

characterized by the deposition of variably sized thrombi of fibrin, platelets, & other blood components on cardiac valves.

In contrast to IE, the **valvular lesions of NBTE are:**

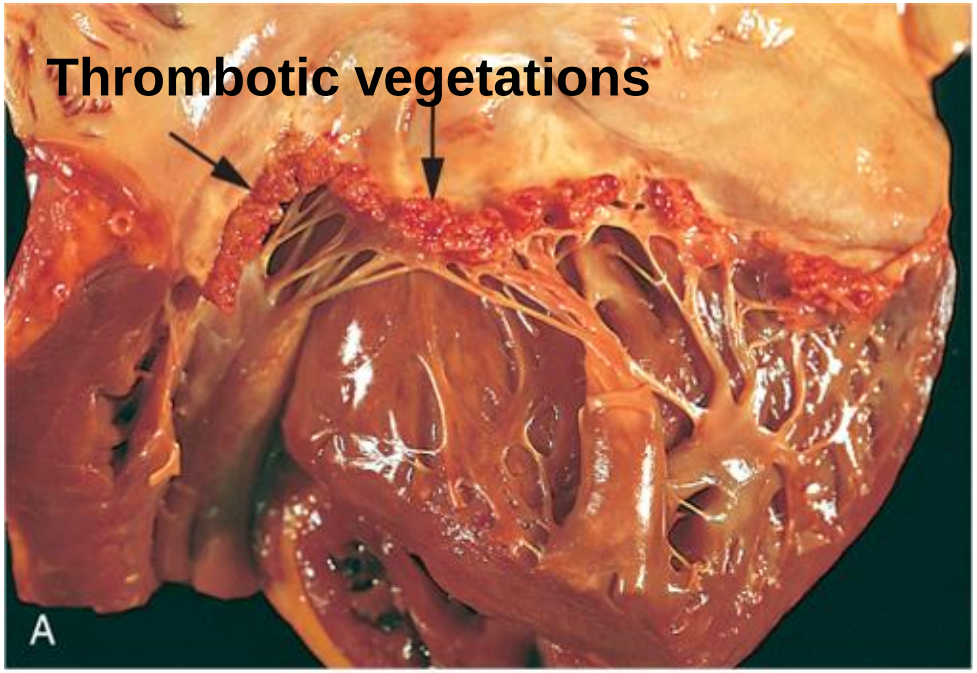
(1) Sterile & do not contain microorganisms.

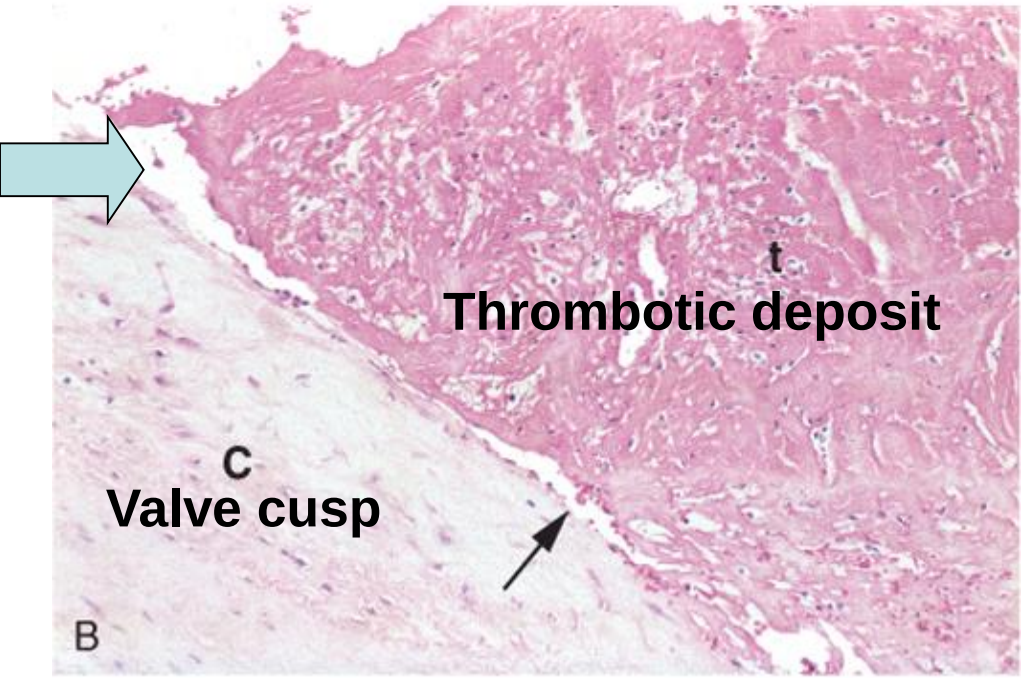
Valvular damage is not a prerequisite for NBTE, which is (2) **usually found on previously ► Normal valves**.

Although NBTE may occur in otherwise healthy individuals, a wide variety of diseases associated with general debility or wasting are associated with an ↑risk of NBTE, hence the alternative term **(*3) Mrantic endocarditis*.**

Morphology

NBTE vegetations are **sterile, (4) nondestructive, & small** (1mm); they occur singly or multiply along the line of closure of the leaflets or cusps **(F11-21).**





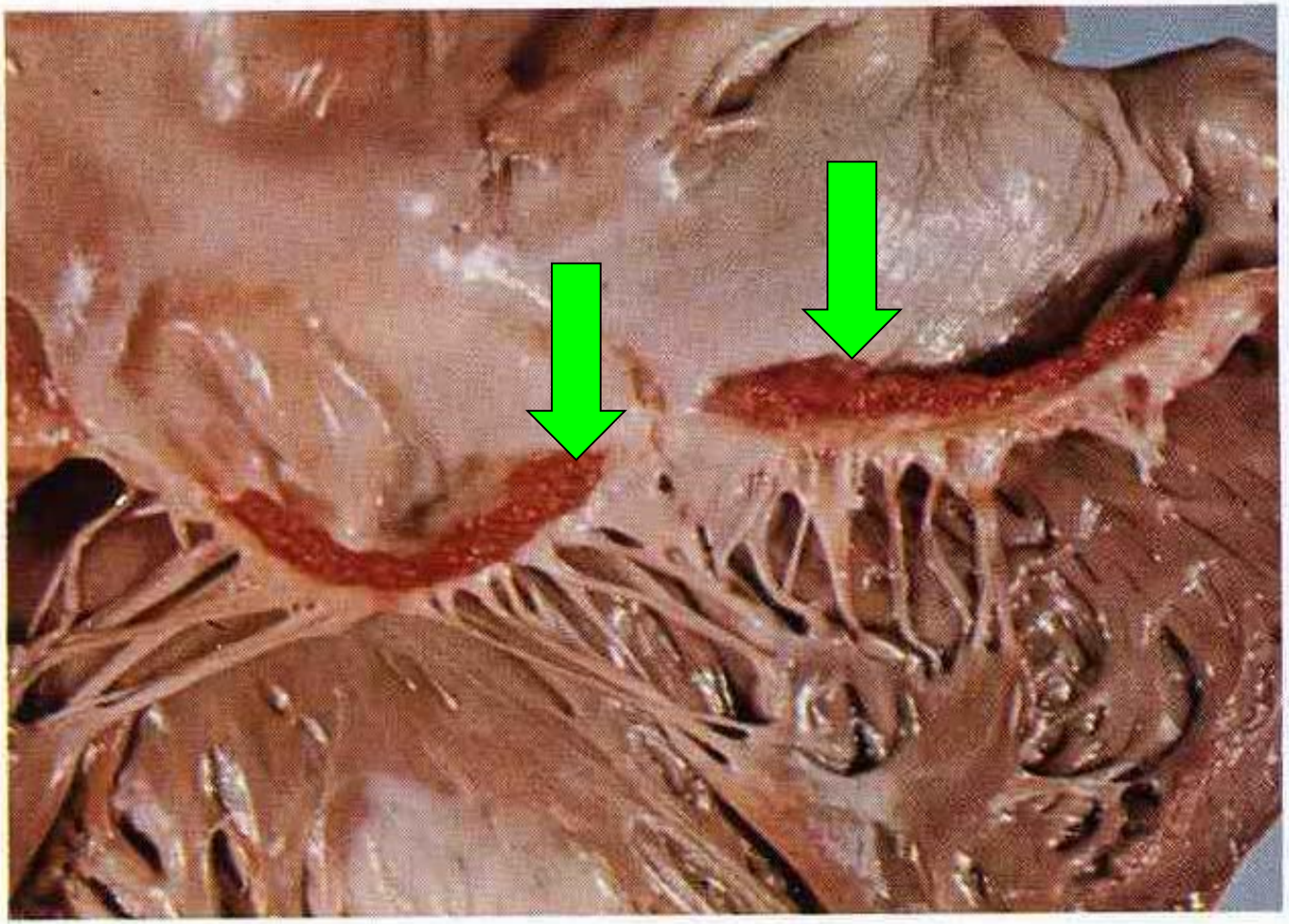
F11-21:

Non bacterial thrombotic endocarditis (NBTE).

A. Complete **row** of thrombotic vegetations along the line of closure of the mitral valve leaflets (arrows).

B. ◙ Bland **Sterile** thrombus, with no inflammation in the valve cusp (c), or in the thrombotic deposit (t) which is **loosely** attached to the cusp (arrow).

F6.36: Non-bacterial (abacterial) thrombotic endocarditis (NBTE); mitral valve. Vegetation on the line of closure of both mitral valve cusps, frequently occur in patients with malignant disease & DIC.



6.36 Terminal (abacterial) endocarditis: mitral valve

◙ H, they are composed of bland thrombus without accompanying inflammation or valve damage.

With time, they can organize into delicate strands of fibrous tissue (so-called Lambl excrescences).

Pathogenesis

NBTE typically occurs in the setting of hypercoagulable states, for example:

1. Sepsis
2. DIC
3. Hyperestrogenic states
4. **Underlying malignancy,** particularly mucinous adenocarcinomas, probably related to the procoagulant effect of circulating mucin &/or tissue factor elaborated by these tumors; indeed, NBTE can be **part of Trousseau syndrome.**
5. Endocardial trauma (e.g., from an **indwelling catheter**) is also a well-recognized predisposing condition.

(II) Libman-Sacks Endocarditis

Are sterile vegetations that can develop on the valves of patients with SLE, presumably because of **immune complex deposition &, thus, have associated inflammation**.

With ↑ use of steroids for treatment of lupus (SLE), Libman-Sacks endocarditis has become **fairly uncommon**.

Morphology

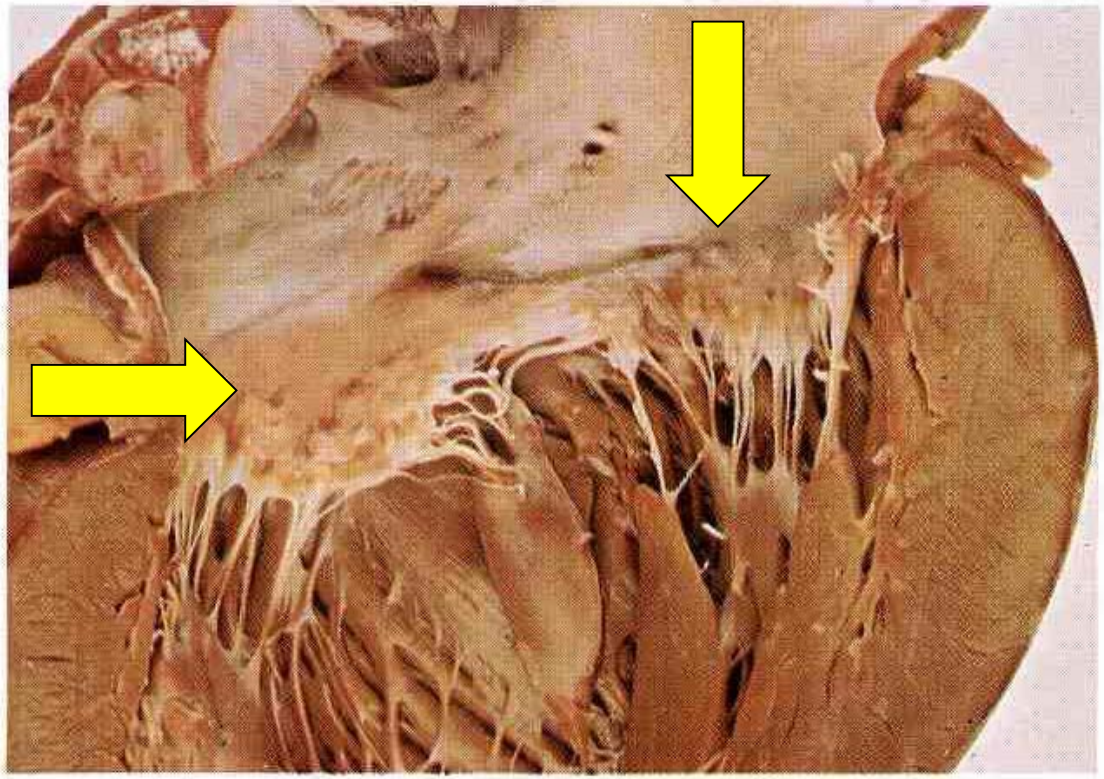
The lesions are small, sterile, granular pink vegetations, 1-4 mm in ∅; they have no special predilection for the lines of valve closure & can be located on the undersurfaces of the atrioventricular valves, on the cords, or even on the atrial or ventricular endocardium

◙ H, the lesions are finely granular, fibrinous eosinophilic vegetations containing nuclear debris.

An intense valvulitis is often present, with fibrinoid necrosis of the valve substance adjacent to the vegetation.

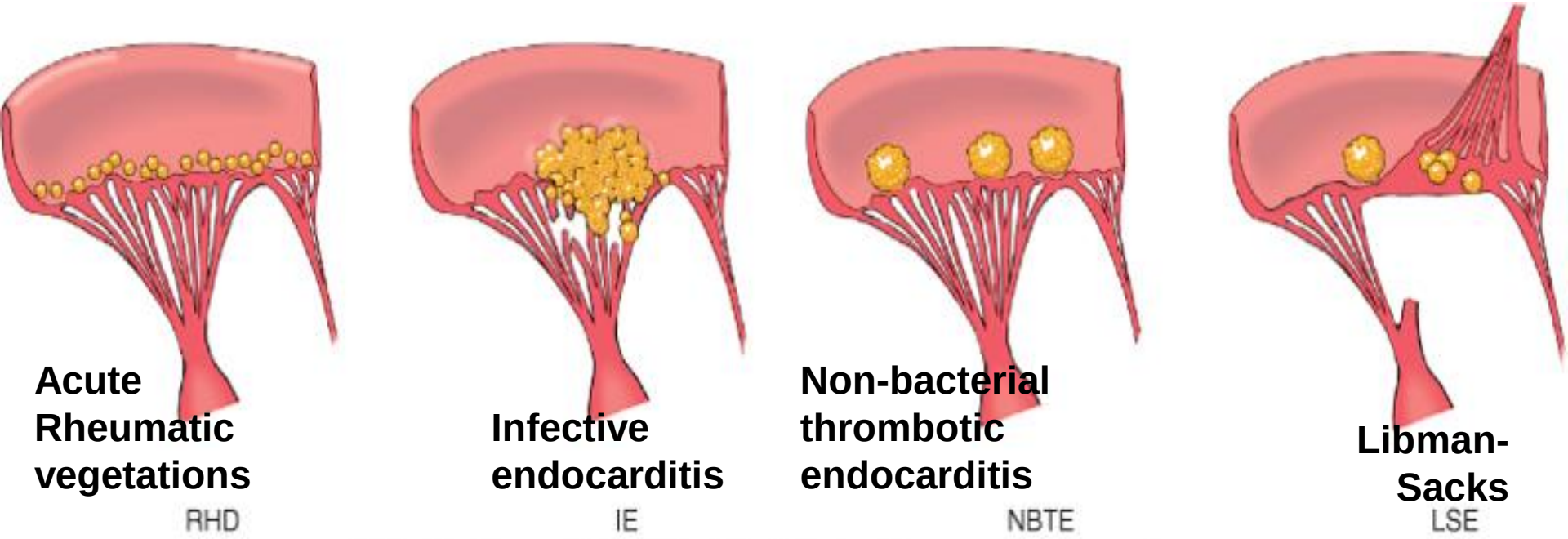
Subsequent fibrosis & **serious deformity can result that resemble chronic RHD.**

F6.39: Libman-Sacks verrucous endocarditis; Manifestation of SLE, been found in about 50% of cases. The superior surface of the mitral valve is covered with small, flat, grey vegetations, **not confined to the line of closure** of the valves. The acute inflammatory process has spread over the surface of the valve to involve its base (right). The chordae are normal.



6.39 Atypical verrucous (Libman-Sacks) endocarditis: mitral valve

F11-22: **Comparison** of **vegetative endocarditis lesions.** **Acute RHD** = row of small, warty verrucae along the lines of closure of the valve leaflets. IE **Infective endocarditis** = large, irregular, destructive vegetations that can extend onto the chordae. **NBTE Non-bacterial thrombotic endocarditis** = small, bland vegetations, usually attached at the lines of closure, one or many may be present as a row. **Libman-Sacks** endocarditis = small vegetations on either or both upper & lower sides of the valve leaflets.



VALVULAR HEART DISEASE

Results in (1) Stenosis or (2) Insufficiency or regurgitation or incompetence, or (3) Both.

Stenosis *is the* ***failure of a valve to open completely,*** *resulting in forward flow obstructing.* Valvular stenosis is always a ►**chronic process,** caused by a **primary cuspal abnormality** (e.g., valve scarring or calcification).

Insufficiency, results from failure of a valve to close completely, *thereby allowing reversed (back) blood flow.* Valvular insufficiency may result from either:

(1) **intrinsic** disease of the **valve cusps,** (valve destruction) or

(2) distortion of the **supporting structures** (e.g., the aortic & mitral **annulus**, tendinous **cords**, **papillary muscles**, & **dilatation** of the ventricular free wall) **without** primary changes in the **cusps.**

Insufficiency can appear ✳ **acutely**, (chordal rupture), or ►**chronically** due to leaflet scarring & retraction (RHD).

Stenosis or regurgitation can occur in **pure forms**, or may **coexist** in the same valve. Valvular disease may affect only a **single valve** (the mitral valve is most commonly affected), or **more than one valve**.

The outcome of valvular disease depends on the valve involved, the degree of impairment, the rate of its development, & the rate & quality of compensatory mechanisms.

☠ For example, **sudden destruction of an aortic valve** cusp by infection may cause massive regurgitation (LV dilatation) & **rapid cardiac failure.**

► In contrast, **rheumatic mitral stenosis** usually develops over years, & its clinical effects (LA dilatation + Pulmonary hypertension + RV hypertrophy & Failure) are remarkably well tolerated.

Abnormal flow through diseased valves typically produces abnormal heart sounds, called ***murmurs.***

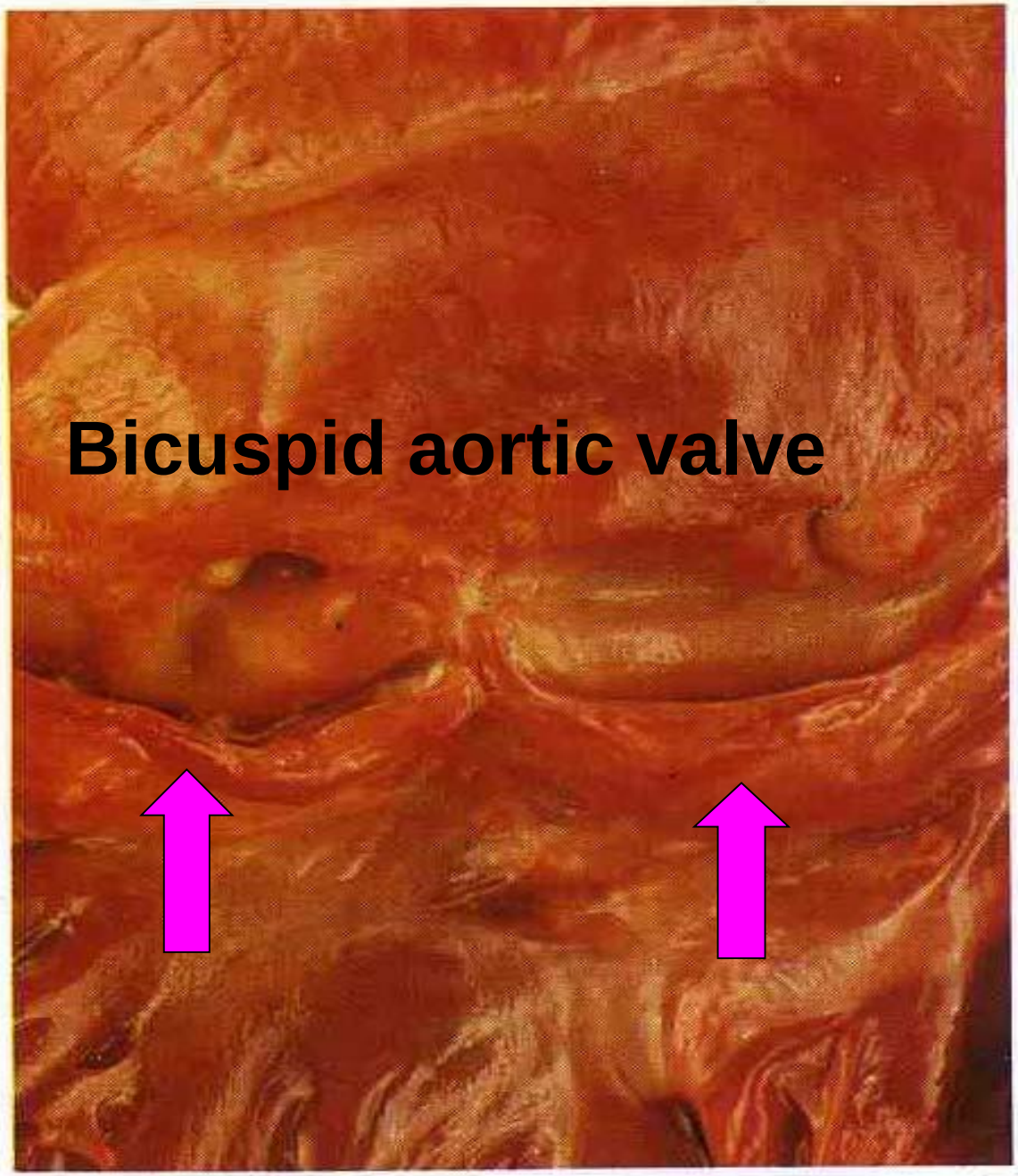
Valve abnormalities can be caused by **congenital** disorders or by **acquired** diseases, summarized in Table 11-4. ***Acquired stenoses of the mitral & aortic valves account for approximately two-thirds of all valve disease.***

Given the repetitive mechanical stresses to which the valves are subjected during life{more than ♫ **40 million cardiac cycles per year** ♫,with a H.R. of 77/minute} associated with substantial deformations during each cycle; the **Degenerative changes** in the cardiac valves are an almost inevitable part of the aging process.

The most common degenerative valvular disease is:

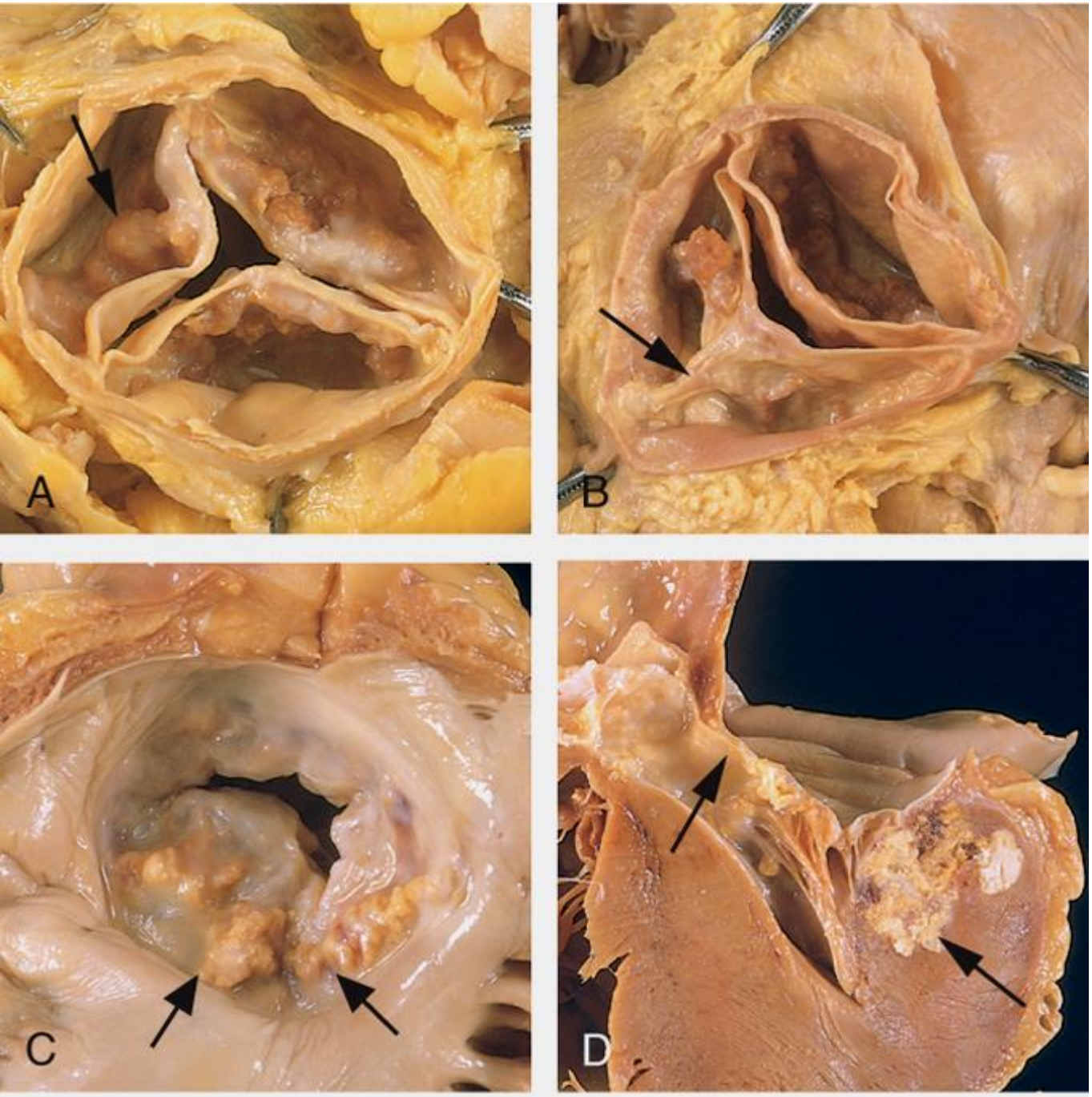
Calcific Aortic Stenosis

✱ ***Is the most common cause of aortic stenosis in the US.*** A consequence of calcification, from progressive age-associated "wear & tear" of either(1) anatomically **normal** aortic valves **(F11-16A**) or (2) **congenitally bicuspid** valves **(F6-7 & 11-16B & 6- 40).**



6.7 Bicuspid aortic valve: heart

F6.7: Bicuspid aortic valve.
A congenital anomaly, occurring in 1.4% of live births. Usually asymptomatic, but the valve cusps are liable for:
(1) **infective endocarditis** &
(2) early degenerative **calcification.**



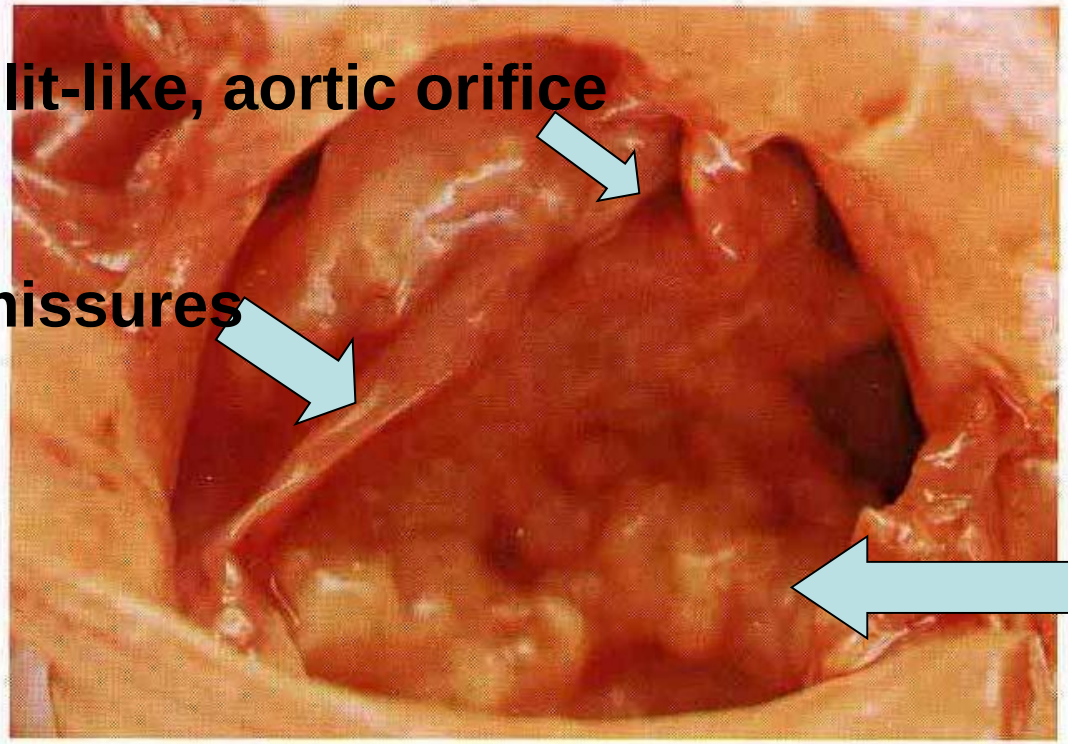
F11-16:

A. Senile calcific aortic valve (3 cusps) with normal commissures .

B. Congenital bicuspid aortic valve with calcific stenosis.

C. Calcified nodules at the base of the anterior mitral leaflet (arrows) and **D.** in the mitral annulus (arrows).

F6.40: Calcific stenosis: aortic valve. The superior surface of the aortic valve, viewed from the first part of the ascending aorta. The **three** cusps are thickened & nodular due to **fibrosis & calcification**. The **commissures are fused** & the free margins of the valve roughened. The **orifice is reduced to a slit-like opening**. The condition is common, degenerative in nature, & usually occurs in elderly people.



6.40 Calcific stenosis: aortic valve

Congenitally ***bicuspid valves*** (i.e., valves with only two functional cusps) occur in approximately **1.4% of live births**. They are asymptomatic throughout early life. However, they are more prone to progressive degenerative calcification **(F 11-16B & 6-7).**

 # The incidence of calcific aortic stenosis is ↑ with the rising average age of the US population.

In **anatomically normal** valves, it typically begins to manifest when patients reach their 70s & 80s; **onset with bicuspid** aortic valves is at 40-50 years.

Morphology

The hallmark of calcific aortic stenosis (normal or bicuspid) is **heaped-up calcified masses** on the outflow side of the cusps; these protrude into the sinuses of Valsalva & mechanically impede valve opening (**F11-16A**).

In calcific aortic stenosis, significant outflow obstruction leads to LV pressure overload with concentric hypertrophy.

Mitral valve calcification primarily involves the valve annulus & is usually asymptomatic unless the calcifications encroach on the adjacent **conduction system (F11-6 C&D).**

Mitral valve myxomatous degeneration

In which one or both mitral leaflets are **"floppy" &** ***prolapse,*** i.e., they **balloon** back into the left atrium during systole.

Mitral valve prolapse is a **primary** form of myxomatous mitral degeneration **affecting 3% to 5% of adults in the US**, women are seven (7) times more frequently than men; as such, it is one of the ✱ **most common forms of valvular heart disease in the west.**

Morphology

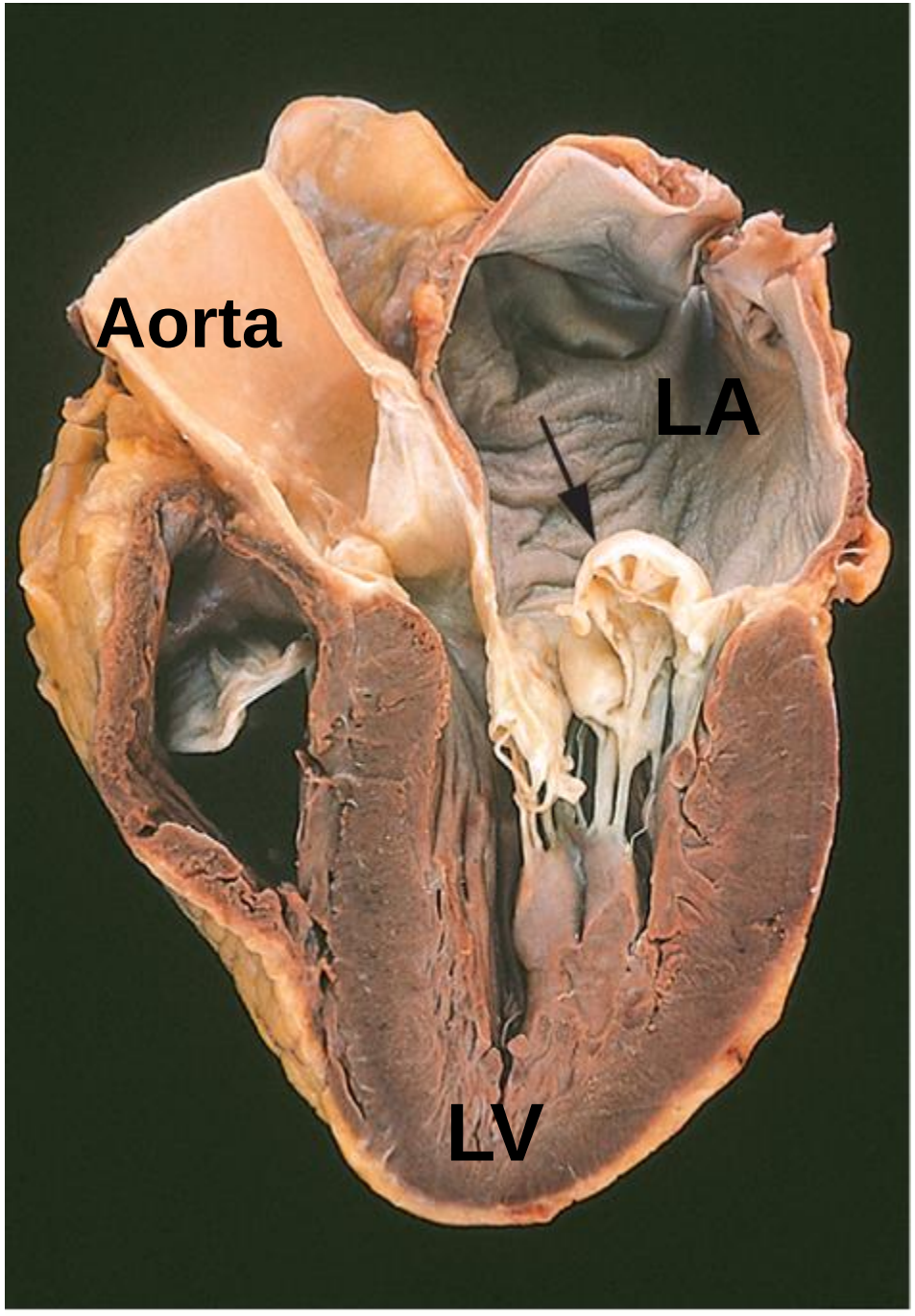
Primary myxomatous degeneration of the mitral valve characterizes by **ballooning** of the mitral leaflets **(F11-17).** The **affected leaflets are enlarged, redundant, thick, & rubbery;** the tendinous cords also tend to be elongated, thinned, & occasionally ruptured.

In mitral valve prolapse, concomitant **tricuspid** valve involvement is common (20% to 40% of cases), & aortic & pulmonic valves can also be affected.

◙ H, the essential change is **thinning of the fibrosa layer of the valve**, on which the structural integrity of the leaflet depends, accompanied by **expansion of the middle spongiosa** layer with increased **deposition of myxomatous** (mucoid) material.

Pathogenesis

The basis for **primary** myxomatous degeneration of the mitral valve is **unknown**. It is a common feature of Marfan syndrome (due to fibrillin-1 mutations).



F11-16: Myxomatous degeneration of the mitral valve.

→ parachute-like, prolapse, hooding, or ballooning of the posterior mitral leaflet into the left atrium (arrow).

→ Note the dilated LA & LV hypertrophy.

CARDIOMYOPATHIES

★ **Most** cardiac diseases are **secondary** to other conditions (e.g., CA, hypertension, or valvular HD), but

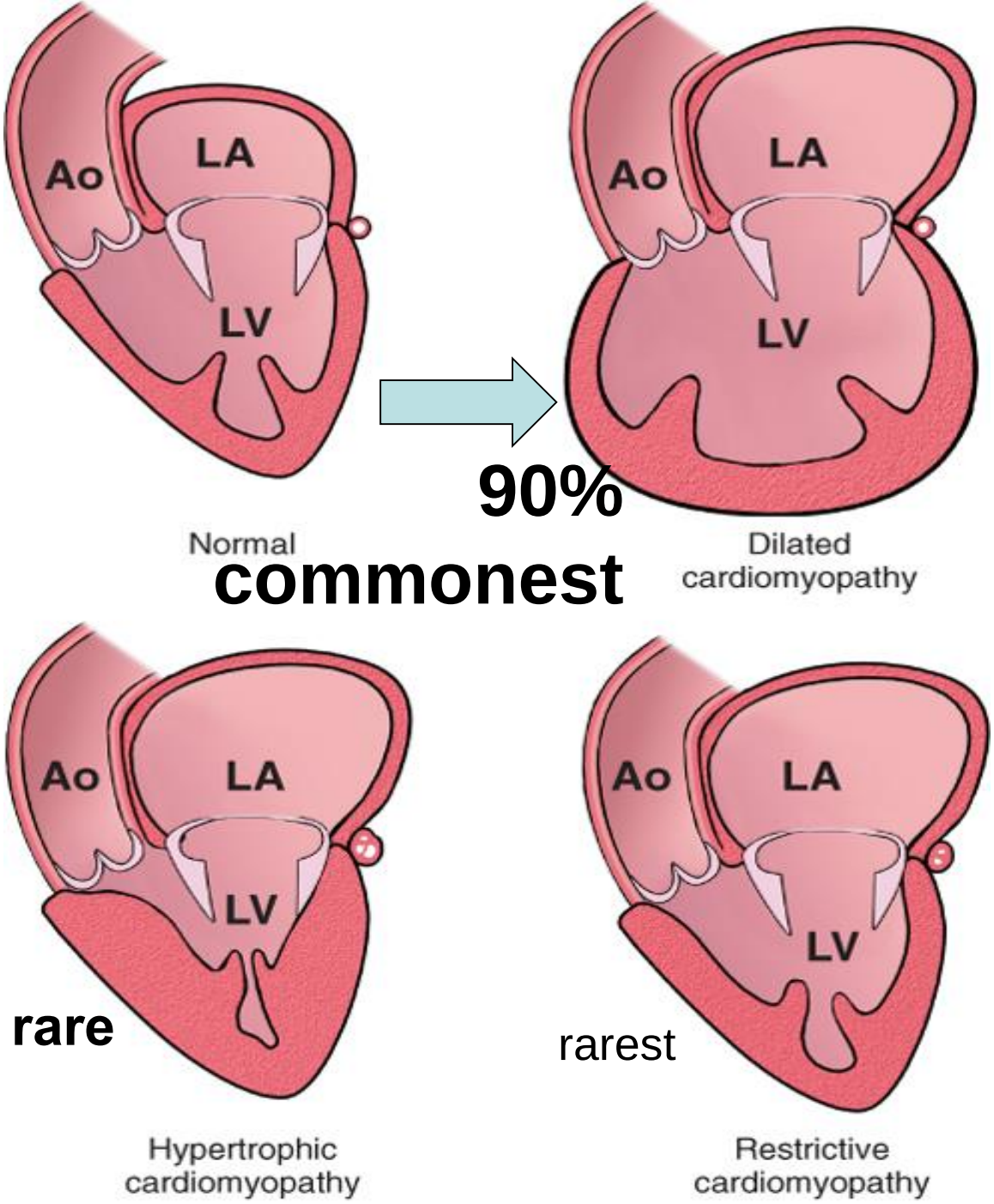
★**Some,** termed **cardiomyopathies** are cardiac diseases attributable to **primary intrinsic** heart muscle diseases resulting in myocardial dysfunction, & **By definition** → there is no primary valve pathology & the coronaries are free of significant atherosclerotic stenosis.

Cardiomyopathy can be classified into 3 groups (F**11-23** & Table 11-5) as follows:

Dilated (commonest, 90%)/ Hypertrophic & Restrictive (rarest) cardiomyopathy

Each of these can be caused by a specific **identifiable cause** or can be **idiopathic.**

Myocarditis are included here, since there is clinical overlap between some cases of myocarditis & dilated cardiomyopathy.



F11-23:
The three distinctive & predominant clinical-pathologic-functional forms of **cardiomyopathies**

Dilated "Congestive" Cardiomyopathy (DCM)

Characterized by **progressive cardiac dilation &** ***contractile (systolic) dysfunction,*** with concurrent hypertrophy.

► Most common type (90% of all cardiomyopathies).

* 25% to 35% of DCM cases have a **familial** (genetic) basis.
* Others result from **acquired** myocardial insults**,** e.g., Viral myocarditis, chronic alcoholism & pregnancy.
* Some DCM are *idiopathic.*

Morphology

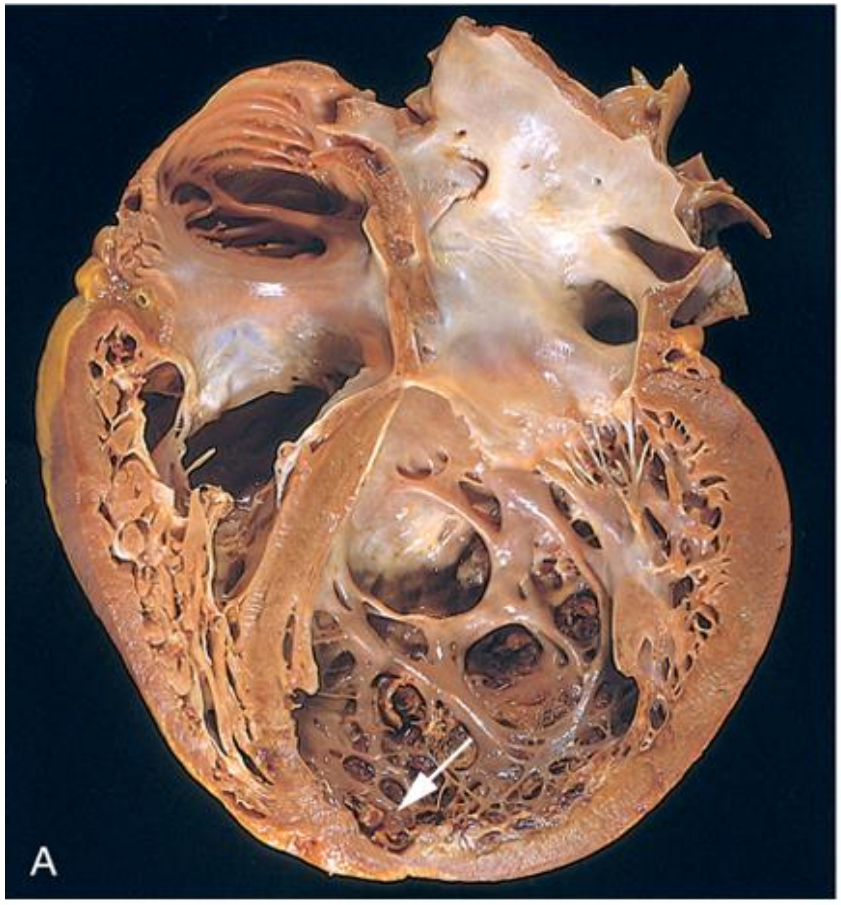
☹ The heart is **enlarged to** 2 to 3 times its normal weight) & **flabby, with dilation of all chambers** (F11-24**).** Because of the wall thinning that accompanies dilation, the ventricular thickness may be less than, equal to, or greater than normal.

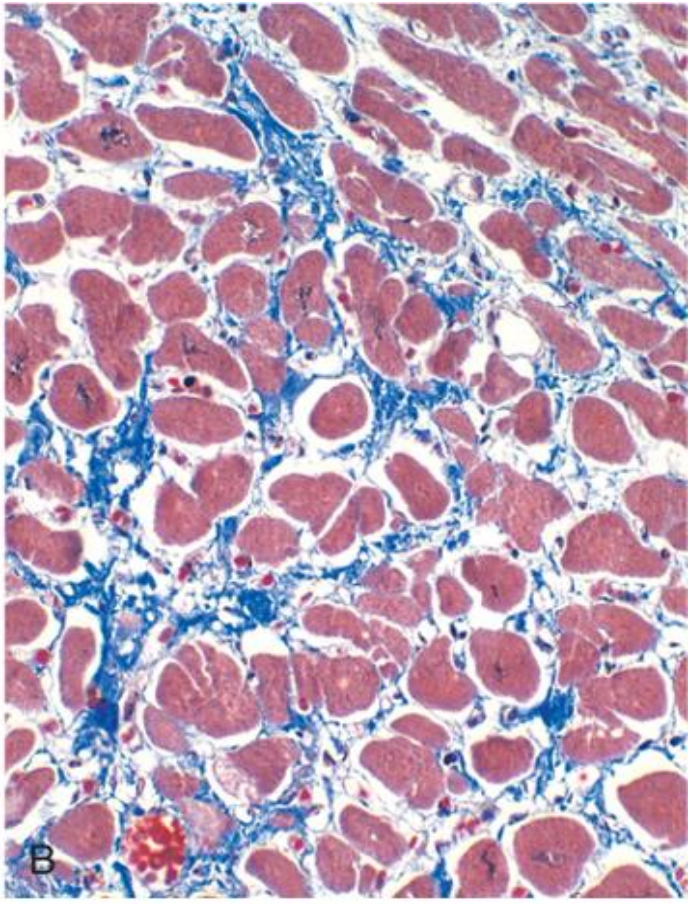
☹ **Mural thrombi** are common & may be a source of thromboemboli.

F11-24: **Dilated cardiomyopathy (DCM).**

A. **Four-chamber dilatation & hypertrophy**, with a small mural thrombus (arrow) in the apex of the LV. There was no coronary artery disease.

B. ◙ Typical myocyte hypertrophy & interstitial fibrosis (Masson trichrome stain collagen blue).





◙ H, most myocytes are **hypertrophied** + with variable interstitial & endocardial fibrosis.

Pathogenesis

The etiology can often only be inferred by the patient's medical **history**, or it is based on **epidemiologic evidence**.

Causes of DCM can be grouped into 4 broad categories:

(1) Viral: Coxsackievirus B & other enteroviruses.

(2) Alcohol or other toxic exposure: Alcohol abuse is strongly associated with development of DCM. Alcohol have a (1) **direct toxic effect on myocardium** & chronic alcoholism can be associated with (2) **thiamine deficiency**, introducing an element of beriberi heart disease.

Certain chemotherapeutic agents, particularly doxorubicin **(Adriamycin), & cobalt, are toxic to myocardium**

(3) Genetic influences. Familial forms of DCM account for 25% to 35% of cases; **autosomal dominant** inheritance is the **predominant pattern**; less common are X-linked, autosomal recessive, & mitochondrial inheritances.

Most of the genetic abnormalities seem to involve the myocyte cytoskeleton.

(4) ***Peripartum cardiomyopathy*** occurs late in gestation or several weeks to months postpartum. The etiology is multifactorial, including pregnancy-**associated-**hypertension, volume overload, & nutritional deficiency.

☺ Fortunately, approximately half of these patients spontaneously recover normal function.

Arrhythmogenic Right Ventricular Cardiomyopathy

A unique, uncommon entity, present with RVF& arrhythmias including SCD. The **RV wall is severely thinned as a result of myocyte replacement by massive fatty infiltration.** Most cases are sporadic, but familial forms do occur with gene defects .

Hypertrophic Cardiomyopathy (HCM)

also known as idiopathic hypertrophic subaortic stenosis is characterized by *myocardial hypertrophy, abnormal diastolic filling,* & in a third of cases-*ventricular outflow obstruction.*

► **The heart is thick-walled, heavy, & hypercontracting**, in striking contrast to the flabby, poorly contractile heart in DCM.

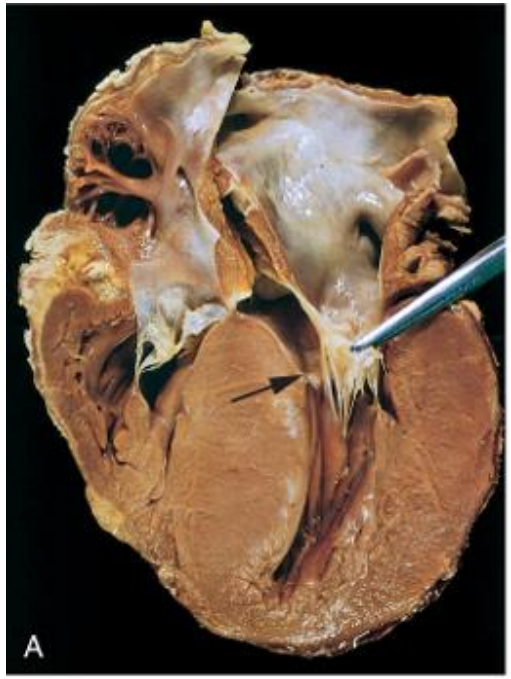
Systolic function is usually preserved in HCM, **but the myocardium do not relax & therefore shows primary diastolic dysfunction.**

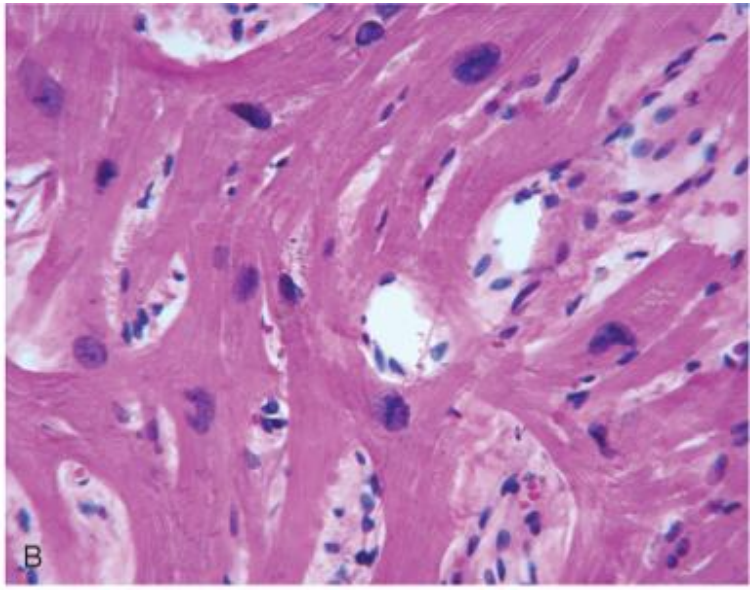
Morphology

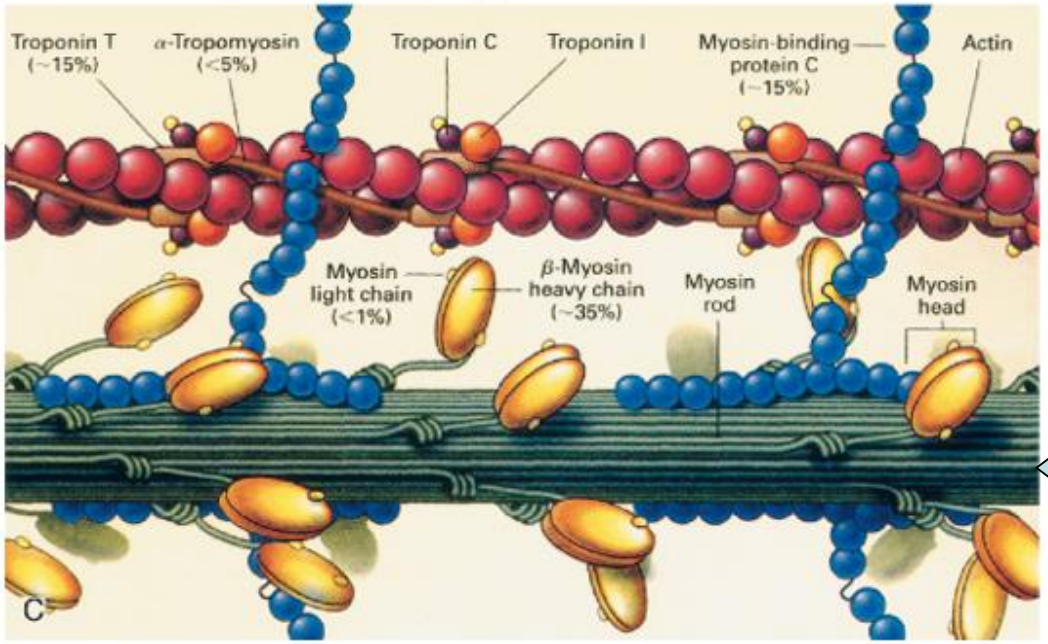
There is massive myocardial hypertrophy without ventricular dilation (F11-25A), involving the IVS more severely (so-called **asymmetrical septal hypertrophy**),**heart weight from** 600 to 1000 g **(Cor-bovinum*)***

The ventricular cavity is compressed into **a "banana-like" configuration (F11-25A**). Often present is an endocardial plaque in the LV outflow tract, as well as a thickening of the anterior mitral leaflet. Both findings reflect contact of the anterior mitral leaflet with the IVS during ventricular systole & correlate with functional LV outflow tract obstruction.

◙The characteristic histologic features in HCM are **severe myocyte hypertrophy, disarray & branching,** & interstitial replacement fibrosis (**F11-25B**).







F11-25: **HCM**.

A. Asymmetrical IVS hypertrophy bulging into the LV out flow tract **"banana-like" configuration of lumen.**

B. Extreme hypertrophy & branching of myocytes

C. Sarcomere of cardiac muscle- sites of mutations.

Pathogenesis

☹ **All cases of HCM are *Genetic,*** caused by missense point **mutations** in one of several genes (more than **100 causal mutations)** have been identified in at least 12 sarcomeric genes encoding the sarcomeric proteins, that form the contractile apparatus of striated muscle (F11-25C), with the β-myosin heavy chain being most frequently affected, followed by myosin-binding protein C & troponin T.

Transmission is **autosomal dominant** with variable expression.

Restrictive Cardiomyopathy

characterized by **LV wall *stiffness, resulting in impaired ventricular filling during diastole. S*ystolic function of the LV is unaffected**. Thus, the functional state can be confused with that of: (1) constrictive pericarditis or (2) HCM.

It can be **idiopathic,** or secondary to associated myocardial involvement by radiation fibrosis, amyloidosis, hemochromatosis, sarcoidosis, or products of inborn errors of metabolism.

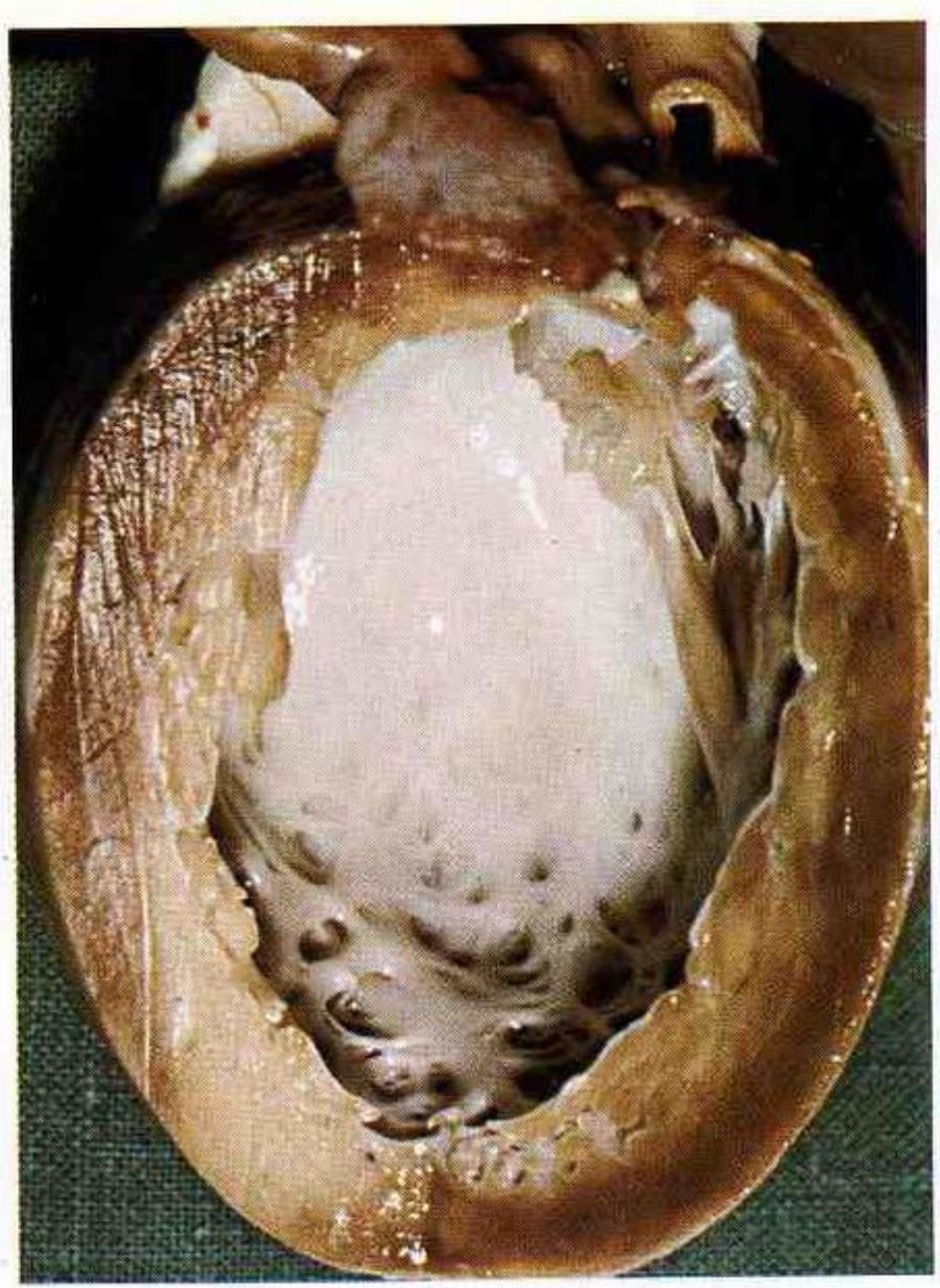
Morphology

In idiopathic restrictive cardiomyopathy, the ventricles are of approximately normal size or slightly enlarged, the cavities are not dilated, & the **myocardium is firm**. Biatrial dilation is commonly observed. ◙ H, there is **interstitial fibrosis**, varying from minimal & patchy to extensive & diffuse. **Endomyocardial biopsy** can reveal disease-specific features (e.g., amyloid, iron overload, sarcoid granulomas).

2 other forms of restrictive cardiomyopathy merit brief mention:

☹ **(1)** ***Endomyocardial fibrosis*** **(Endocardial fibroelastosis)** is principally a disease of **children & young adults in Africa & other tropical areas (F6-22) & (F6-8)** ; *it is characterized by* ***dense fibrosis*** *of the ventricular endocardium & subendocardium extending from the apex up to the tricuspid & mitral valves, which* markedly diminishes the volume & compliance of affected chambers & so causes a restrictive physiology**.**

► **Worldwide, this is the most common form of restrictive cardiomyopahy**.



6.8 Endocardial fibroelastosis: heart

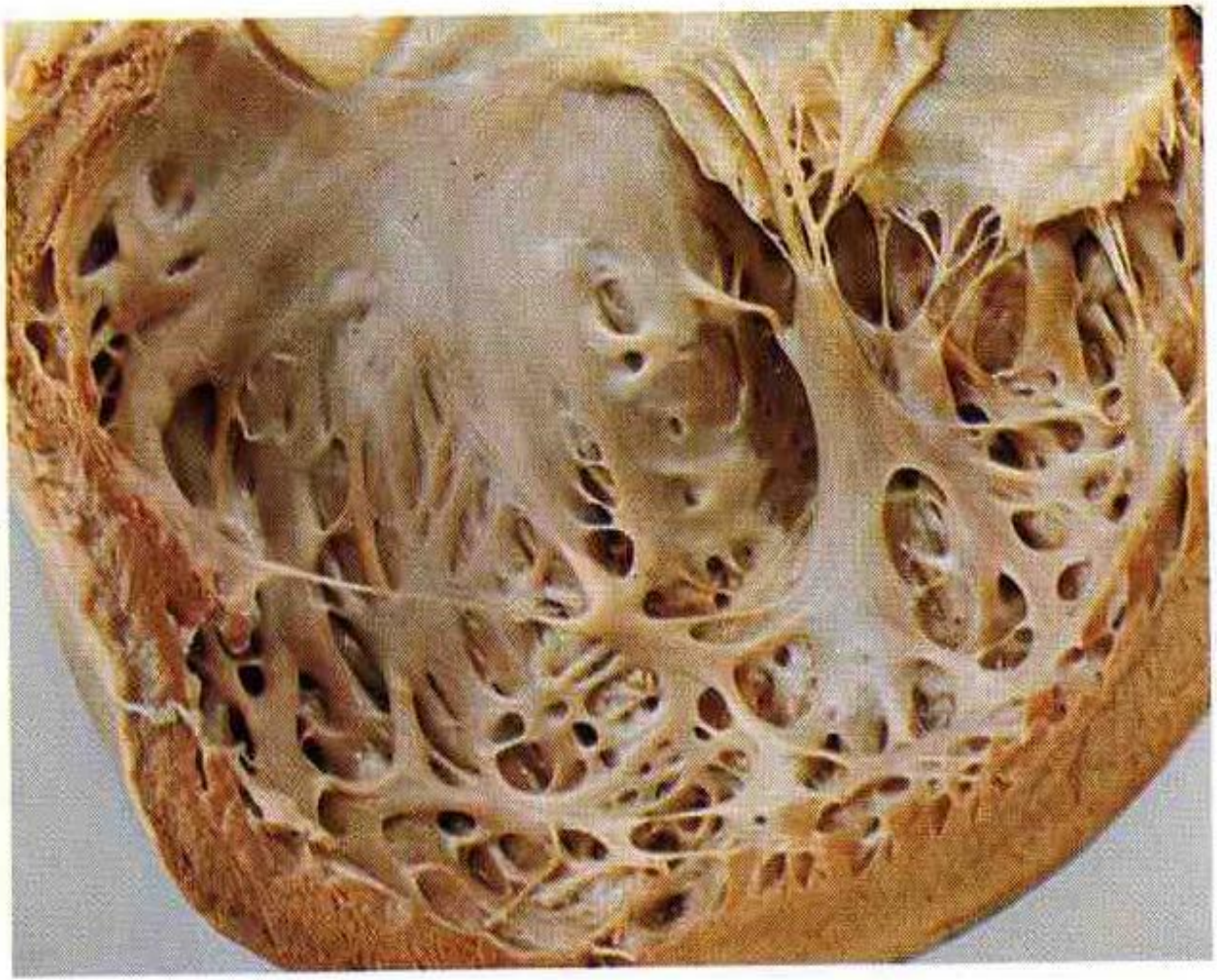
F6.8: Endocardial fibroelastosis: Heart of a neonate.

☹ The entire endocardium of the LV is covered with a layer of pearly grey-white tissue, consist of collagen & elastic fibers. Mural thrombi formation is rare. The LV wall is hypertrophied.

☼ Principally, it is a disease of children & young adults in Africa & other tropical areas of **unknown etiology**.

F6.22: Endocardial fibroelastosis: heart.

The **LV is greatly dilated** & greyish-white **fibro-elasti**c tissue covers the endocardial surface, including that of the papillary muscles of the mitral valve.



6.22 Fibroelastosis and mural thrombus: heart

(2)***Loeffler endomyocarditis*** also causes **endocardial fibrosis**, typically with **mural thrombi**; however, it is not geographically restricted, & there is often an **associated peripheral hypereosinophilia**.

Myocarditis

inflammation of the myocardium, resulting in myocardial injury.

In myocarditis, the inflammatory process is the cause of- rather than a response to-myocardial injury.

Morphology

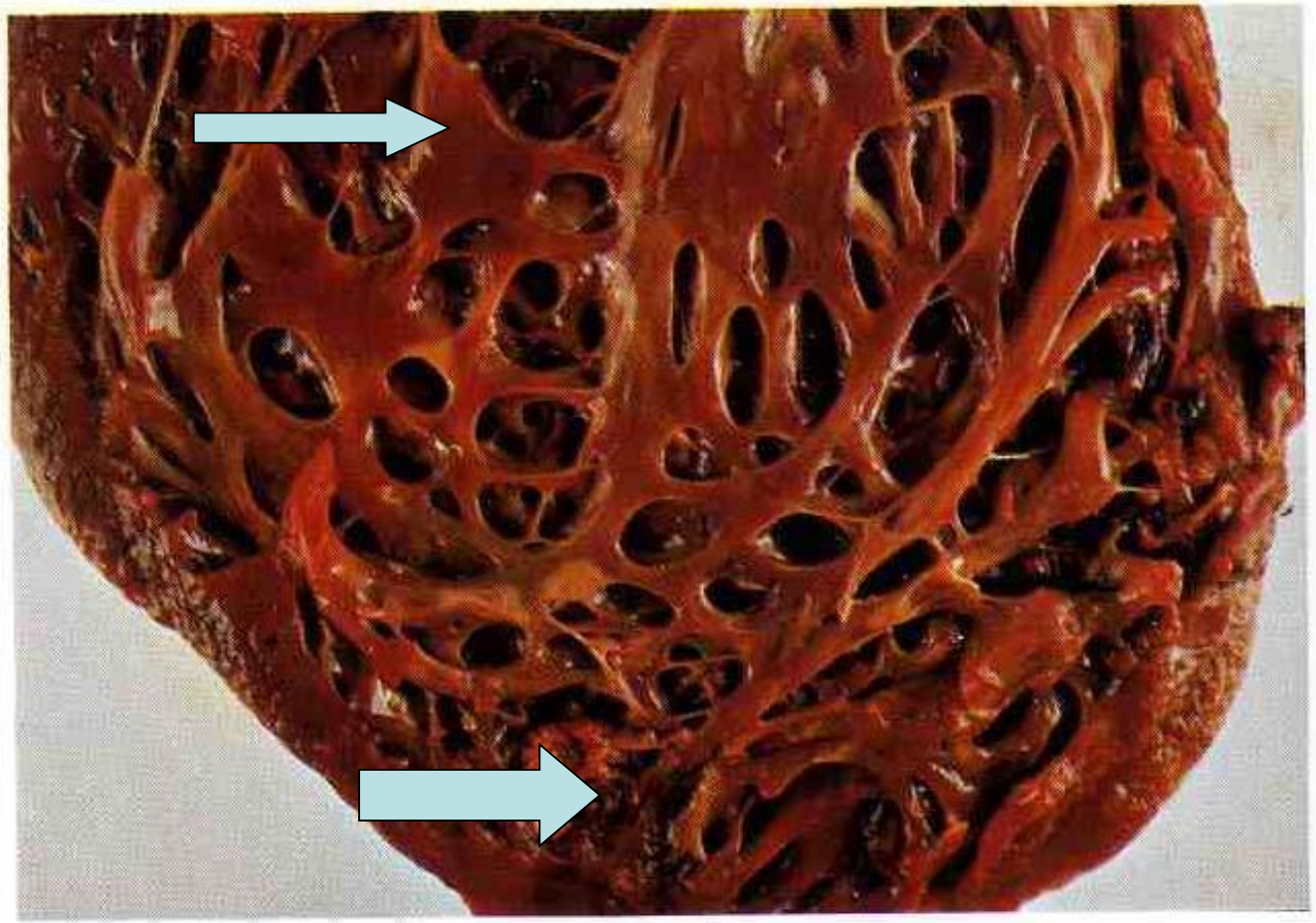
During active myocarditis the heart may appear normal or dilated. The ventricular myocardium is typically **flabby** & often mottled by patchy or diffuse foci of pallor &/or hemorrhage. **Mural thrombi** can be present.

◙ H, active myocarditis shows (1) an interstitial inflammatory infiltrate, with (2) focal necrosis of myocytes adjacent to the inflammatory cells **(F11-26**).

▼ **Lymphocytic myocarditis** is most common **(F11-26A**).

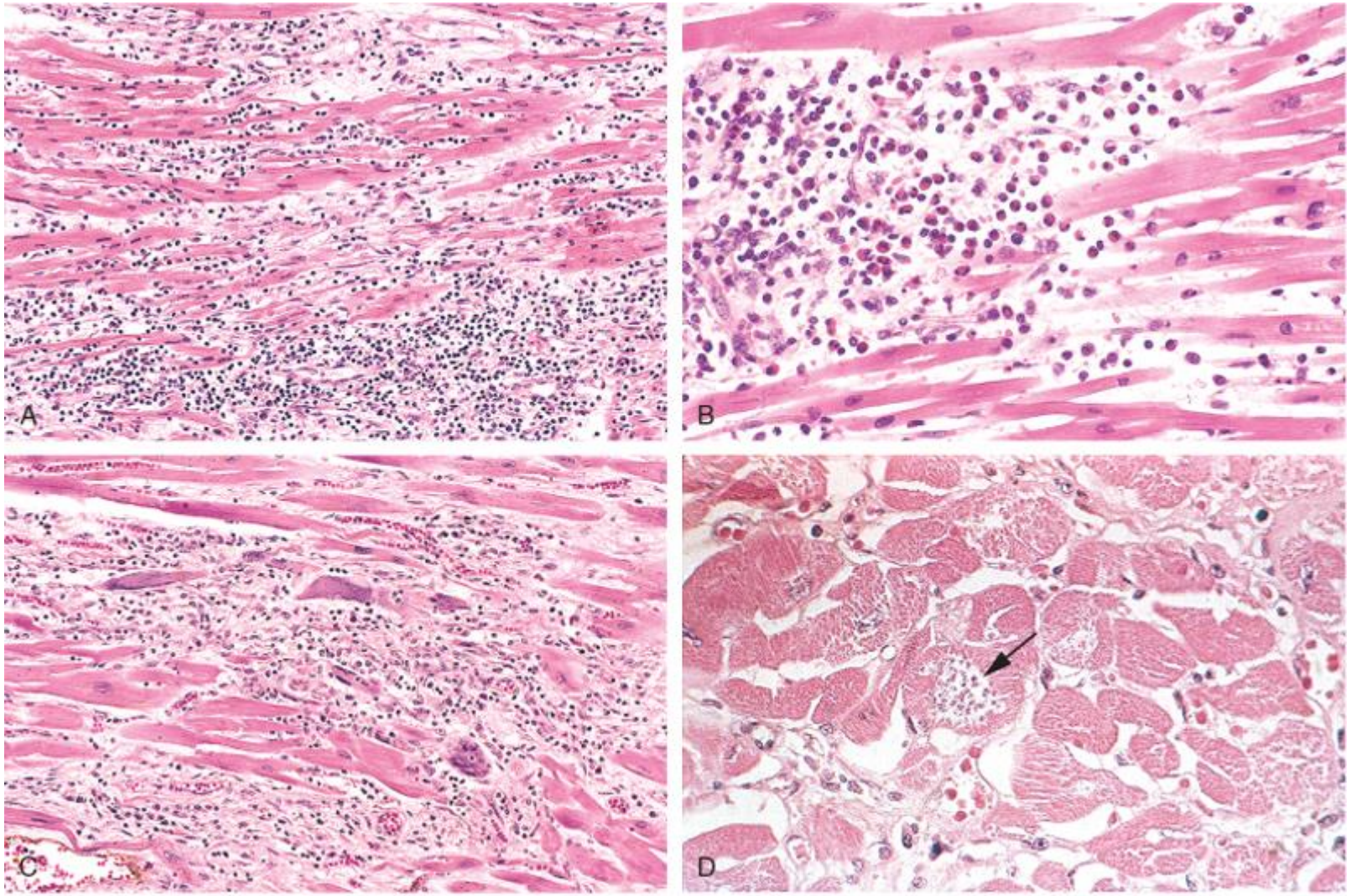
If the patient survives, inflammatory lesions either resolve, leaving no residual changes, or heal by progressive fibrosis.

F6.23: Viral myocarditis: heart. The ventricle is dilated, flabby-looking & minimally hypertrophied. The muscle is red-brown & hemorrhagic mottling being well seen over the trabeculae carneae (arrow, upper center). Small portions of mural thrombi are present (lower arrow).



6.23 Viral myocarditis: heart

F11-26: **Myocarditis**: **A**. Lymphocytic. **B.** Drug-hypersensitivity, with eosinophilic infiltration. **C**. Giant-cell & extensive loss of muscle. **D.** Chagas disease, with muscle fiber distended by trypanosomes (arrow).



▼**Hypersensitivity myocarditis** has interstitial & perivascular infiltrates composed of lymphocytes, macrophages, & a high proportion of eosinophils.

▼**Giant-cell myocarditis** characterized by widespread inflammatory cellular infiltrates containing multinucleate giant cells (formed by macrophage fusion) interspersed with lymphocytes, eosinophils, & plasma cells.

It probably represents the aggressive end of the spectrum of lymphocytic myocarditis, & there is at least focal-& frequently extensive-necrosis **(F11-26C**).

This variant carries **a poor prognosis**.

▼**Chagas myocarditis** is distinctive by virtue of the parasitization of scattered myofibers by **trypanosomes accompanied** by an inflammatory infiltrate of neutrophils, lymphocytes, macrophages, & occasional eosinophils **(F11-26D).**

Pathogenesis

Viral infections are the most common cause of myocarditis in the US. Coxsackieviruses A & B & other enteroviruses account for most of the cases. Less common agents include cytomegalovirus, HIV.

☹ In most cases, the injury is caused by an immune response directed against virally infected cells ; this is **analogous** to the damage inflicted by virus-specific T cells on **hepatitis** virus-infected liver cells.

☹***Nonviral infectious causes of myocarditis;***

Trypanosoma cruzi is the agent of **Chagas disease**. Chagas disease affects as much as half the population in endemic areas of South America, & myocardial involvement can be found in 80% of infected individuals, with 10% of patients die during an acute attack.

Toxoplasma gondii (household **cats** are the most common vector) can cause myocarditis

Trichinosis is the most common helminthic disease with associated cardiac involvement. Myocarditis occurs in 5% of patients with Lyme disease, a systemic illness caused by the bacterial spirochete ***Borrelia burgdorferi.***

Noninfectious causes of myocarditis include systemic diseases of immune origin, such as **SLE & polymyositis**. Drug hypersensitivity reactions ***(hypersensitivity myocarditis)*** can also occur in response to any of a wide range of agents; these are typically benign & only in rare circumstances lead to CHF or sudden death.

PERICARDIAL DISEASE

Include inflammatory conditions & effusions.
lesions are almost always associated with disease in other portions of the heart, surrounding structures, or to a systemic disorders.

Pericarditis

Primary pericarditis is uncommon; mostly caused by infection. ***Viruses are usually responsible,*** which may cause myocarditis at the same time.

Secondary pericarditis is mostly due **to acute MI, cardiac surgery, irradiation to the mediastinum, or pleuritis.**

The most common **systemic** disorder associated with pericarditis is → **uremia.** Less common causes include **rheumatic fever, SLE , & metastatic malignancies.**

Pericarditis can (1) cause **pressure effect** on the heart,
(2) **resolve** without significant sequelae, or
(3) **progress to a chronic fibrosing process.**

Morphology: of **acute pericarditis:**

In **viral** pericarditis or **uremia** (F6-15), the exudate is typically **fibrinous,** (so-called **bread & butter** pericarditis).

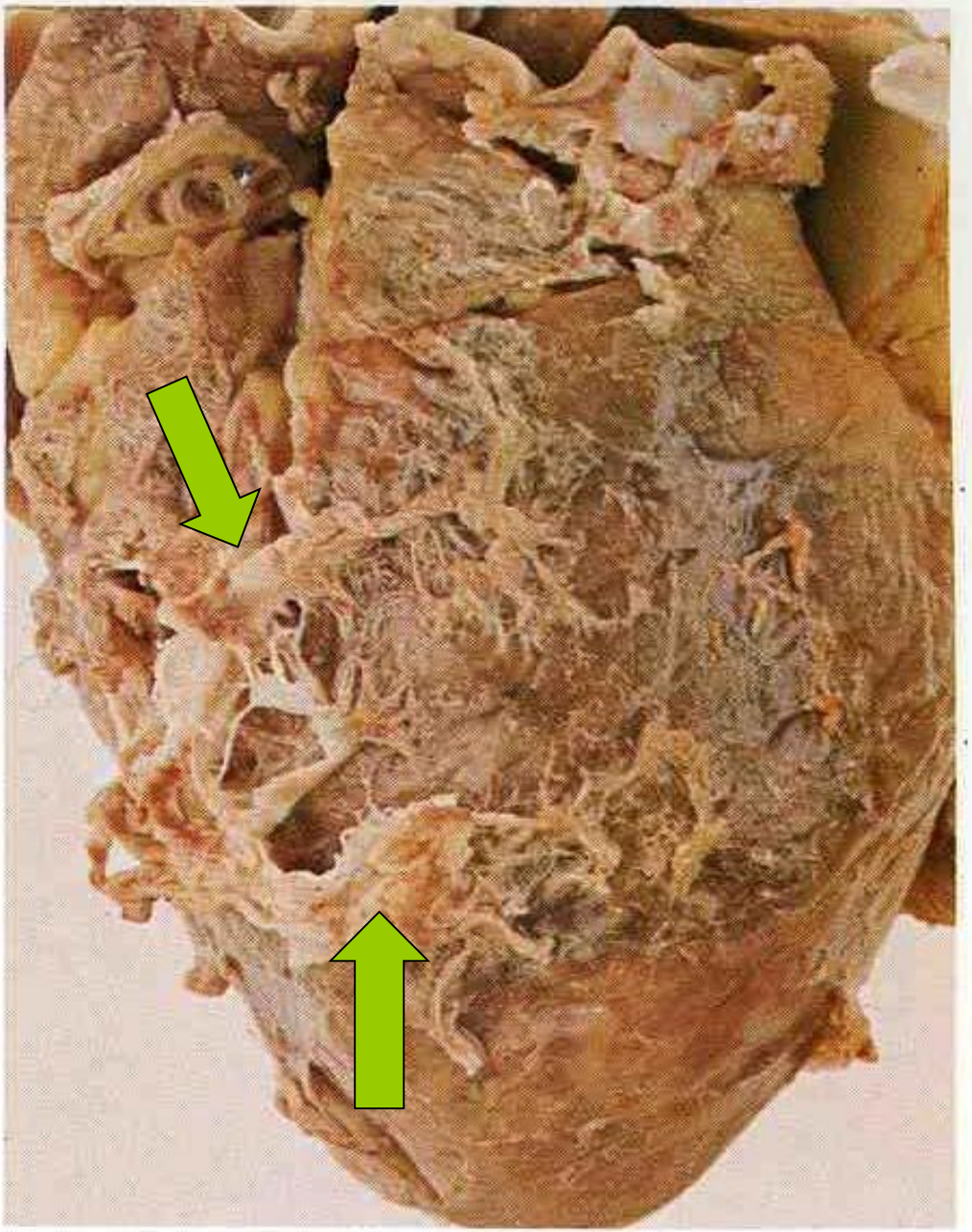
In acute bacterial pericarditis the exudate is **fibrinopurulent or suppurative,** with pus (**icing-sugar**) (F11-27 & 6-16).

Tuberculous (TB) pericarditis can show areas of caseation.

Pericarditis due to **malignancy** may show (a) **fibrinous exudate**, (b) **bloody effusion, and/or (c)** irregular masses of **metastases** can be grossly evident.

Acute fibrinous or fibrinopurulent pericarditis usually **resolves**. Extensive suppuration or caseation heals by fibrosis only, so-called **(chronic pericarditis).**

Chronic pericarditis apperance ranges from delicate adhesions to dense, fibrotic scars that obliterate the sac. In extreme cases the heart is so completely encased by dense fibrosis, which may calcified, that it cannot expand normally during diastole, so-called **constrictive pericarditis.**

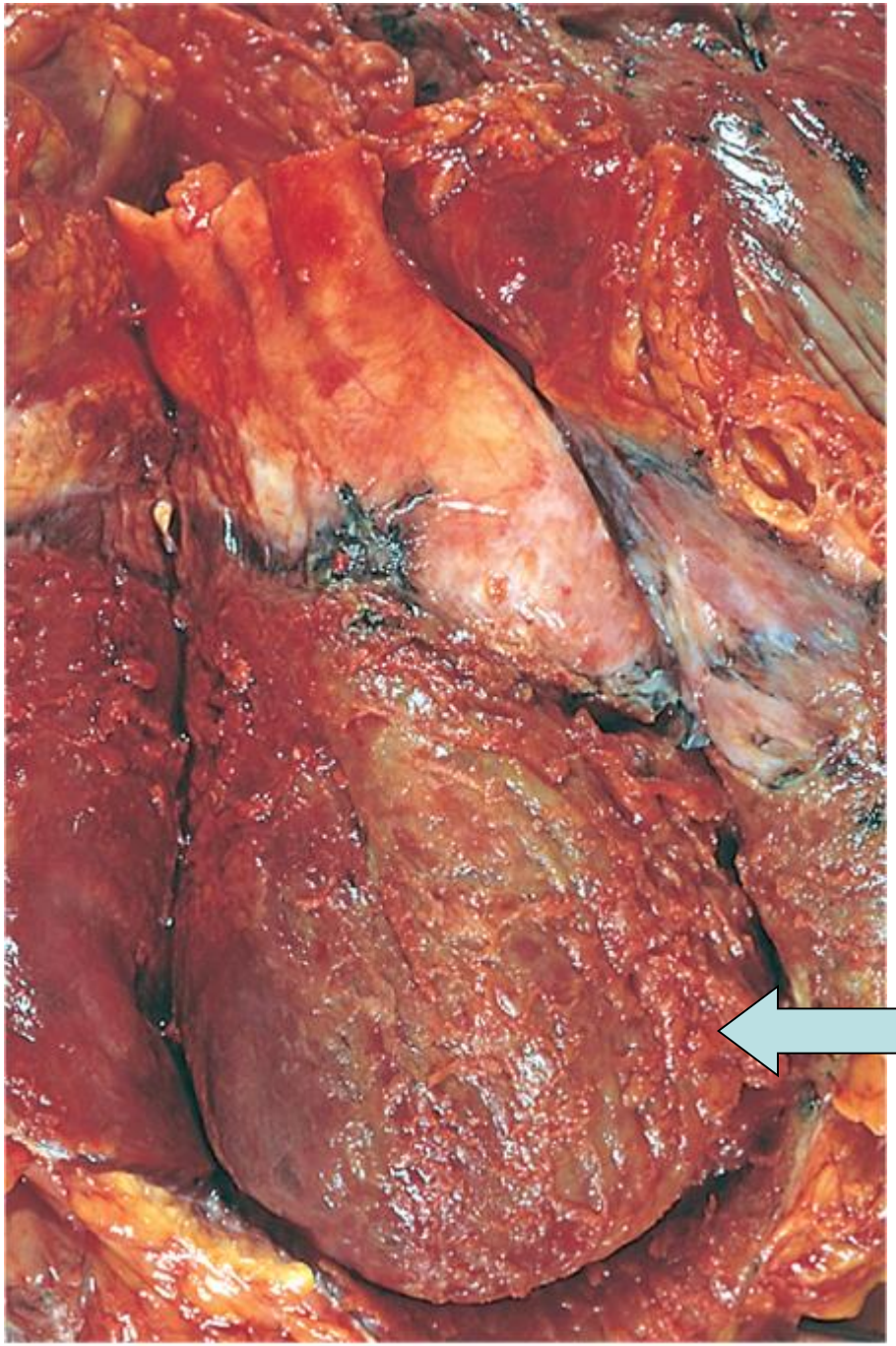


6.15 Uraemic pericarditis: heart

F6.15: Uraemic pericarditis: heart.

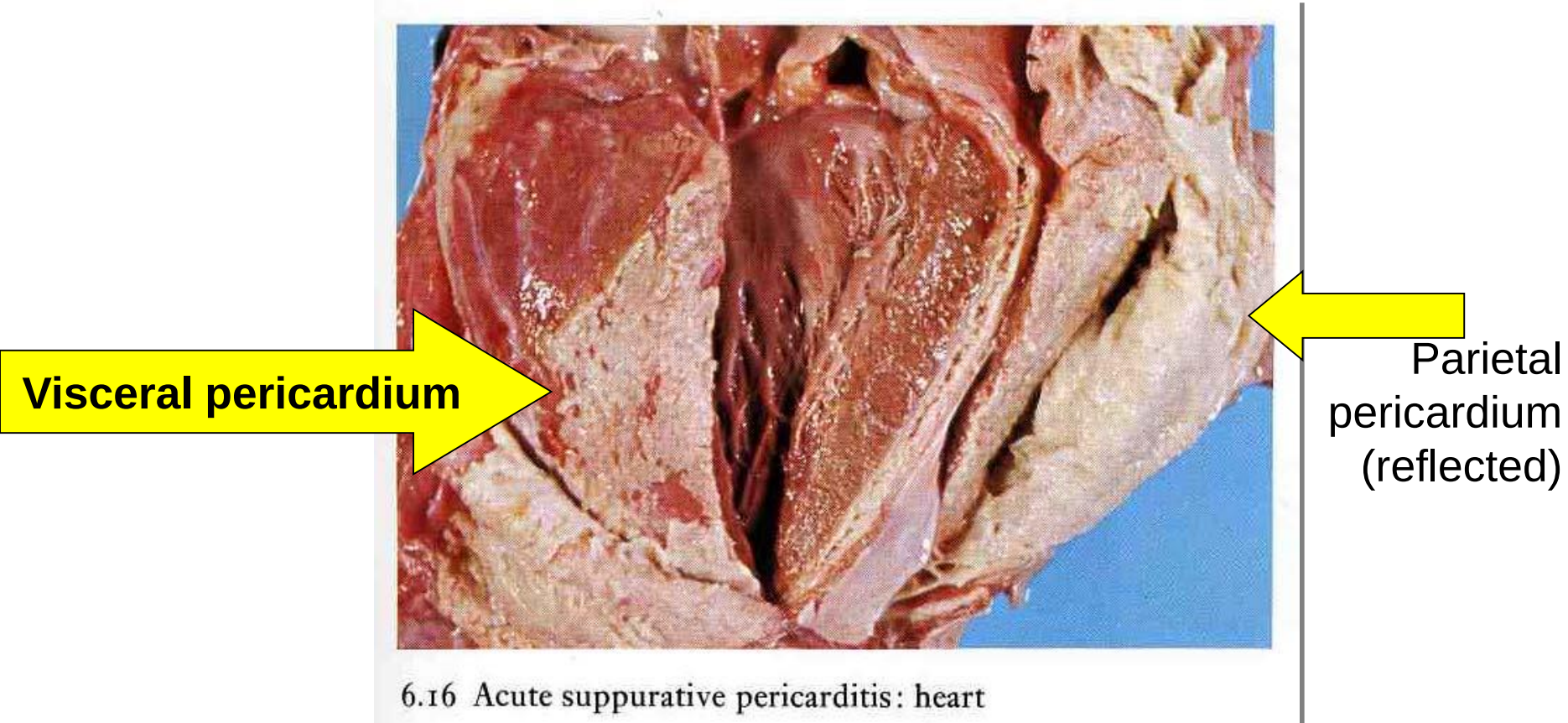
Sterile & usually fibrinous pericarditis.

The epicardial surface is covered with grey-white strands of fibrin some of which appear contracted & white as a result of organization (so-called, **bread & butter appearance).**



F 11-27 **Acute suppurative pericarditis**, with purulent exudate. An extension from a pneumonia.

F6.16: Acute suppurative pericarditis: heart. Caused by pyogenic organisms (e.g., staph., strept. & pneumococci). Both visceral & parietal pericardium (reflected) are covered with a yellowish-green **purulent exudate**. Organization, fibrosis & occasional calcification of exudate may result in adhesions, with partial or even complete obliteration of the pericardial sac (Chronic restrictive pericarditis with CHF).



6.16 Acute suppurative pericarditis: heart

Pericardial Hemorrhages & Effusions

☹ **Hemopericardium: means accumulation of blood** (with/without clot) in the pericardial sac, usually caused by **ruptured MI** (F6-73), or aortic dissection (DeBakey type I & II), causing **fatal *cardiac tamponade.***

☺ Normally, there is about 30 to 50 mL of thin, clear, straw-colored (serous) fluid in the pericardial sac.

☹ **Pericardial effusion**: means abnormal accumulation of excessive fluid in the pericardial sac.

In addition to the inflammatory states described above, it occurs in a number of settings, including:

Serous: CHF, hypoalbuminemia of any cause

Serosanguinous (blood stained effusion): blunt chest trauma, TB, & malignancy.

Chylous: mediastinal lymphatic channels obstruction (usually by tumor), resulting in accumulation of lymph in the pericardial sac.

The effects of pericardial effusions depend on the ability of the parietal pericardium to stretch, this depends on the amount of fluid & the rate of its accumulation.

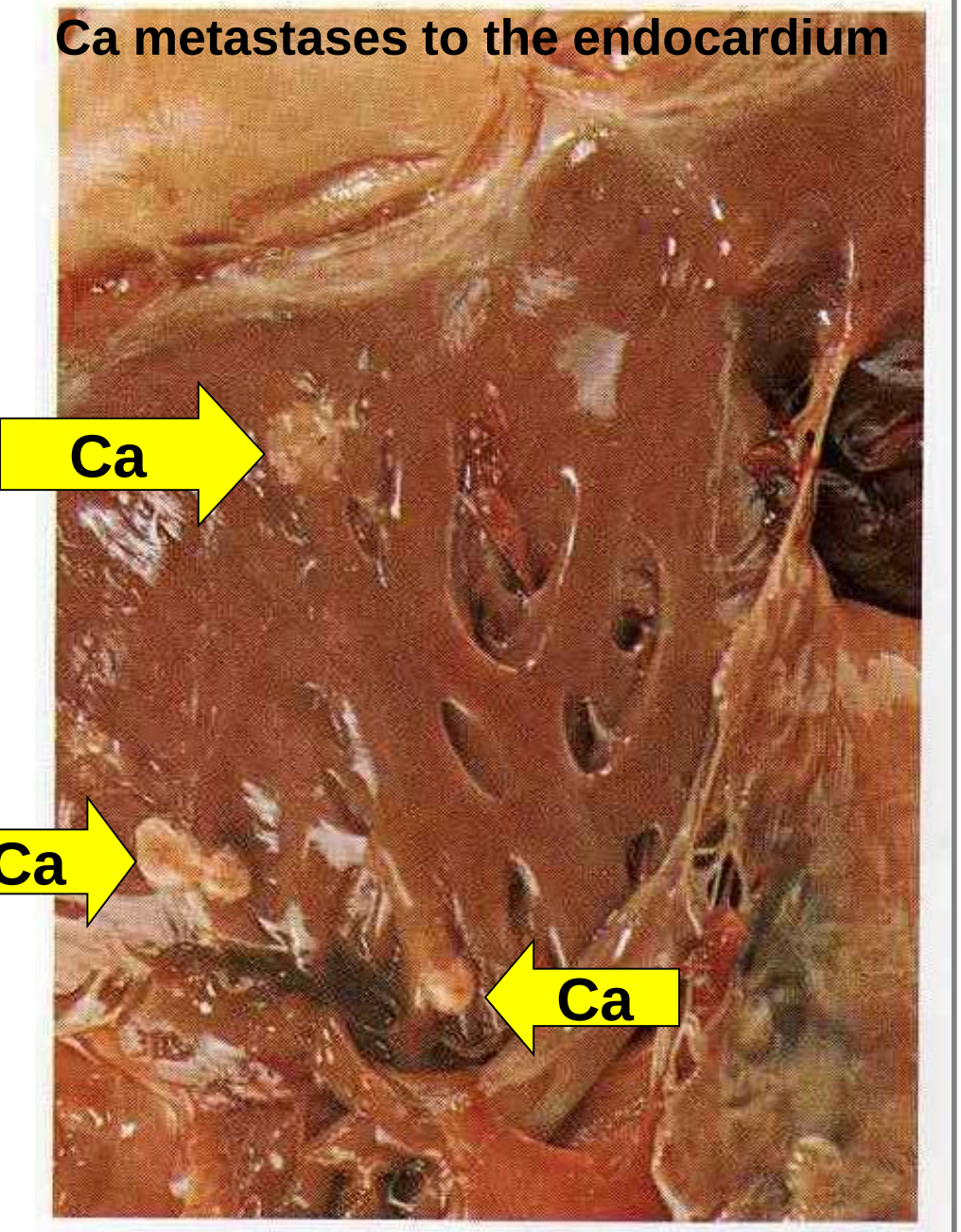
☺ Thus, **slowly** accumulating effusions, even as large as 1000 mL-can be tolerated without clinical manifestation.
☹ In contrast, **rapidly** developing collections of fluid of as little as 250 mL (e.g., from ruptured MI or ruptured aortic dissection) can restrict diastolic cardiac filling to produce ☠ **fatal *cardiac tamponade.***

CARDIAC TUMORS

Metastatic Neoplasms

The most common tumor of the heart is a metastatic tumor; tumor metastases to the heart occur **in about 5% of patients dying of cancer.** Certain tumors have a higher predilection to spread to the heart. In descending order, these tumors are:

carcinoma of the lung, lymphoma, breast cancer, leukemia, melanoma, carcinomas of the liver, & colon.



6.8o Secondary carcinoma: heart

F6.80: Secondary carcinoma; heart.

Four small pinkish-white **secondary deposits** (from **primary breast carcinoma**) are present at the infundibulum (upper part) of the right ventricle.

☹Tumor metastases to the heart occur in about 5% of patients dying of cancer. Mostly, **ca. lung, breast, lymphoma, leukemia, melanoma, ca. liver & colon.**

Primary Neoplasms

Primary cardiac tumors are uncommon; in addition, most primary cardiac tumors are also (thankfully) **benign**.

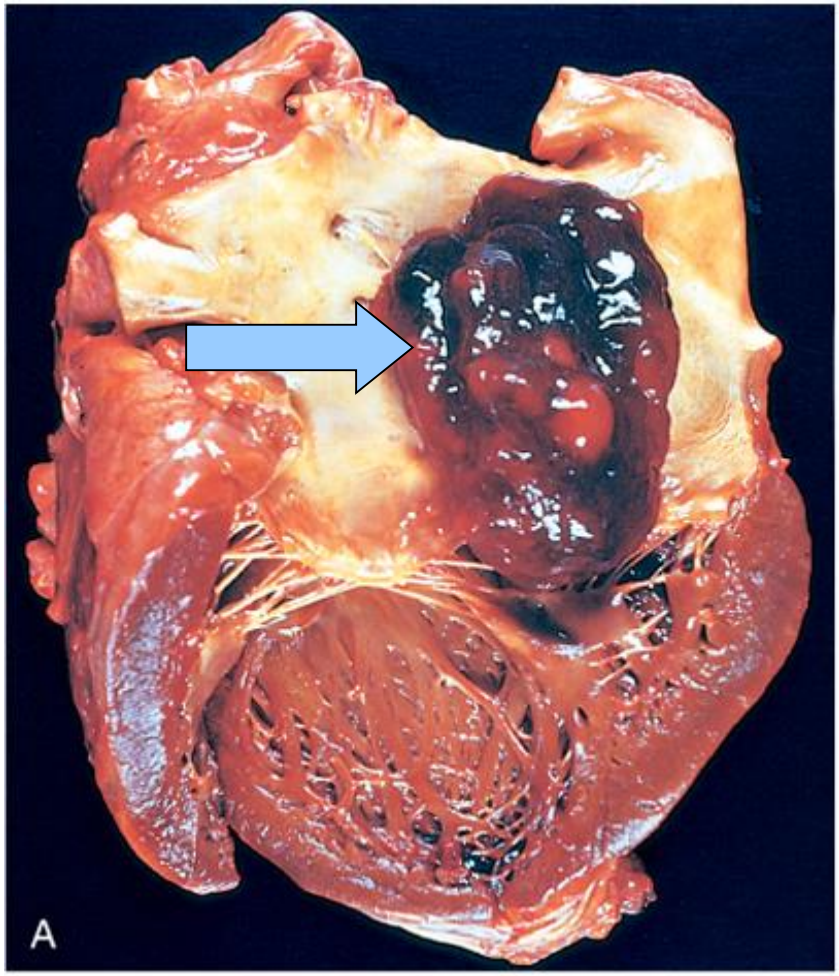
The five most common have no malignant potential & account for 80% to 90% of all primary heart tumors. In descending order of frequency , adults primary cardiac tumors are:

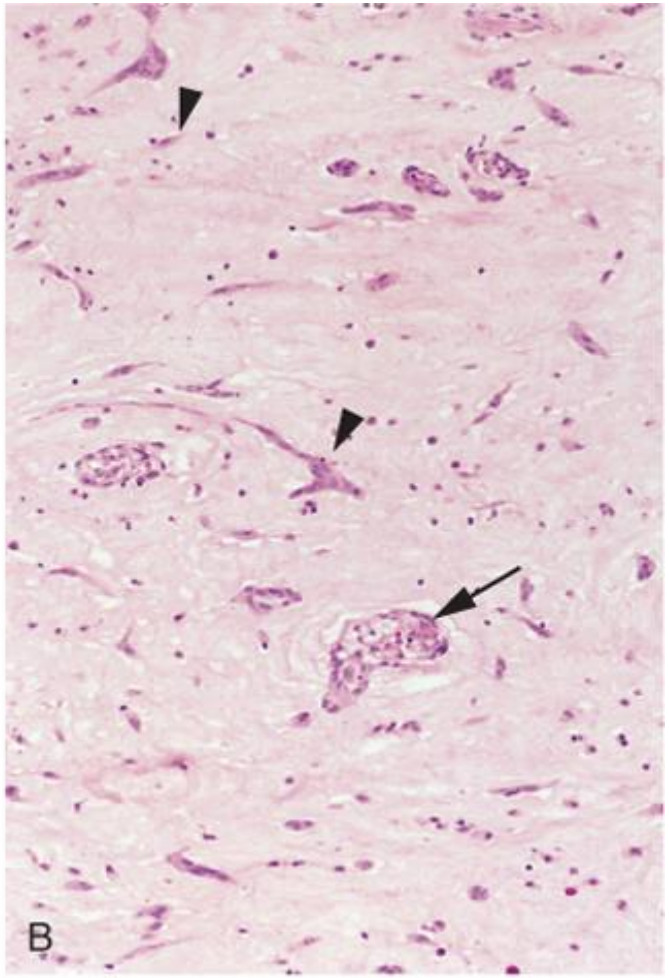
☺ myxomas, fibromas, lipomas, papillary fibroelastomas, rhabdomyomas &
☹ angiosarcomas (this last one is malignant).
Myxomas & rhabdomyomas are significant.

Myxomas

Myxomas are the most common primary tumor of the **adult heart** (**F11-28 & 6-77 & 78)**). Roughly 90% are located in the atria, with the left atrium accounting for 80% of those.

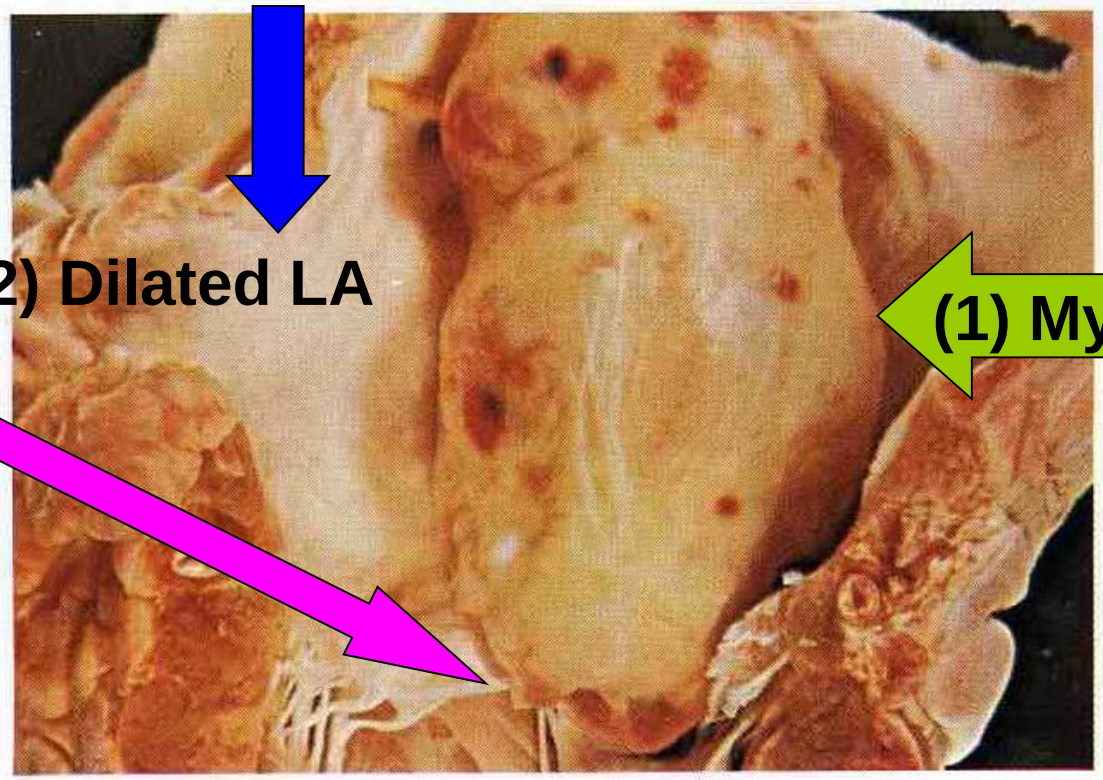
F11-28: A. **Left atrial myxoma:** large pedunculated tumor arising from fossa ovalis & extending into the mitral valve orifice. B. scattered myxoma cells (arrowheads) in a rich amorphus ECM.





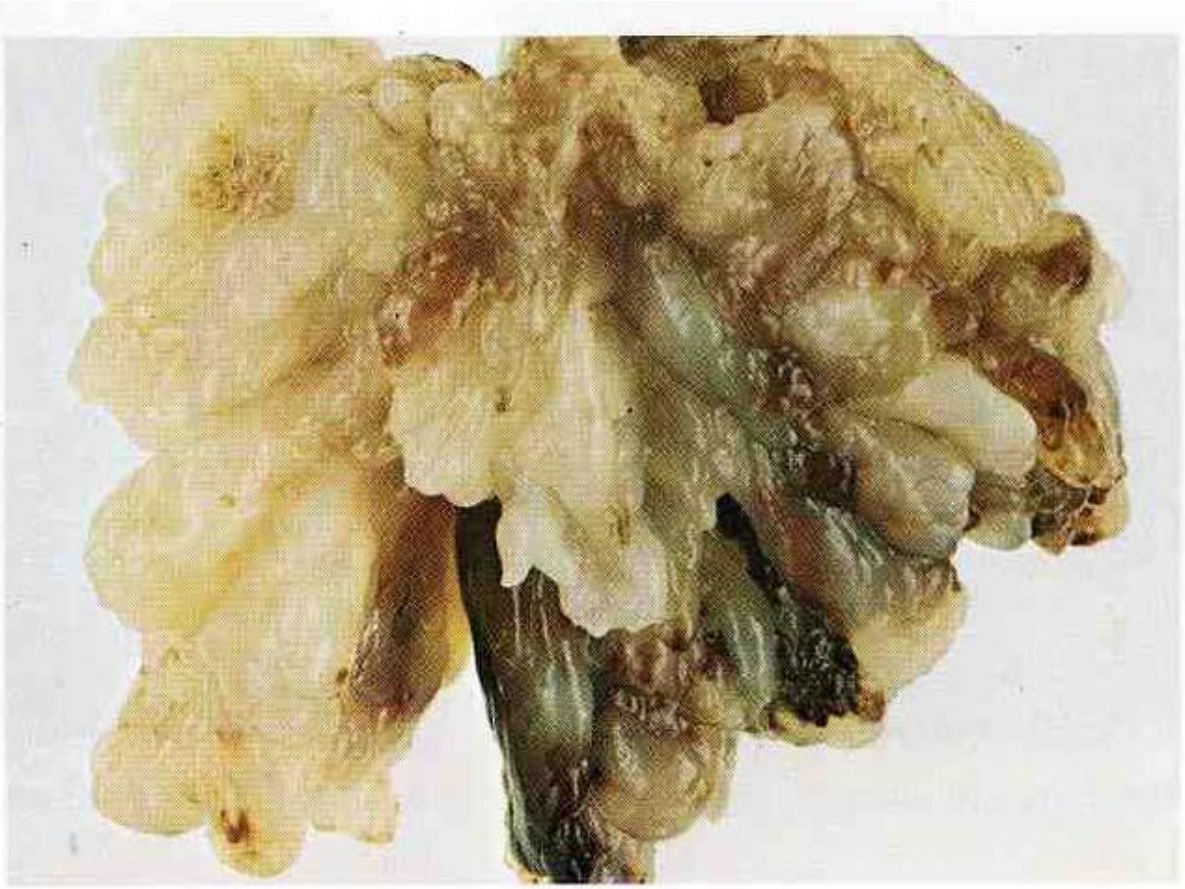
F6.77: Myxom: atrium. The **commonest primary intracardiac tumor**, 75% occurring in the left atrium, near the fossa ovalis. (1) The atrium contains large**10X5X5cm**, smooth, ovoid, gelatinous pale-yellow tumor, with focal surface hemorrhage, projects into the mitral valve orifice (causing **intermittent valve obstruction, or ☠ sudden death**).

(2) The atrium is dilated & its wall shows endocardial fibrosis.



6.77 Myxoma: atrium

<u>F6.78: Myxom: atrium,</u> <u>commonest</u> primary intracardiac tumor. Pedunculated, lobular, & **villous left atrial myxoma**, removed from a16-year-old girl. The surface is glistening, cream-colored with pale brownish areas of hemorrhage.



6.78 Myxoma: atrium

Morphology

Myxomas are **single,** mostly **located at the fossa ovalis (atrial septum).** They range from small (<1 cm) to impressive **(≤10 cm) (F6.77) , sessile or pedunculated masses (**F11-28A) vary from globular hard masses **(F6.77)** to soft, translucent, villous lesions with a gelatinous (**F6.78)** appearance.

Pedunculated myxomas **(F6.77)** are often sufficiently mobile to **swing** into the mitral or tricuspid valves during systole, **causing intermittent obstruction (which may cause sudden death).**

- H, myxomas are composed of stellate, multinucleated myxoma cells with hyperchromatic nuclei, admixed with cells showing endothelial, smooth muscle, &/or fibroblastic differentiation, all embedded in an abundant acid mucopolysaccharide ground substance (F**11-28B).** Hemorrhage, poorly organizing thrombus, & mononuclear inflammation are also usually present.

Rhabdomyomas

Are the most frequent primary tumor of the heart **in infants & children**; they are frequently discovered because of an **obstruction** of a valvular orifice or cardiac chamber. They occur with high frequency in patients with tuberous sclerosis.

Morphology

Rhabdomyomas are generally *small, gray-white myocardial masses up to several centimeters in diameter that* ***protrude into the*** **ventricular chambers.**

◙ H, they have a mixed population of cells; the most characteristic of which are **spider cells**, large, rounded, or polygonal cells, containing numerous glycogen-laden vacuoles separated by strands of cytoplasm running from the plasma membrane to the centrally located nucleus.

♥ End of Heart diseases: 81W + 51F = 132 Slides.

@ 21/2/2021.Lectures prepared by

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