CARDIOMYOPATHY

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Learning Objectives

a. Definition of Cardiomyopathy
b. Classification
c. Morphologic features
   - Grossly
   - Microscopically

Introduction

- **MYOCARDIAL DISEASE**

  I. **Myocarditis**

  - Inflammatory involvement of the myocardium

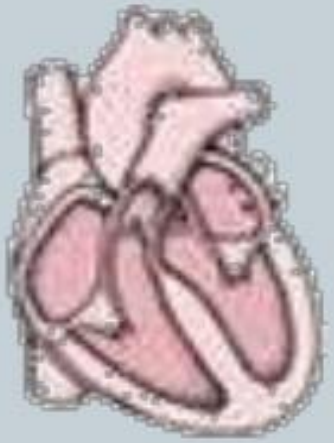
  II. **Cardiomyopathy**

  - A non-inflammatory myocardial involvement with unknown (primary) or known (secondary) etiology.

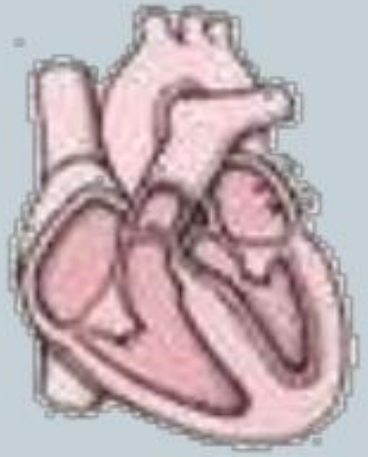
CARDIOMYOPATHY

- Cardiomyopathy literally means **disease of the heart muscle** but the term was originally coined to restrict its usage to **myocardial disease of unknown cause**.
- The WHO definition of cardiomyopathy also excludes heart muscle diseases of known etiologies.

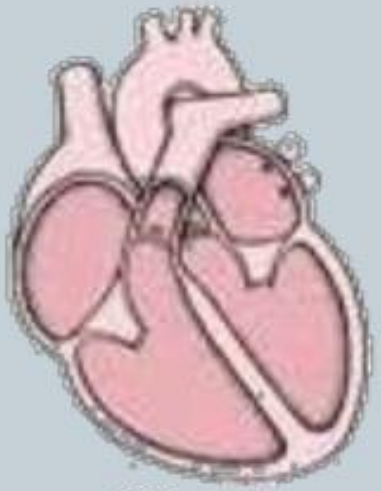
Cardiomyopathy



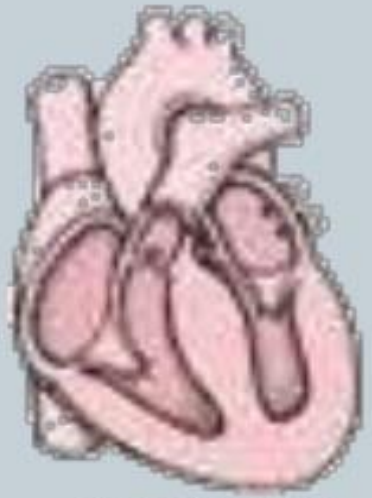
Normal



Restrictive Cardiomyopathy



Dilated Cardiomyopathy



Hypertrophic Cardiomyopathy

- However, the term **cardiomyopathy** has been loosely used by various workers for myocardial diseases of known etiology as well e.g.
  i. alcoholic cardiomyopathy,
  ii. amyloid cardiomyopathy,
  iii. ischaemic cardiomyopathy
- This controversy is resolved by classifying all cardiomyopathies into two broad groups:
  a) **primary cardiomyopathy**
  b) **secondary cardiomyopathy**
     - myocardial disease with known underlying cause.

A. PRIMARY CARDIOMYOPATHY

- This is a group of myocardial diseases of unknown cause
- **Pathophysiologic categories**

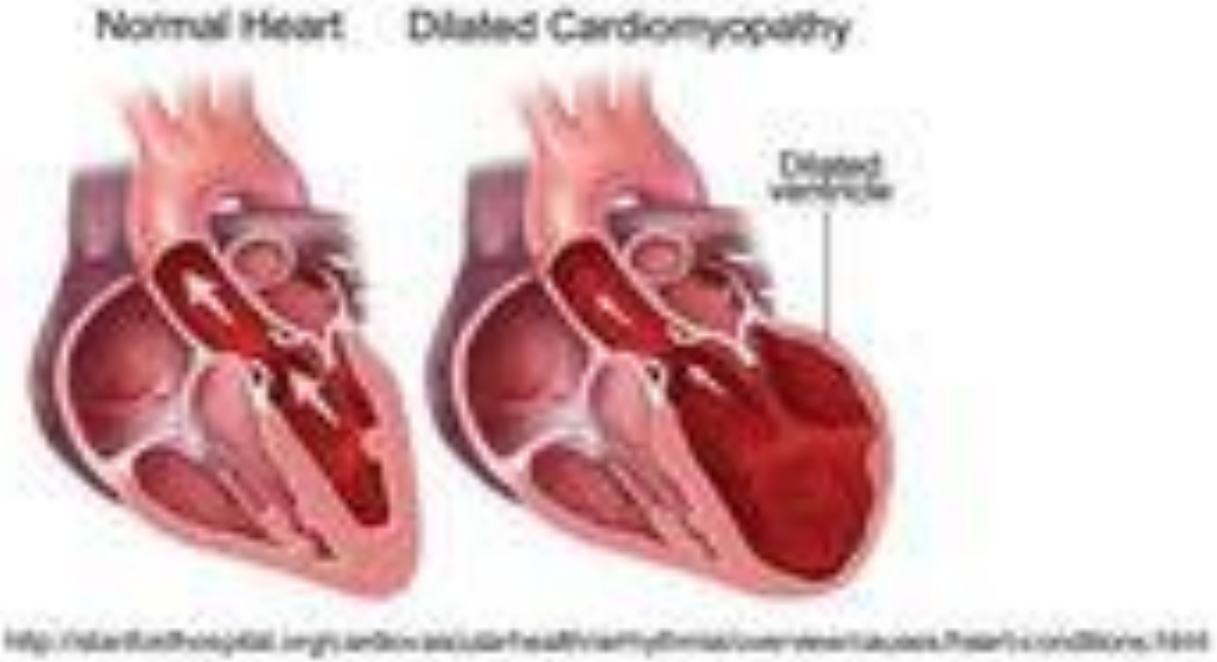
1. Idiopathic dilated (congestive) cardiomyopathy.
2. Idiopathic hypertrophic cardiomyopathy.
3. Idiopathic restrictive or obliterative or infiltrative cardiomyopathy.

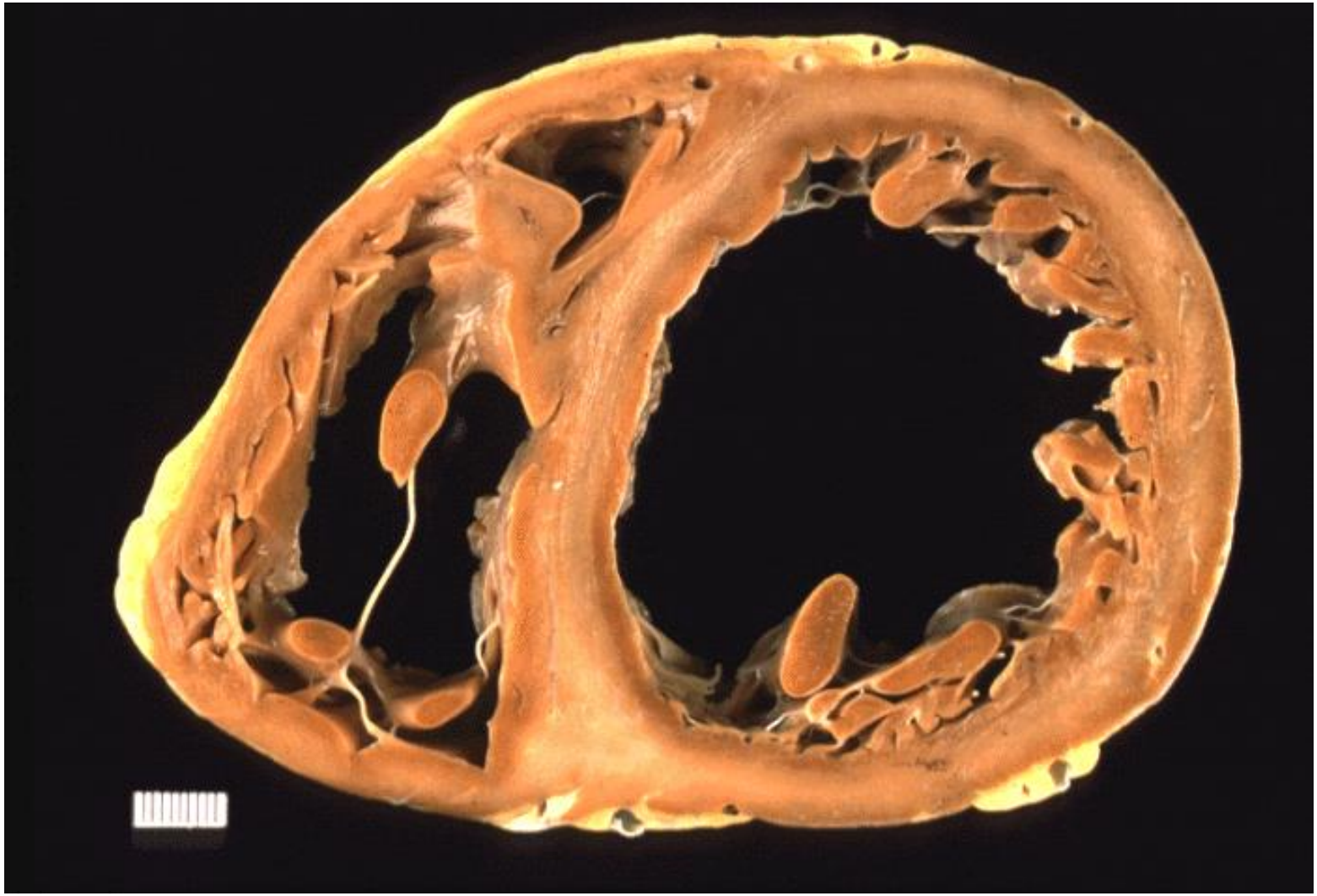
a)Idiopathic Dilated (Congestive) Cardiomyopathy

- This type of cardiomyopathy is characterised by gradually progressive cardiac failure along with dilatation of all the four chambers of the heart.
- The condition occurs more often in adults and the average survival from onset to death is less than 5 years

Dilated Cardiomyopathy

- Compared to a normal heart, an enlarged & dilated left ventricle is less efficient pumping blood to the rest of the body





Associated Conditions

I. Possible association of **viral myocarditis** (especially coxsackievirus B) with dilated cardiomyopathy, due to presence of viral nucleic acids in the myocardium,

II. Association with **toxic damage from cobalt** and c**hemotherapy** with doxorubicin and other anthracyclines

III. **Inherited mutations** have been implicated due to occurrence of disease in families. Mutations in certain sarcomere proteins such as cardiac troponin-T and I, β-and α-myosin, and α-cardiac actin have been observed. Abnormality in protein

iv) Chronic alcoholism has been found associated with dilated cardiomyopathy. It may be due to thiamine deficiency induced by alcohol and resulting in **beri-beri heart disease**

v) Peripartum association has been observed in some cases. Poorly-nourished women may develop this form of cardiomyopathy within a month before or after delivery (peripartum cardiomyopathy).

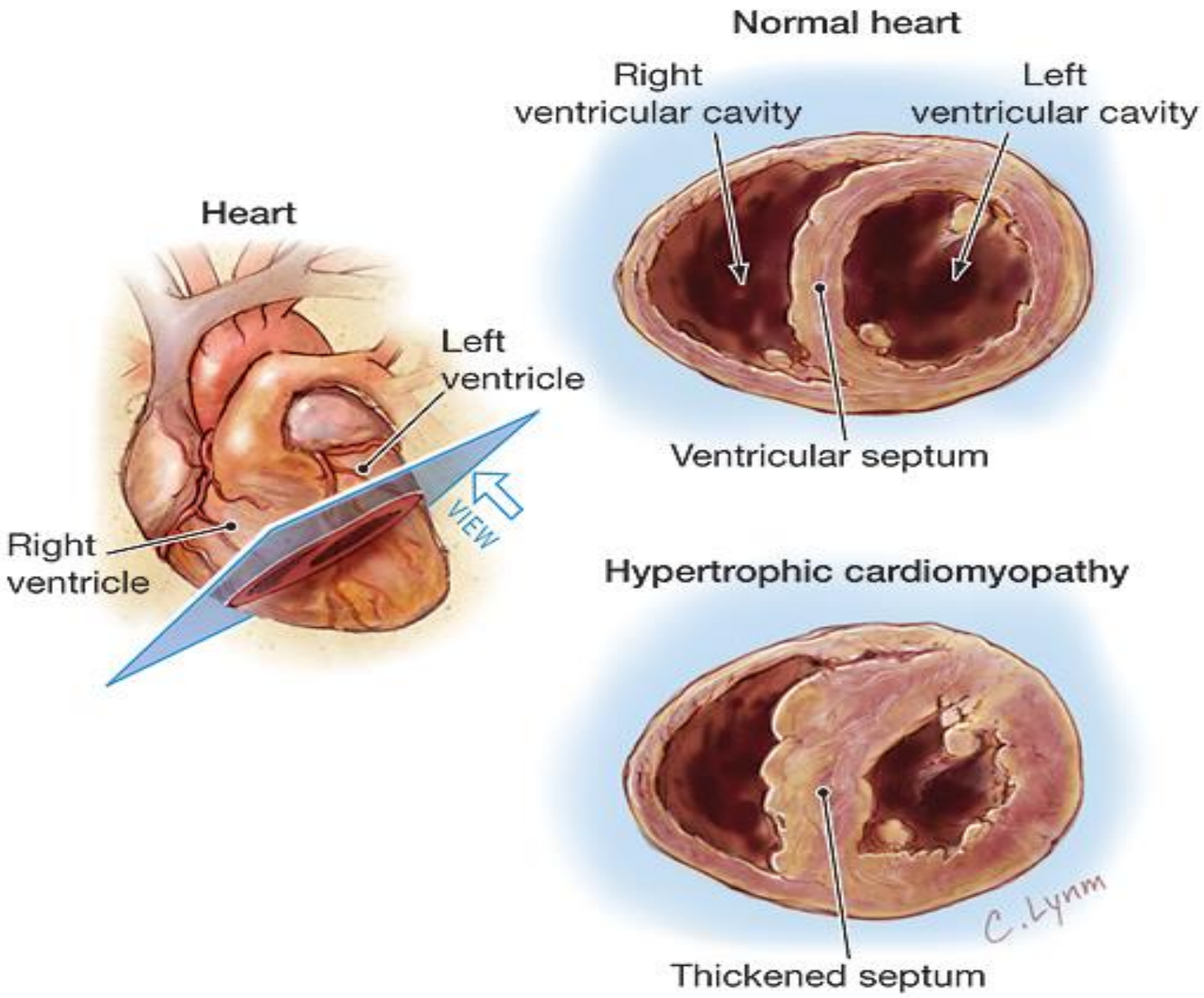
MORPHOLOGIC FEATURES

- **Grossly,**
  - the heart is enlarged and increased in weight (up to 1000 gm).
  - The most characteristic feature is **prominent dilatation** of all the four chambers giving the heart typical **globular appearance**.
  - **Thickening of the ventricular walls** even if present is masked by the ventricular dilatation
  - The endocardium is thickened and mural thrombi are often found in the ventricles and atria.
  - The cardiac valves are usually normal.

- **Microscopically:**
  - The endomyocardial biopsies or autopsy examination of the heart reveal non-specific and variable changes.
  - There may be;
    - **hypertrophy of some myocardial fibres** and **atrophy of others**.
    - degenerative changes and small areas of interstitial fibrosis
    - focal mononuclear inflammatory cell infiltrate.

2. Idiopathic Hypertrophic Cardiomyopathy

- This form of cardiomyopathy is known by various synonyms like
  - ❖Asymmetrical hypertrophy
  - ❖Hypertrophic subaortic stenosis
  - ❖Teare's disease.
- The disease occurs more frequently between the age of 25 and 50 years.
- It is often asymptomatic but becomes symptomatic due to heavy physical activity causing
  a) dyspnoea,
  b) angina,
  c) congestive heart failure and
  d) even sudden death


Normal heart
Right ventricular cavity
Left ventricular cavity
Ventricular septum
Heart
Left ventricle
Right ventricle
VIEW
Hypertrophic cardiomyopathy
C. Lynn
Thickened septum

Etiologic factors

i) **Autosomal dominant** inheritance of the disease is available in about half the cases suggesting genetic factors in its causation.

ii) **Inherited mutations in genes encoding for sarcomere proteins** have been reported in much larger number of cases of hypertrophic cardiomyopathy than those of dilated cardiomyopathy.

iii) **Other contributory factors are**:

- increased circulating level of catecholamines,
- myocardial ischaemia as a result of thickened vasculature of the myocardium
- abnormally increased fibrous tissue in the myocardium due to hypertrophy.

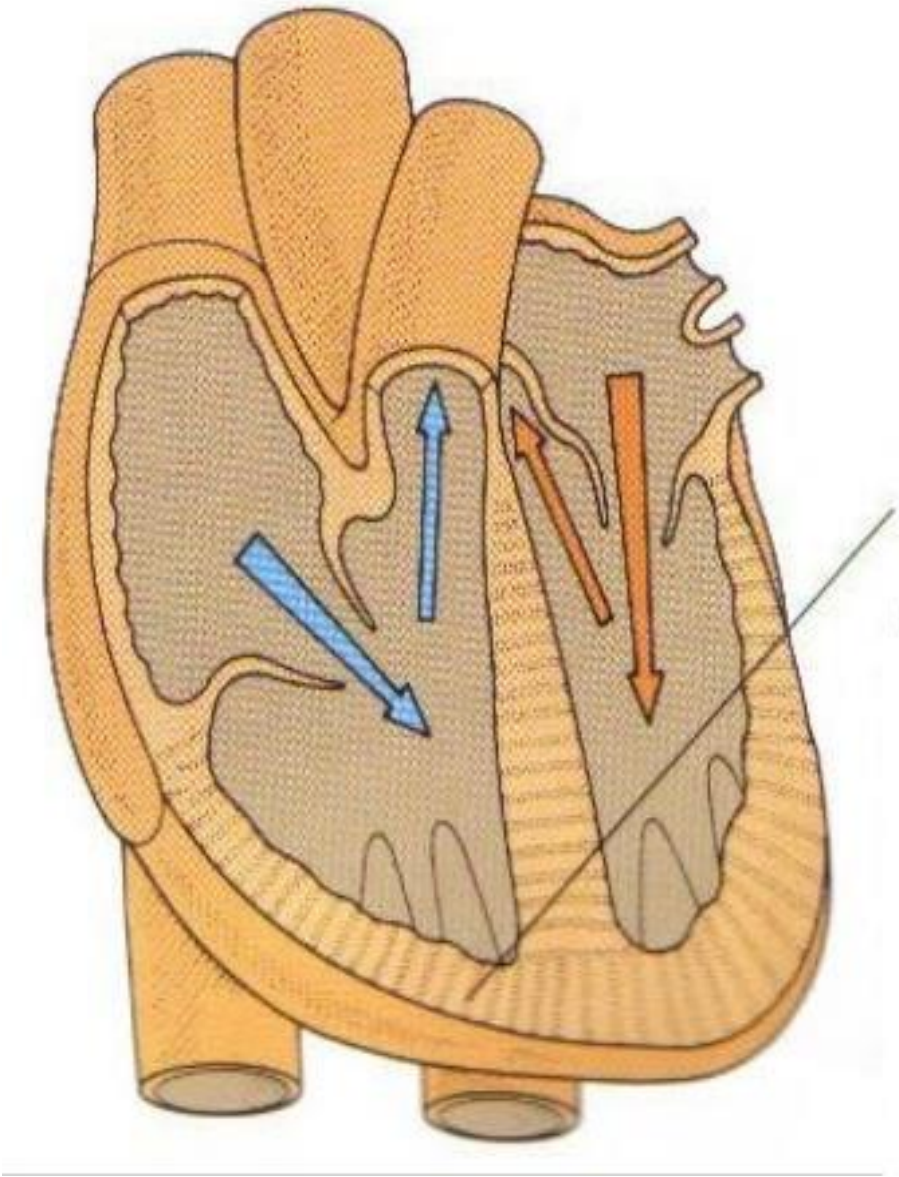
MORPHOLOGIC FEATURES

- **Grossly;**
  - ❖cardiac enlargement,
  - ❖increase in weight,
  - ❖normal or small ventricular cavities,
  - ❖myocardial hypertrophy- which is typically **asymmetrical** and affects the interventricular septum more than the free walls of the ventricles

- **Microscopically**
  - myocardial **cell disorganisation** in the ventricular septum(classical feature).
  - The bundles of myocardial fibres are **irregularly and haphazardly arranged** rather than the usual parallel pattern and are separated by bands of interstitial fibrous tissue.
  - The individual muscle cells show **hypertroph**y and large **prominent nuclei**.

3. Idiopathic Restrictive (Obliterative or Infiltrative) Cardiomyopathy

- This form of cardiomyopathy is characterised by restriction in ventricular filling due to reduction in the volume of the ventricles.
- The common feature in this heterogeneous group of conditions producing restrictive cardiomyopathy is abnormal diastolic function



Restrictive Cardiomyopathy

Rigid ventricular wall

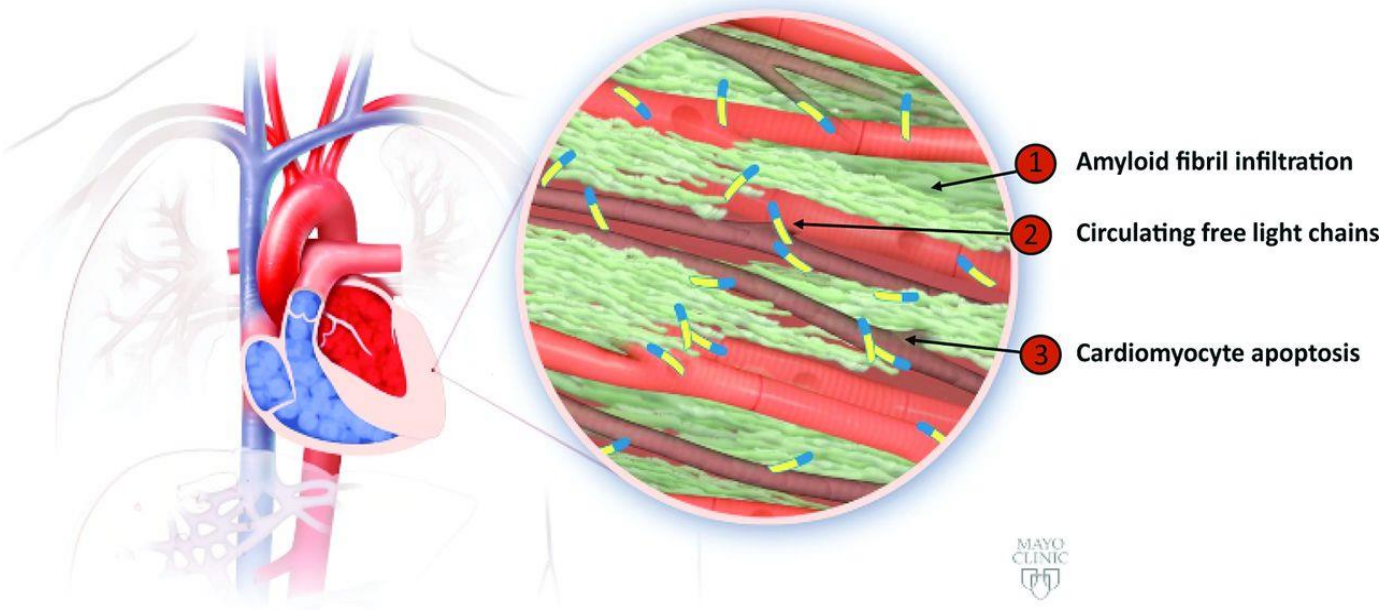
- Poor ventricular compliance is major abnormality in restrictive cardiomyopathies, and inadequate filling of the ventricular cavities occurs during diastole and results in clinical manifestations

Types of Restrictive cardiomyopathy

a) Cardiac amyloidosis
b) Endocardial fibroelastosis
c) Endomyocardial fibrosis
d) Löeffler's endocarditis (Fibroplastic parietal endocarditis with peripheral blood eosinophilia)
e) Other forms of restrictive cardiomyopathy.

I) CARDIAC AMYLOIDOSIS

- Amyloidosis of the heart may occur in any form of systemic amyloidosis or may occur as isolated organ amyloidosis in amyloid of aging and result in subendocardial deposits



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II) ENDOCARDIAL FIBROELASTOSIS

- unusual and uncommon form of heart disease occurring predominantly in **infants and children under 2 years** of age and less often in adults.
- The **infantile form** is clinically characterised by
  - ❖sudden breathlessness,
  - ❖cyanosis,
  - ❖cardiac failure and
  - ❖death
- whereas the symptoms in the **adult form** last for longer duration

ENDOCARDIAL FIBROELASTOSIS

- This condition has been called
  - fetal endocarditis,
  - endocardial fibrosis,
  - prenatal fibroelastosis,
  - elastic tissue hyperplasia, and
  - endocardial sclerosis.

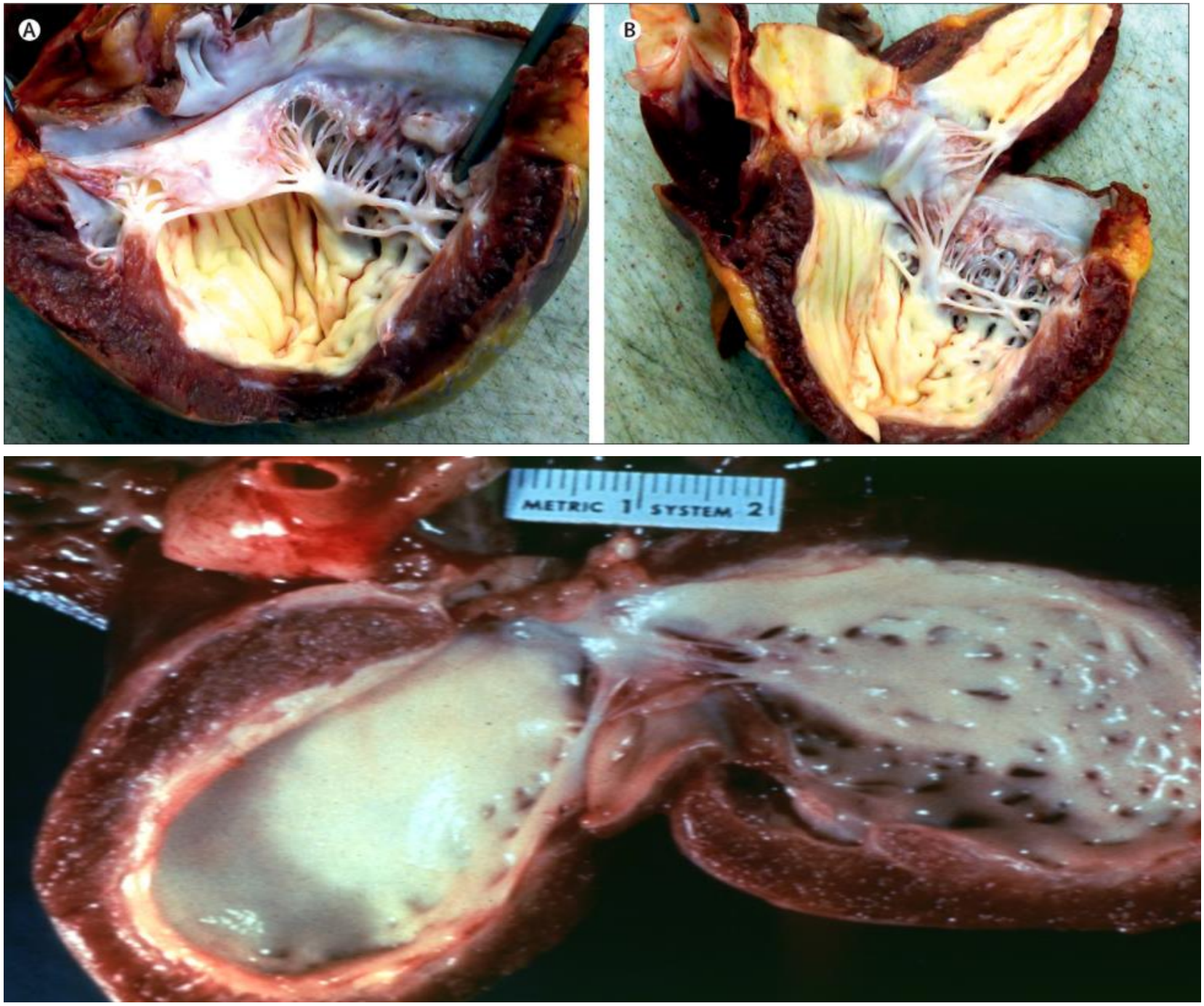
ETIOLOGY

- The etiology of the condition remains obscure. However, a number of theories have been proposed.
  - The infantile form is believed to be **congenital in origin** occurring due to the effect of intrauterine endocardial anoxia, while adult form may be induced by anoxia-causing lesions such as anomalous coronary arteries, metabolic derangements influencing myocardial function etc.

- **haemodynamic pressure overload** such as in congenital septal defects and coarctation of the aorta
- an expression of **genetic disorder** as noticed in twins, triplets and siblings.
- a form of **connective tissue disorder**
- **Certain factors causing myocardial injury** may initiate the endocardial disease such as in thiamine deficiency (beri-beri heart disease) or from preceding idiopathic myocarditis.
- **Lymphatic obstruction** of the heart has been suggested by some as the causative mechanism.

MORPHOLOGIC FEATURES

- **Grossly,**
  - The characteristic feature is the **diffuse or patchy, rigid, pearly-white thickening** of the mural endocardium
  - In decreasing frequency;
    - Left ventricle is predominantly involved, then
    - left atrium,
    - right ventricle and
    - right atrium
    - left heart valves involvement,
    - Presences of mural thrombi.
  - Enlargement of the heart is present and is mainly due to left ventricular hypertrophy but the volume of the chamber is decreased


A
B
METRIC 1 SYSTEM 2

- **Microscopically,**
  - the typical finding is the proliferation of the collagen and elastic tissue (**fibroelastosis**) comprising the thickened endocardium.
  - The fibroelastosis generally **does not extend** into the subjacent myocardium.
  - The lesion is **devoid of inflammatory cells**.

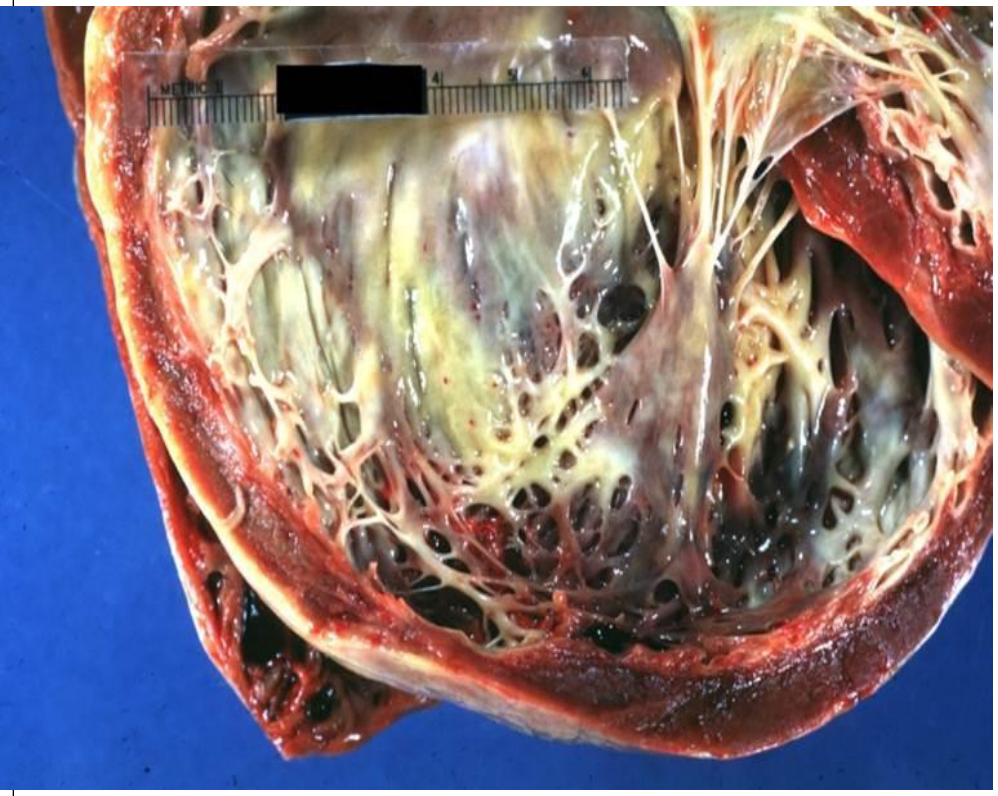
III) ENDOMYOCARDIAL FIBROSIS

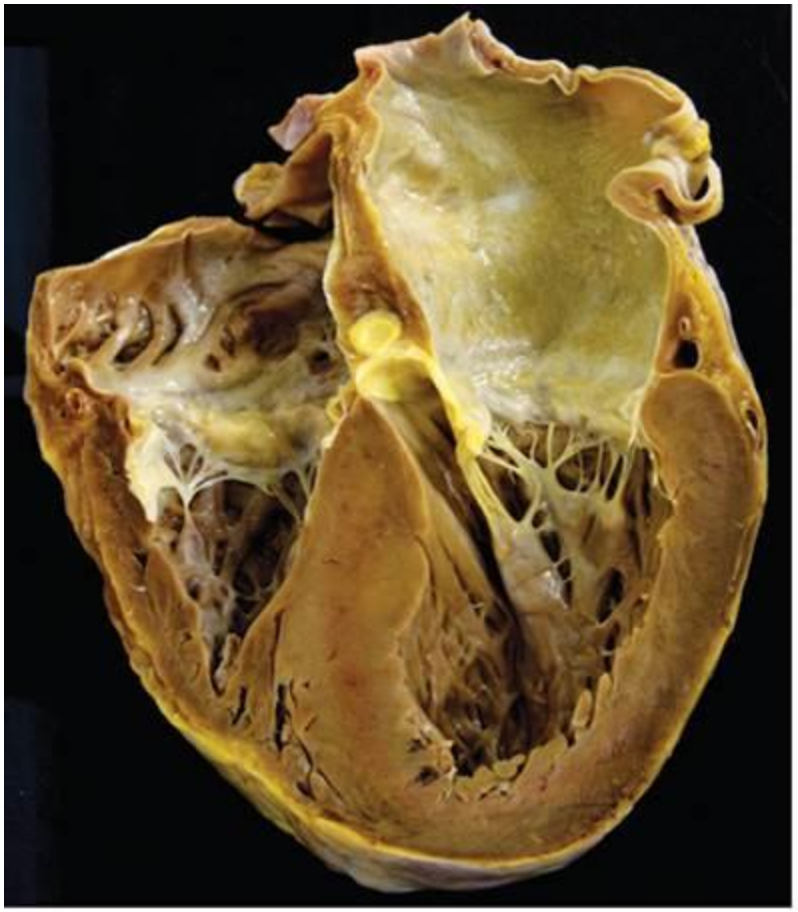
- This form of restrictive cardiomyopathy is a tropical condition prevalent in Africa, especially in Uganda and Nigeria, but some cases occur in South India, Sri Lanka, Malaysia and tropical South America.
- It is seen in children and young adults.
- The clinical manifestations consist of congestive heart failure of unknown cause just as in adult variety of endocardial fibroelastosis.
- The etiology of the condition remains obscure but the geographic distribution suggests the role of certain factors like malnutrition, viral infections and heavy consumption of banana (rich in serotonin).

MORPHOLOGIC FEATURES

- **Grossly,**
  - Its characterised by **fibrous scarring** of the ventricular endocardium that extends to involve the inner third of the myocardium.
  - The **atrioventricular valve** leaflets are often affected but the semilunar valves are uninvolved.
  - Mural thrombi may be present.
  - The heart may be **normalsized or hypertrophied** but the volume of the affected chambers is diminished due to fibrous scarring.

- **Microscopically**
  - the endocardium and parts of inner third of the myocardium show **destruction of normal tissue and replacement by fibrous tissue**.
  - The condition differs from endocardial fibroelastosis in having mononuclear inflammatory cell infiltrate and lacking in elastic tissue.
  - The superficial layer may show dense **hyalinised** connective tissue and even **calcification.**

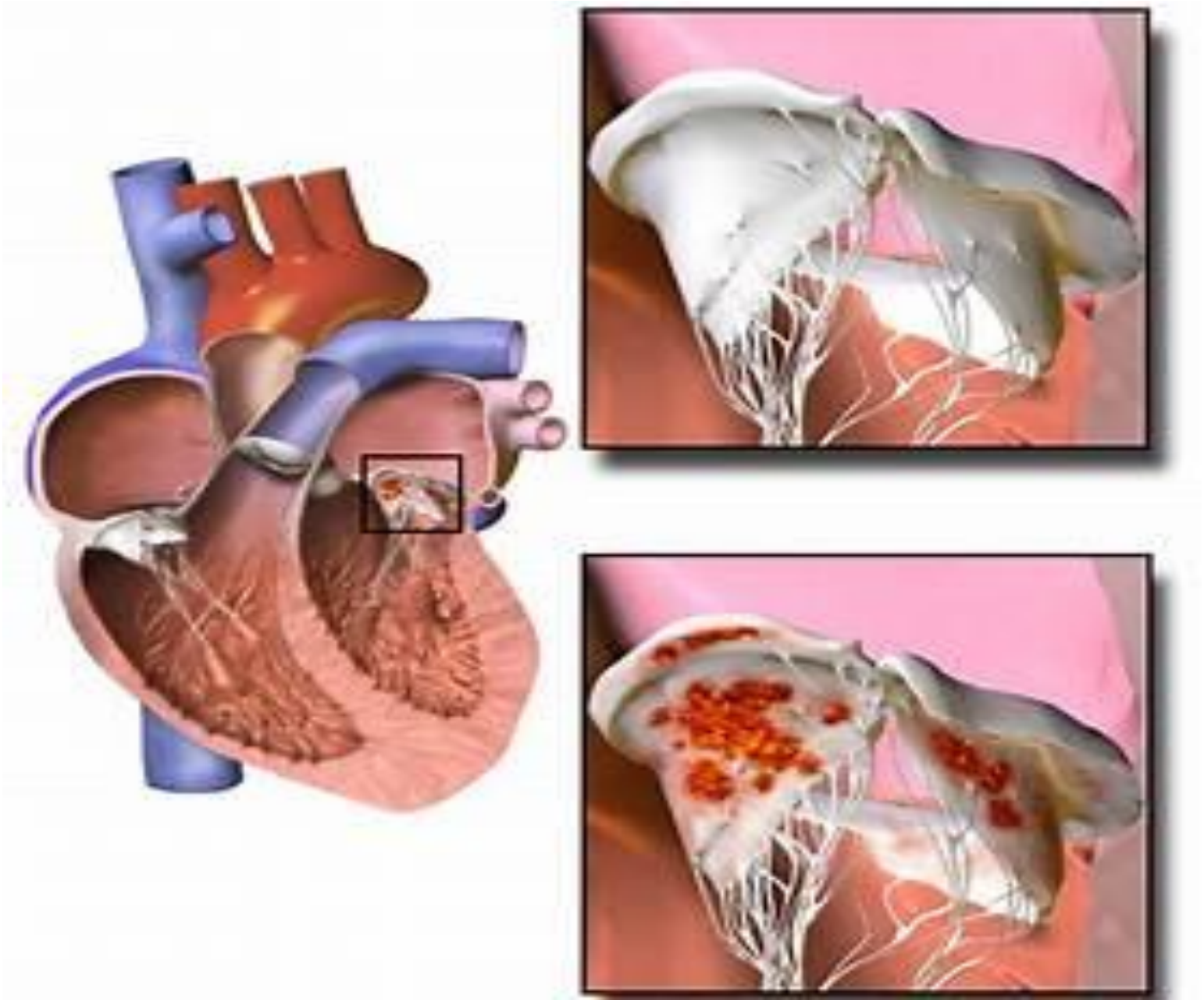




Source: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine, 18th Edition*: www.accessmedicine.com

IV) LÖEFFLER'S ENDOCARDITIS

- Also known as'fibroplastic parietal endocarditis with peripheral blood eosinophilia',
- Its considered by some as a variant of the entity described above, endomyocardial fibrosis.
- However, it differs from the latter in following respects:
  a) There is generally a peripheral blood eosinophilic leucocytosis.
  b) The inflammatory infiltrate in the endocardium and in the part of affected myocardium chiefly consists of eosinophils.
  c) The condition has a worse prognosis.



B. SECONDARY CARDIOMYOPATHY

- This is a group of myocardial diseases of known etiologies or having clinical associations
- The main entities included:

  1. **Nutritional disorders** e.g. chronic alcoholism, thiamine deficiency causing beri-beri heart disease (Chapter 9).

  2. **Toxic chemicals** e.g. cobalt, arsenic, lithium and hydrocarbons.

  3. **Drugs** e.g. cyclophosphamide, adriamycin, catecholamines.

  4. **Metabolic diseases** e.g. amyloidosis, haemochromatosis, glycogen storage diseases, hypo-and hyperthyroidism, hypoand hyperkalaemia.

5. **Neuromuscular diseases** e.g. Friedreich's ataxia, muscular dystrophies.

6. **Infiltrations** e.g. from leukaemia and carcinoma.

7. **Connective tissue diseases** e.g. rheumatoid arthritis, systemic sclerosis, dermatomyositis, lupus erythematosus.