RESTRICTIVE CARDIOMYOPATHY

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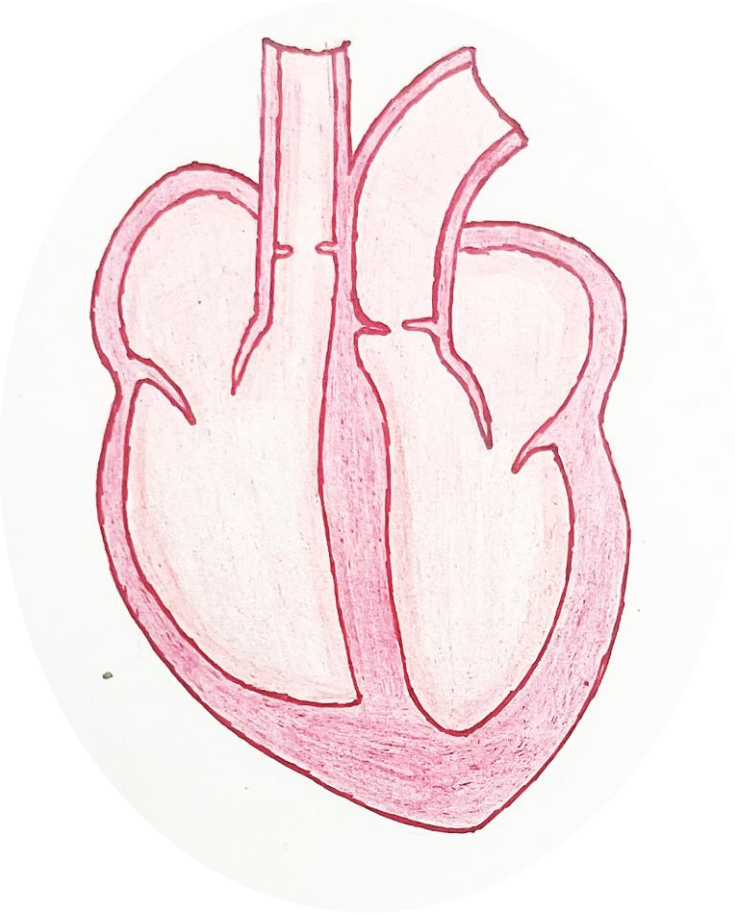
TIRUPATHI

CARDIOMYOPATHY

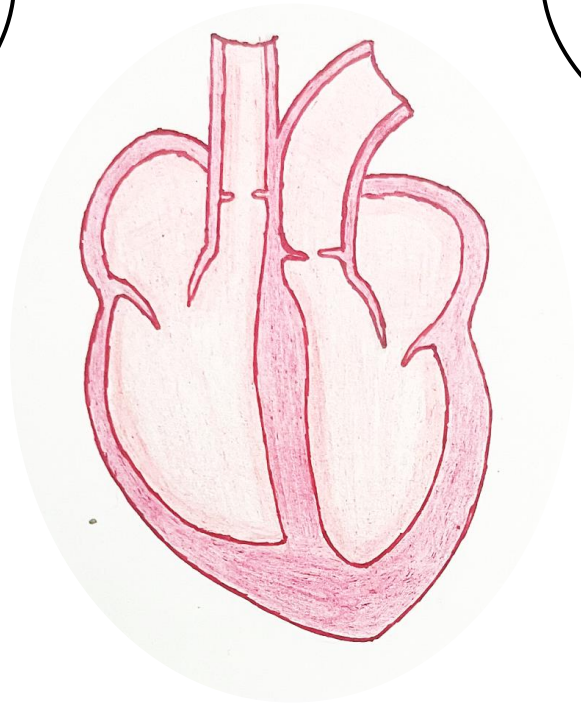
- Cardiomyopathies are a heterogeneous group of diseases, resulting from abnormality in myocardium associated with abnormalities in mechanical and/or electrical dysfunction that usually exhibit inappropriate ventricular hypertrophy or dilatation



CARDIOMYOPATHY

Secondary cardiomyopathy

Myocardial involvement as a component of a systemic or multiorgan disorder (e.g. hemochromatosis, amyloidosis)



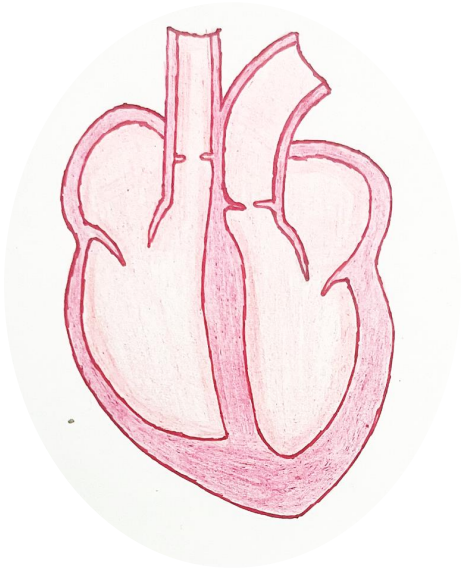
Primary cardiomyopathy

Primarily involving heart muscle

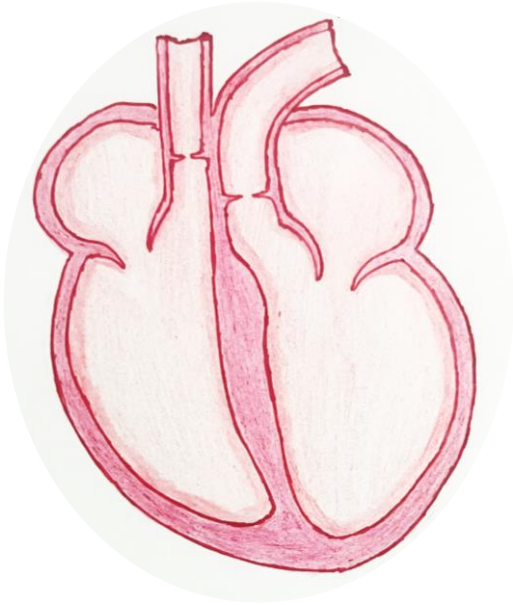
CARDIOMYOPATHY

- Types of cardiomyopathies are determined by clinical, functional and pathologic patterns

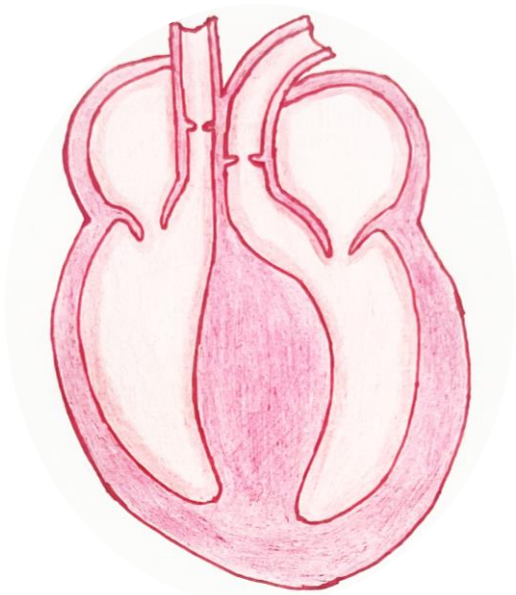
Normal heart



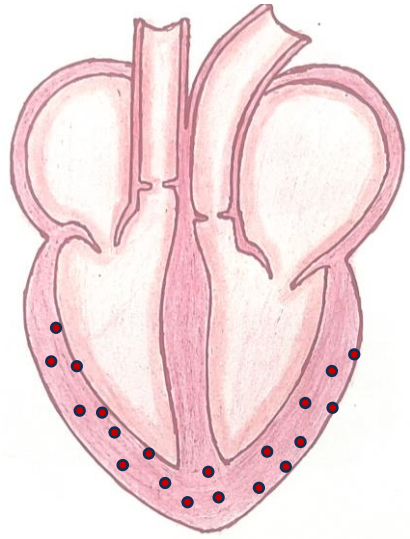
Dilated cardiomyopathy



Hypertrophic cardiomyopathy



Restrictive cardiomyopathy



Among the three major patterns, DCM is most common (90% of cases), and restrictive cardiomyopathy is the least frequent

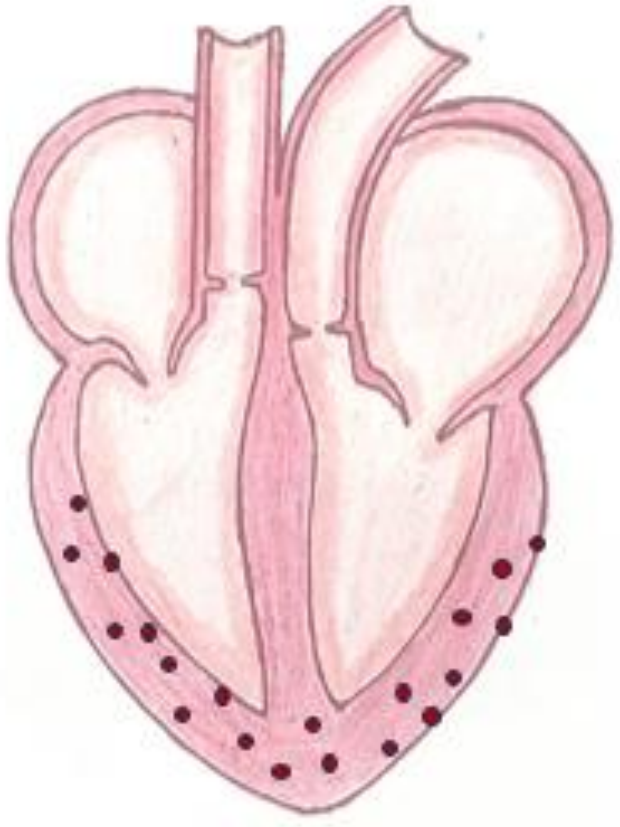
CARDIOMYOPATHY

Functional pattern	Left ventricular ejection fraction	Mechanism of heart failure	Causes of phenotype
Dilated	< 40%	Impairment of contractility (systolic dysfunction)	Genetic, alcohol, peripartum, myocarditis, hemochromatosis, chronic anemia, doxorubicin (Adriamycin), chagas disease, idiopathic
Hypertrophic	50 – 80%	Impairment of compliance (Diastolic dysfunction)	Genetic, Friedreich ataxia, storage diseases, infants of diabetic mother
Restrictive	45 – 90%	Impairment of compliance (Diastolic dysfunction)	Amyloidosis, radiation induced fibrosis, idiopathic

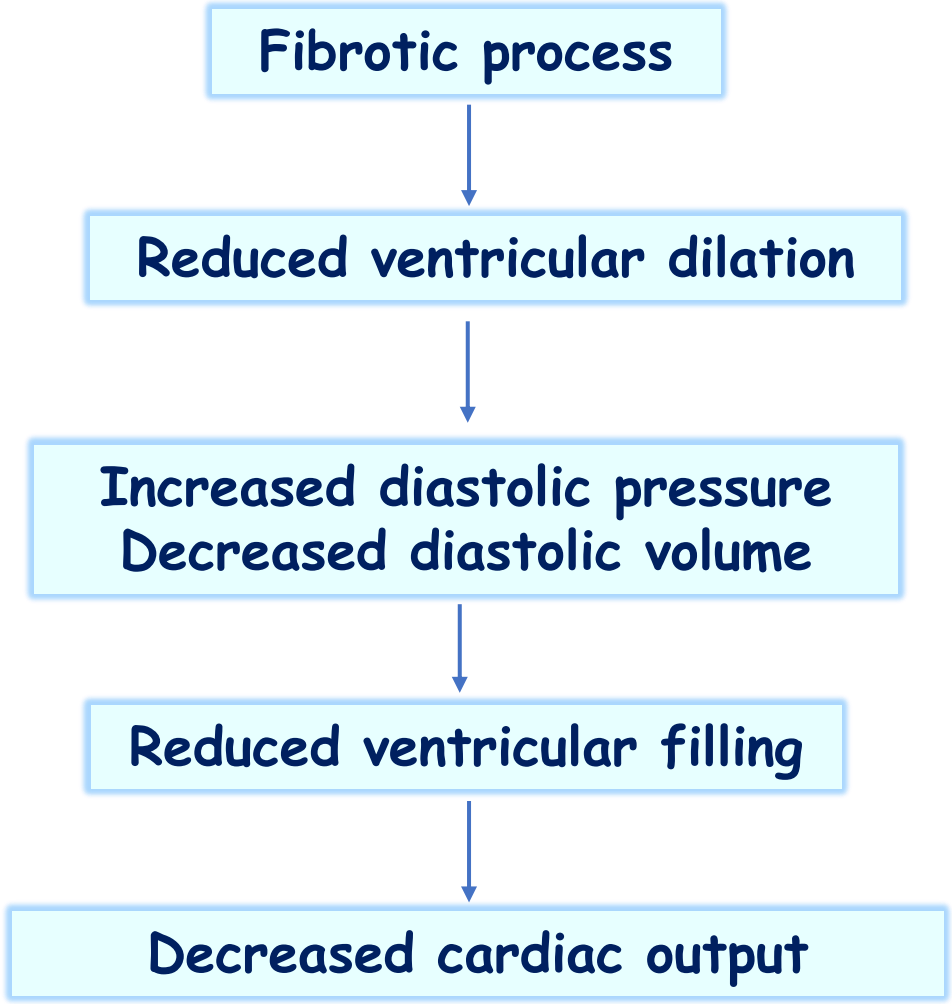
RESTRICTIVE CARDIOMYOPATHY

- Primary disorder of heart muscle characterized by decrease in ventricular compliance resulting in impaired ventricular filling during diastole

- Contractile (systolic) function of the left ventricle is usually unaffected

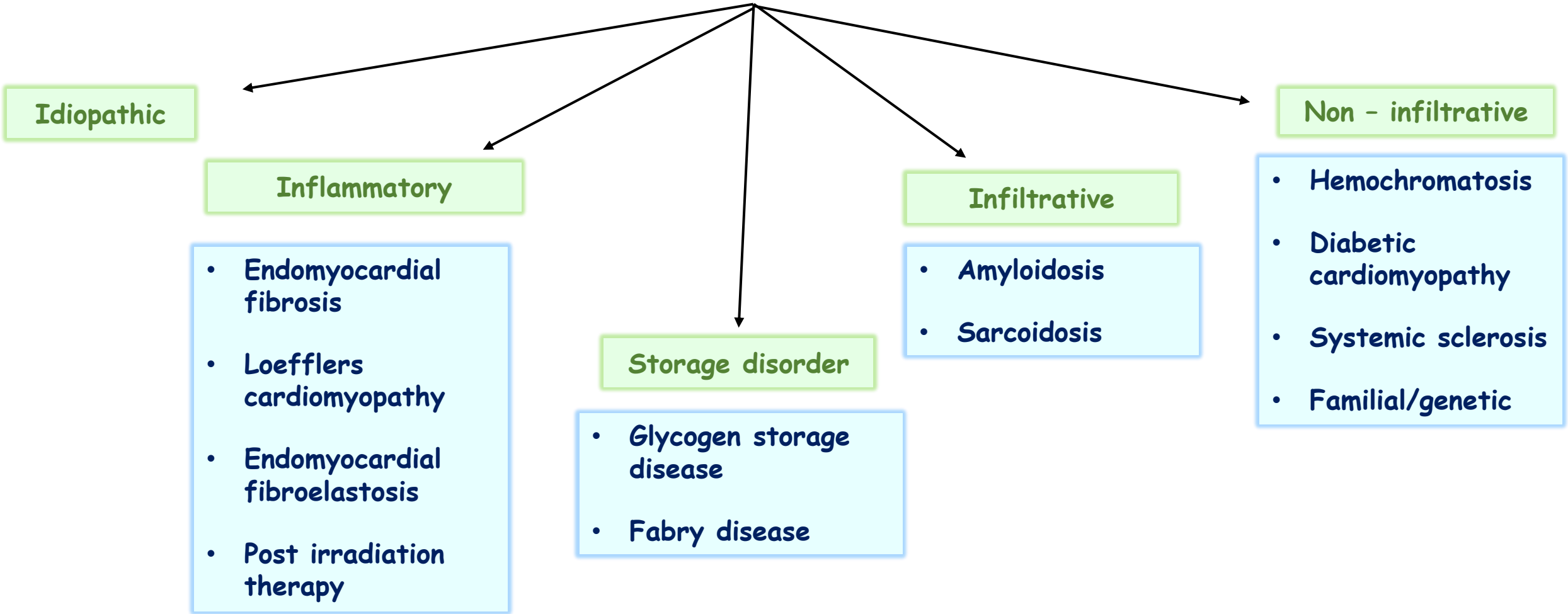


RESTRICTIVE CARDIOMYOPATHY



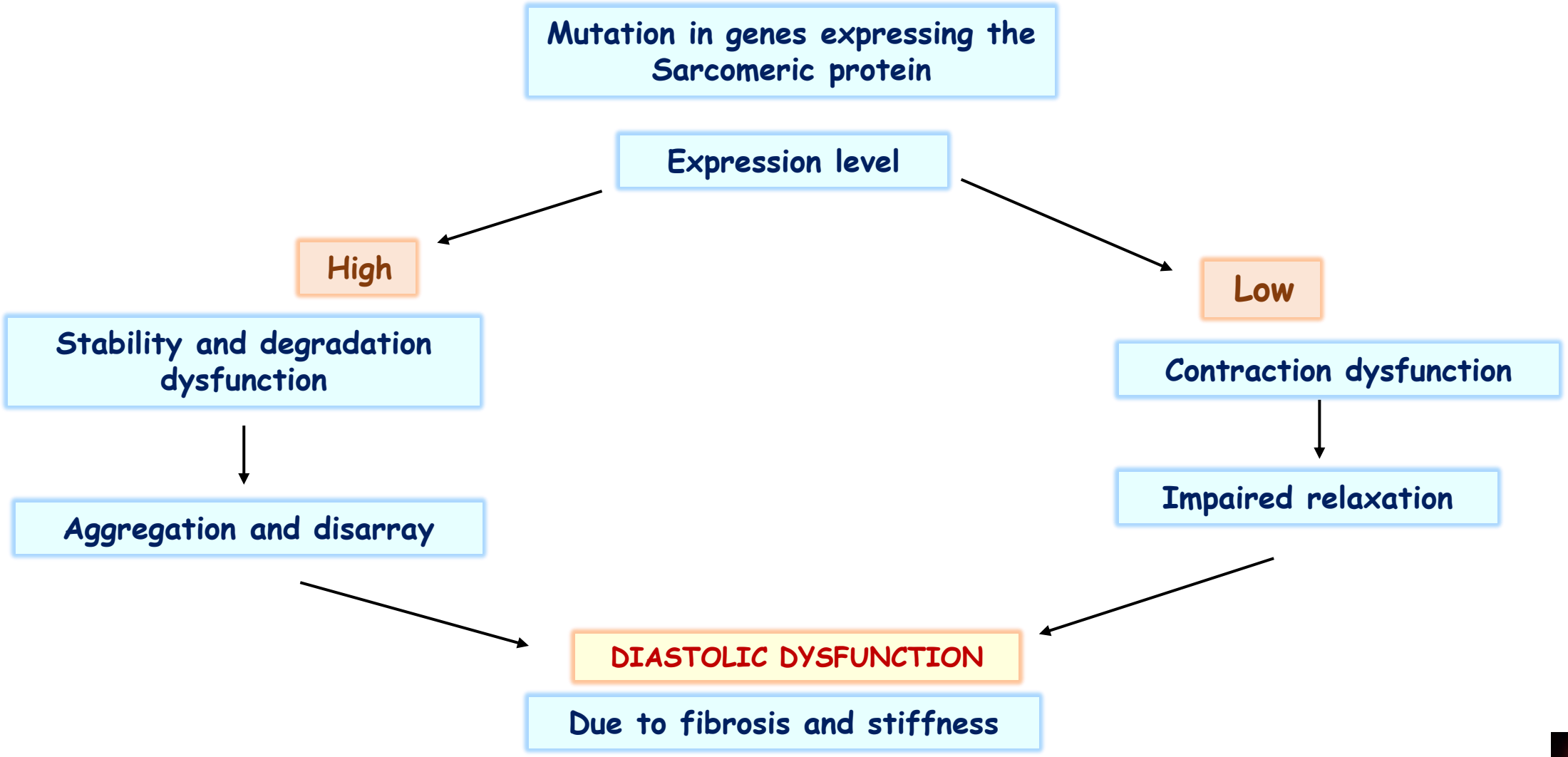
RESTRICTIVE CARDIOMYOPATHY

Etiopathogenesis

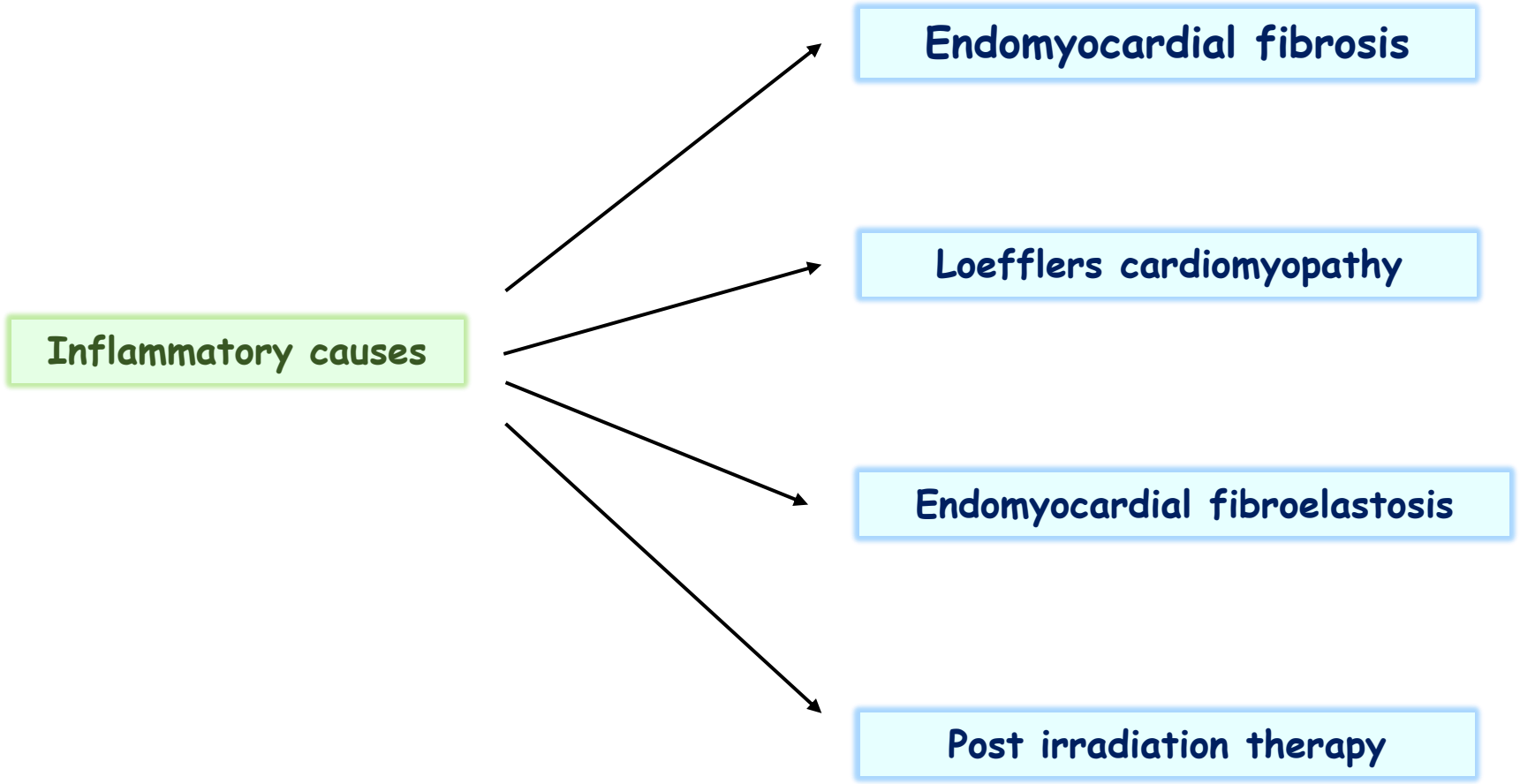


RESTRICTIVE CARDIOMYOPATHY

Genetic causes



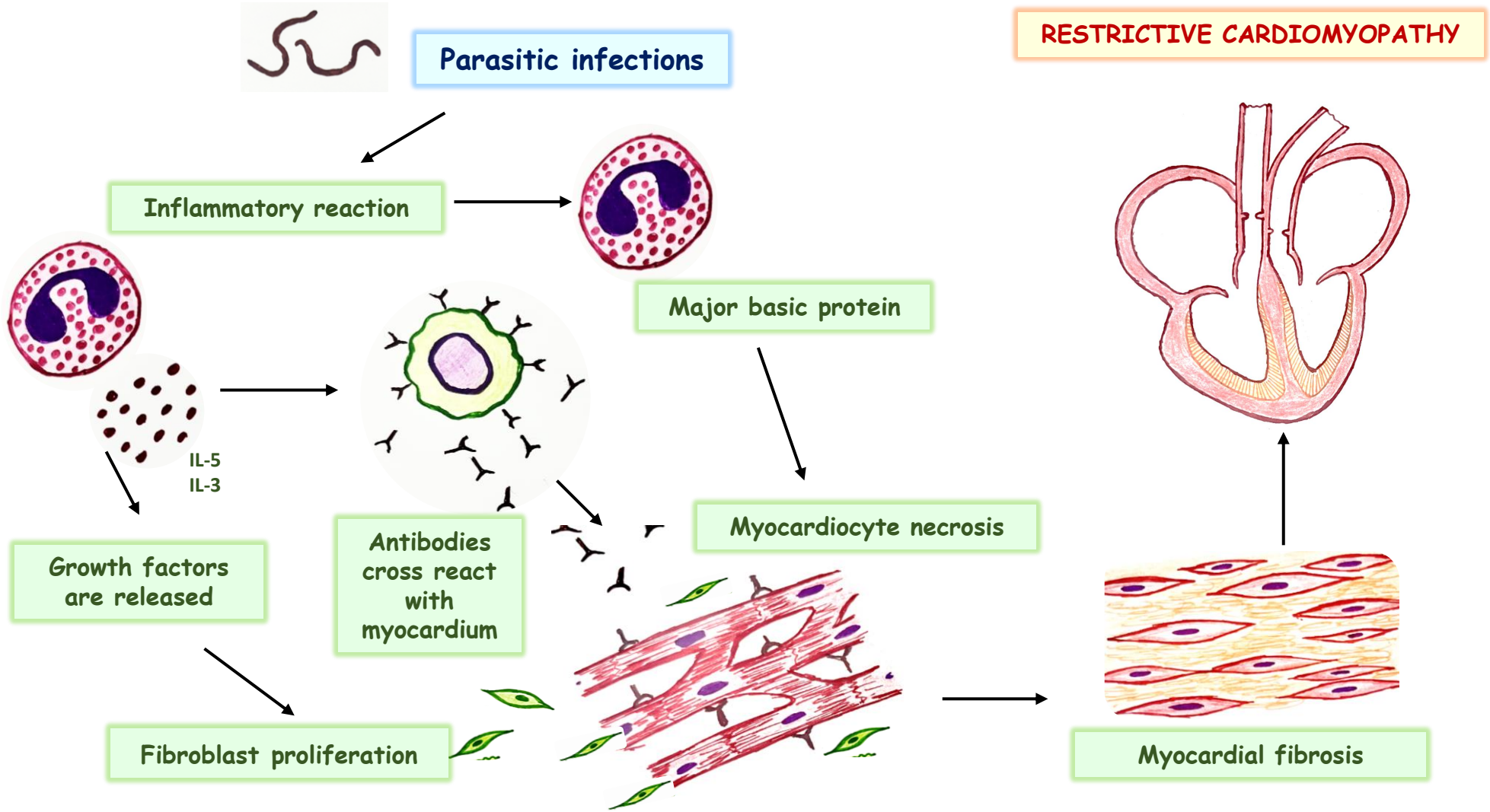
RESTRICTIVE CARDIOMYOPATHY



RESTRICTIVE CARDIOMYOPATHY

Endomyocardial fibrosis

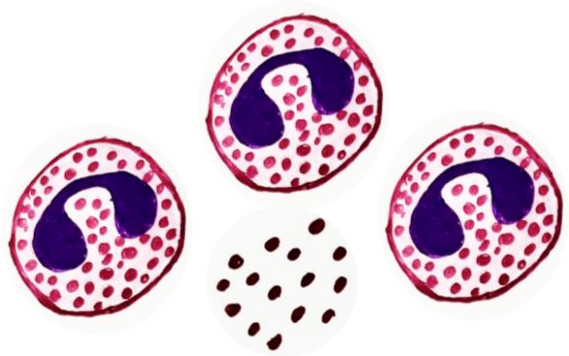
Commonly seen in children and young adults of Africa and other tropical areas



RESTRICTIVE CARDIOMYOPATHY

Loeffler endomyocarditis

Primary eosinophilia
Chronic eosinophilic leukemia or hypereosinophilc syndrome



Secondary eosinophilia
Parasitic infections or allergic conditions

Peripheral eosinophilia and eosinophilic infiltrates in multiple organs, including the heart

Major basic protein from eosinophils

Myocardiocyte necrosis

FIBROSIS

THROMBUS FORMATION ON THE NECROTIC SURFACE

RESTRICTIVE CARDIOMYOPATHY

Endocardial fibroelastosis

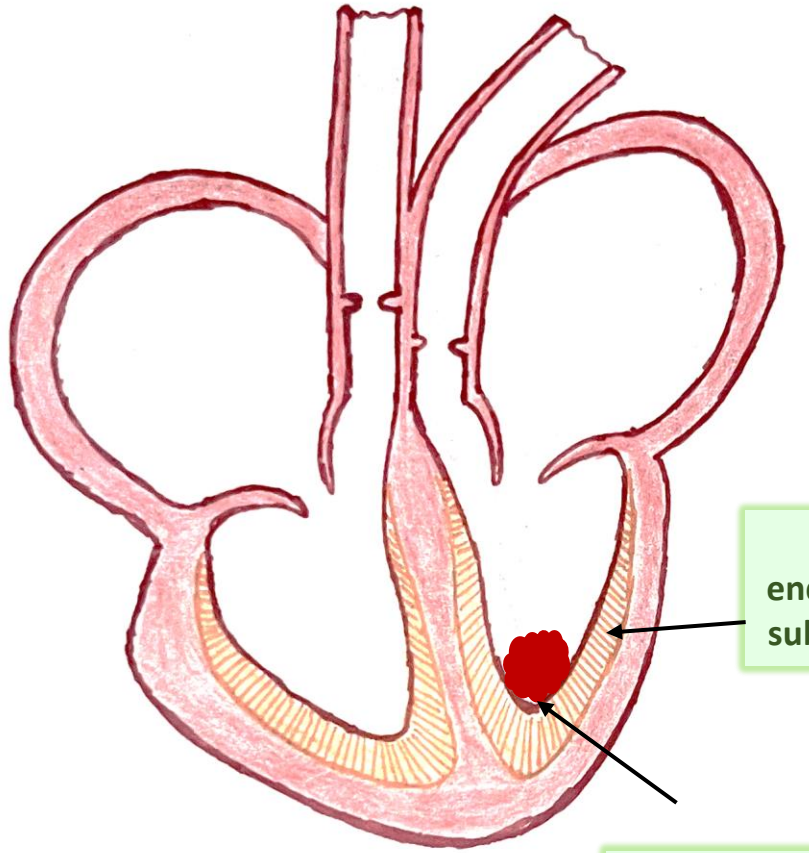
- Uncommon heart disease characterized by fibroelastic thickening that typically involves the left ventricular endocardium
- Most common in the first 2 years of life
- Accompanied by aortic valve obstruction or other congenital cardiac anomalies
- Represent a common morphologic end-point of several different insults including viral infections (e.g., intrauterine exposure to mumps) or mutations in the gene for tafazzin, which affects mitochondrial inner membrane integrity
- Diffuse involvement may be responsible for rapid and progressive cardiac decompensation and death

RESTRICTIVE CARDIOMYOPATHY

Endomyocardial fibrosis

Morphology

- Characterized by fibrosis of the ventricular endocardium and subendocardium that extends from the apex upward, often eventually involving the tricuspid and mitral valves
- The fibrous tissue markedly diminishes the volume and compliance of affected chambers and so causes a restrictive functional defect
- Ventricular mural thrombi may develop



RESTRICTIVE CARDIOMYOPATHY

Radiation

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Release of reactive oxygen species

↓

Myocardiocyte damage

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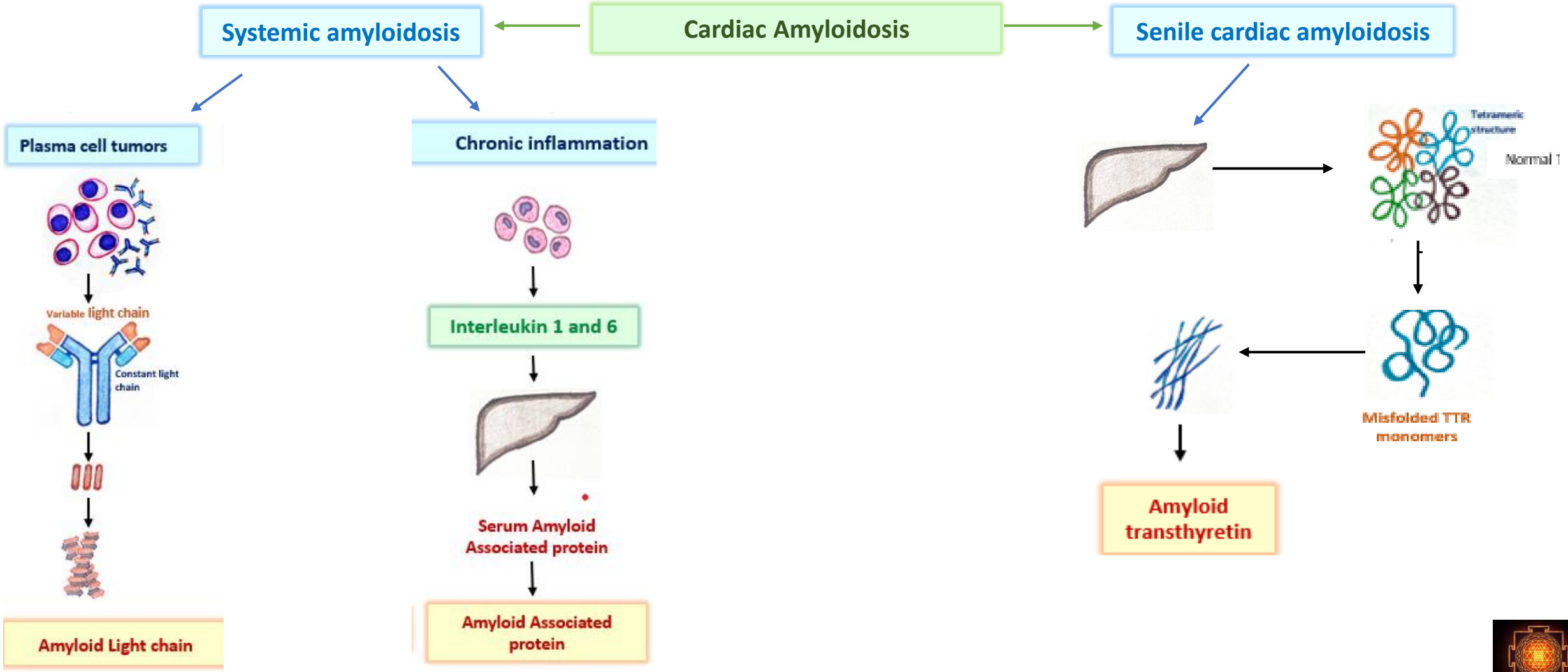
Myocardial fibrosis

RESTRICTIVE CARDIOMYOPATHY

Amyloidosis

- Amyloidosis is an important form of restrictive cardiomyopathy resulting from the extracellular accumulation of protein fibrils that form insoluble β-pleated sheets

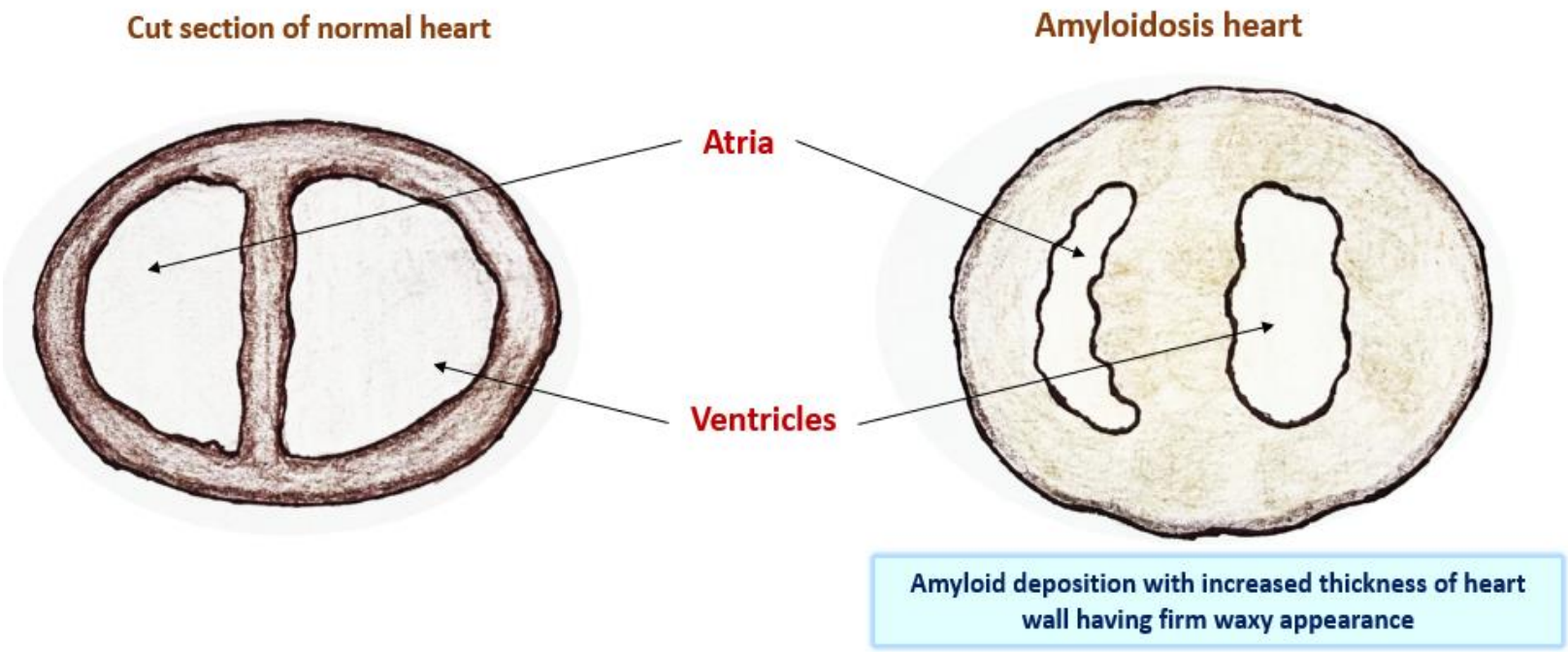


RESTRICTIVE CARDIOMYOPATHY

Amyloidosis

Morphology

- Heart varies in consistency from normal to firm and rubbery
- Chambers are usually of normal size but can be dilated and have thickened walls
- Small, semitranslucent nodules resembling drips of wax may be seen on the atrial endocardial surface, particularly on the left

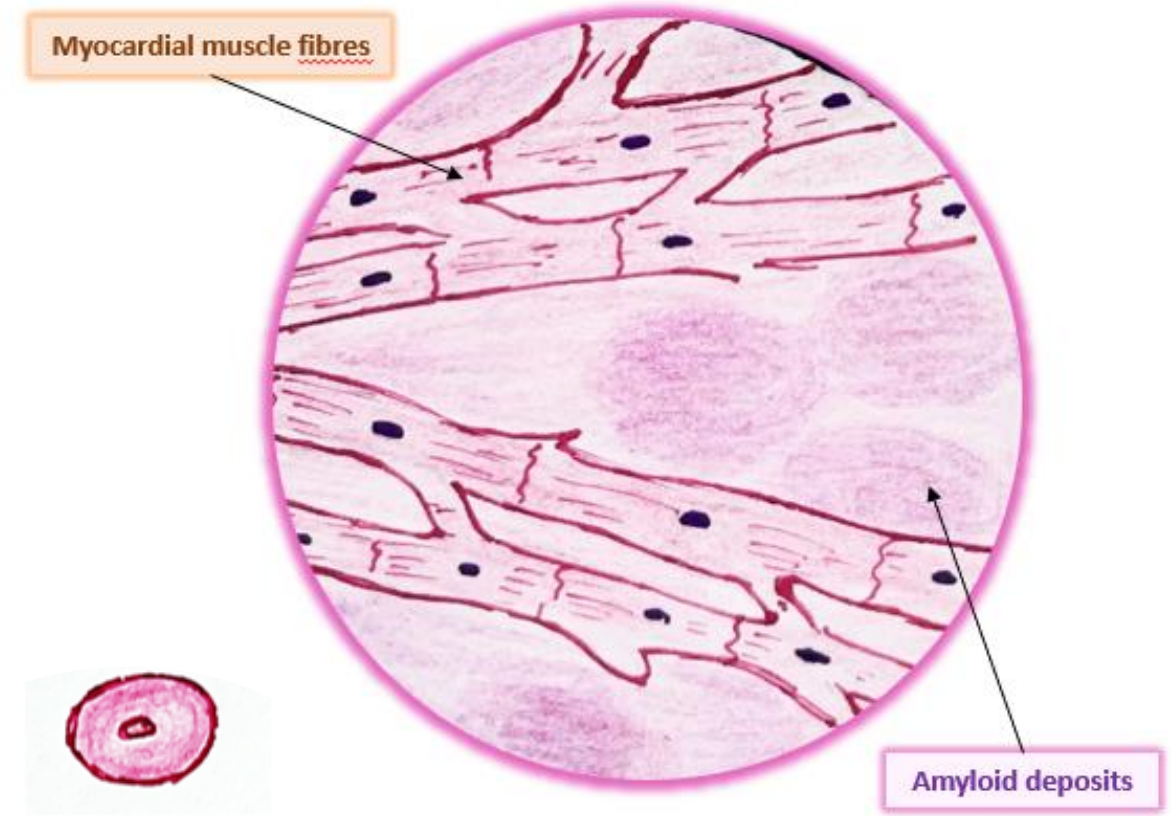


RESTRICTIVE CARDIOMYOPATHY

Amyloidosis

- Histologically, hyaline eosinophilic deposits of amyloid may be found in the interstitium, conduction tissue, valves, endocardium, pericardium, and small intramural coronary arteries

- Intramural arteries and arterioles may have sufficient amyloid in their walls to compress and occlude their lumens, inducing myocardial ischemia ("small-vessel disease")



Amyloidosis of blood vessels leading to ischemia

RESTRICTIVE CARDIOMYOPATHY

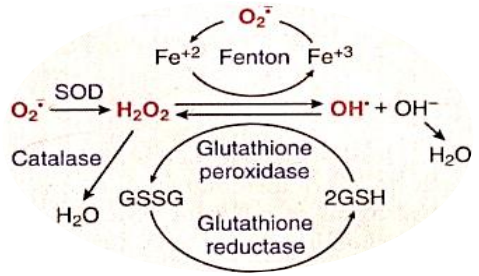
SARCOIDOSIS

- Sarcoidosis is granulomatous disorder affecting multi system but most commonly involving lungs
- Cardiac sarcoidosis is rare and constitutes 10% of cases of sarcoidosis
- Cardiac sarcoidosis involves endocardium, myocardium, and pericardium, but most frequently involve myocardium
- It involves base of the interventricular septum, hence affects conduction system
- Extensive involvement of myocardium causes restrictive cardiomyopathy affecting left ventricle.
- Right ventricle can be directly affected by sarcoidosis or as a consequence of pulmonary fibrosis, pulmonary hypertension, or left ventricular dysfunction

RESTRICTIVE CARDIOMYOPATHY

Hemochromatosis

Non transferrin bound iron (Free Fe) in myocardium



Activate fibroblasts

Proliferation and differentiation to myofibroblast

Fibrosis

RESTRICTIVE CARDIOMYOPATHY

Produces ROS via fenton's reaction

Oxidative stress

- Impaired coupling of excitation and contraction
- Impaired contraction and relaxation of myocardium
- Elevated cytoplasmic Ca 2+ levels
- Lipid peroxidation causing membrane damage including mitochondria affecting oxidative phosphorylation and ATP deficiency
- Damage to DNA and mitochondrial DNA
- Ferroptosis (Iron mediated cell death)

RESTRICTIVE CARDIOMYOPATHY

STORAGE DISORDERS

GLYCOGEN STORAGE DISEASE

Cell organelle dysfunction, enzyme deficiency and disturbed molecular transport

Infiltration of cardiac myocytes with stored substrate (storage disorders)

CARDIOMYOPATHY AND VALVULAR DYSFUNCTION

FABRYS DISEASE

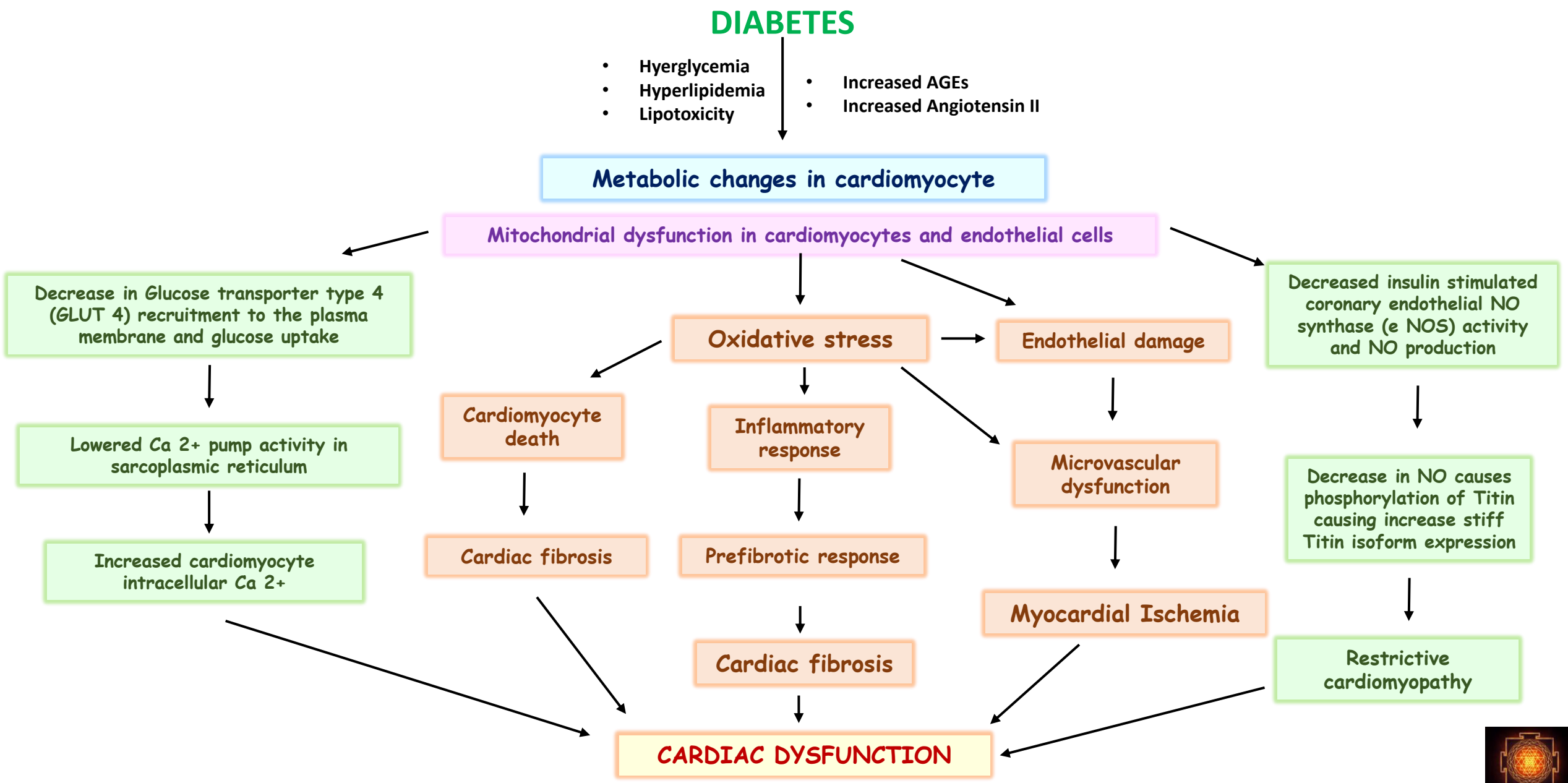
Caused by deficiency of α-galactosidase A lysosomal enzyme

Accumulation of Globotriaosylceramide (Gb3) in lysosomes of cardiomyocytes, valvular fibroblasts and conduction system

Initially LVH and papillary muscle hypertrophy

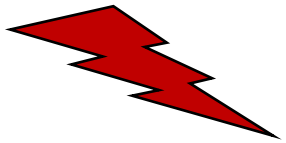
LATER DIASTOLIC DYSFUNCTION WITH RESTRICTIVE CARDIOMYOPATHY

RESTRICTIVE CARDIOMYOPATHY



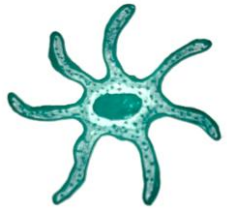
RESTRICTIVE CARDIOMYOPATHY

SYSTEMIC SCLEORSIS



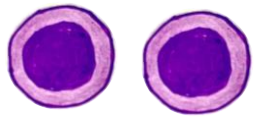
Unknown stimuli

Stimulation of APC



Antigen presenting cell

Stimulation of CD4+ T cells



Increased Growth factors

Increased cytokines

Stimulation of fibroblast activity

Excess production of collagen

- Microvascular abnormalities like concentric intimal hypertrophy of small coronary arteries leading to ischemia
- Cardiomyocyte damage and myocardial fibrosis

Myocardial pathology

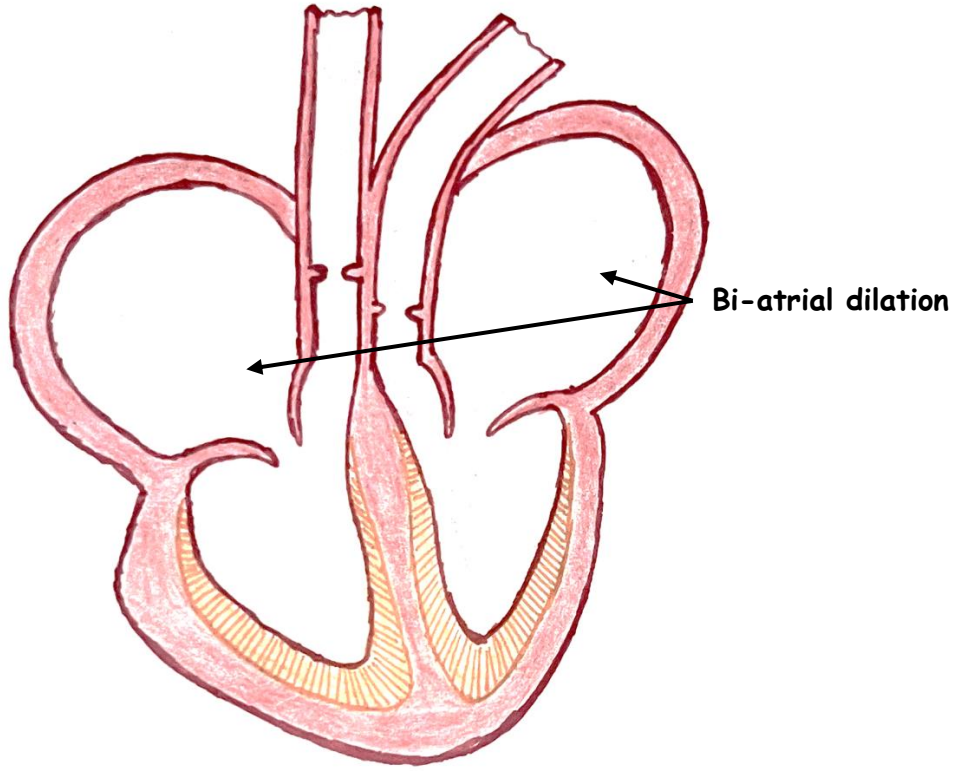
Systemic / pulmonary small vessel pathology

- Thickened intima
- Narrowed lumen
- Ischemia

RESTRICTIVE CARDIOMYOPATHY

Morphology

- Non-specific, although bi-atrial dilation is commonly observed due to restricted ventricular filling and pressure overloads
- ventricles are of approximately normal size and later diminished volume, and the myocardium is largely unremarkable
- Microscopically, there can be patchy or diffuse interstitial fibrosis, varying from minimal to extensive



RESTRICTIVE CARDIOMYOPATHY

Treatment

- Treatment of the underlying cause
- Heart transplatation

SUMMARY

RESTRICTIVE CARDIOMYOPATHY

Definition : Disorder of heart muscle causing decreased compliance resulting in impaired ventricular filling

Causes

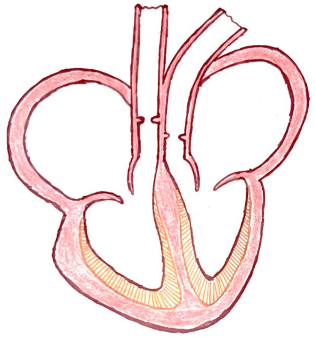
- **Idiopathic**
- **Inflammatory**
  - Endomyocardial fibrosis
  - Loefflers cardiomyopathy
  - Endomyocardial fibroelastosis
  - Post irradiation therapy
- **Storage disorder**
  - Glycogen storage disease
  - Fabry disease
- **Infiltrative**
  - Amyloidosis
  - Sarcoidosis
- **Non-infiltrative**
  - Hemochromatosis
  - Diabetic cardiomyopathy
  - Systemic sclerosis
  - Familial/genetic

Morphology

Fibrosis of ventricular endocardium, sub-endocardium and later myocardium causing diminished compliance

Bi atrial dilation and normal ventricular size

Later there can diminished volume of ventricles



Treatment

- Treatment of the underlying cause
- Heart transplatation


Thank
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