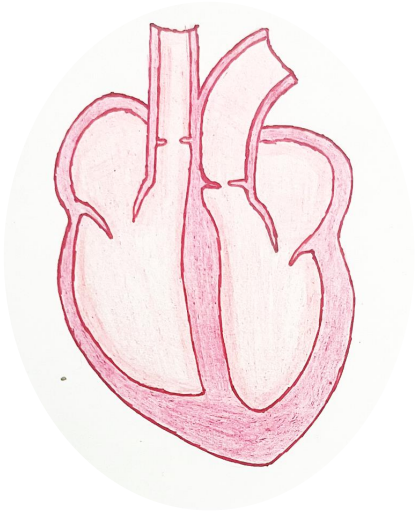
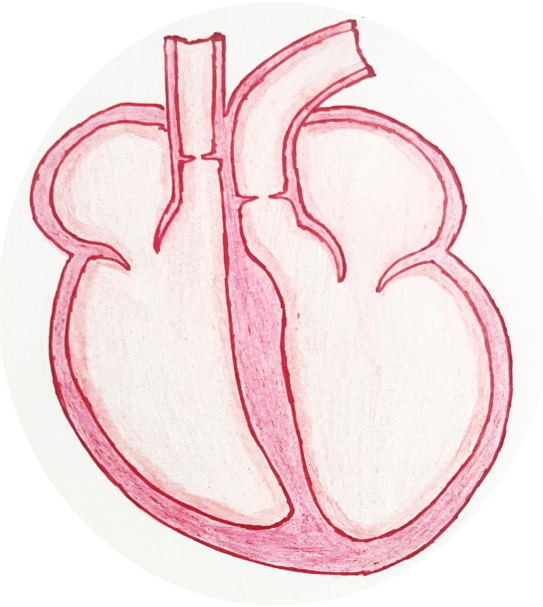


DILATED CARDIOMYOPATHY



Dr.V.Shanthi

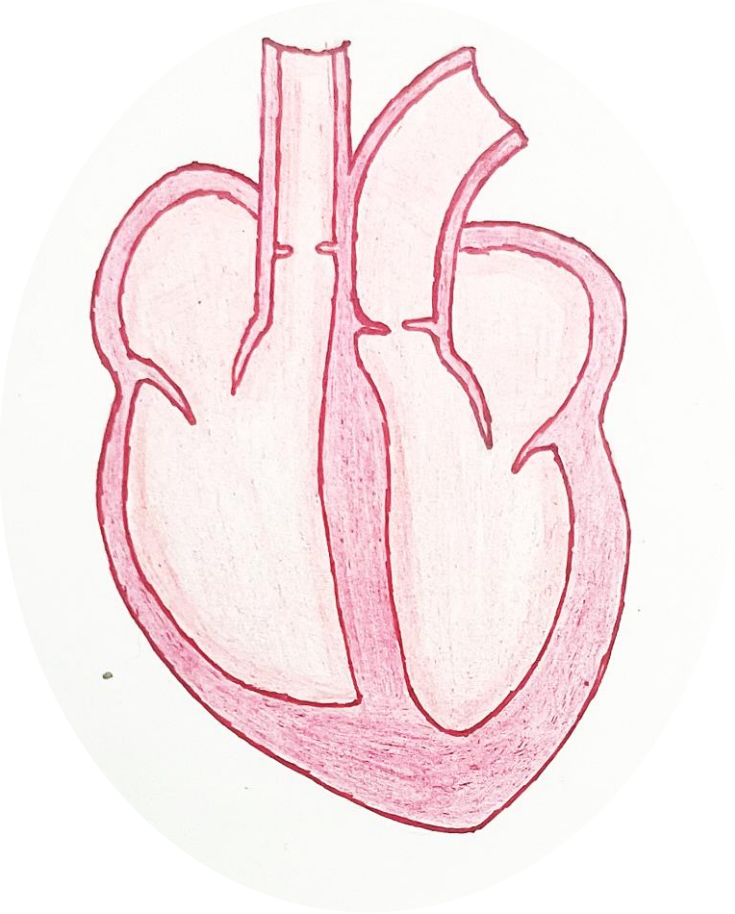
Associate Professor, Pathology

Sri Venkateswara Institute of Medical Sciences

TIRUPATHI

CARDIOMYOPATHY

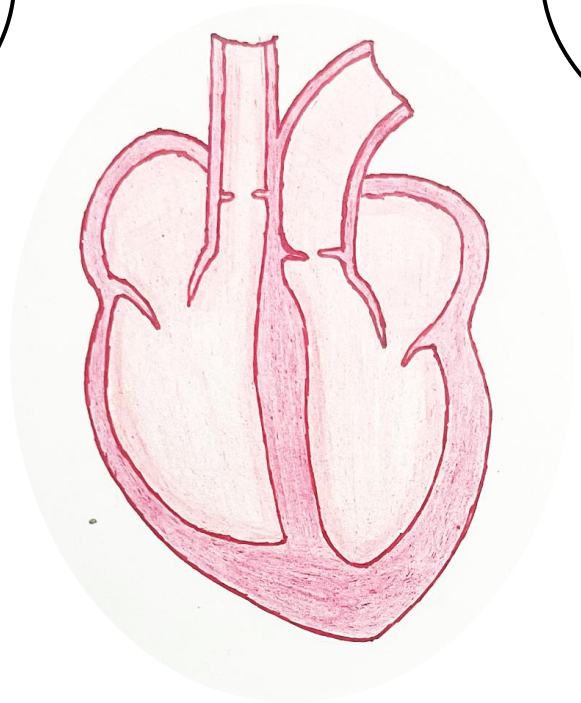
- Cardiomyopathies are a heterogeneous group of diseases, resulting from abnormality in myocardium associated with abnormalities in mechanical and/or electrical dysfunction that usually exhibit inappropriate ventricular hypertrophy or dilatation



CARDIOMYOPATHY

Secondary cardiomyopathy

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



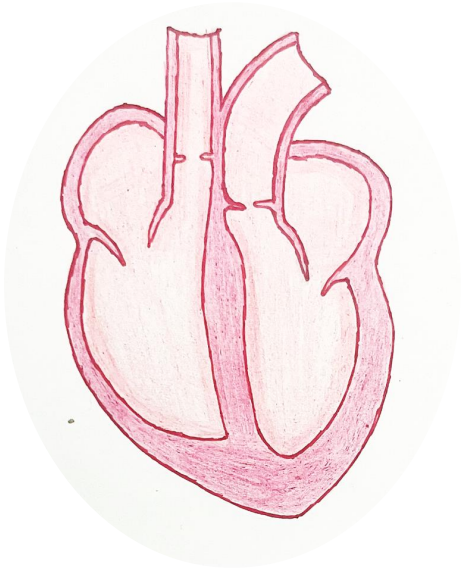
Primary cardiomyopathy

Primarily involving heart muscle

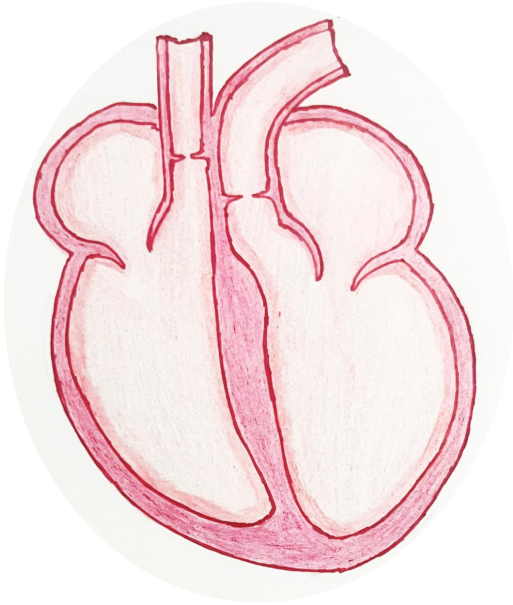
CARDIOMYOPATHY

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

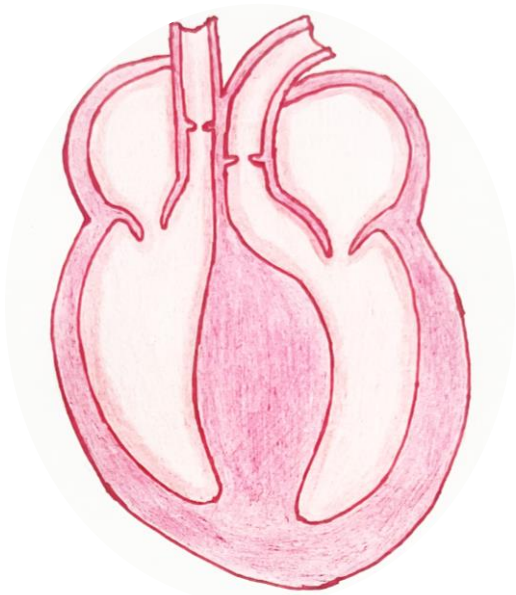
Normal heart



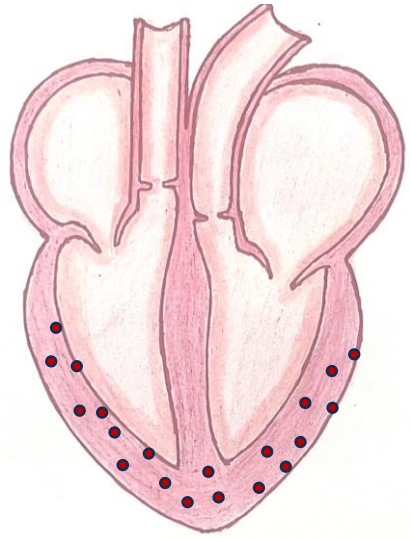
Dilated cardiomyopathy



Hypertrophic cardiomyopathy



Restrictive cardiomyopathy



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

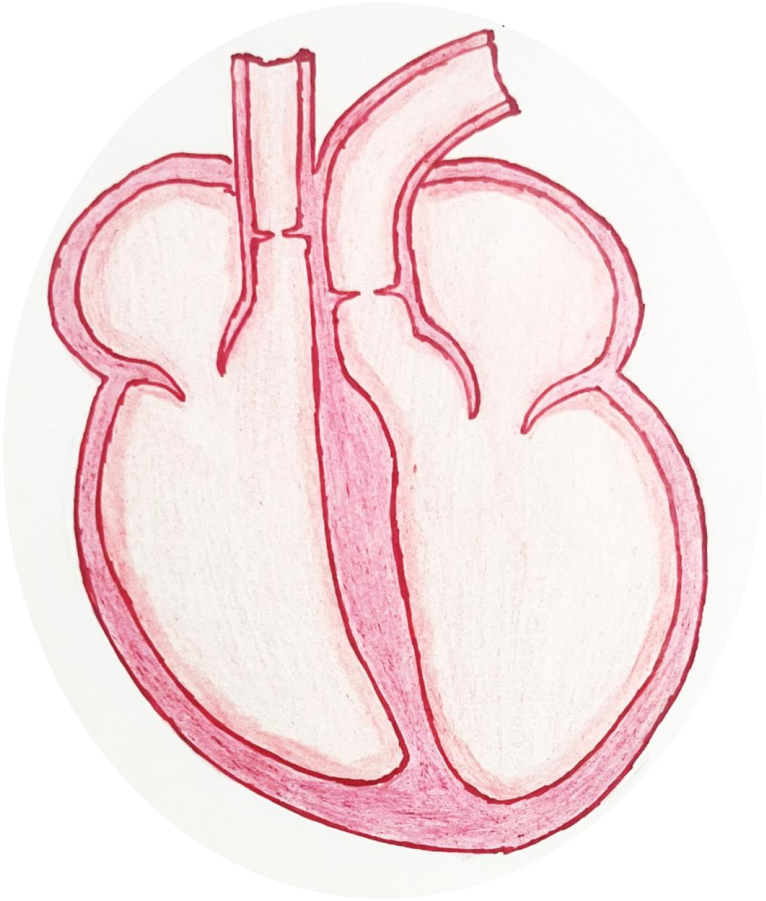
CARDIOMYOPATHY

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

DILATED CARDIOMYOPATHY

- Dilated cardiomyopathy is characterized by progressive cardiac dilation and contractile (systolic) dysfunction, usually with concomitant hypertrophy

- Also called as congestive cardiomyopathy



DILATED CARDIOMYOPATHY

Idiopathic – most common

Causes of dilated cardiomyopathy

Alcohol abuse

Ethanol toxicity or a secondary nutritional disturbance

Takotsubo cardiomyopathy

Increased psycological stress "Heart broken syndrome"

Beriberi heart disease

Thiamine deficiency

Cobalt poisoning

In tainting in beer production

Supraphysiologic stress

Tachycardia,hyperthyroidism, tumors that elaborate epinephrine (pheochromocytoma)

Genetic causes

Viral myocarditidis

Coxsackie B virus

Doxorubicin toxicity

Iron overload

- Hemochromatosis
- Excessive blood transfusion

- Chronic coaciane use
- Chemotherapy drugs
- Chagas disease

Pregnancy

pregnancy-associated hypertension, volume overload, nutritional deficiency, and/or other subtle metabolic derangements

DILATED CARDIOMYOPATHY

Alcoholic cardiomyopathy

Genetic factors

- HLA subtypes
- Alcohol dehydrogenase enzyme allele

Non- genetic factors

- Thiamine deficiency
- Direct toxicity to cardiac muscle
  - Mitochondrial damage
  - Oxidative stress injury
  - Modification of actin and myosin structure
  - Alteration of calcium homeostasis

DILATED CARDIOMYOPATHY

Thiamine derivative TPP, is a cofactor involved in citric acid cycle and also in breakdown of sugars. Citric acid is involved in regulation of carbohydrate, lipids and aminoacid metabolism

Thiamine deficiency

Wet beri-beri

↓

Increase in pyruvate + lactate + Adenosine

↓

Vasomotor depression leading to decrease in peripheral vascular resistance

↓

Increased venous blood flow

↓

Increase in cardiac preload

Wet beri beri
Right sided heart failure +pulmonary hypertension + high cardiac output

Dry beri beri
Peripheral neuropathy such as motor weakness and areflexia due to decreased production of neurotransmitters like GABA and glutamic acid

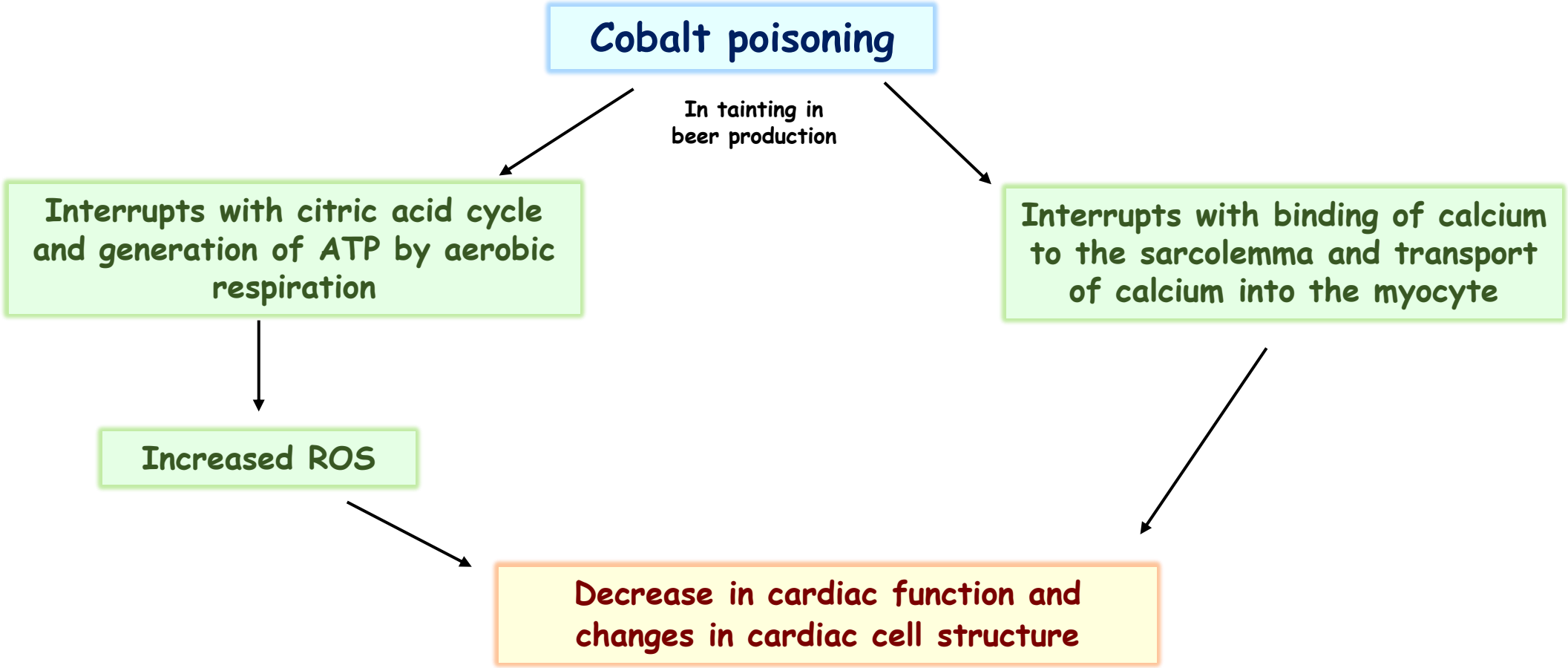
Myocardial dysfunction

↓

CARDIAC FAILURE

DILATED CARDIOMYOPATHY

ETIOLOGY



DILATED CARDIOMYOPATHY

ETIOLOGY

HEMOCHROMATOSIS

IRON DEPOSITION

↓

Occurs initially in ventricular myocardium, then atrial myocardium and conduction system

Iron in myocytes

Impairs calcium transport and impaired excitation- contraction coupling

ROS production through Fentons reaction

Diastolic and ventricular dysfunction

DILATED CARDIOMYOPATHY

ETIOLOGY

Coxsackie B virus

↓

Viral protease 2A can cleave the cytoskeletal dystrophin protein in cardiomyocytes, disrupting the Dystrophin glycoprotein complex

↓

Loss of sarcolemmal integrity and increasing myocyte permeability

↓

DILATED CARDIOMYOPATHY

DILATED CARDIOMYOPATHY

ETIOLOGY

Doxorubicin toxicity

- Increased ROS causing oxidative stress
  - Induces and activates p53
    - Apoptosis of cardiomyocytes
- Downregulation of α – actin, myosin light and heavy chains, troponin-I and Desmin proteins
  - Myofibrillar loss and decreased myocardial contractile function
- Down regulation of sarcoplasmic reticular ATPase
  - Anormal myocardial diastolic function

CARDIOMYOPATHY

DILATED CARDIOMYOPATHY

ETIOLOGY

CHAGAS DISEASE — Caused by Trypanosoma cruzi

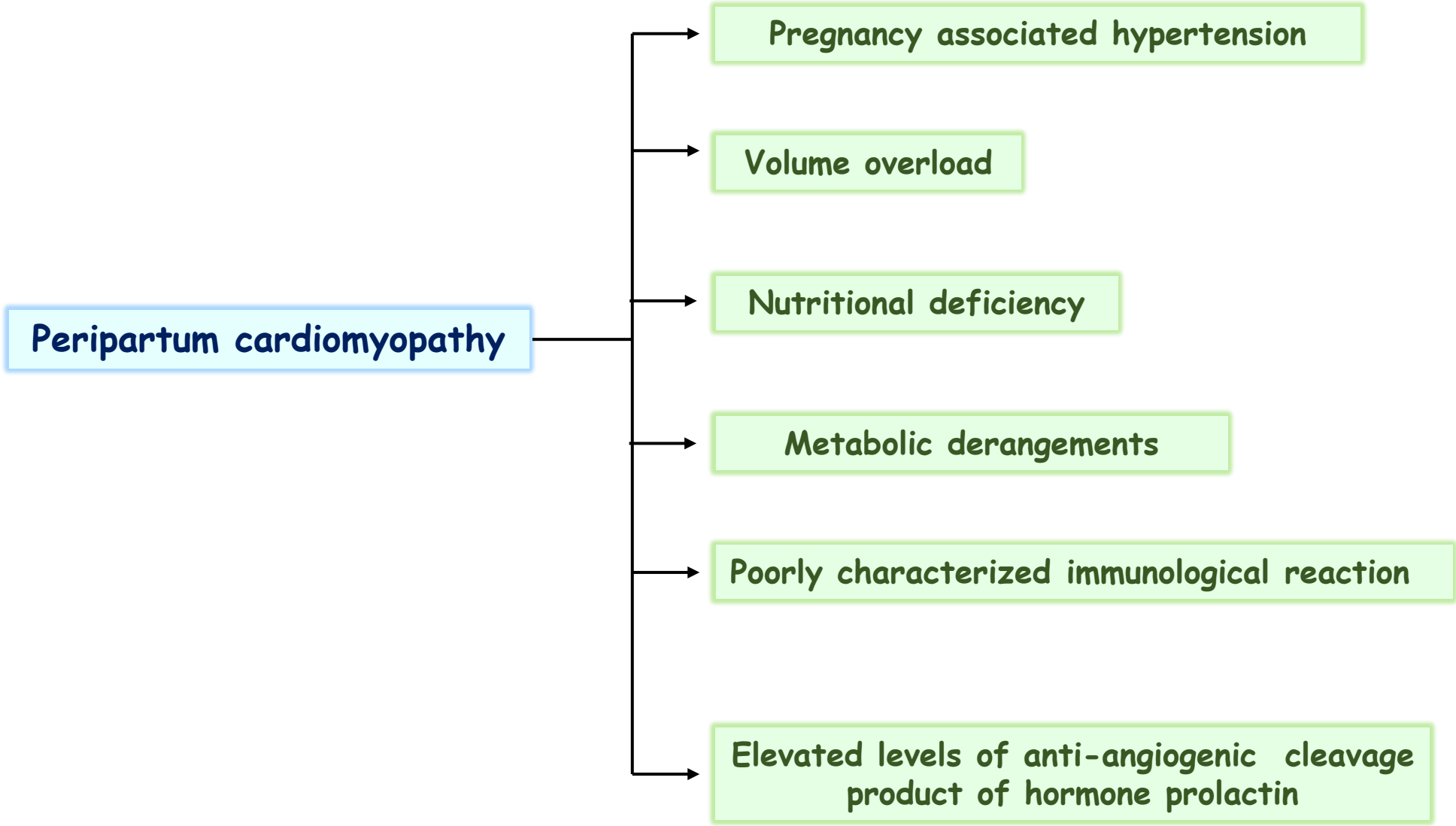
Wide spread immunological reaction involving heart, GIT, meninges and peripheral nervous system

- Myocarditis
  - Myocyte necrosis
- Endocarditis
  - Causes thrombi formation
- Involvement of sinus node and conduction system of heart

DILATED CARDIOMYOPATHY

DILATED CARDIOMYOPATHY

ETIOLOGY



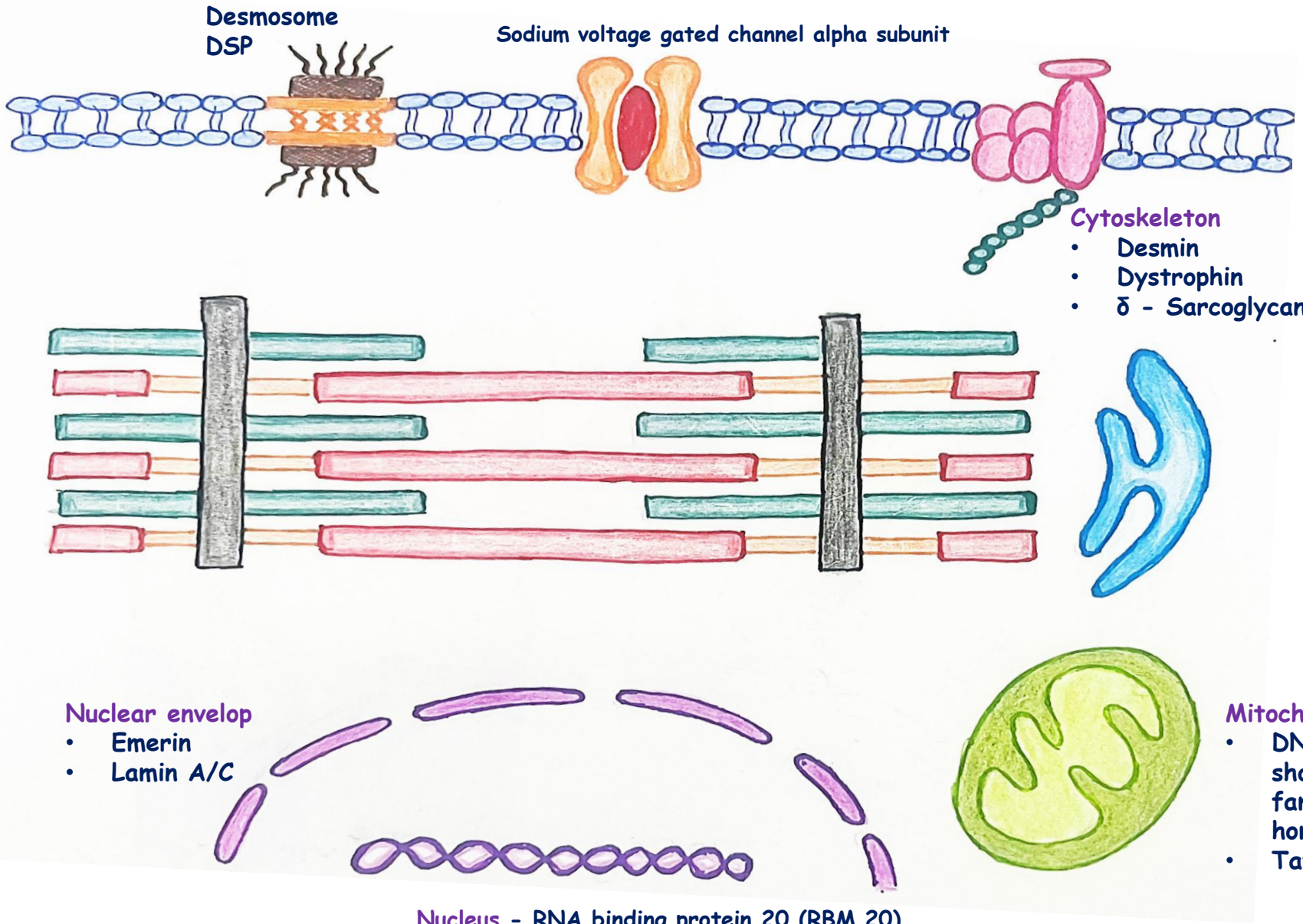
DILATED CARDIOMYOPATHY - ETIOLOGY

Genetic causes

Sarcomere

Genes affected are that encode for

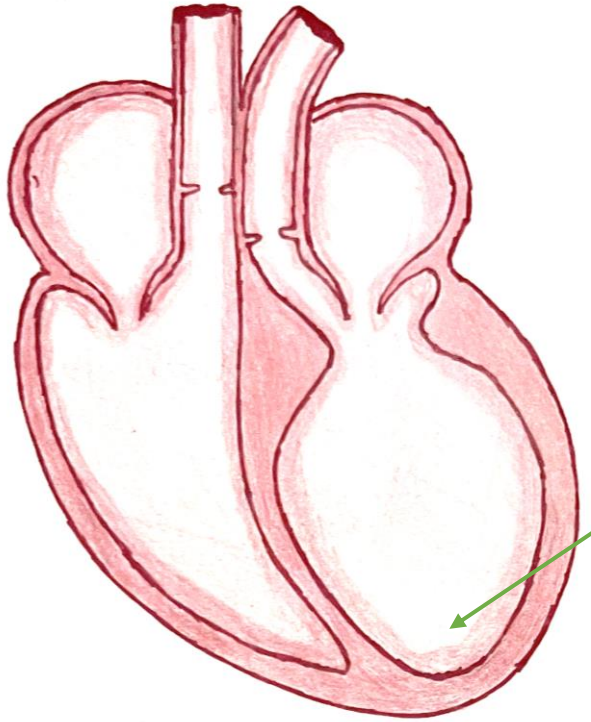
- Alpha cardiac actin
- Beta myosin heavy chain
- Cardiac Troponin C
- Cardiac Troponin T
- Cardiac Troponin I
- Tropomyosin alpha 1 chain
- Titin



DILATED CARDIOMYOPATHY - ETIOLOGY

Takotsubo cardiomyopathy

- Increased psycological stress "Heart broken syndrome"
- Left ventricular apex is most often affected, leading to "apical ballooning" that resembles a takotsubo, Japanese for "fishing pot for trapping octopus"



Enlarged left ventricle forms shape like an octopus pot which shows apical ballooning

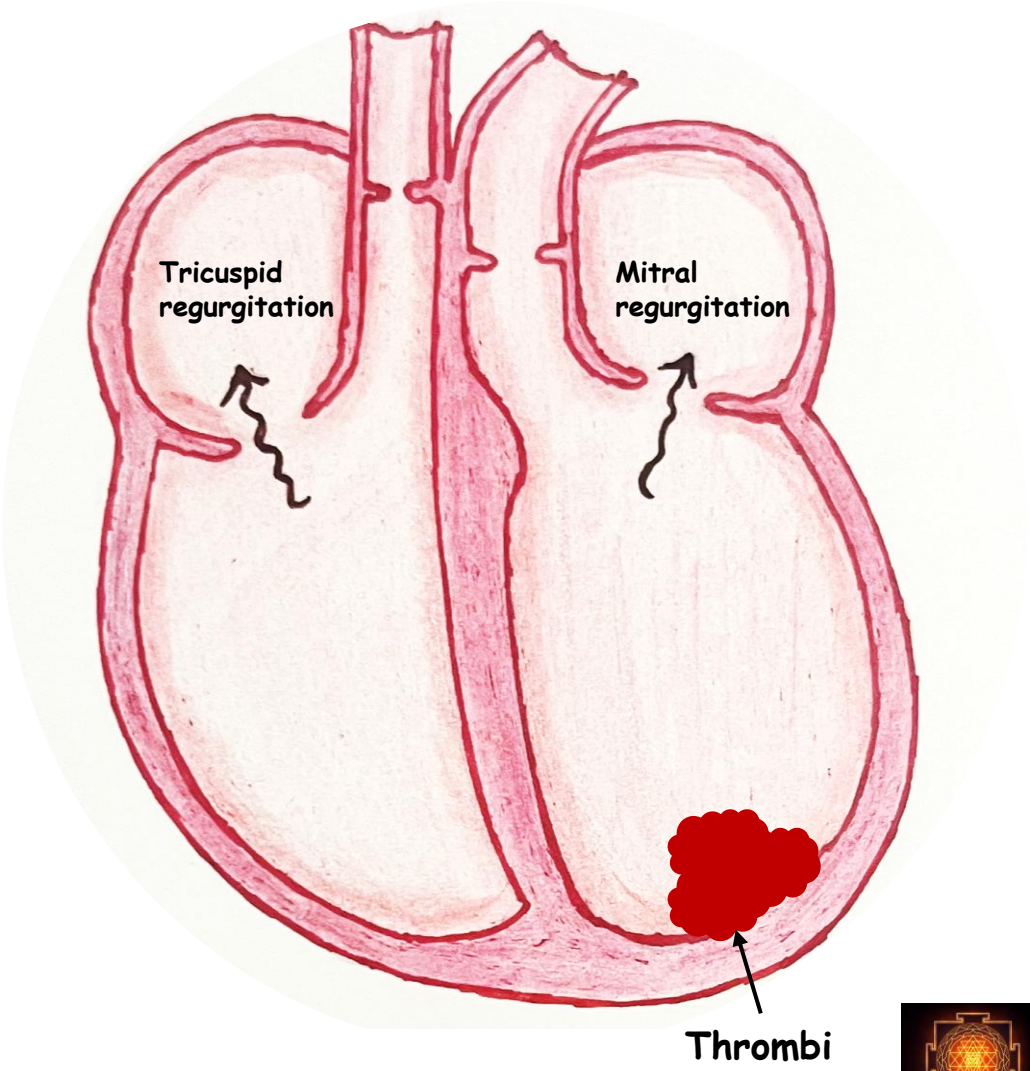
Japanese octopus pot – Tako - tsubo

DILATED CARDIOMYOPATHY

MORPHOLOGY

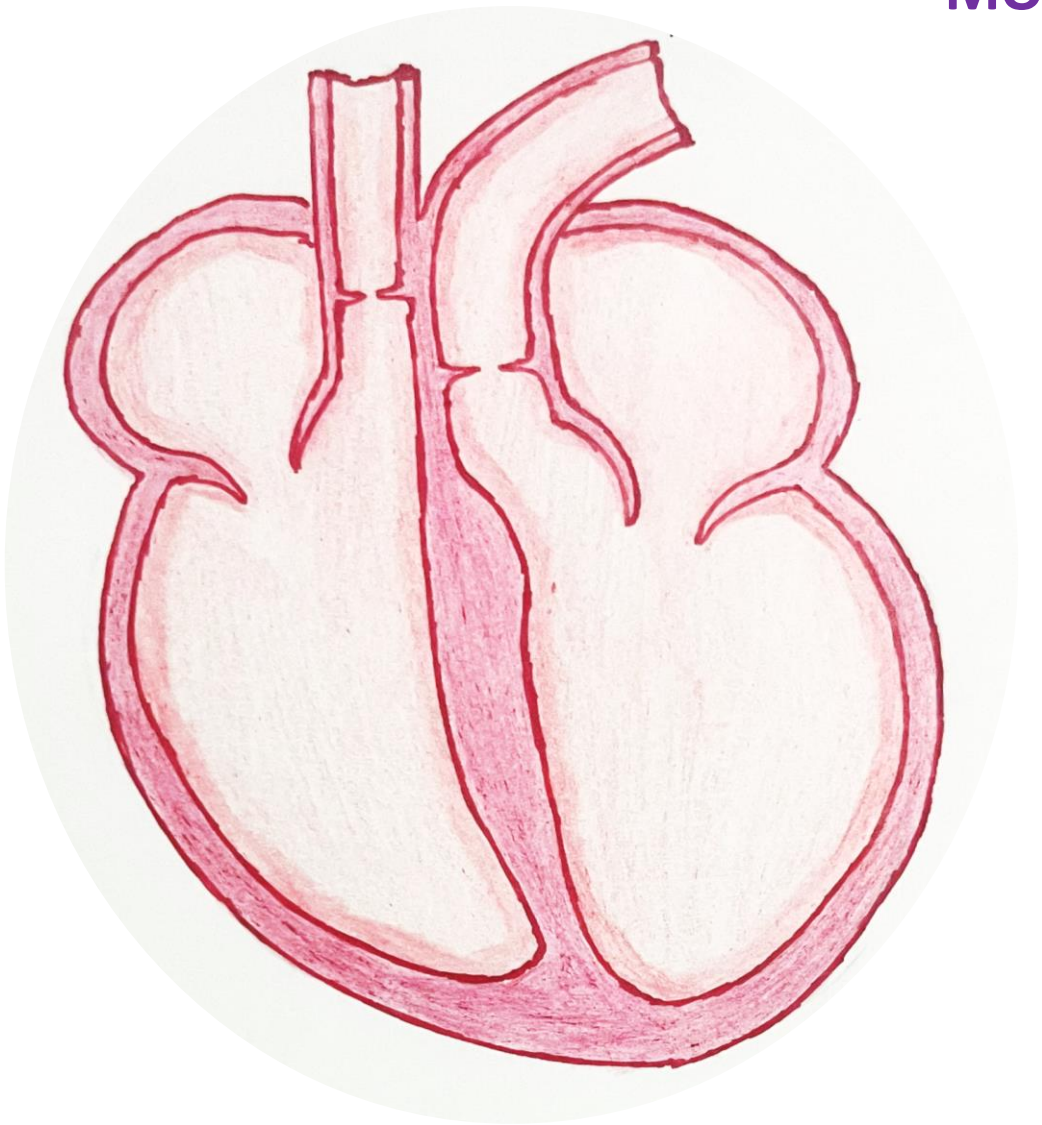
Morphology

- Heart is typically enlarged, flabby and heavy (often weighing two to three times normal)
- Mural thrombi can result from relative stasis of the blood
- Heart should have no primary valvular alterations, to consider DCM
- if mitral (or tricuspid) regurgitation is present, it results from left (or right) ventricular chamber dilation (functional regurgitation)

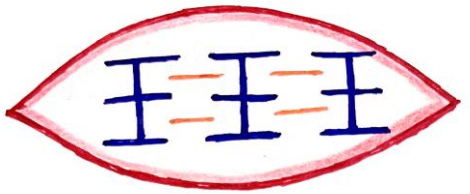


DILATED CARDIOMYOPATHY

MORPHOLOGY

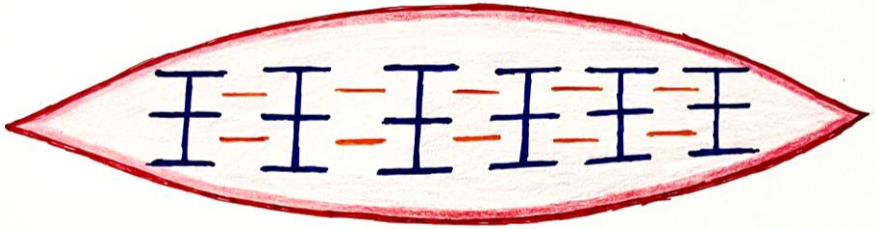


Normal myocardiocyte



Sarcomere

Myocyte in dilated cardiomyopathy

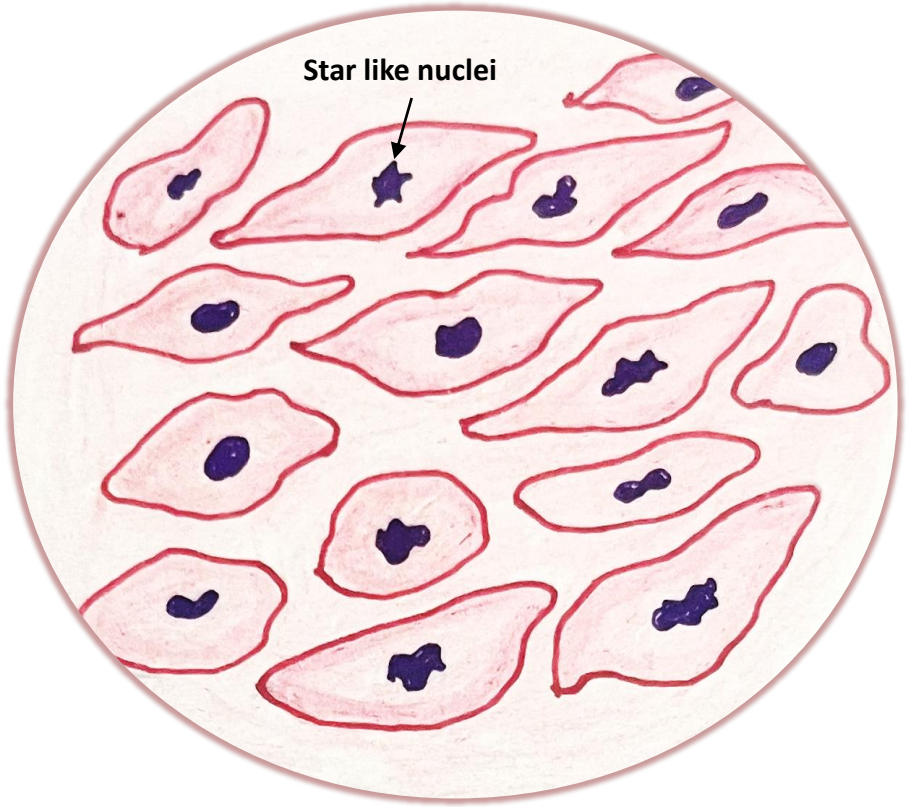


Sarcomere increased in series

DILATED CARDIOMYOPATHY (DCM)

Morphology

- Histologic abnormalities in DCM are nonspecific
- Muscle cells are hypertrophied with enlarged nuclei, but some are attenuated, stretched, and irregular
- DCM caused by truncating mutations in the titin gene, myocytes may exhibit hyperchromatic, highly distorted "Ninja star"-like nuclei



DILATED CARDIOMYOPATHY (DCM)

Clinical features

- Fundamental defect in DCM is ineffective contraction
- Affects individuals between the ages of 20 and 50 years
- Presents with progressive signs and symptoms of CHF including dyspnea, easy fatigability, and poor exertional capacity
- In end-stage DCM, the cardiac ejection fraction typically is less than 25% (normal is 50% to 65%)
- Secondary mitral regurgitation and abnormal cardiac rhythms are common
- Embolism from intracardiac thrombi can occur
- Peripheral edema due to further right ventricular dysfunction
- Death usually results from progressive cardiac failure or arrhythmia

SUMMARY

Definition: progressive cardiac dilation and contractile dysfunction

B D I G C^5 P A S T

CAUSES

- **Alcohol** – Direct toxicity to myocyte
- **Beri beri** – Decreased peripheral resistance and myocardium dysfunction
- **Chagas disease** – immunological damage
- **Cox-sackie virus-** cleaves cytoskeletal proteins
- **Cobalt poisoning-** Increased ROS and interrupts calcium transport into myocyte
- **Chemotherapy drugs-** toxicity to myocardiocytes
- **Cocaine use-** toxicity to myocardiocytes
- **Doxorubicin-** apoptosis of cardiomyocytes and Down regulation of sarcoplasmic reticular ATPase
- **Genetic-** mutations of genes encoding for sarcolemmal, mitochondrial, endoplasmic reticulum proteins and ion channel transport proteins
- **Supraphysiologic stress-** Tachycardia, hyperthyroidism, tumors that elaborate epinephrine (pheochromocytoma)
- **Takotsubo cardiomyopathy-** Increased psychological stress
- **Hemochromatosis-** increased ROS, impaired calcium transport
- **Pregnancy-** volume overload, HTN, nutritional deficiency etc

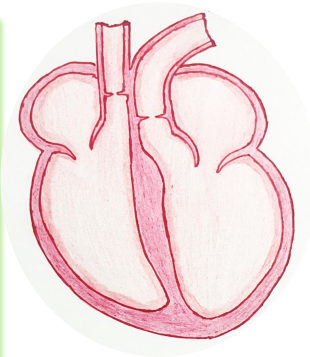
Morphology –

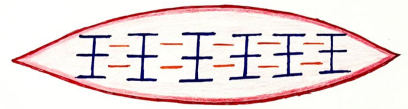
Gross – enlarged flabby

Sarcomeres are arranged in series so the length increases

Microscopy –

- Muscle cells are hypertrophied with enlarged nuclei, but some are attenuated, stretched, and irregular
- Truncating mutations in the titin gene, myocytes may exhibit hyperchromatic, highly distorted "Ninja star"-like nuclei





Clinical features

- Dyspnea and fatigue (LV dysfunction)
- Peripheral edema (rt. Ventricular dysfunction
- Mural thrombi and mitral valve regurgitation
- Death – progressive cardiac failure and arrhythmia

THANK YOU