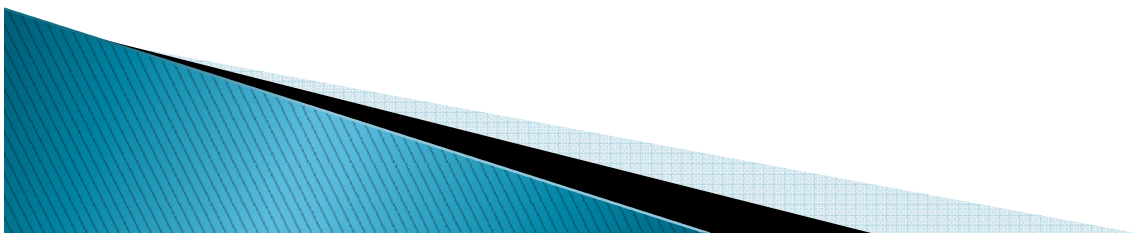
Cardiomyopathies

Dr Rodney Itaki
Lecturer
Anatomical Pathology Discipline

University of Papua New Guinea
School of Medicine & Health Sciences
Division of Pathology

Case 1

- A 8 y.o normally developed has chronic progressive exercise intolerance. Exam shows T=37.1, PR=70bpm, RR=14/min, BP=100/60 mmHg.
- How will you investigate to make a diagnosis?



Case 2

- A 56 y.o man with long history of alcohol use has experienced increased fatigue & decreased exercise tolerance for 2 yrs. Exam showed T=36.9, PR=75bpm, RR=17/min, BP=115/75 mmHg. Auscultation reveals diffuse crackles. Abdomen is distended with fluid thrill & bilateral pitting edema is present.

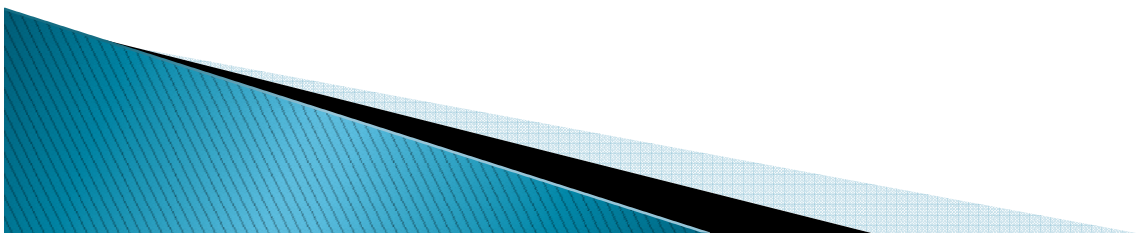
- What is the diagnosis? How would you confirm the diagnosis?
- What is the patho-physiology of his condition?

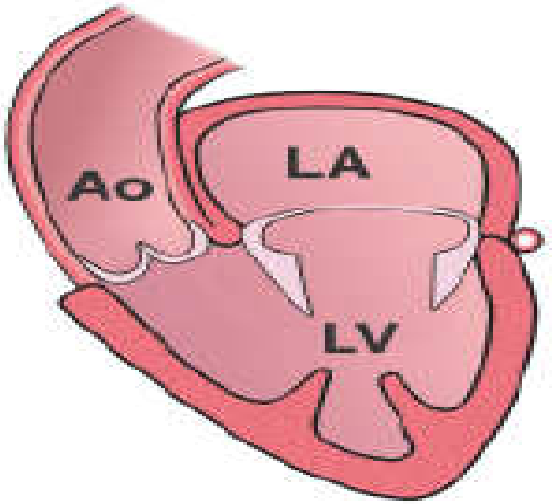
General Considerations

- Cardiomyopathy: term describing primary non-inflammatory disease of the myocardium.
- Not associated with hypertension, congenital heart disease, valvular disease or coronary artery disease.
- The only curative treatment for cardiomyopathy is cardiac transplantation.
- Characterised by unexplained **ventricular dysfunction** (HF unresponsive to digitalis, ventricular enlargement,, ventricular arrhythmias.

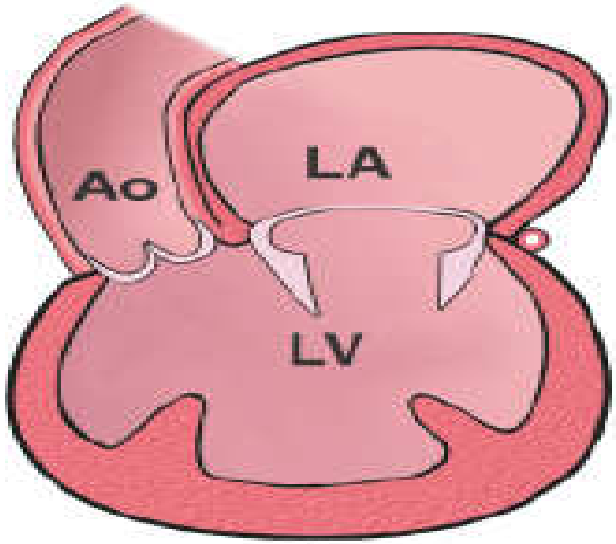
Clinicopathological Forms

- 3 major clinicopathological entities described:
- Dilated (Congestive) cardiomyopathy
- Hypertrophic cardiomyopathy
- Restrictive cardiomyopathy

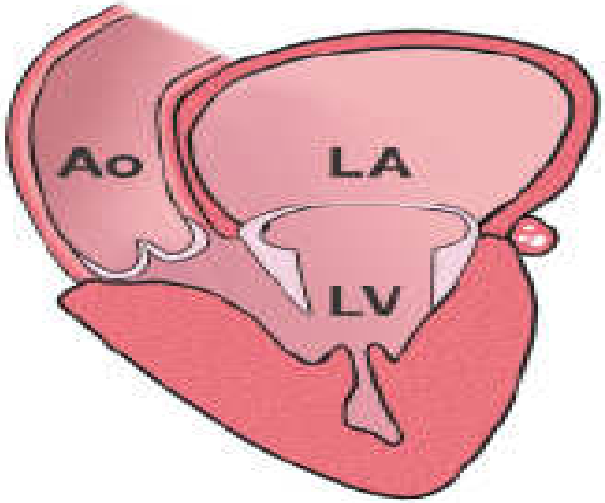




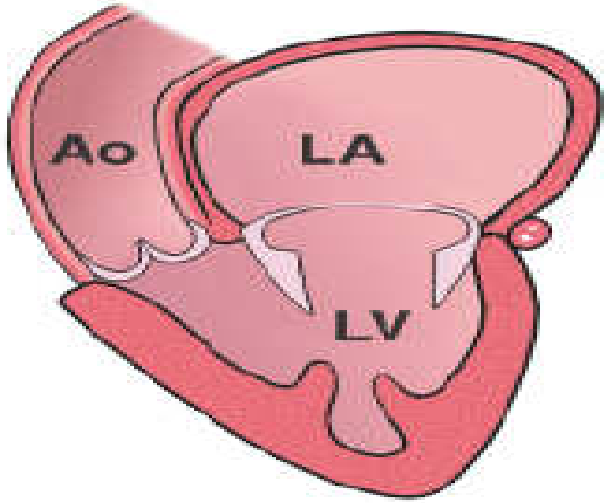
Normal



Dilated cardiomyopathy



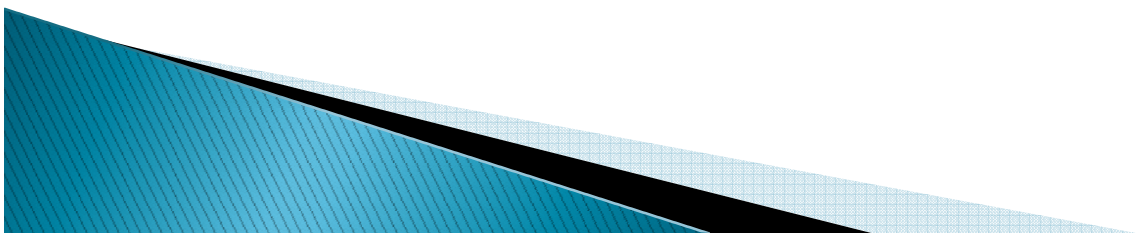
Hypertrophic cardiomyopathy



Restrictive cardiomyopathy

Dilated Cardiomyopathy

- Most common form
- Characterised by: 4 chamber hypertrophy & dilation; both right sided & left sided intractable heart failure (systolic failure).
- This leads to systolic failure i.e heart can not contract.
- Etiology: unknown most cases. Some cases related to alcoholism (alcohol cardiomyopathy), thiamine deficiency (beribri heart disease) or prior myocarditis (virus – coxsackie B, enteroviruses)



DCM – Alcohol Cardiomyopathy

- Alcohol abuse strongly associated with development of DCM.
- ?ethanol toxicity or one of its metabolites.
- Acetaldehyde, a metabolite of alcohol has direct toxic effect on the myocardium.
- Chronic alcoholism may be associated with thiamine deficiency (beriberi heart disease).
- Drugs – direct toxicity to myocardium: doxorubicin, adiramycin and cobalt in cancer treatment.

Beriberi heart disease

- Thiamine is widely available in diet but low in refined foods.
- Thiamine is absorbed from the gut & undergoes phosphylation to produce thiamine pyrophosphate, functionally active coenzyme form of the vitamine.
- Has 3 major functions:
  - Regulation of oxidative decarboxylation of α-keto acids, leading to ATP synthesis
  - Acts as cofactor for transketolase in the pentose phosphate pathway
  - Maintains neural membranes for normal nerve conduction (peripheral nerves mostly).
- Deficiency is associated with: peripheral vasodilation, pale, flabby myocardium, four chamber dilation leading to thin myocardial walls.

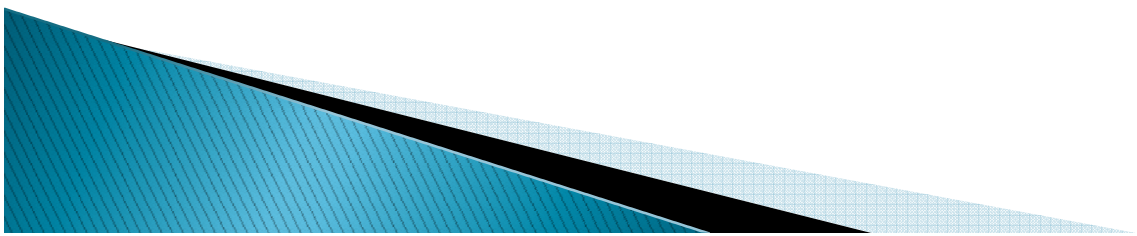
Clinical Features – DCM

- DCM occur at any age but common 20-60.
- Presents with slow progressive congestive HF.
- End stage patient can have ejection fraction of 25% (normal: 50-65%).
- 50% will die in 2 years after diagnosis.
- 25% will survive more than 5 years after diagnosis.
- Death due to progressive cardiac failure.
- Embolism from intra-cardiac thrombus can occur.

Pathology

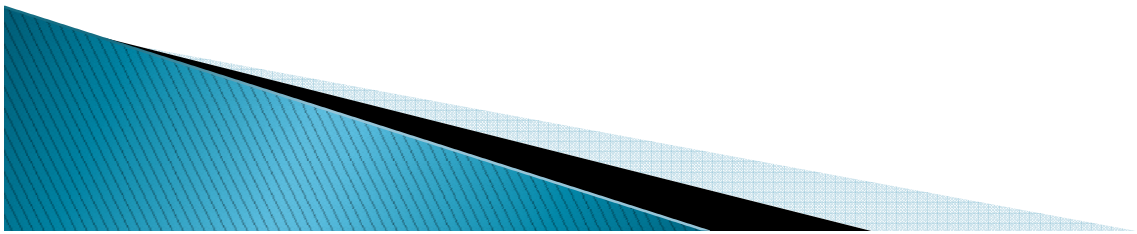
- Grossly enlarged and heavy; 2-3x normal weight.
- Large, flabby with dilated 4 chambers.
- Thin myocardial wall.

- Microscopy: non-specific changes. Muscle cells hypertrophied with enlarged nuclei. Attenuated and stretched myocardial cells. Interstitial and endocardial fibrosis.



Hypertrophic Cardiomyopathy

- Also known as idiopathic hypertrophic subaortic stenosis & hypertrophic obstructive cardiomyopathy.
- Oftern inherited as an autosomal dominant disorder.
- Charactersed by:
  - Hypertrophy of all 4 chambers.
  - Hypertrophy of the ventricular septum (asymmetric septal hypertrophy).
  - Abnormal diastolic filling
  - 1/3 of cases will show intermittent left ventricular outflow obstruction
- HCM – ventricles cannot dilate i.e diastolic failure.



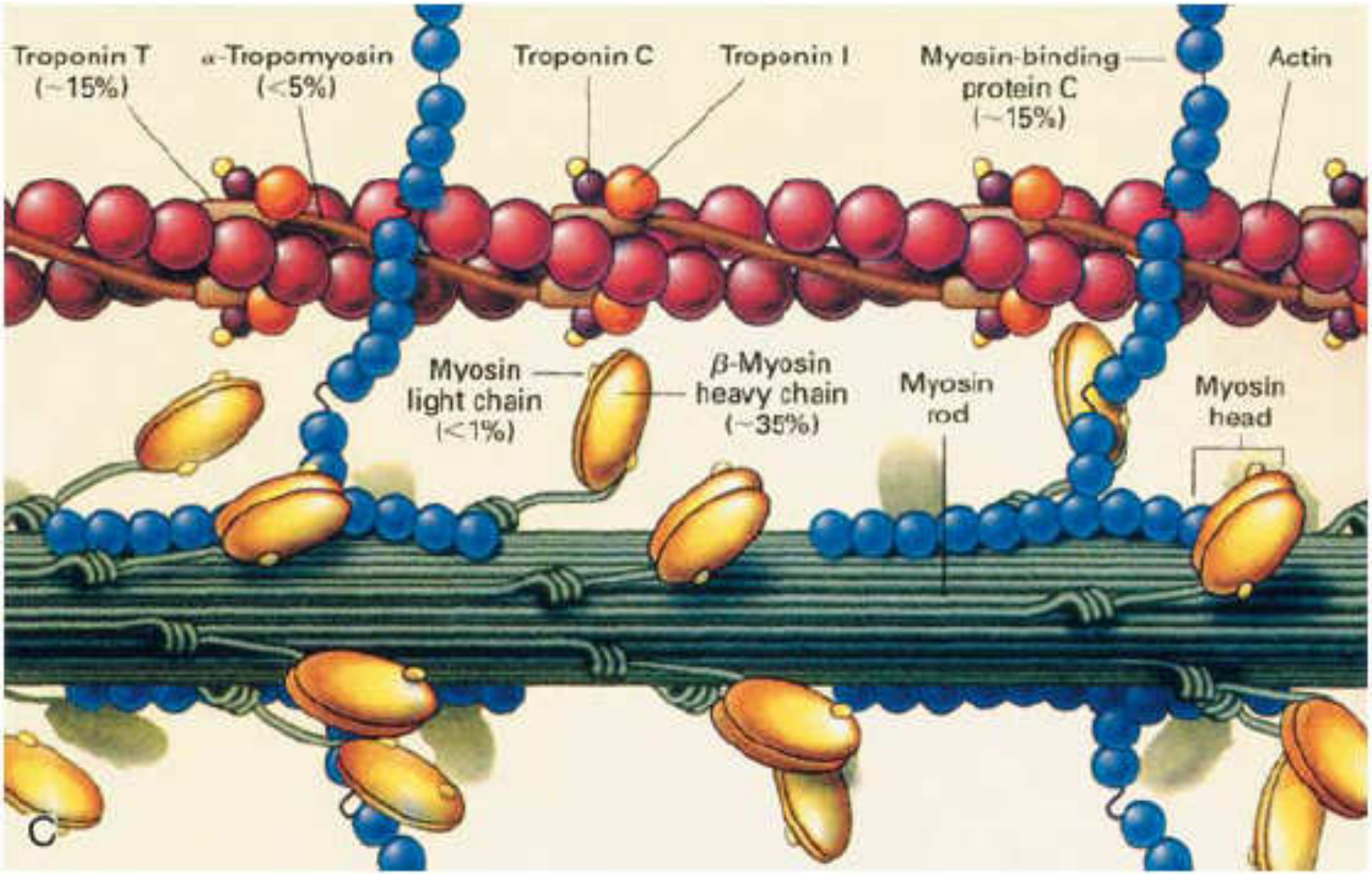
HCM – Clinical Features

- Reduced chamber size, poor compliance with reduced stroke volume resulting from impaired diastolic filling of the massively hypertrophied left ventricle.
- Exertional dyspnoea
- Harsh systolic murmur may be audible – from ventricular outflow obstruction.
- Angina pain from focal myocardial ischaemia (even in the absence of concomitant CAD).
- AF with mural thrombus common.
- Common cause for sudden death in young people/athletes.

HCM – Pathogenesis

- Familial with autosomal dominant pattern of transmission and variable expression.
  - Reminder of cases is sporadic.
- 4 genes code for proteins of the cardiac contractile elements (sarcomeres): β-myosin heavy chain, cardiac troponin T, α-tropomyosin & myosin-binding protein C.
- In HCM defect in any one of the 4 genes.
- Common mutation is in coding for β-myosin heavy chain.
- More than 50 distinct mutations have been reported in the literature. Maybe more now?
- Sequence of events leading to HCM poorly understood.

Genetic Mutations in HCM

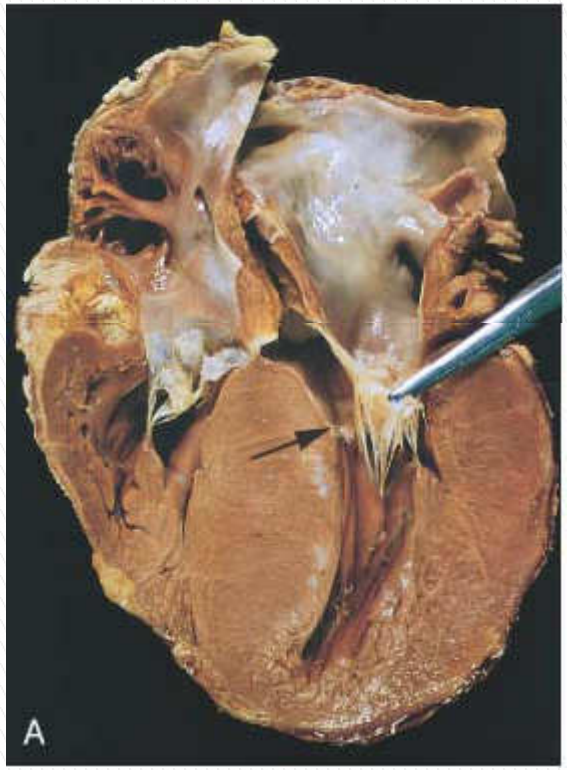


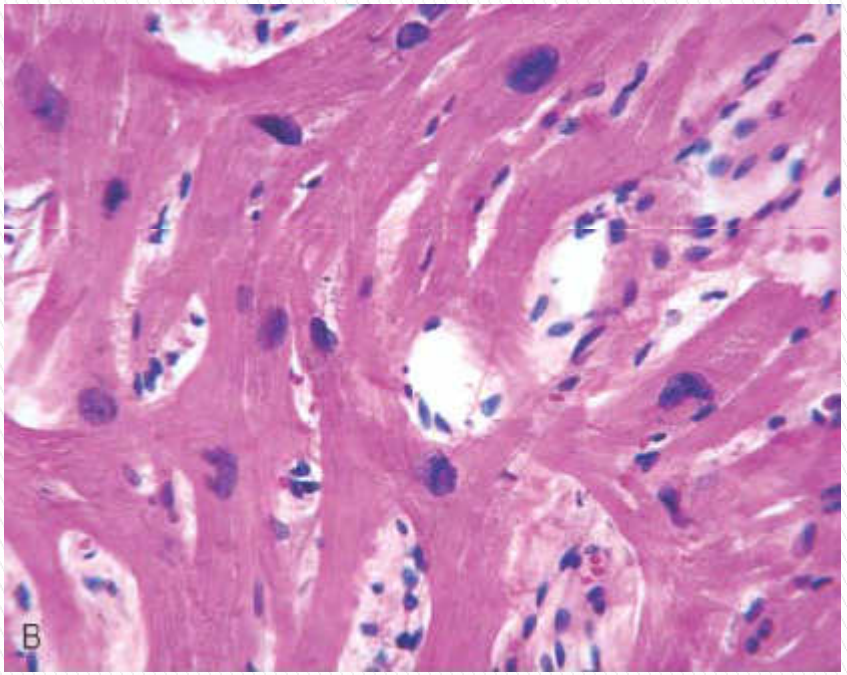
Ref: Robins Pathological Basis of Diseases, 7th Ed.

Pathology

- Massively myocardial hypertrophy without ventricular dilation.
- Disproportionate thickening of the ventricular septum as compared to free wall of the ventricle = "Asymmetric septal hypertrophy".
- 10% of cases hypertrophy is symmetric.
- Cut section: ventriclar cavity is round-to-oval and maybe compressed into a banana-like configuration by bulging enlarged septum.
- Enlarged septum most prominent in the subaortic region.

- Micro: extensive myocyte hypertrophy, hapharzard disarray of bundles of myocytes, interstitial fibrosis.

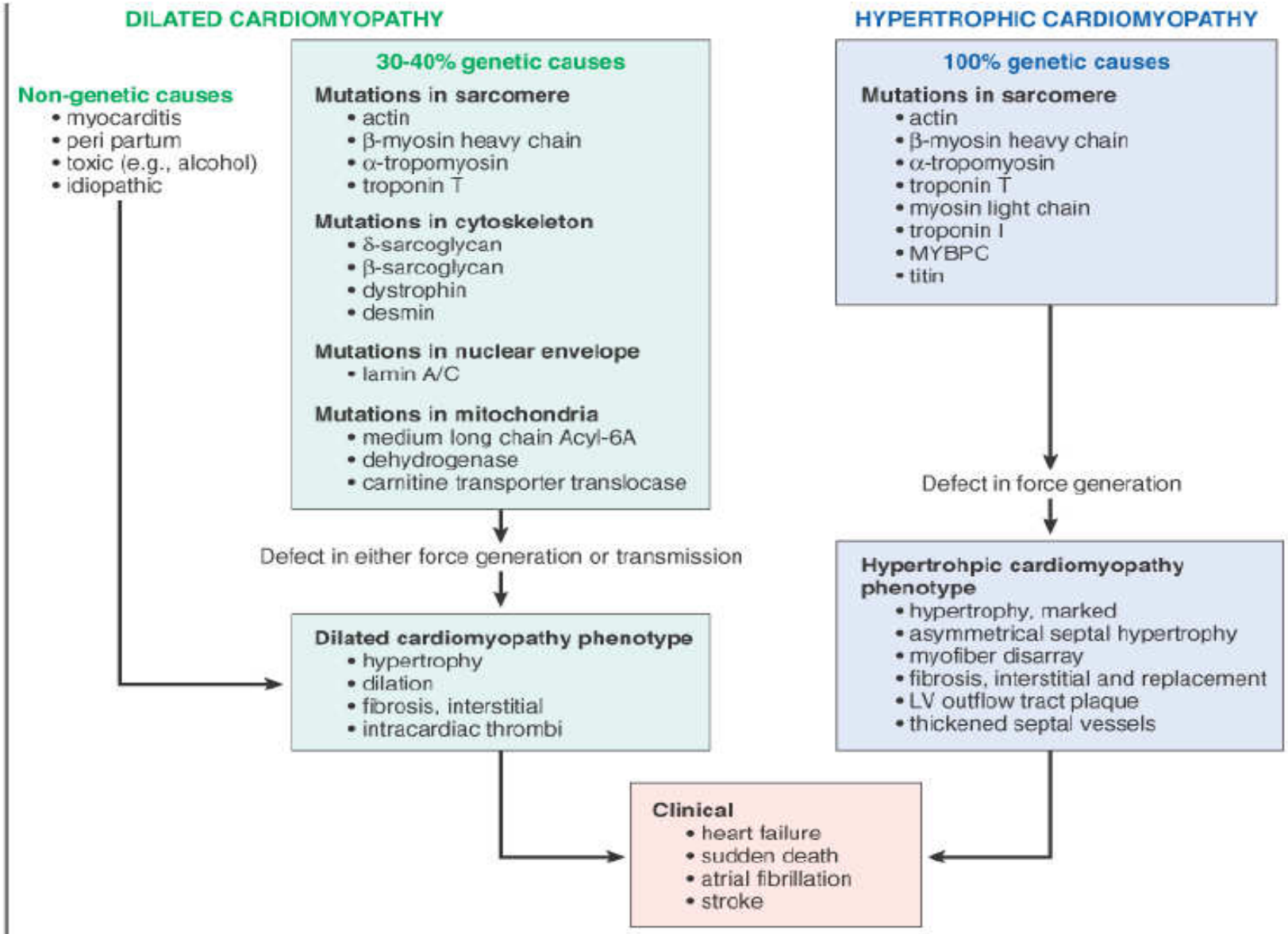




Banana-like configuration

Hapazard dissary of bundles of myocytes

Ref: Robins Pathological Basis of Diseases, 7th Ed.



Ref: Robins Pathological Basis of Diseases, 7th Ed.

Restrictive Cardiomyopathy

- Rare form of cardiomyopathy.
- Characterised by non-compliance of ventricles resulting in impaired ventricular filling during diastole.
  - Leading to **diastolic failure.**
- Functional state can be confused with constrictive pericarditis or HCM.

- **Etiology**: idiopathic or infiltrative pathological conditions e.g. amyloidosis, sarcoidosis, metastatic tumor or products of inborn errors of metabolism.
- Radiation fibrosis of myocardium in patients undergoing treatment for cancer.
- Rare causes include: endomyocardial fibrosis, Loeffler endomyocarditis & Endocardial fibroelastosis

Pathology

- Idiopathic Restrictive Cardiomyopathy:
  - Ventricles are normal or slightly enlarged.
  - Ventricle cavity not usually dilated.
  - Atriums both dilated.
  - Diffuse of patchy interstitial fibrosis microscopically

Diagnosis

- Good history & examination
- CXR
- Echocardiography
- ECG
- Cardiac muscle biopsy
- Specific tests where required e.g. Genetic tests, vitamin levels,

END

Reference: Robins Pathological Basis of Diseases, 6th & 7th Ed.

Download PDF copies of seminar notes at:

www.pathologyatsmhs.wordpress.com