CVS module – 6
Cardiomyopathies, Myocarditis and cardiac tumor

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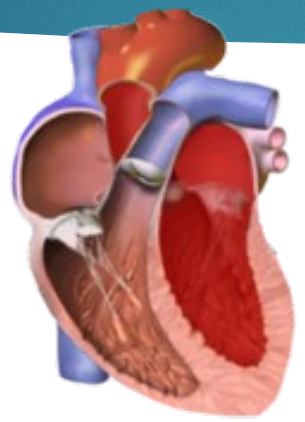
Cardiomyopathies

- Cardiac diseases due to intrinsic myocardial dysfunction.

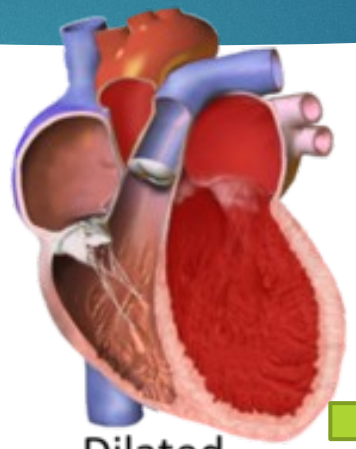
- May be :
- primary: that confined to the myocardium
- Secondary: presenting as the cardiac manifestation of a systemic disorder.

- Clinically they are classified into three major types:
- Dilated cardiomyopathy (DCM) (90% of cases)
- Hypertrophic cardiomyopathy (HCM)
- Restrictive cardiomyopathy(RCM).

Types

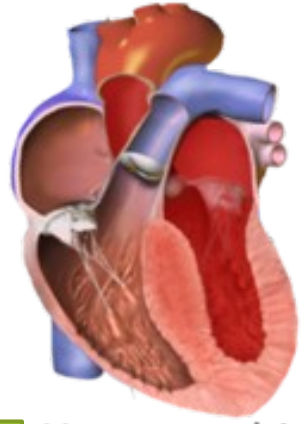


Normal



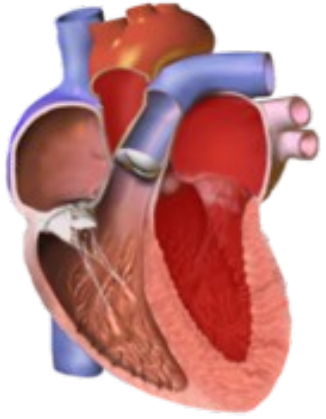
Dilated

flabby, poorly contractile



Hypertrophic

thick-walled,
heavy, and hypercontractile



Restrictive

Table 11.5 Cardiomyopathies: Functional Patterns, Causes

Functional Pattern	Left Ventricular Ejection Fraction*	Mechanisms of Heart Failure	Causes	Secondary Myocardial Dysfunction (Mimicking Cardiomyopathy)
Dilated	<40%	Impairment of contractility (systolic dysfunction)	Genetic; alcohol; peripartum; myocarditis; hemochromatosis; chronic anemia; doxorubicin (Adriamycin); sarcoidosis; idiopathic	Ischemic heart disease; valvular heart disease; hypertensive heart disease; congenital heart disease
Hypertrophic	50%–80%	Impairment of compliance (diastolic dysfunction)	Genetic; Friedreich ataxia; storage diseases; infants of diabetic mothers	Hypertensive heart disease; aortic stenosis
Restrictive	45%–90%	Impairment of compliance (diastolic dysfunction)	Amyloidosis; radiation-induced fibrosis; idiopathic	Pericardial constriction

*Range of normal values is approximately 50% to 65%.

1. Dilated Cardiomyopathy

- Dilated cardiomyopathy (DCM) is characterized by a poorly contracting dilated left ventricle with a normal or reduced left ventricular wall thickness
- DCM is the most common cause of congestive cardiac failure (CCF).
- It occurs more frequently in men than women and is most common between ages 20 and 60 years.
- By definition, valvular and vascular lesions (e.g., atherosclerotic coronary artery disease) that can cause cardiac dilation secondarily are absent.

Pathogenesis

- In most cases, no definite cause is identifiable, but causes can be classified as:

- Genetic : in 20% to 50% of cases, either as:
- autosomal dominant : mutations affecting cytoskeletal proteins or proteins that link the sarcomere to the cytoskeleton.
- X-linked : mutations in dystrophin, a cell membrane protein that physically couples the intracellular cytoskeleton to the ECM.

Pathogenesis. Cont.

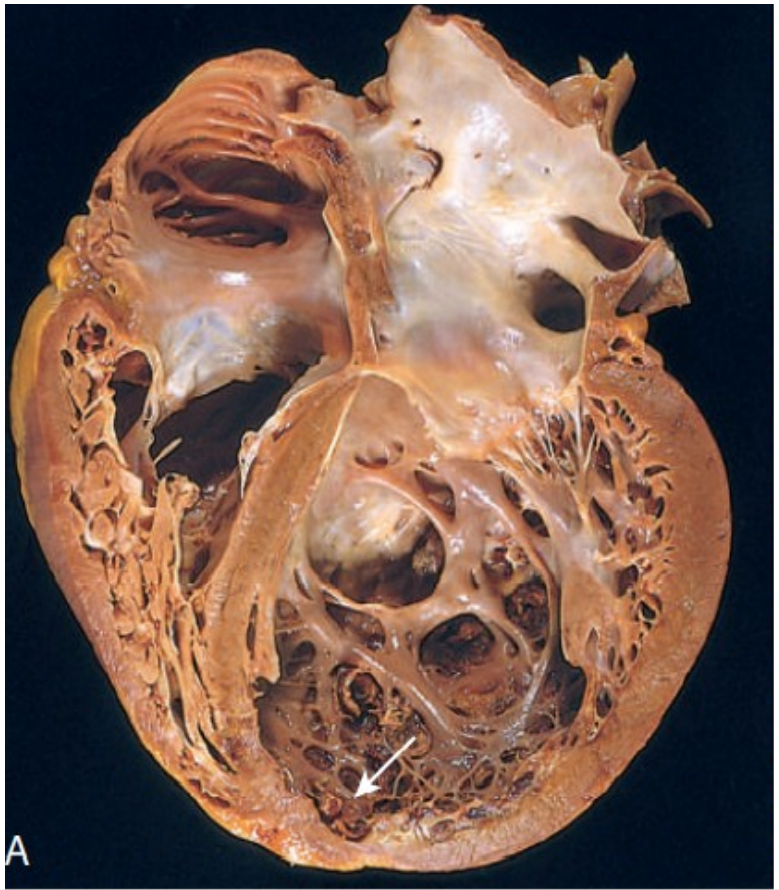
- Acquired causes such as:

- Infections: e.g. coxsackievirus, adenovirus.
- Nutritional deficiency: carnitine selenium deficiencies
- Cardiotoxins: e.g. Adriamycin: a chemotherapeutic drug.
- Puerperium: usually occur late in gestation or several weeks to months postpartum.
- Due to pregnancy-associated hypertension, volume overload, nutritional deficiency, gestational diabetes.
- Alcohol :
- direct toxic effect on the myocardium.
- thiamine deficiency

Gross Morphology

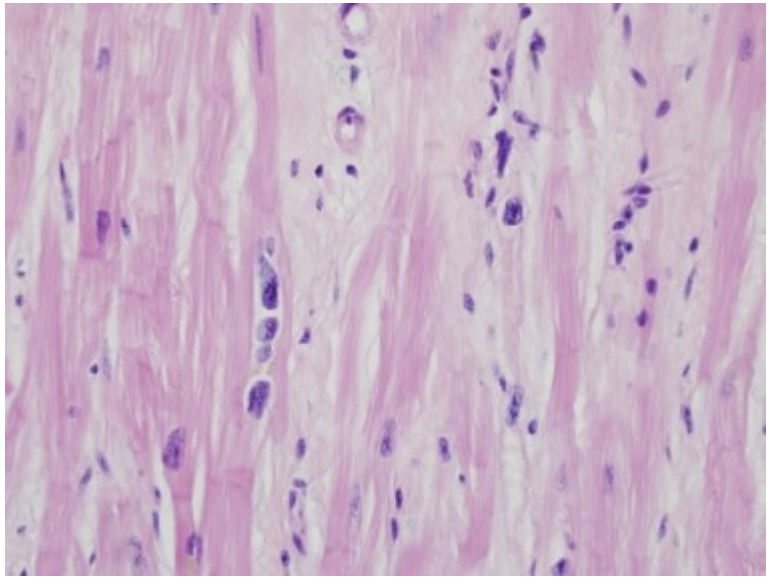
- The heart assumes a globular shape.
- ventricular chamber dilatation.
- atrial enlargement.
- Mural thrombi are often present

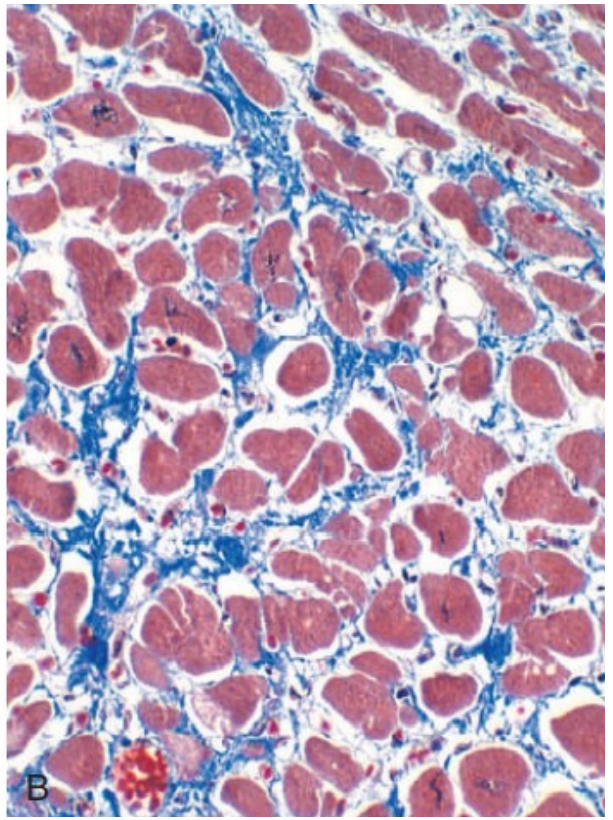
and may be a source of thromboemboli.



Histological features

- The characteristic histologic abnormalities in DCM are nonspecific.
- Myocytes exhibit hypertrophy with enlarged nuclei.
- interstitial and endocardial fibrosis,





Clinical features

- The fundamental defect in DCM is ineffective contraction.

- It typically manifests with signs of slowly progressive CHF, including dyspnea, easy fatigability, and poor exertional capacity.
- Secondary mitral regurgitation .
- abnormal cardiac rhythms.
- embolism from intracardiac (mural) thrombi.

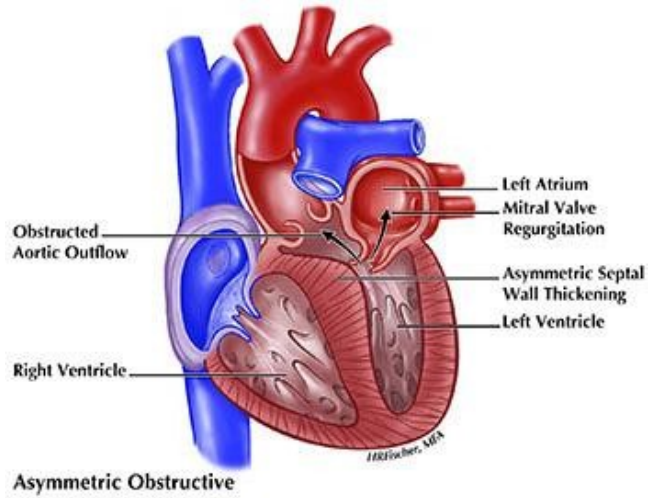
- Cardiac transplantation is the only definitive treatment.

2. Hypertrophic Cardiomyopathy

- Hypertrophic cardiomyopathy (HCM) is defined by the presence of increased left ventricular (LV) wall thickness (in a non dilated chamber) that is not explained by abnormal loading conditions ?

- Typically associated with defective diastolic filling, and ventricular outflow obstruction.

- Systolic function usually is preserved in HCM, but the myocardium does not relax and therefore exhibits primary diastolic dysfunction



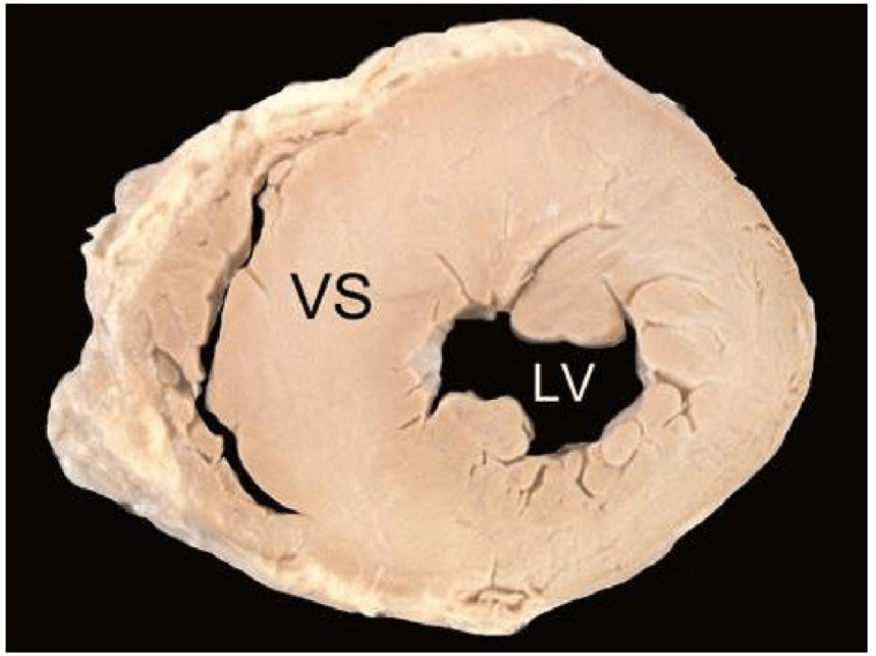
Pathogenesis

- Most cases of HCM are caused by mutations (usually autosomal dominant) in one of the proteins that form the contractile apparatus:

- β-myosin heavy chain is most frequently involved.
- myosin-binding protein C .
- troponin T.

Gross MORPHOLOGY

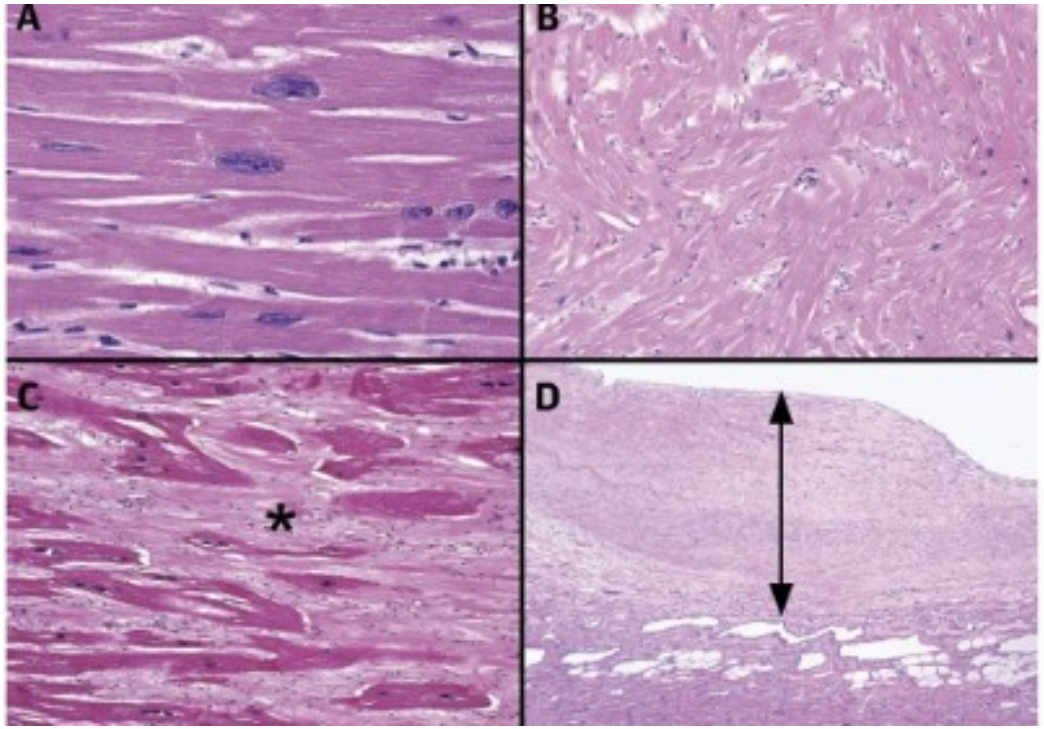
- Hypertrophic cardiomyopathy is marked by massive myocardial hypertrophy without ventricular dilation.



Histological features

- The characteristic histologic features in HCM are marked myocyte hypertrophy, haphazard myocyte (and myofiber) disarray, and interstitial fibrosis

- A) Myocyte hypertrophy.
- (B) myocyte disarray.
- (C) interstitial (pericellular-type) fibrosis (asterisk).
- (D) endocardial fibrosis (double-headed arrow).



Clinical Features

- HCM typically manifests during the postpubertal growth spurt.
- characterized by massive left ventricular hypertrophy associated with reduced stroke volume(due to impaired diastolic filling and overall smaller chamber size).
- Reduced cardiac output and a secondary increase in pulmonary venous pressure cause exertional dyspnea.
- A combination of massive hypertrophy, high left ventricular pressures, and compromised intramural arteries frequently leads to myocardial ischemia (with angina), even in the absence of concomitant CAD.

Clinical Features

- So Major clinical problems include :

- atrial fibrillation with mural thrombus formation.
- ventricular fibrillation leading to sudden cardiac death.
- CHF.

- In almost one third of cases of sudden cardiac death in athletes younger than 35 years of age, the underlying cause is HCM.

3. Restrictive Cardiomyopathy

- Restrictive cardiomyopathy is characterized by a primary decrease in ventricular compliance, resulting in impaired ventricular filling during diastole.

- May be:
- idiopathic.
- Or associated with systemic diseases that affect the myocardium, e.g.: radiation fibrosis, amyloidosis, sarcoidosis, or products of inborn errors of metabolism.

Commonest forms of restrictive cardiomyopathy include:

- 1. Cardiac amyloidosis :
- caused by the deposition of extracellular proteins (amyloid).

- can occur in the setting of:
  - systemic amyloidosis (e.g., multiple myeloma).
  - or restricted to the heart (e.g., senile cardiac amyloidosis).

- 2. Endomyocardial fibrosis :
- characterized by dense diffuse fibrosis of the ventricular endocardium and subendocardium, often involving the tricuspid and mitral valves
- is principally a disease of children and young adults.
- The fibrous tissue markedly diminishes the volume and compliance of affected chambers, resulting in a restrictive physiology.
- Causes:
- nutritional deficiencies.
- inflammation related to helminthic infections with hypereosinophilia.

Myocarditis

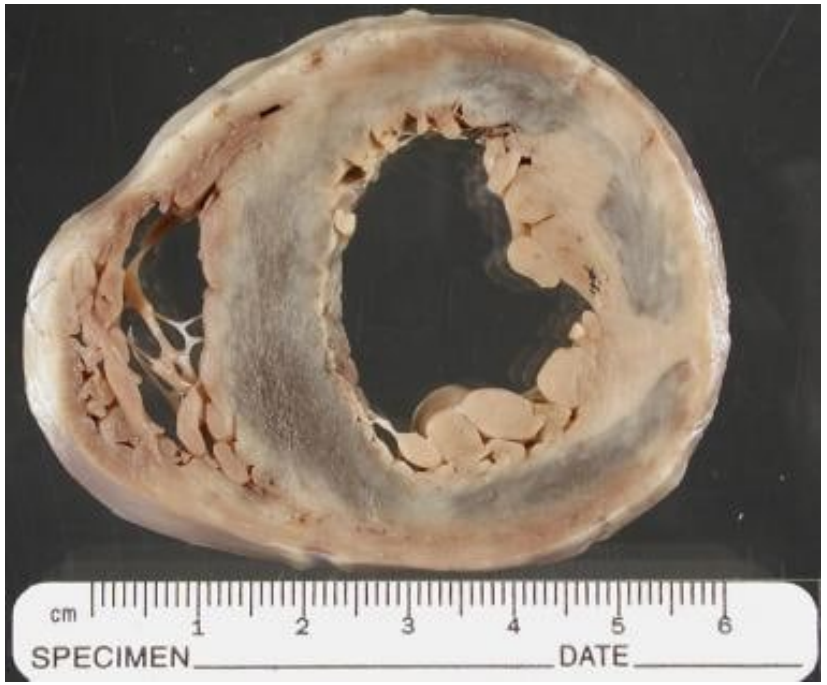
- Myocarditis is an inflammatory disease of the myocardium caused by different infectious and noninfectious triggers.

- Classified according to the cause into:
- Infectious:
- Viral infections, e.g.: coxsackie viruses A and B , enteroviruses, Cytomegalovirus (CMV), human immunodeficiency virus (HIV).

- Noninfectious:
- systemic diseases of immune origin, such as systemic lupus erythematosus and polymyositis.
- Drug hypersensitivity reactions (hypersensitivity myocarditis)

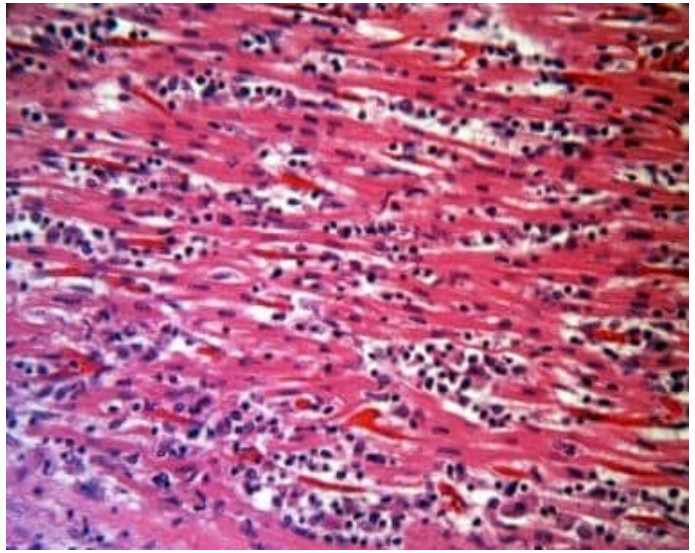
Gross Morphology

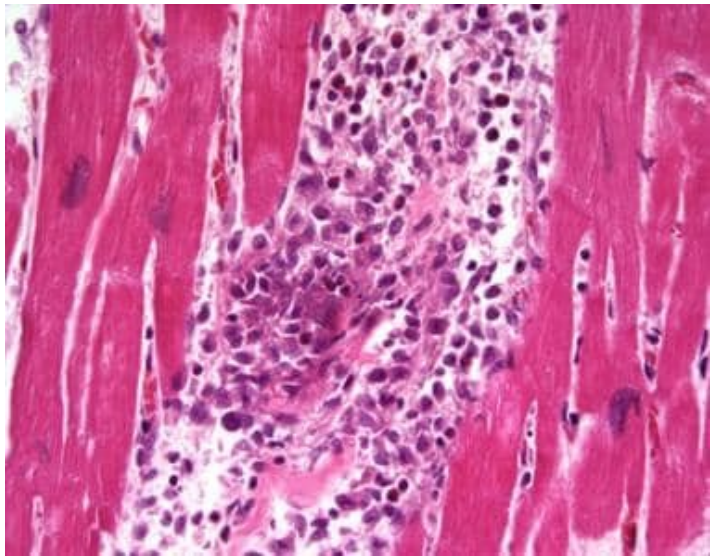
- In acute myocarditis, the heart may appear normal or dilated.
- in advanced stages, the myocardium typically is flabby and pale and hemorrhagic areas.
- Mural thrombi may be present.

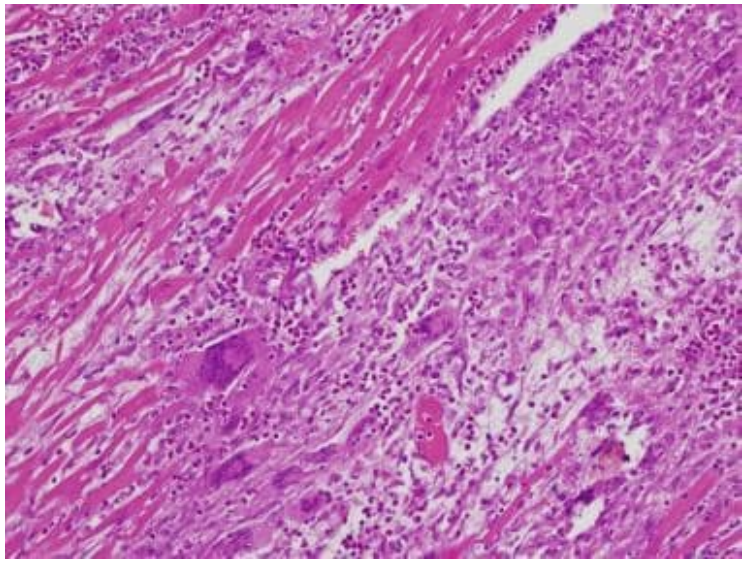


Histological features myocarditis is characterized by:

- edema and myocyte injury.
- interstitial inflammatory infiltrates:
- Lymphocytic type: numerous lymphocytes.
- hypersensitivity myocarditis: abundant eosinophils.
- Giant cell myocarditis: containing multinucleate giant cells







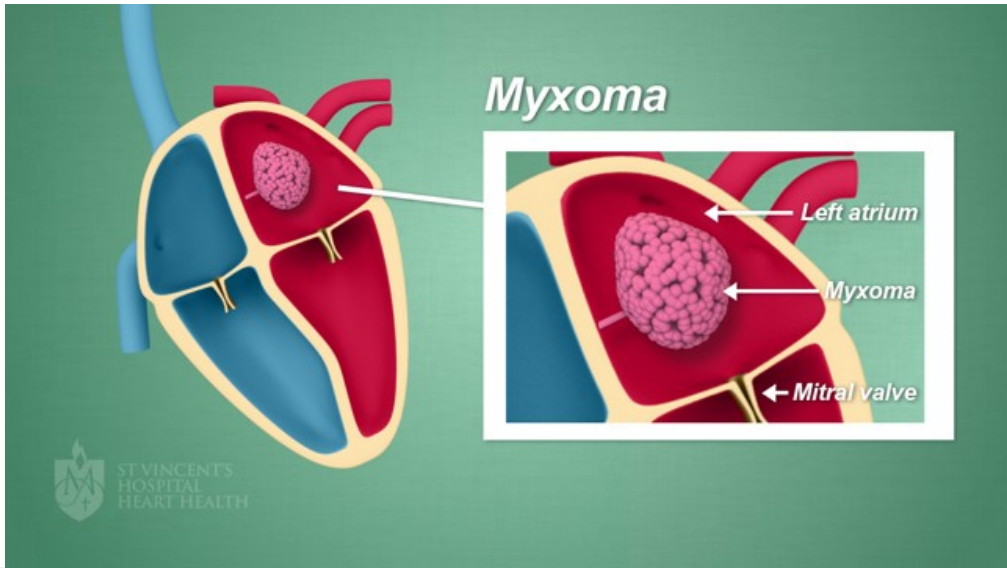
Cardiac Tumors

- cardiac tumors are rare. Cardiac tumors comprise primary and secondary metastatic tumors.
- Primary tumors:
- Primary cardiac tumors are uncommon; and usually benign.
- In descending order of frequency, the most common tumors are:
  - Myxomas (most common).
  - Fibromas.
  - Lipomas.
  - papillary fibroelastomas.
  - Rhabdomyomas (most frequent in infants and children, they often regress spontaneously).

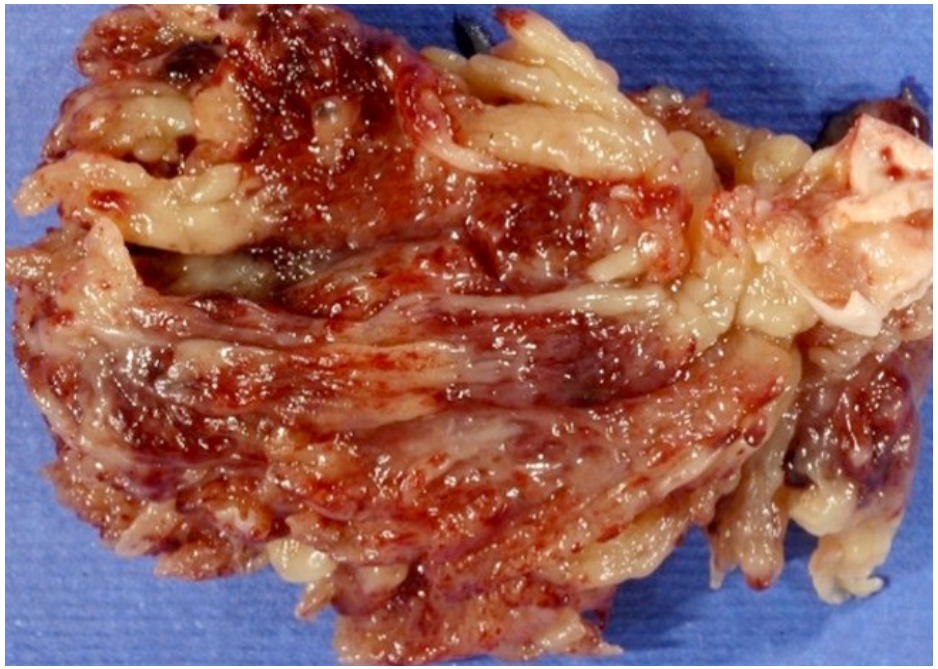
- Angiosarcomas constitute the most common primary malignant tumor of the heart.

Myxoma

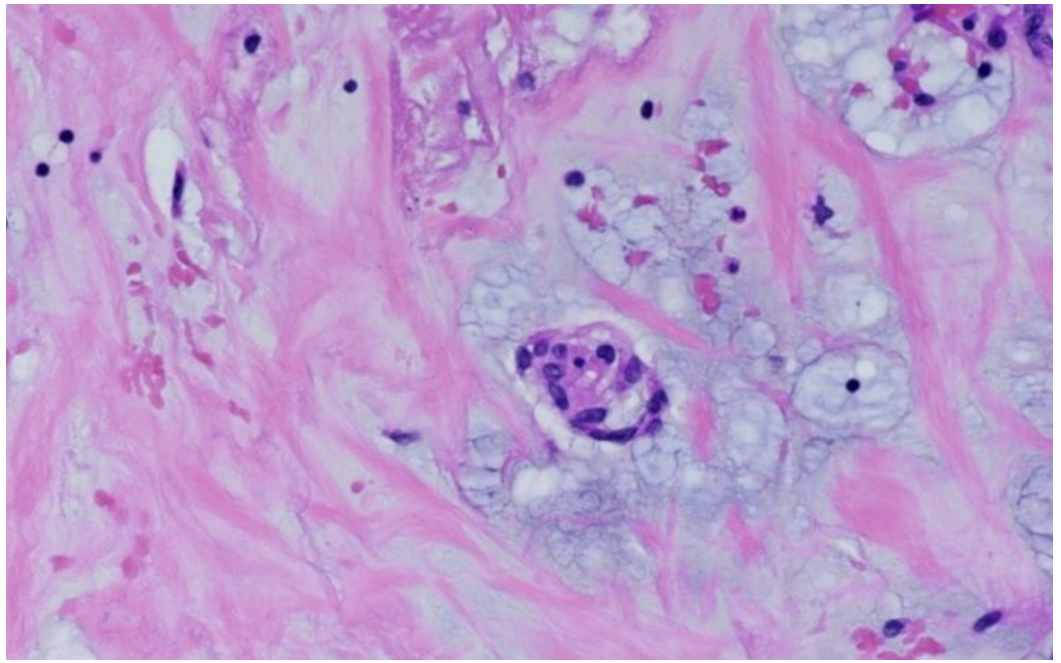
- Most common primary tumors of the heart, usually single in sporadic forms and mainly located in the left atrium.
- May cause sudden death, usually due to mitral valve obstruction.
- clinical manifestations:
- valvular “ball-valve” obstruction.
- embolization.
- fever and malaise.
- Echocardiography is the diagnostic modality of choice.
- surgical resection is almost uniformly curative.



Morphology



Grossly : appear as sessile or pedunculated mass.



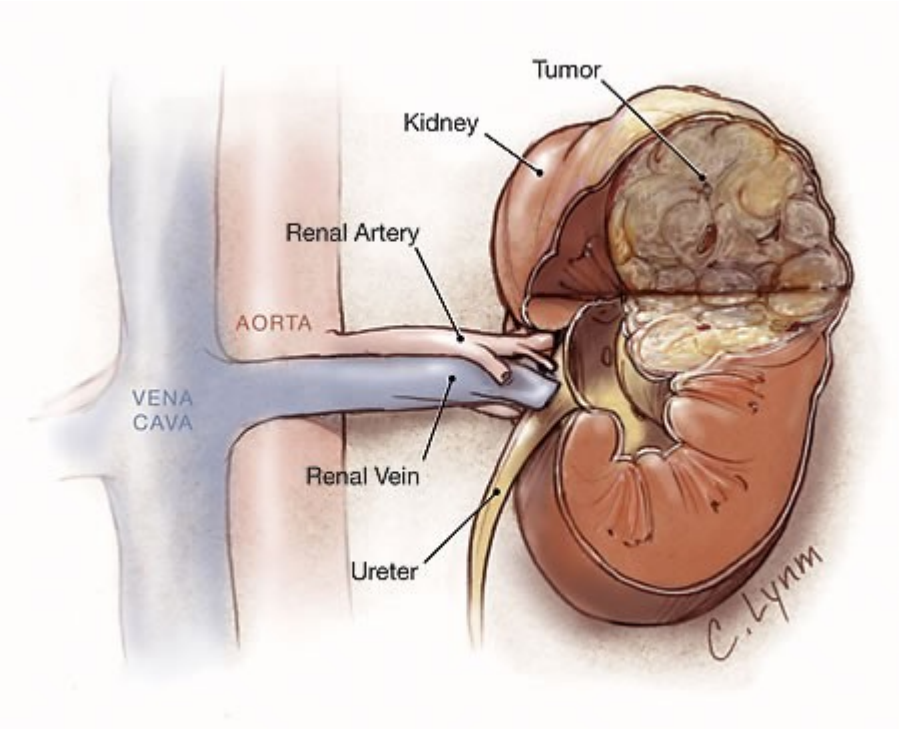
Microscopic: neoplastic cells within myxoid stroma

Table 11.6 Cardiovascular Effects of Noncardiac Neoplasms

Direct Consequences of Tumor
Pericardial and myocardial metastases
Large vessel obstruction
Pulmonary tumor emboli
Indirect Consequences of Tumor (Complications of Circulating Mediators)
Nonbacterial thrombotic endocarditis
Carcinoid heart disease
Pheochromocytoma-associated heart disease
Myeloma-associated amyloidosis
Effects of Tumor Therapy
Chemotherapy
Radiation therapy

Secondary cardiac tumors

- The most frequent metastatic tumors involving the heart are:
- carcinomas of the lung.
- Carcinoma of the breast.
- melanomas.
- leukemia's and lymphomas.



- Metastases can reach the heart and pericardium by:
- lymphatic extension.
- hematogenous seeding
- direct contiguous extension.
- venous extension

Carcinoid Heart Disease

- The carcinoid syndrome results from bioactive compounds such as serotonin released by carcinoid tumors (tumor arising from Neuroendocrine cells).
- Cardiac lesions typically do not occur until there is a massive hepatic metastasis since the liver normally inactivates circulating mediators before they can affect the heart.
- Classically, endocardium and valves of the right heart are primarily affected since they are the first cardiac tissues bathed by the mediators.

- The mediators elaborated by carcinoid tumors include serotonin (5-hydroxytryptamine), kallikrein, bradykinin, histamine, prostaglandins, and tachykinins.

- systemic manifestations include :
- Flushing.
- diarrhea.
- Dermatitis.
- bronchoconstriction.