# Cardiovascular system

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TOPICS:

- CARDIOMYOPATHIES.
- MYOCARDITIES.
- PERICARDIAL DISEASE.
- CARDIAC TUMORS.

# CARDIOMYOPATHIES

- ✓ **Cardiomyopathies** (literally, “heart muscle diseases”): Cardiac diseases attributable to intrinsic myocardial dysfunction.
- ✓ These can be primary—that is, principally

confined to the myocardium—or secondary presenting as the cardiac manifestation of a systemic disorder.

- For purposes of general diagnosis and therapy, **three** time-honored clinical, functional, and pathologic patterns are recognized:

1. Dilated cardiomyopathy (DCM) (including arrhythmogenic right ventricular cardiomyopathy)
2. Hypertrophic cardiomyopathy (HCM)
3. Restrictive cardiomyopathy

# 1-Dilated Cardiomyopathy

- characterized by *progressive cardiac dilation and contractile (systolic) dysfunction,* usually with concurrent hypertrophy; regardless of cause, the clinicopathologic patterns are similar.

# At least five general pathways can lead to end-stage DCM :

• Genetic causes. DCM has a hereditary basis in 20% to 50% . They Could be:

1. Autosomal dominant inheritance is the predominant pattern, most commonly involving mutations in encoding cytoskeletal proteins, or proteins that link the sarcomere to the cytoskeleton.

2. X-linked DCM is most frequently associated with dystrophin gene mutations affecting the cell membrane protein that physically couples the intracellular cytoskeleton to the ECM.).

3. Mutations of genes in the mitochondrial genome.

• Infection. Mostly viral in origin.

• Alcohol or other toxic exposure.

. Peripartum cardiomyopathy occurs late in gestation or several weeks to months postpartum. The etiology is likely to be multifactorial.

• Iron overload in the heart can result either from hereditary hemochromatosis or from multiple transfusions.

# MORPHOLOGY

- ✓ The heart in DCM characteristically is enlarged (up to 2-3 times the normal weight) and flabby, with dilation of all chambers).
- ✓ The characteristic histologic abnormalities in  is DCM secondary to iron overload, in which marked accumulation of intramyocardial hemosiderin is demonstrable by staining with Prussian blue.
- ✓ Most myocytes exhibit hypertrophy with enlarged nuclei, but many are attenuated, stretched, and irregular. There is also variable interstitial and endocardial fibrosis, with scattered areas of replacement fibrosis.
- ✓ Mural thrombi are often present.

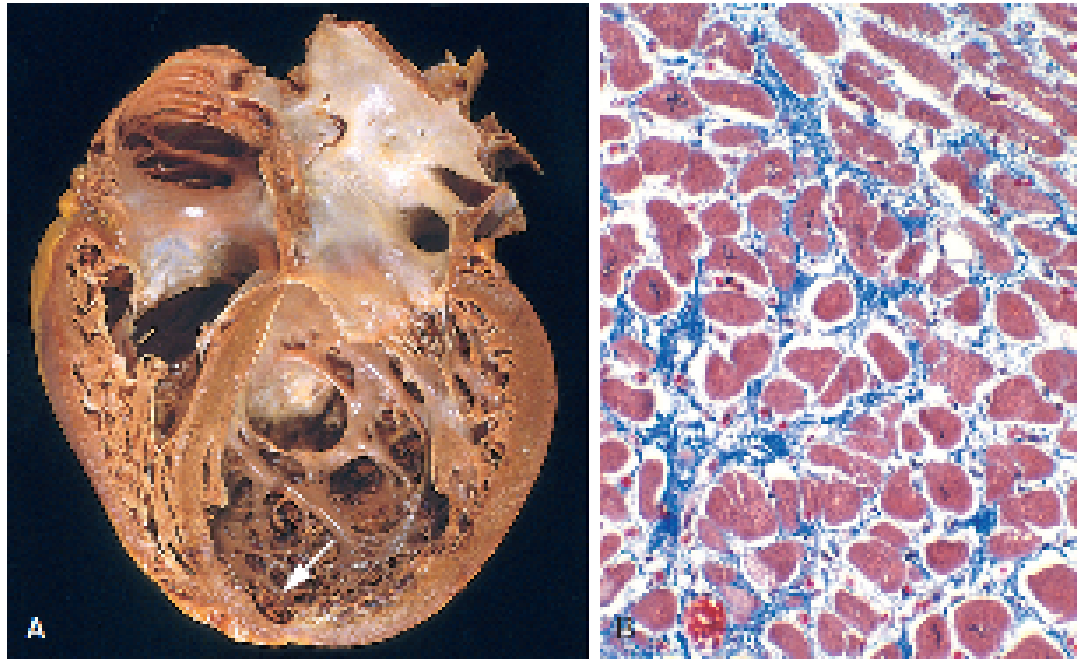


Figure 10–26 Dilated cardiomyopathy (DCM). A, Four chamber dilation and hypertrophy are evident. A small mural thrombus can be seen at the apex of the left ventricle (arrow). B, The nonspecific histologic pattern in typical DCM, with myocyte hypertrophy and interstitial fibrosis (collagen is blue in this Masson trichrome–stained preparation).

# Clinical Features

- DCM can occur at any age but most commonly is diagnosed between the ages of 20 and 50 years.
- It typically manifests with signs of slowly progressive CHF, including Dyspnea and easy fatigability.
- The fundamental defect in DCM is ineffective contraction. Thus, in end-stage DCM, the cardiac ejection fraction typically is less than 25%.
- Secondary mitral regurgitation and abnormal cardiac rhythms are common, and embolism from intracardiac (mural) thrombi can occur.
- Half of the patients die within 2 years.
- Cardiac transplantation is the only definitive treatment. Implantation of long-term ventricular assist devices is being increasingly utilized.

# *Arrhythmogenic Right Ventricular Cardiomyopathy*

- Is an autosomal dominant disorder of cardiac muscle with variable penetrance.
- It classically manifests with right sided heart failure and rhythm disturbances that can cause sudden cardiac death.
- Morphologically, the right ventricular wall is severely thinned owing to myocyte replacement by massive fatty infiltration and lesser amounts of fibrosis.
- Many of the mutations involve genes encoding

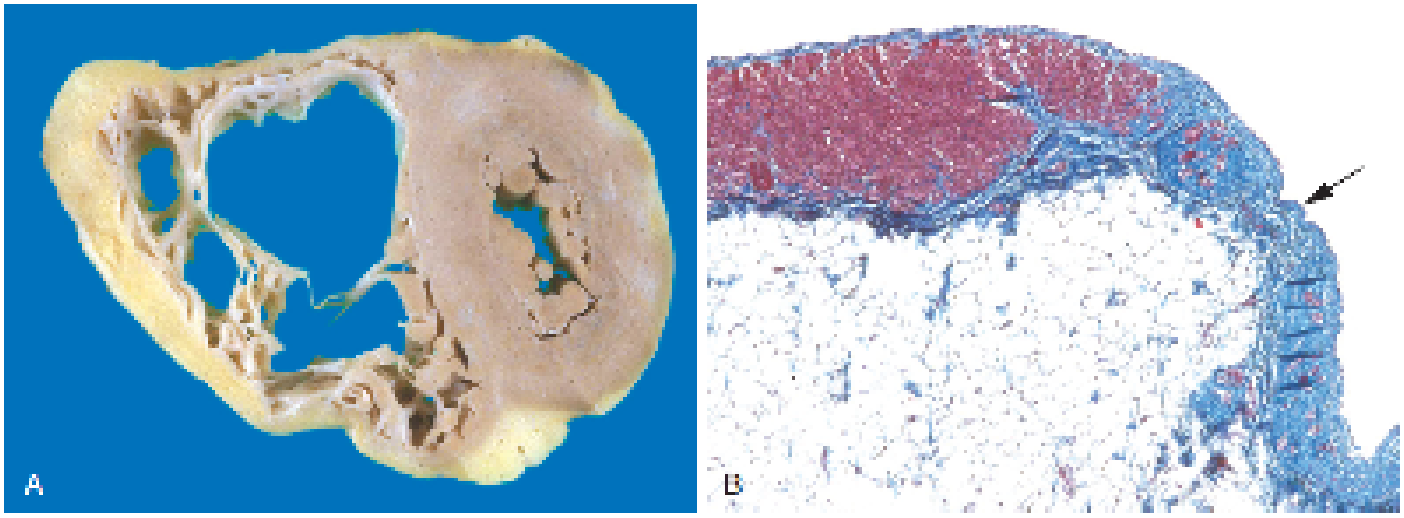


Figure 10–27 Arrhythmogenic right ventricular cardiomyopathy. A, The right ventricle is markedly dilated with focal, almost transmural replacement of the free wall by adipose tissue and fibrosis. The left ventricle has a grossly normal appearance in this heart. It can be involved (albeit to a lesser extent) in some instances. B, The right ventricular myocardium (red) is focally replaced by fibrous connective tissue (blue, arrow) and fat (Masson trichrome stain).

# Hypertrophic cardiomyopathy (HCM)

- Characterized by *myocardial hypertrophy, defective diastolic filling,* and—in a third of cases—*ventricular outflow obstruction.*
- The heart is thick-walled, heavy, and  hypercontractile.
- Systolic function usually is preserved in HCM, but the myocardium does not relax and therefore exhibits primary diastolic dysfunction.
- HCM needs to be distinguished clinically from disorders causing ventricular stiffness (e.g., amyloid deposition) and ventricular hypertrophy (e.g., aortic stenosis and hypertension).
- **HCM is fundamentally a disorder of sarcomeric proteins. Of these, β-myosin heavy chain is most frequently affected**.

# MORPHOLOGY

- ✓ Classically, there is disproportionate thickening of the ventricular septum relative to the left ventricle free wall (so-called **asymmetric septal hypertrophy**); nevertheless, in about 10% of cases of HCM, concentric hypertrophy is seen. On longitudinal sectioning, the ventricular cavity loses its usual round-to-ovoid shape and is compressed into a “banana-like” configuration.

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

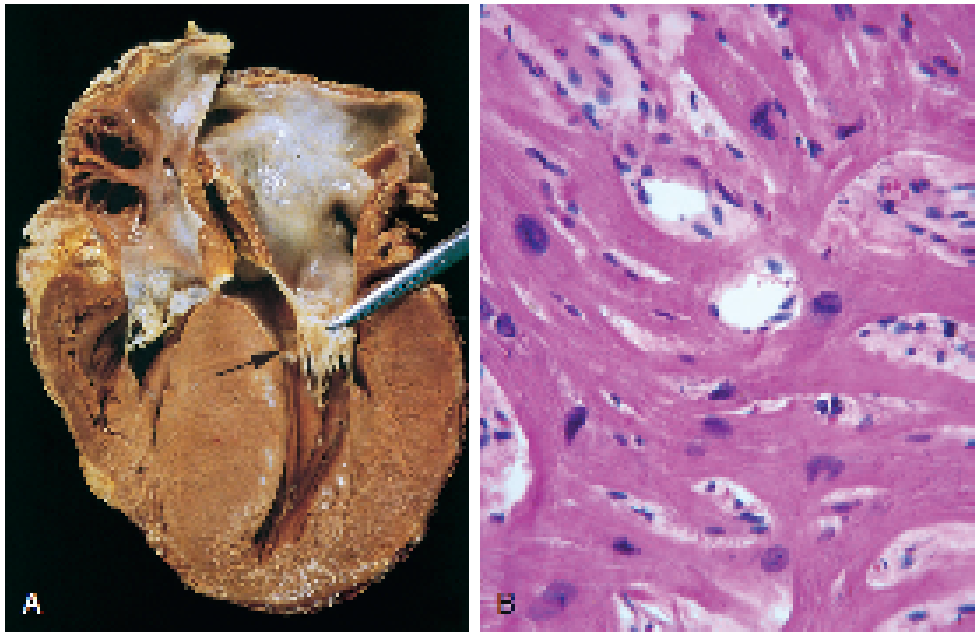


Figure 10–28 Hypertrophic cardiomyopathy with asymmetric septal hypertrophy. A, The septal muscle bulges into the left ventricular outflow tract, giving rise to a "banana shaped" ventricular lumen, and the left atrium is enlarged. The anterior mitral leaflet has been moved away from the septum to reveal a fibrous endocardial plaque (arrow) (see text). B, Histologic appearance demonstrating disarray, extreme hypertrophy, and characteristic branching of myocytes, as well as interstitial fibrosis.

# Clinical Features

- Although HCM can present at any age it typically manifests during the postpubertal growth spurt.
- In almost one third of the cases of sudden cardiac death in athletes under the age of 35, the underlying cause is HCM.
- Atrial and ventricular fibrillations with mural thrombus formation, infective endocarditis of the mitral valve, CHF, and sudden death.
- Most patients are improved by therapy that promotes ventricular relaxation or partial surgical excision.

# Restrictive Cardiomyopathy

- Characterized by a *primary decrease in ventricular compliance, resulting in impaired ventricular filling during diastole* (simply put, the wall is *stiffer*).
- Restrictive cardiomyopathy can be idiopathic or associated with systemic diseases that also happen to affect the myocardium also happen to affect the myocardium, for example:

* Radiation fibrosis.

* Amyloidosis.

* Products of inborn errors of metabolism.

- ✓ *Amyloidosis* is caused by the deposition of extracellular proteins with the predilection for forming insolubleβ-pleated sheets. Cardiac amyloidosis can occur with systemic amyloidosis or can be restricted to the heart, particularly in the case of *senile cardiac amyloidosis.*

- ✓ *Endomyocardial fibrosis* is principally a disease of children and young adults in Africa and other tropical areas;

. It is characterized by dense diffuse fibrosis of the ventricular endocardium and subendocardium, often involving the tricuspid and mitral valves.

. Endomyocardial fibrosis has been linked to nutritional deficiencies and/or inflammation related to helminthic infections (e.g., hypereosinophilia); worldwide, it is the most common form of restrictive cardiomyopathy.

- ✓ *Loeffler endomyocarditis* also exhibits endocardial fibrosis, typically associated with formation of large mural thrombi, but without geographic predilection. Histologic examination typically shows peripheral hypereosinophilia and eosinophilic tissue infiltrates.

# MORPHOLOGY

- ✓ The ventricles are of approximately normal size or only slightly enlarged, the cavities are not dilated, and the myocardium is firm.
- ✓ Microscopic examination reveals variable degrees of interstitial fibrosis.

**Table 10–6** 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 diseases; 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%–65%.

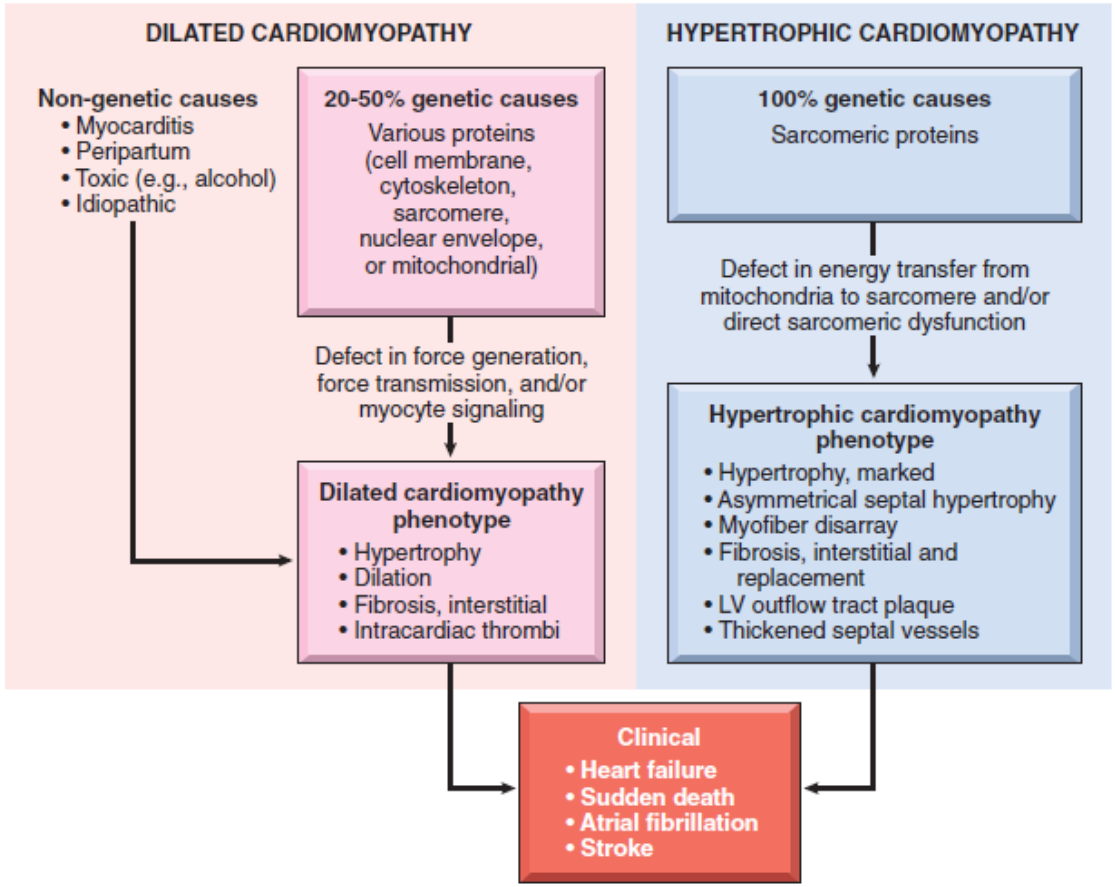


**Figure 10–25** Causes and consequences of dilated and hypertrophic cardiomyopathy. A significant fraction of dilated cardiomyopathies—and virtually all hypertrophic cardiomyopathies—have a genetic origin. Dilated cardiomyopathies can be caused by mutations in cytoskeletal, sarcomeric, nuclear envelope, or mitochondrial proteins; hypertrophic cardiomyopathies typically are caused by sarcomeric protein mutations. Although the two forms of cardiomyopathy differ in cause and morphology, they have common clinical end points. LV, left ventricle.

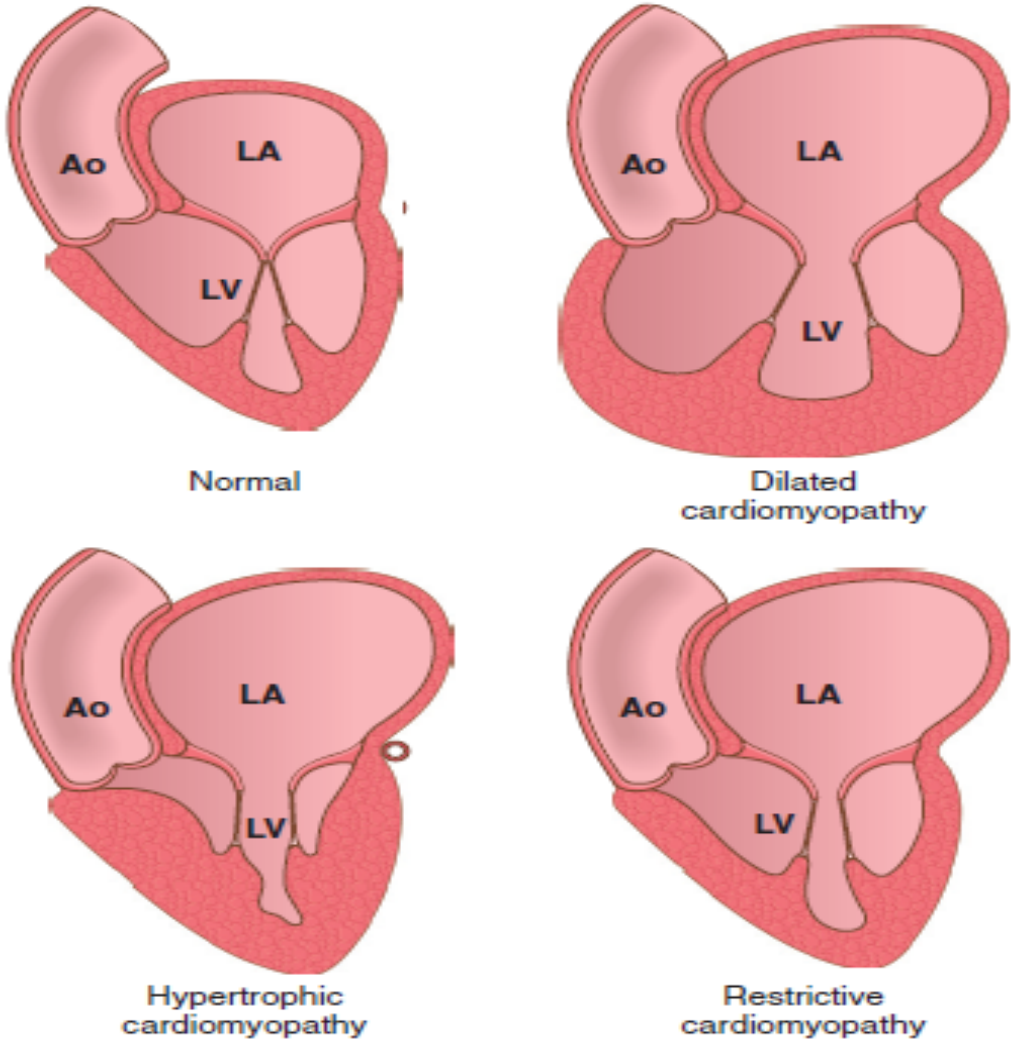


**Figure 10–24** The three major forms of cardiomyopathy. Dilated cardiomyopathy leads primarily to systolic dysfunction, whereas restrictive and hypertrophic cardiomyopathies result in diastolic dysfunction. Note the changes in atrial and/or ventricular dilation and in ventricular wall thickness. Ao, aorta; LA, left atrium; LV, left ventricle.

# Myocarditis

Myocarditis encompasses a diverse group of clinical entities in which infectious agents and/or inflammatory processes primarily target the myocardium.

## ❑ Infectious causes

1-Viral infections are the most commoncause of myocarditis, with coxsackieviruses A and B and other enteroviruses accounting for a majority of the cases.

2-The nonviral infectious causes of myocarditis :

- ✓ The protozoan Trypanosoma cruzi is the agent of Chagas disease.
- ✓ Toxoplasma gondii (household cats are the most common vector), particularly in immunocompromised persons.
- ✓ Trichinosis is the most common helminthic disease with associated cardiac involvement.

## ❑ Noninfectious causes

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

# MORPHOLOGY

In acute myocarditis, the heart may appear normal or dilated; in advanced stages, the myocardium typically is flabby and often mottled with pale and hemorrhagic areas.

**Microscopically**, active myocarditis is characterized by edema, interstitial inflammatory infiltrates, and myocyte injury .

- In **hypersensitivity myocarditis**, interstitial and perivascular infiltrates are composed of lymphocytes, macrophages, and a high proportion of eosinophils.

- **Giant cell myocarditis** is a morphologically distinctive entity characterized by widespread inflammatory cellular infiltrates containing multinucleate giant cells.

- **Chagas myocarditis** is characterized by the parasitization of scattered myofibers by trypanosomes accompanied by an inflammatory infiltrate of neutrophils, lymphocytes, macrophages, and occasional eosinophils.

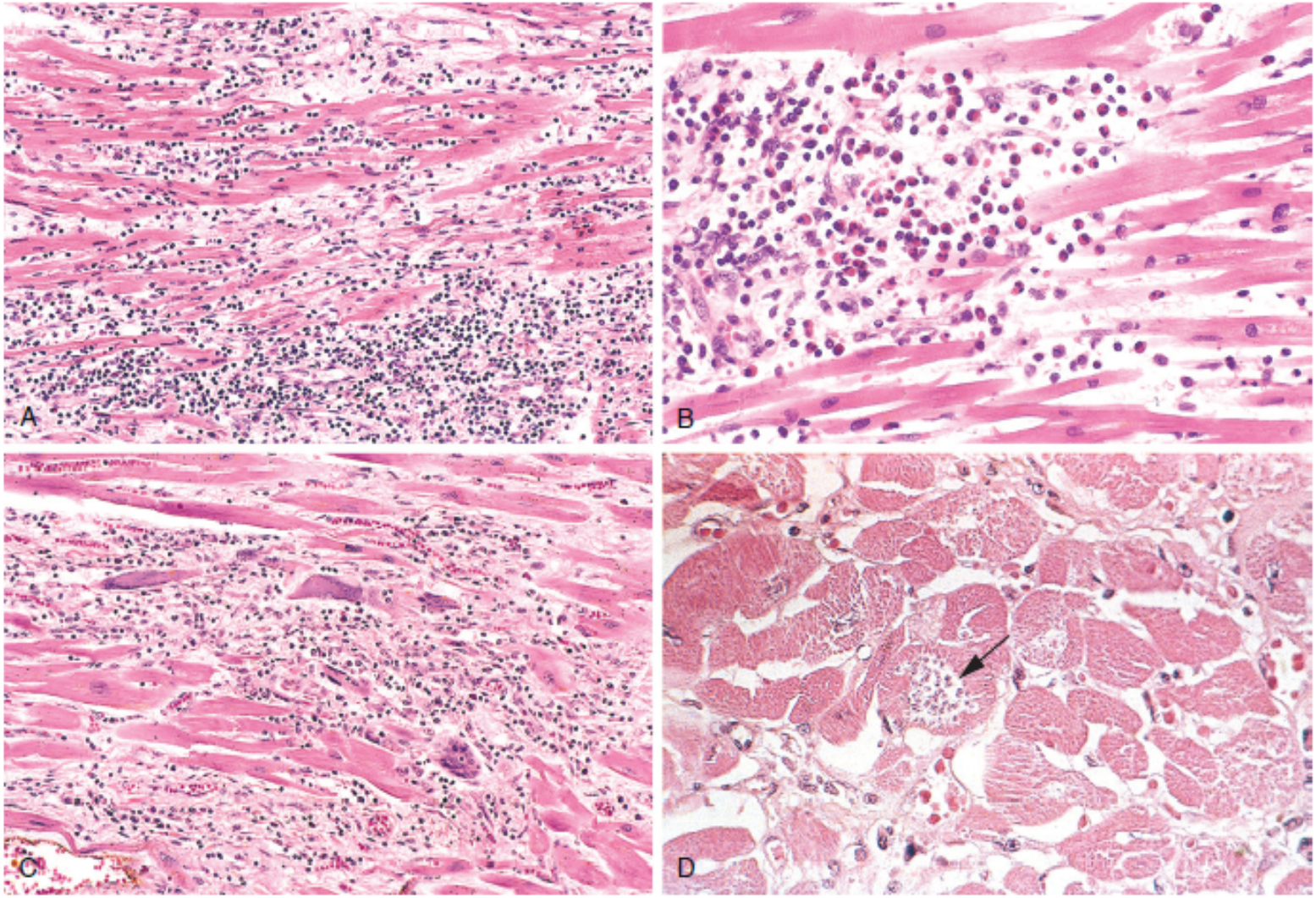


**Figure 10–29** Myocarditis. **A,** Lymphocytic myocarditis, with edema and associated myocyte injury. **B,** Hypersensitivity myocarditis, characterized by perivascular eosinophil-rich inflammatory infiltrates. **C,** Giant cell myocarditis, with lymphocyte and macrophage infiltrates, extensive myocyte damage, and multinucleate giant cells. **D,** Chagas myocarditis. A myofiber distended with trypanosomes (*arrow*) is present, along with mononuclear inflammation and myofiber necrosis.

# PERICARDIAL DISEASE

# 1-Pericarditis

- Primary pericarditis is uncommon. It most often is due to

viral infection (typically with concurrent myocarditis),

although bacteria, fungi, or parasites may also be involved.

- In most cases, pericarditis is secondary to acute MI, cardiac surgery, radiation to the mediastinum, or processes involvingother thoracic structures (e.g., pneumonia or pleuritis).

*Uremia is the most common systemic disorder associated

with pericarditis.

Pericarditis can:

(1) Cause immediate hemodynamic complications if it elicits a large effusion (resulting in cardiac *tamponade*).

(2) Resolve without significant sequelae.

(3) Progress to a chronic fibrosing process.

# Clinical Features

- Atypical chest pain (not related to exertion and worse in recumbency)
- Pominent friction rub.
- Cardiac tamponade, with declining cardiac output and consequentshock.
- Chronic constrictive pericarditis produces a combination of right-sided venous distention and low cardiac output, similar to the clinical picture in restrictive cardiomyopathy.

# MORPHOLOGY

Tuberculous pericarditis:

Exhibits areas of caseation

Acute viral pericarditis or uremia:

The exudate typically is fibrinous, imparting an irregular, shaggy appearance to the pericardial surface (so-called “bread and butter” pericarditis).

Pericarditis due to malignancy

Associated with an exuberant, shaggy fibrinous exudate and a bloody effusion.

Acute bacterial pericarditis:

The exudate is fibrinopurulent (suppurative), often with areas of frank pus .

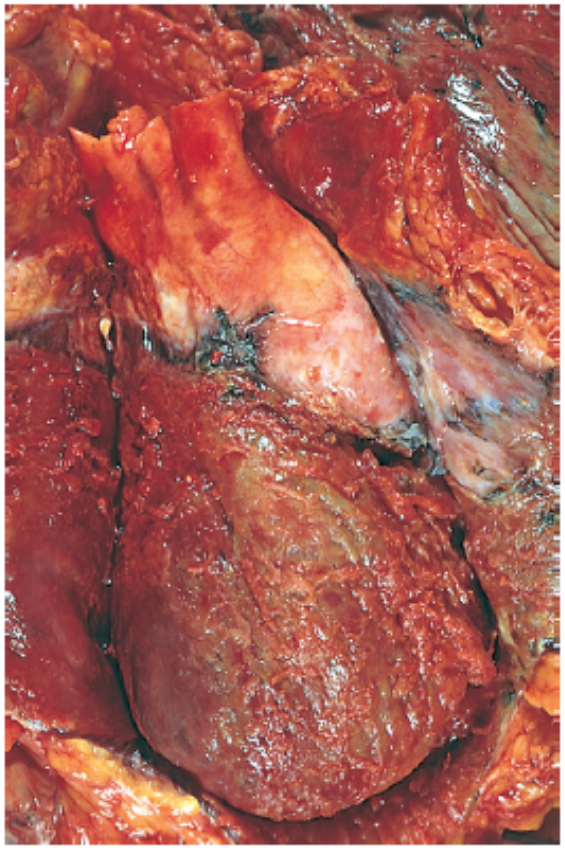

**Figure 10–30** Acute suppurative (purulent, exudative) pericarditis, caused by extension from a pneumonia.

# 2-Pericardial Effusions

- Normally, the pericardial sac contains at most 30 to 50 mL of clear, serous fluid.

1. Serous and/or fibrinous effusions in excess of this amount occur most commonly in the setting of pericardial inflammation.
2. Serous: congestive heart failure, hypoalbuminemia of any cause
3. Serosanguineous: blunt chest trauma, malignancy, ruptured MI or aortic dissection
4. Chylous: mediastinal lymphatic obstruction

- The consequences of pericardial accumulations depend on the volume of fluid and the ability of the parietal pericardium to stretch.

- slowly accumulating effusions—even as large as 1000 mL—can be welltolerated

rapidly developing collections of as little as 250 mL can so restrict diastolic cardiac filling as to produce potentially fatal cardiac tamponade.

# CARDIAC TUMORS

- Tumor metastases constitute the most common malignancy of the heart.
- Primary cardiac tumors are uncommon; moreover, most also are (fortunately) benign.
- The five most common have nomalignant potential and account for 80% to 90% of all primary heart tumors. In descending order of frequency, these are myxomas, fibromas, lipomas, papillary fibroelastomas, and rhabdomyomas. Angiosarcomas
- Clinical Features:
  1. Valvular “ball-valve” obstruction.
  2. Embolization.
  3. Syndrome of constitutional signs and symptoms including fever and malaise.
- Echocardiography is the diagnostic modality of choice, and surgical resection is almost uniformly curative.

- Myxomas are the most common primary tumors of the adult heart.

Roughly 90% are atrial, with the left atrium accounting for 80% of those.

* Histologically, myxomas are composed of stellate, frequently multinucleated myxoma cells (typically with hyperchromatic nuclei), admixed with cells showing endothelial,

smooth muscle, and/or fibroblastic differentiation.

- Rhabdomyomas are the most frequent primary tumors of the heart in infants and children; they frequently are discovered owing to valvular or outflow obstruction. Cardiac rhabdomyomas occur with high frequency in patients with tuberous sclerosis caused by mutations in the TSC1 or TSC2 tumor suppressor genes.

* Histologic examination shows a mixed population of cells; most characteristic, however, are large, rounded, or polygonal cells containing numerous glycogen-laden vacuoles separated by strands of cytoplasm running from the plasma membrane to the centrally located nucleus, so-called spider cells.

- Lipomas are localized, poorly encapsulated masses of adipose tissue; these can be asymptomatic, create ball-valve obstructions (as with myxomas), or produce arrhythmias.

- Papillary Fibroelastomas usually are only incidentally identified lesions, although they can embolize. Generally located on valves, they form distinctive clusters (up to 1 cm in diameter) of hairlike projections.

*Histologic examination shows myxoid connective tissue containing abundant mucopolysaccharide matrix and laminated elastic fibers, all surrounded by endothelium.

- Cardiac Angiosarcomas.

*Histologic examination revealed lesions ranging from plump atypical endothelial cells that form vascular channels (to undifferentiated spindle cell tumors without discernible blood vessels.

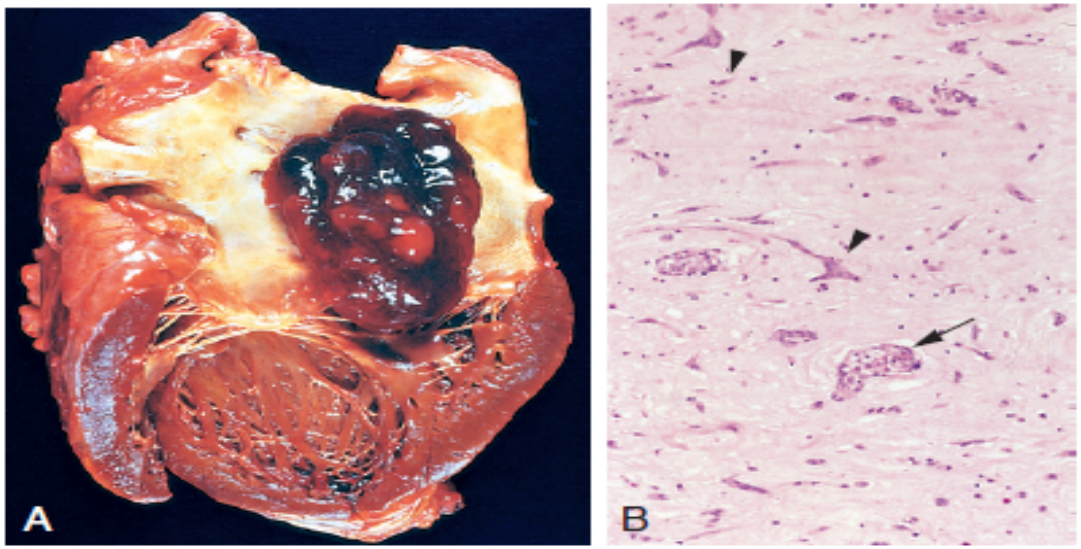


**Figure 10–31** Atrial myxoma. **A,** A large pedunculated lesion arises from the region of the fossa ovalis and extends into the mitral valve orifice. **B,** Abundant amorphous extracellular matrix contains scattered multinucleate myxoma cells (*arrowheads*) in various groupings, including abnormal vascular formations (*arrow*).