

# Myocarditis and Cardiomyopathies

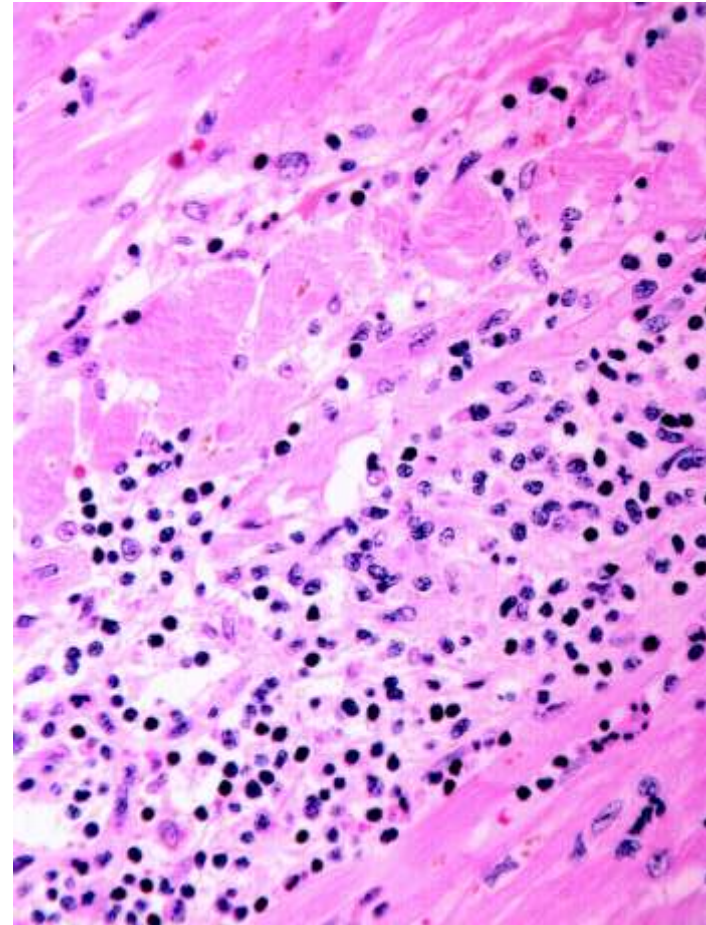
LECTURE IN INTERNAL MEDICINE FOR V COURSE STUDENTS

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# Myocarditis

# Plan of the Lecture

- Definition
- Epidemiology
- Risk factors
- Etiology
- Mechanisms
- Classification
- Clinical investigation
- Diagnosis
- Treatment
- Prognosis
- Prophylaxis
- Abbreviations
- Diagnostic and treatment guidelines



# Definition

Myocarditis is an inflammatory disease of the myocardium with a wide range of clinical presentations, from subtle to devastating, diagnosed by established histological, immunological and immunohistochemical criteria.

# Epidemiology

- Incidence is usually estimated at 1-10 cases per 100,000 persons.
- Incidence of positive right ventricular biopsy findings in patients with suspected myocarditis is highly variable (ranging from 0-80%).
- According to estimates, as many as 1-5% of patients with acute viral infections may have involvement of the myocardium.
- No particular race predilection is noted for myocarditis except for peripartum cardiomyopathy that appears to have a higher incidence in patients of African descent.
- The incidence of myocarditis is similar between males and females.
- Patients are usually fairly young.

# Risk Factors and Etiology: 1

Worldwide, the most common cause is Chagas' disease, an illness endemic to Central and South America that is due to infection by the protozoan *Trypanosoma cruzi*.

## Infections

- Viral (adenovirus, parvovirus B19, coxsackie virus, human immunodeficiency virus (HIV), enterovirus, rubella virus, poliovirus, cytomegalovirus, human herpesvirus, and possibly hepatitis C),
- Protozoan (*Trypanosoma cruzi* causing *Chagas disease* and *Toxoplasma gondii*),
- Bacterial (*Brucella*, *Corynebacterium diphtheriae*, *gonococcus*, *Haemophilus influenzae*, *Actinomyces*, *Tropheryma whipplei*, *Vibrio cholerae*, *Borrelia burgdorferi*, leptospirosis, and Rickettsia, *Mycoplasma pneumoniae*).

# Risk Factors and Etiology: 2

- Fungal (*Aspergillus*).
- Parasitic (ascaris, *Echinococcus granulosus*, *Paragonimus westermani*, schistosoma, *Taenia solium*, *Trichinella spiralis*, visceral larva migrans, and *Wuchereria bancrofti*).
- Bacterial myocarditis is rare in patients without immunodeficiency.
- Toxins (drugs, including alcohol, anthracyclines, chemotherapy, antipsychotics, also some designer drugs such as mephedrone).
- Immunologic (allergic (acetazolamide, amitriptyline), rejection after a heart transplant, autoantigens (scleroderma, systemic lupus erythematosus, sarcoidosis, Kawasaki disease, etc. ), toxins (arsenic, toxic shock syndrome toxin, carbon monoxide, or snake venom), heavy metals (copper or iron).
- Physical agents (electric shock, hyperpyrexia, and radiation).

# Mechanisms

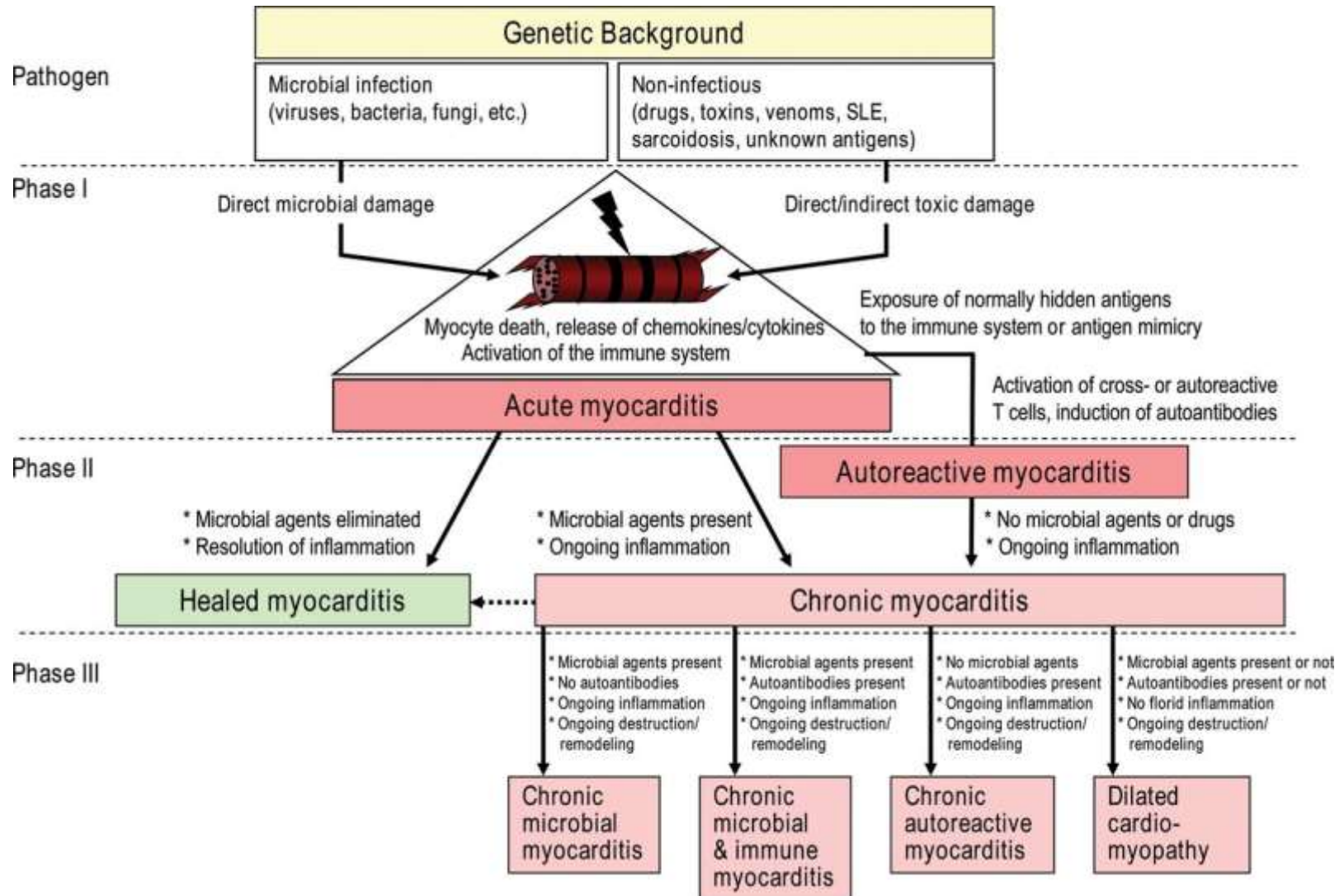
## (Viral and Autoimmune)

- There is evidence for viral and autoimmune mechanisms, acting in individuals with or without a genetic predisposition.
- Enteroviruses that preferentially enter cardiomyocytes via specific receptors cause severe cytopathic effects due to virus replication in the first 2 weeks post-infection.
- As a consequence, a humoral and cellular immune response, mainly consisting of macrophages and CD4+ and CD8+ T-lymphocytes, leads to the elimination of the infectious agent within 2 weeks following infection.
- The ongoing infection and inflammation trigger autoimmune reactions in the heart, most likely as a result of myocyte necrosis and subsequent release of self-antigens previously hidden to the immune system.



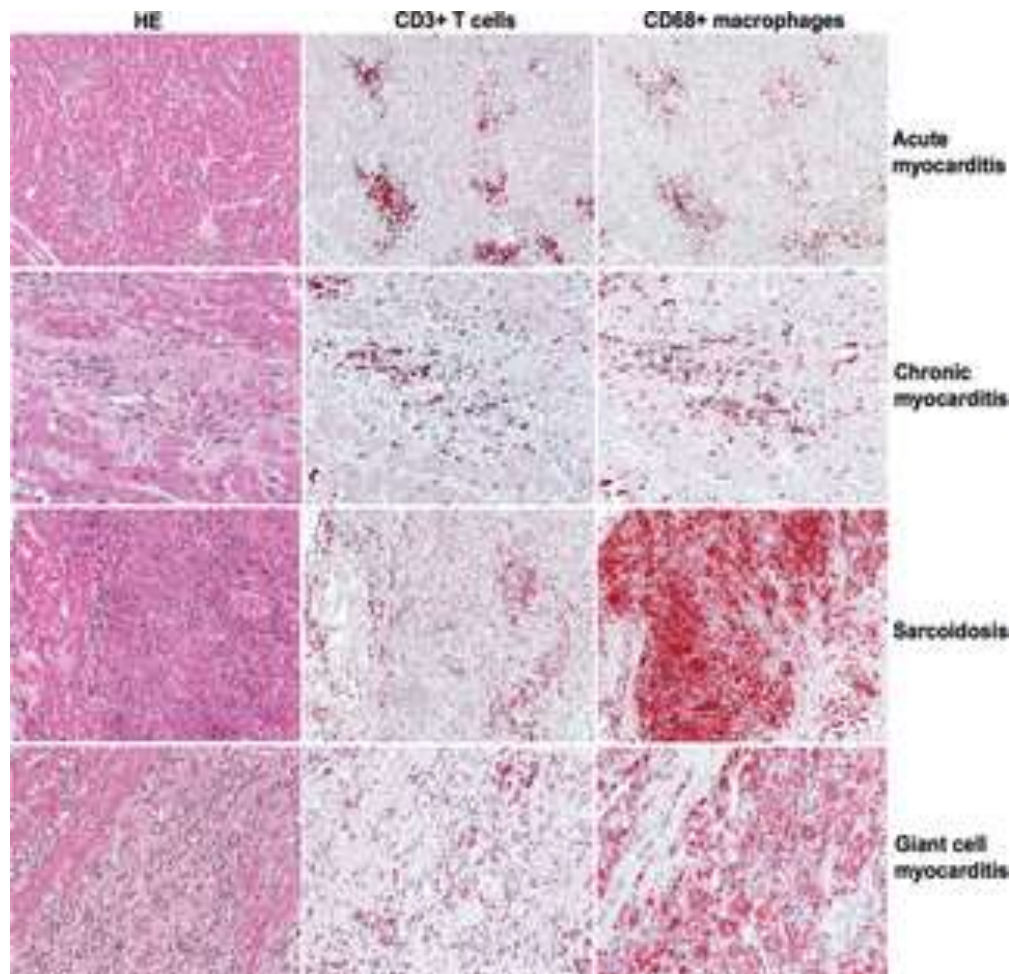
# Mechanisms

## (From Myocarditis to Dilated Cardiomyopathy)



# Mechanisms

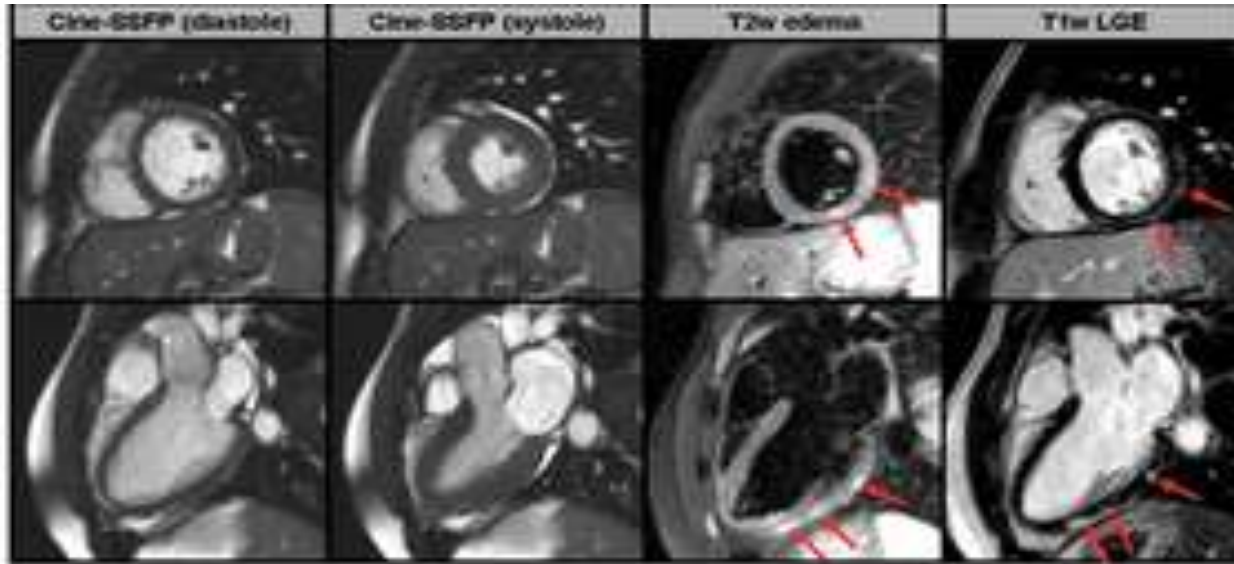
## (Histopathology and Immunopathology)



Acute lymphocytic myocarditis (first row), chronic lymphocytic myocarditis (second row), sarcoidosis (third row), and giant cell myocarditis (fourth row). Left column = haematoxylin-eosin; middle column = staining with anti-CD3 antibody (pan T lymphocyte marker); right column = staining with anti-CD68 antibody (macrophage marker).

# Mechanisms

## (Histopathology and Immunopathology)



Short-axis (upper line) and long-axis (lower line) images of a patient with acute myocarditis. In the first two columns, cine-SSFP images are shown in diastole and systole and suggest absence of any wall motion abnormality. In the next column, T2-weighted edema images demonstrate the presence of patchy focal edema in the subepicardium of the inferolateral wall (red arrows). In the last column, T1-weighted late gadolinium enhancement (LGE) images demonstrate presence of subepicardially distributed LGE (red arrows) which is typical for acute myocarditis.

# Classification

## (International Classification of Diseases (ICD))

I01.2 Acute rheumatic myocarditis

I40.0 Infective myocarditis

I40.1 Isolated myocarditis

I40.8 Other acute myocarditis

I40.9 Acute myocarditis, unspecified

I41\* Myocarditis in diseases classified elsewhere

I41.0\* Myocarditis in bacterial diseases classified elsewhere (diphtheritic (A36.8†), gonococcal (A54.8†), meningococcal (A39.5†), syphilitic (A52.0†), tuberculous (A18.8†))

I41.1\* Myocarditis in viral diseases classified elsewhere (influenzal myocarditis (acute) (J10.8†, J11.8†, J09†, B26.8†))

I41.2\* Myocarditis in other infectious and parasitic diseases classified elsewhere (Chagas disease (chronic) (B57.2†, B57.0†, B58.8†))

I41.8\* Myocarditis in other diseases classified elsewhere (rheumatoid myocarditis (M05.3†), sarcoid myocarditis (D86.8†))

I51.4 Myocarditis, unspecified (myocardial fibrosis)

# Classification

## (Etiology, Cell Type, Clinical Type)

Etiology	Cell type	Clinical type
Virus	Lymphocytic type	Acute
Bacteria	Giant cell type	Fulminant
Fungi	Eosinophilic type	Chronic
Rickettsia	Granulomatous type	(prolonged)
Spirochetes		(latent)
Protozoa, parasites		
Other causes of infection		
Drugs, chemical substances		
Allergy, autoimmune		
Collagen disease, Kawasaki disease		
Sarcoidosis		
Radiation, heat stroke		
Unknown cause, idiopathic		

# Classification

## (Lieberman' Classification)

- Fulminant myocarditis: follows a viral prodrome; distinct onset of illness consisting of severe cardiovascular compromise with ventricular dysfunction and multiple foci of active myocarditis; either resolves spontaneously or results in death.
- Acute myocarditis: less distinct onset of illness, with established ventricular dysfunction; may progress to dilated cardiomyopathy.
- Chronic active myocarditis : less distinct onset of illness, with clinical and histologic relapses; development of ventricular dysfunction associated with chronic inflammatory changes (including giant cells).
- Chronic persistent myocarditis: less distinct onset of illness; persistent histologic infiltrate with foci of myocyte necrosis but without ventricular dysfunction (despite symptoms, e.g., chest pain, palpitations).



# Classification

## (The Dallas Classification (1987))

### Initial biopsy:

- Myocarditis: myocardial necrosis, degeneration, or both, in the absence of significant coronary artery disease with adjacent inflammatory infiltrate with or without fibrosis,
- Borderline myocarditis: inflammatory infiltrate too sparse or myocyte damage not apparent,
- no myocarditis,

### Subsequent biopsy:

- Ongoing (persistent) myocarditis with or without fibrosis,
- Resolving (healing) myocarditis with or without fibrosis,
- Resolved (healed) myocarditis with or without fibrosis.

# Classification

## (WHO Marburg Criteria (1996))

First biopsy:

1. Acute (active) myocarditis: a clear-cut infiltrate (diffuse, focal or confluent) of  $\geq 14$  leukocytes/mm<sup>2</sup> (preferably activated T-cells).
2. Chronic myocarditis : an infiltrate of  $\geq 14$  leukocytes/mm<sup>2</sup> (diffuse, focal or confluent, preferably activated T-cells).
3. No myocarditis: No infiltrating cells or  $< 14$  leukocytes/mm<sup>2</sup>.

Subsequent biopsies:

1. Ongoing (persistent) myocarditis. Criteria as in 1 or 2 (features of an acute or chronic myocarditis).
2. Resolving (healing) myocarditis. Criteria as in 1 or 2 but the immunological process is sparser than in the first biopsy.
3. Resolved (healed) myocarditis. Corresponds to the Dallas classification.



# Clinical Investigation

## (Signs and Symptoms)

- The clinical signs of myocarditis include fever, cardiac rhythm disturbance (tachycardia, bradycardia, and arrhythmia), hypotension, gallop rhythm, rales, jugular venous dilatation, and cardiac tamponade.
- Flu-like symptoms: chills, fever, headache, muscle aches, general malaise.
- Cardiac symptoms (a few hours to a few days after the initial signs and symptoms): heart failure, chest pain due to pericardial irritation, symptoms associated with heart block and arrhythmia.
- Gastrointestinal symptoms: decreased appetite, nausea, vomiting, and diarrhea.

# Clinical Investigation

## (Course of the Disease)

- The primary signs and symptoms and disease progression of myocarditis are relatively easy to grasp.
- The inflammatory phase lasts one to two weeks, and is followed by a recovery phase.
- Myocarditis causes myocardial necrosis and inflammation, which result in cardiac dysfunction and failure.
- Myocarditis usually manifests in an otherwise healthy person and can result in rapidly progressive (and often fatal) heart failure and arrhythmia

# Clinical Investigation

## (Specific Findings in Special Cases)

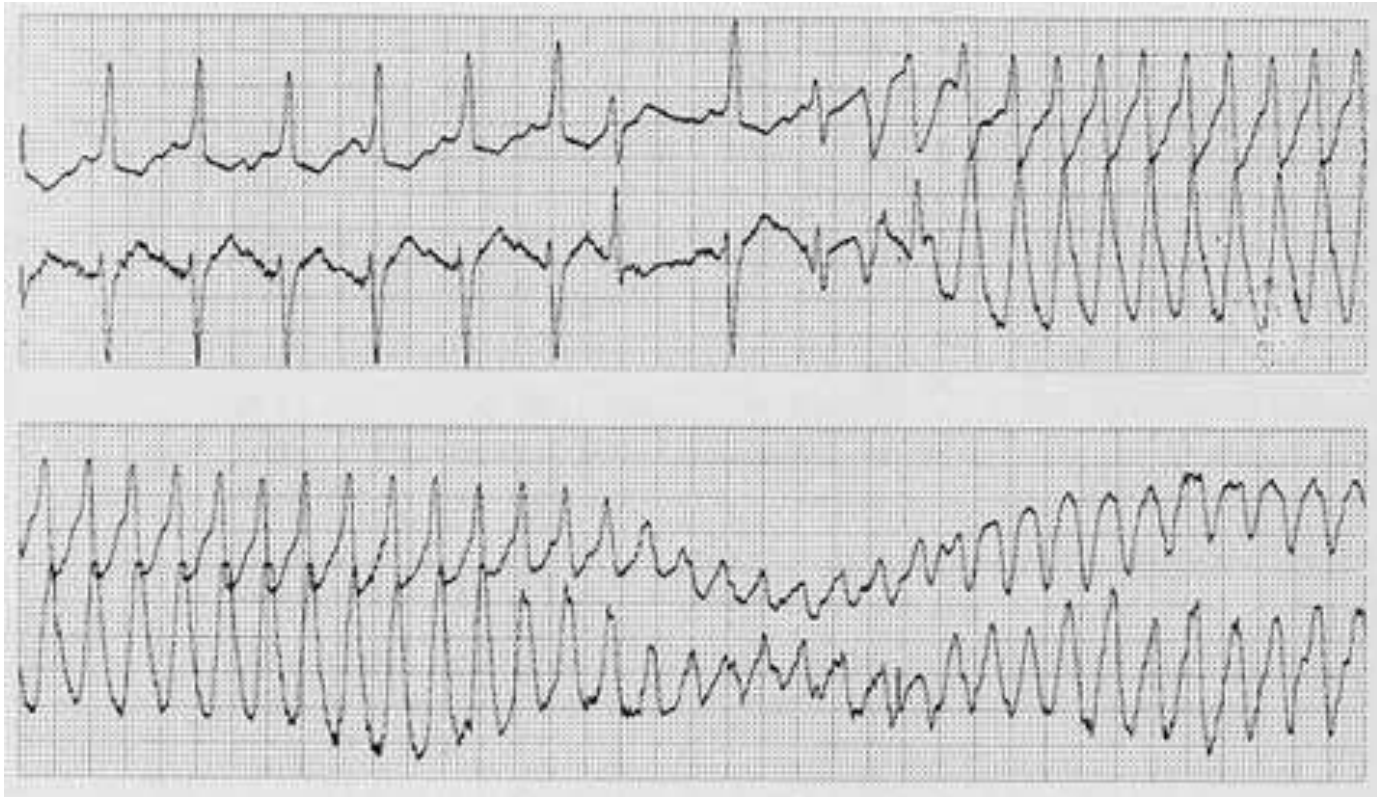
- Sarcoid myocarditis: lymphadenopathy, also with arrhythmias, sarcoid involvement in other organs (up to 70%),
- Acute rheumatic fever: usually affects heart in 50-90%; associated signs, such as erythema marginatum, polyarthralgia, chorea, subcutaneous nodules (Jones criteria),
- Hypersensitive/eosinophilic myocarditis: pruritic maculopapular rash and history of using offending drug,
- Giant cell myocarditis: sustained ventricular tachycardia in rapidly progressive heart failure,
- Peripartum cardiomyopathy: heart failure developing in the last month of pregnancy or within 5 months following delivery.

# Diagnosis

## (Instrumental)

- Chest X-Ray: visualizing cardiac enlargement and pulmonary congestion.
- Electrocardiography (ECG): abnormal ST-T waves, conduction block, gradual increase in the width of the QRS complex, potentially fatal arrhythmias.
- Echocardiography: transient wall thickening, reduced wall motion, reduced cardiac chamber size, pericardial effusion.
- Cardiac Magnetic Resonance (CMR) and magnetic resonance imaging (MRI): visualization the regions of the heart affected by inflammation.
- Cardiac catheterization including endomyocardial biopsy: to detect myocardial degeneration, myocyte necrosis, inflammatory infiltrates, and/or interstitial edema of the myocardium.

# Diagnosis (ECG)



Ventricular tachycardia (rapid ventricular rhythm disorder) in myocarditis.

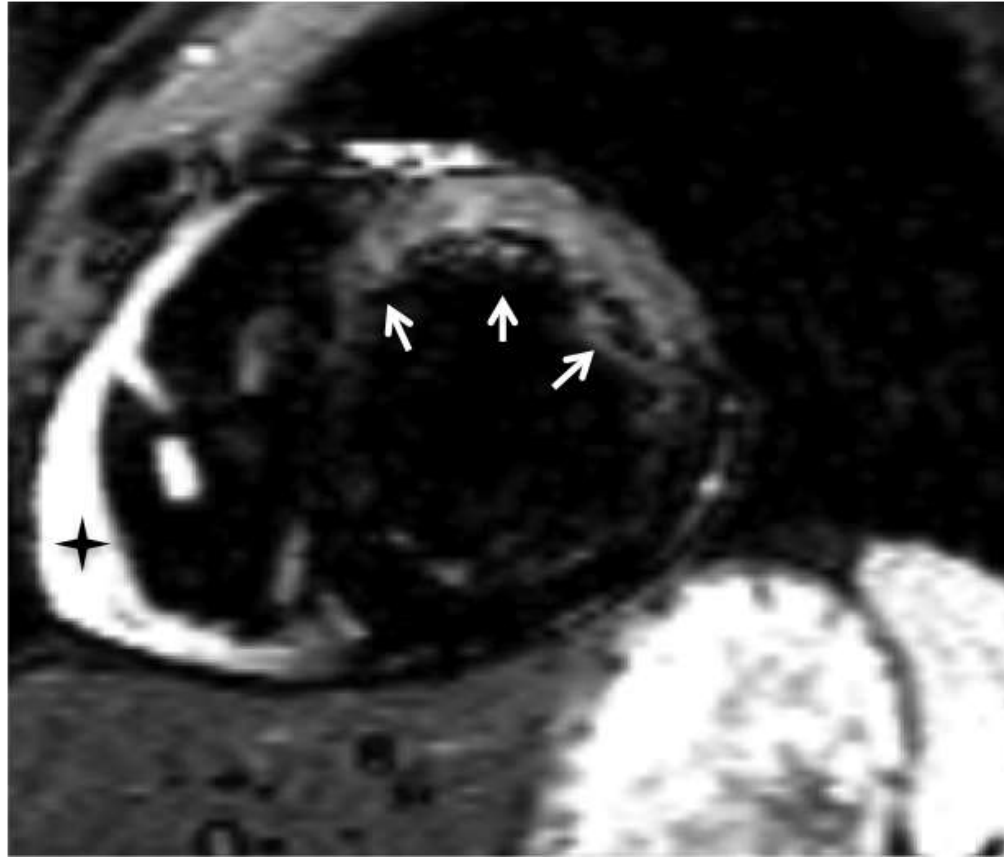
# Diagnosis (Echocardiography)



Circulatory disorder (red) in an acute myocarditis.

# Diagnosis

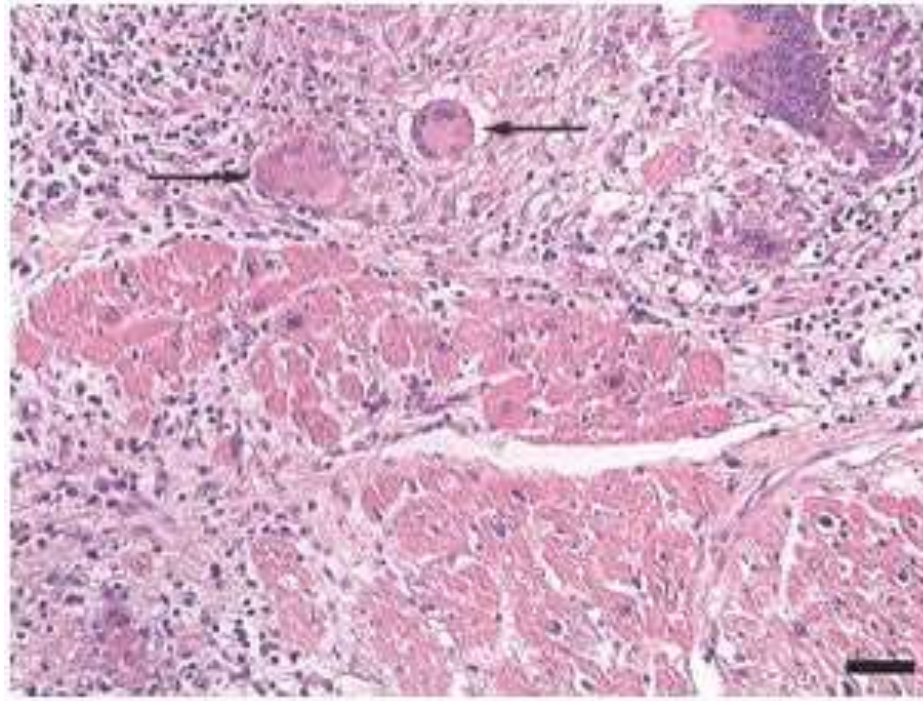
## (Magnetic Resonance Imaging)



Representation of edema in acute myocarditis (arrow indicators).  
A pericardial effusion, aka fluid around the heart (star).

# Diagnosis

## (Endomyocardial Biopsy)



Hematoxylin and eosin staining of the biopsy sample reveals extensive myocyte necrosis, cellular inflammation and the formation of multinucleated giant cells (arrows).



# Diagnosis

## (Diagnostic Criteria for Acute Myocarditis in Endomyocardial Biopsy)

- Infiltration of many large or small mononuclear cells\* (occasionally, a few polymorphonuclear leukocytes and multinucleated giant cells appear).
- Rupture, fusion and disappearance of cardiomyocytes.
- Interstitial edema (occasionally with fibril formation).

\*Cell infiltrates are often observed adjacent to cardiomyocytes.

# Diagnosis

## (Laboratory Studies)

- Complete blood count (CBC): leukocytosis (may demonstrate eosinophilia),
- Elevated erythrocyte sedimentation rate (and other acute phase reactants, such as C-reactive protein),
- Rheumatologic screening : to rule out systemic inflammatory diseases,
- Elevated cardiac enzymes: transient elevation of C-reactive protein (CRP), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), the MB form creatine kinase (CK-MB), and cardiac troponin T in blood; troponin T is especially useful for immediate diagnosis, however, which type of it, T or I, is more useful for diagnosis has not been determined.
- Serum viral antibody titers: for viral myocarditis.

# Diagnosis (Viral Infection)

- Viral infection is confirmed if the viral antibody titer is at least four times higher in an acute phase serum sample than in a sample obtained in remission phase collected at least two weeks apart.
- However, only approximately 10% of patients with viral infection exhibit a positive antibody titer.
- Polymerase chain reaction (PCR) is more useful for identifying the genomes of viruses causing myocarditis, but is not commonly performed.

# Diagnosis

## (Differential Diagnoses)

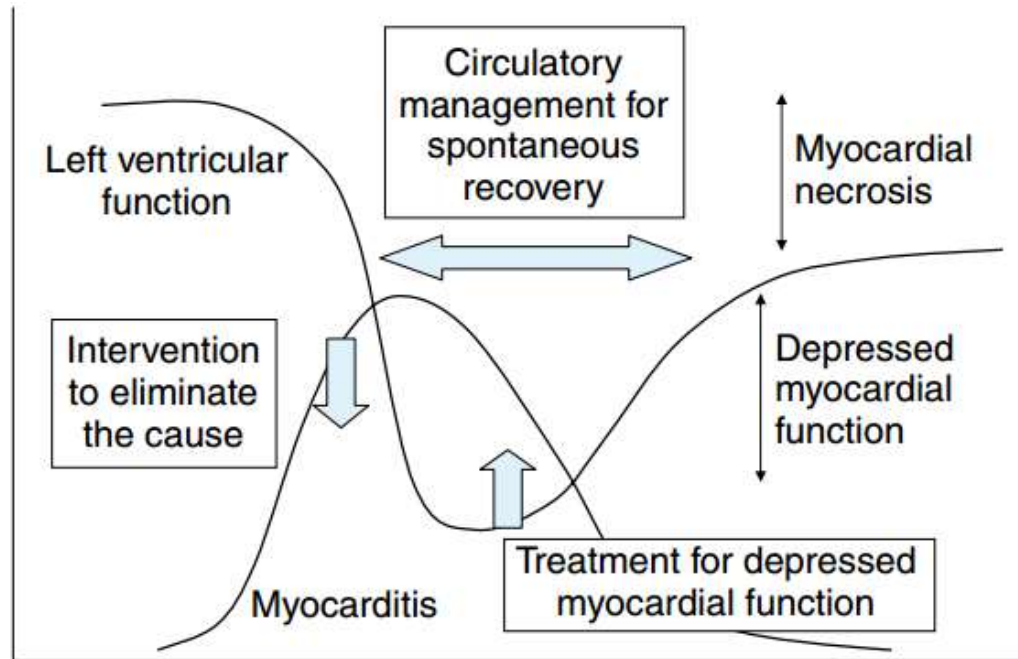
- Alcoholic Cardiomyopathy
- Cardiac Tamponade
- Cardiogenic Shock
- Chagas Disease (American Trypanosomiasis)
- Cocaine-Related Cardiomyopathy
- Coronary Artery Atherosclerosis
- Dilated Cardiomyopathy
- Hypertrophic Cardiomyopathy
- Peripartum Cardiomyopathy
- Restrictive Cardiomyopathy

# Treatment

## (Diet and Physical Activity)

- Patients should consume a low-sodium diet similar to that for heart failure management.
- Physical activity should be restricted to reduce the work of the heart during the acute phase of myocarditis, especially when there is fever, active systemic infection, or heart failure.
- Terms of physical activity limitation:
  - 10 – 14 days – mild myocarditis (up to ECG normalization),
  - 4 – 6 weeks – moderate myocarditis (up to normalization of heart size),
  - individually – severe myocarditis (up to decreasing of HF severity and disappearance of rhythm disorders).

# Treatment (Tasks)



Myocarditis is treated in three ways: (1) intervention to eliminate the cause, (2) intervention to improve hemodynamic compromise, and (3) intervention in cardiac dysfunction.

# Treatment

## (Etiotropic)

- Antibiotic therapy only after the confirmation of the etiological factor (diphtheria).
- Antiviral drugs only for proven viral myocarditis (etiologic agent is known AND sensitive to antiviral drug), however, beneficial effects are seen only if therapy is started prior to inoculation or soon thereafter.
- Nevertheless, antiviral therapy may be considered in acute, fulminant myocarditis, in institutional outbreaks and in laboratory-acquired cases.

# Treatment

## (Intensive Immunosuppressive Therapy)

- Intensive immunosuppressive therapy (e.g., corticosteroids, azathioprine, cyclosporine, muromonab-CD3/OKT3) has been shown to have some benefit only in small-scale clinical studies in the treatment of giant cell myocarditis and has not been validated in large clinical trials.
- At this time, immunosuppressive therapy is not recommended for myocarditis until clear evidence is available from the results of multicenter trials.



# Treatment

## (Pathogenetic Pharmacotherapy)

- Vasodilators (e.g., nitroglycerin, sodium nitroprusside),
- Angiotensin-converting enzyme inhibitors (e.g., enalapril)
- Diuretics (e.g., furosemide),
- Anticoagulation may be advisable as a preventive measure, although no definitive evidence is available,
- Antiarrhythmics can be used cautiously, although most antiarrhythmic drugs have negative inotropic effects that may aggravate heart failure; supraventricular arrhythmias should be converted electrically,
- Inotropic drugs (e.g., dobutamine, milrinone) may be necessary for severe decompensation, although they are highly arrhythmogenic.

# Treatment

## (Supportive Care and Surgical Intervention)

- Hemodynamic and cardiac monitoring,
- Administration of supplemental oxygen,
- Fluid management,
- Temporary transvenous pacing for complete heart block,
- Cardiac transplantation,
- Extreme cases: ventricular assist device or percutaneous circulatory support; left ventricular assistive devices (LVADs) and extracorporeal membrane oxygenation.

# Consultations

- Cardiothoracic surgery,
- Infectious disease and/or rheumatology consultations.



Rheumatic heart disease.

# Prognosis

- In the acute phase, myocarditis management of cardiac pump failure and potentially fatal arrhythmias is the main clinical challenge.
- The prognosis of myocarditis varies depending on the pathogenesis and type of disease.
- Patients who survive fulminant myocarditis have a good prognosis.
- Predictors of death or need for heart transplantation include syncope, low ejection fraction, and left bundle-branch block, all indicators of advanced cardiomyopathy.

# Prophylaxis

- Vaccination should reduce the incidence of myocarditis caused by measles, rubella, mumps, poliomyelitis, and influenza.
- The development of vaccines for other cardiotropic viruses may prevent viral myocarditis in the future.

# Abbreviations

ACE - angiotensin converting  
enzyme

CMR - cardiac magnetic  
resonance

ECG - electrocardiogram

MRI - magnetic resonance  
imaging

HIV - human immunodeficiency  
virus

LVADs - left ventricular assistive  
devices

# Diagnostic and treatment guidelines

Current state of knowledge on etiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases

Guidelines for Diagnosis and Treatment of Myocarditis

2015 ESC Guidelines for the management of infective endocarditis

2015 ESC Guidelines for the diagnosis and management of pericardial diseases

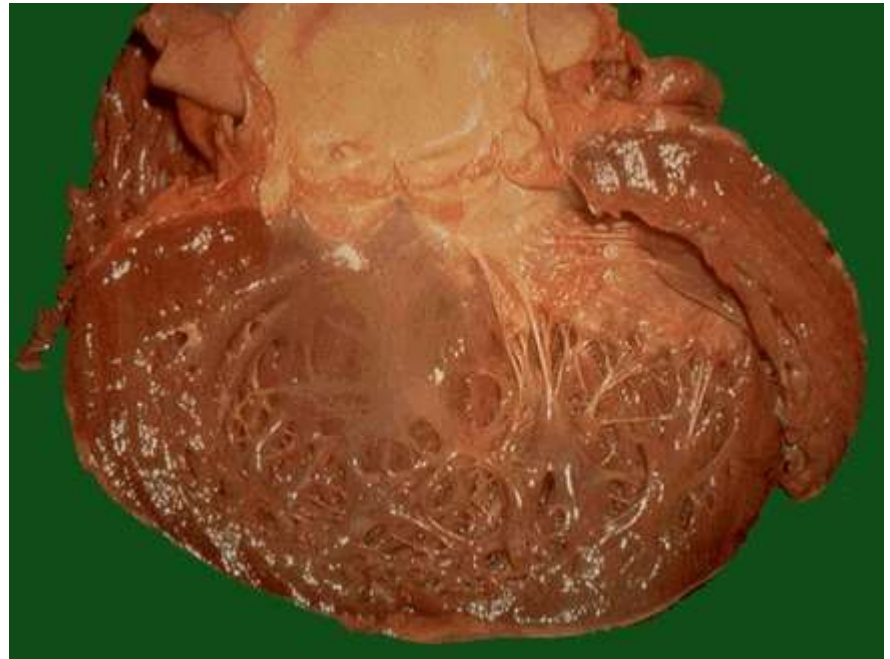
Update on Myocarditis

# Cardiomyopathies



# Plan of the Lecture

- Definition
- Epidemiology
- Risk factors
- Etiology
- Mechanisms
- Classification
- Clinical investigation
- Diagnosis
- Treatment
- Prognosis
- Prophylaxis
- Abbreviations
- Diagnostic and treatment guidelines



A large, dilated left ventricle typical of a dilated, or congestive, cardiomyopathy.

# Definition

Cardiomyopathies are defined by structural and functional abnormalities of the ventricular myocardium that are unexplained by flow-limiting coronary artery disease or abnormal loading conditions and historically have been subdivided into primary disease, in which the heart is the only involved organ, and secondary forms where the cardiomyopathy is a manifestation of a systemic disorder.

# Epidemiology

## (Dilated Cardiomyopathy)

- The estimated prevalence of dilated cardiomyopathy (DCM) is 1:2500.
- The incidence of DCM discovered at autopsy is estimated to be 4.5 cases per 100,000 population per year, whereas the clinical incidence is 2.45 cases per 100,000 population per year.
- DCM is the most common type, occurring mostly in adults 20 to 60.
- Men are more likely in men than in women.

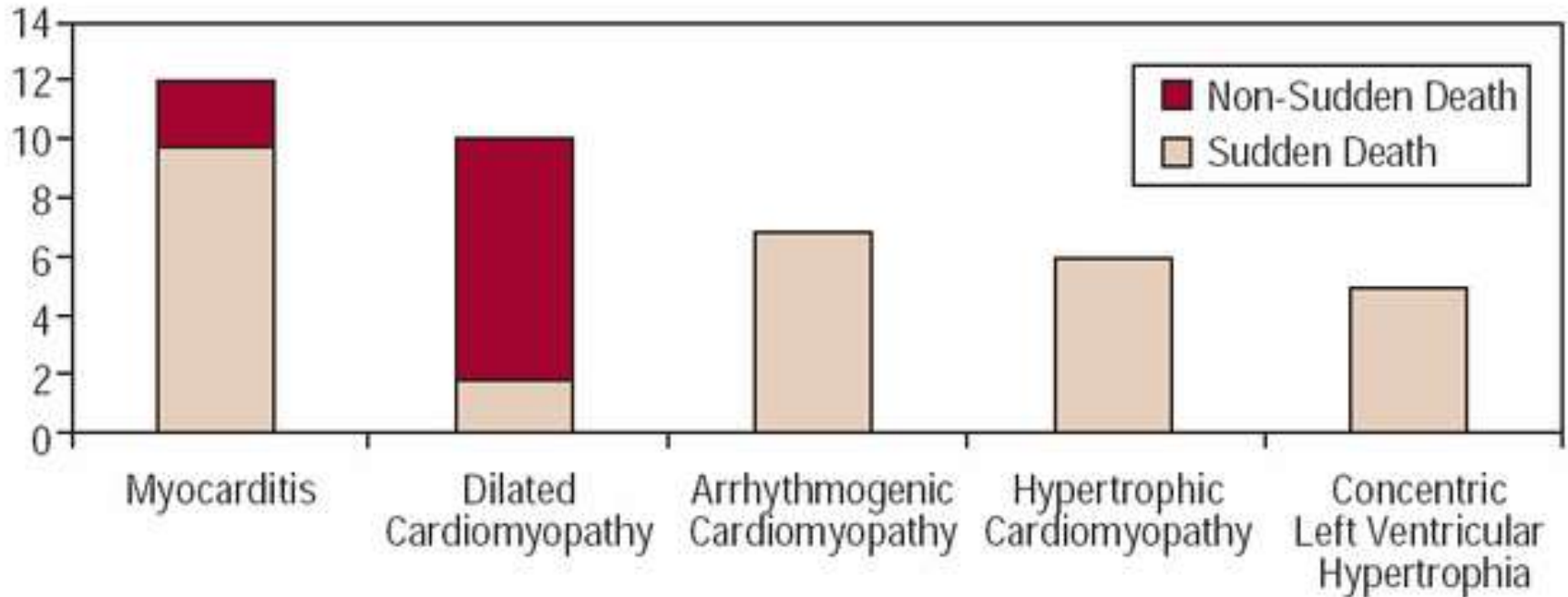
# Epidemiology

## (Hypertrophic Cardiomyopathy)

- Hypertrophic cardiomyopathy (HCM) occurs with an incidence of 1 in 500 people in the general population and is the most common cause of sudden death in children and adults under 35 years.
- The mean age is 57 (16 to 87) years.
- HCM is autosomal dominant with no known sex predilection.
- Sudden death is most common in young patients, and death from heart failure or stroke occurs more frequently in middle age and beyond.
- Apical HCM is seen much more commonly in Asian people.

# Epidemiology

(Distribution of Myocardial Diseases According to the Manner of Death)



# Risk Factors and Etiology

## (Dilated Cardiomyopathy)

- DCM can be familial, primary without family history, or secondary (associated with or caused by other conditions).
- Familial DCM (at least 25% of cases of DCM), is usually autosomal dominant, with X-linked autosomal recessive and mitochondrial inheritance occurring less frequently.
- Approximately 2 of 3 patients have no known family history (sporadic DCM) and about 15% of sporadic cases arise from chronic myocarditis, leading to scarring and heart failure.
- Noninflammatory etiologies and associations include alcoholism, anthracycline drugs, ingestion of metals, autoimmune and systemic disorders, and mitochondrial disorders.
- The distinction between the cause and risk factor(s) DCM is sometimes blurred.

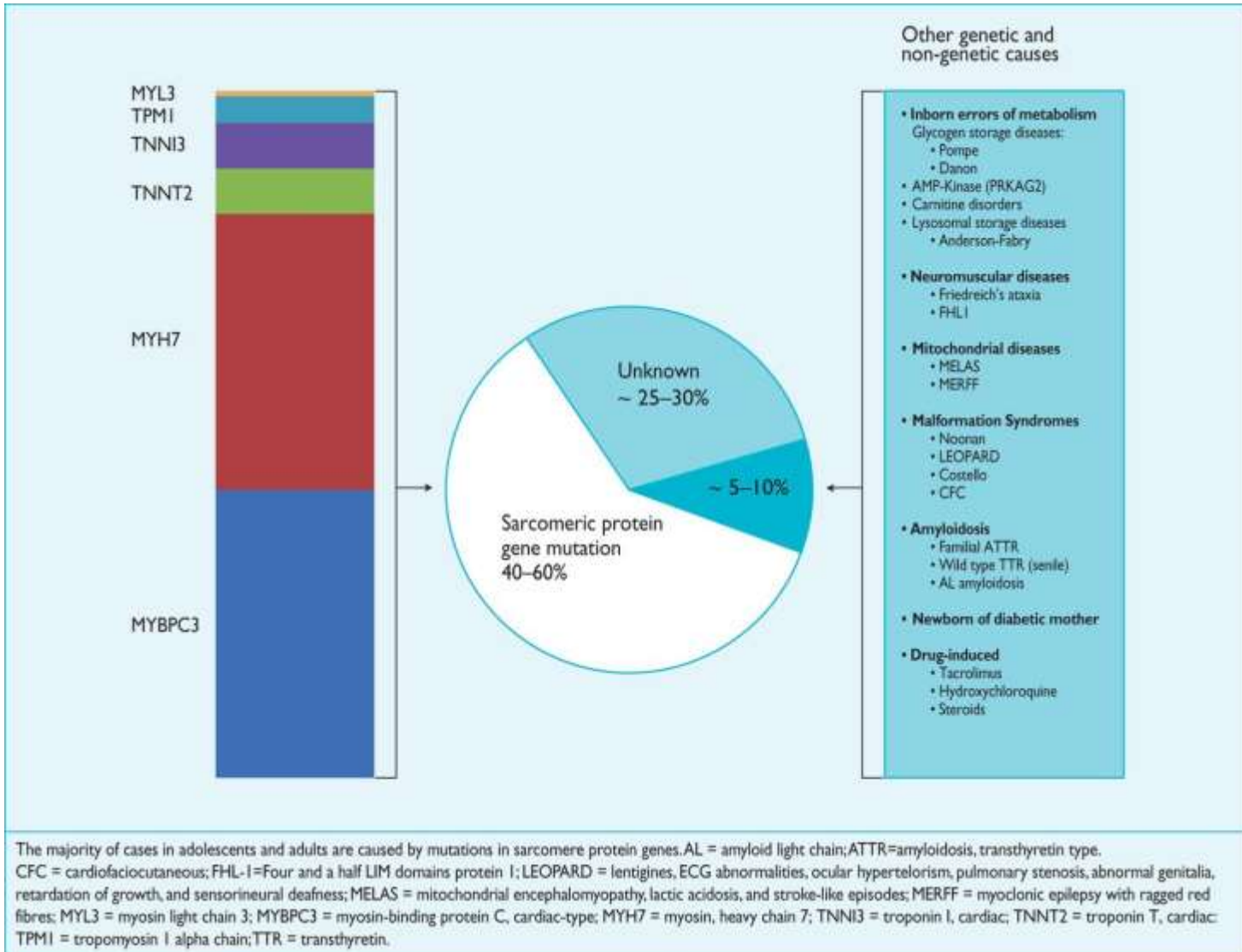
# Risk Factors and Etiology

## (Hypertrophic Cardiomyopathy)

- Abnormal calcium kinetics leads to the inappropriate myocardial hypertrophy and specific features of HCM, particularly in patients with diastolic functional abnormalities (abnormal myocardial calcium kinetics and abnormal calcium fluxes from an increase in the number of calcium channels result in an increase in intracellular calcium concentration, which may produce hypertrophy).
- Genetic causes: familial HCM occurs as an autosomal dominant Mendelian-inherited disease in approximately 50% of cases (at least 6 different genes on at least 4 chromosomes are associated with HCM, with more than 50 different mutations discovered thus far).  
Familial HCM.
- Other possible causes: abnormal sympathetic stimulation; abnormally thickened intramural coronary arteries; subendocardial ischemia; cardiac structural abnormalities.

# Risk Factors and Etiology

## (Diverse Etiology of Hypertrophic Cardiomyopathy)





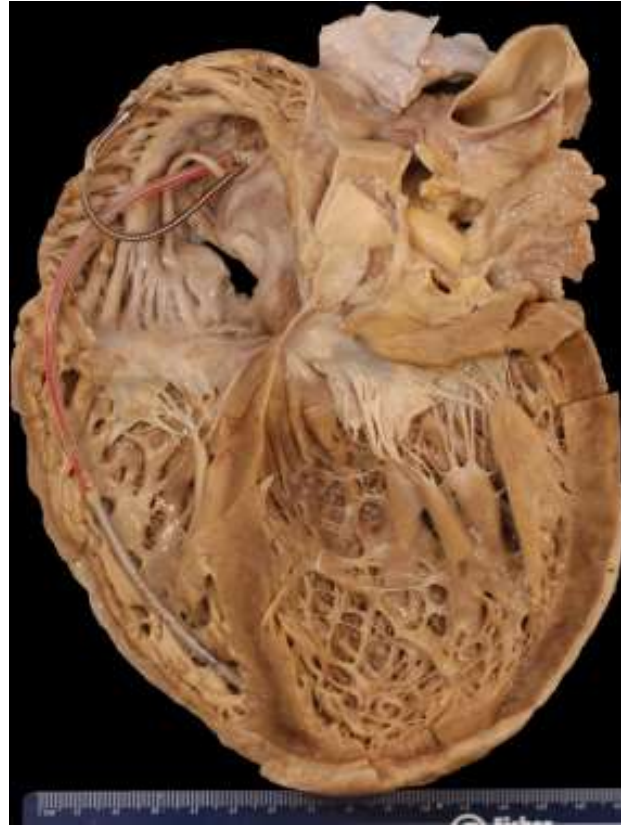
# Mechanisms

## (Dilated Cardiomyopathy: Gross Findings)

- Cardiomegaly is a requisite for the diagnosis of DCM (the mean heart weight is about 600 g).
- Typically, 4-chamber dilatation that is greater in the ventricles than the atria is found.
- LV wall thickness is often normal, in contrast to hypertensive cardiomyopathy with failure.
- Mitral insufficiency may result from papillary muscle dysfunction secondary to LV and changes in LV wall shape, and tricuspid regurgitation results from annular dilatation.
- Mural thrombi are common in patients who do not receive anticoagulation.
- Mild diffuse or patchy endocardial fibrosis is frequent and is likely a result of cardiac dilatation.

# Mechanisms

## (Dilated Cardiomyopathy: Gross Findings)



Gross heart specimen from a patient with DCM who died in end-stage heart failure. Defibrillator leads are in the right heart. The ventricles are dilated more than the atria.

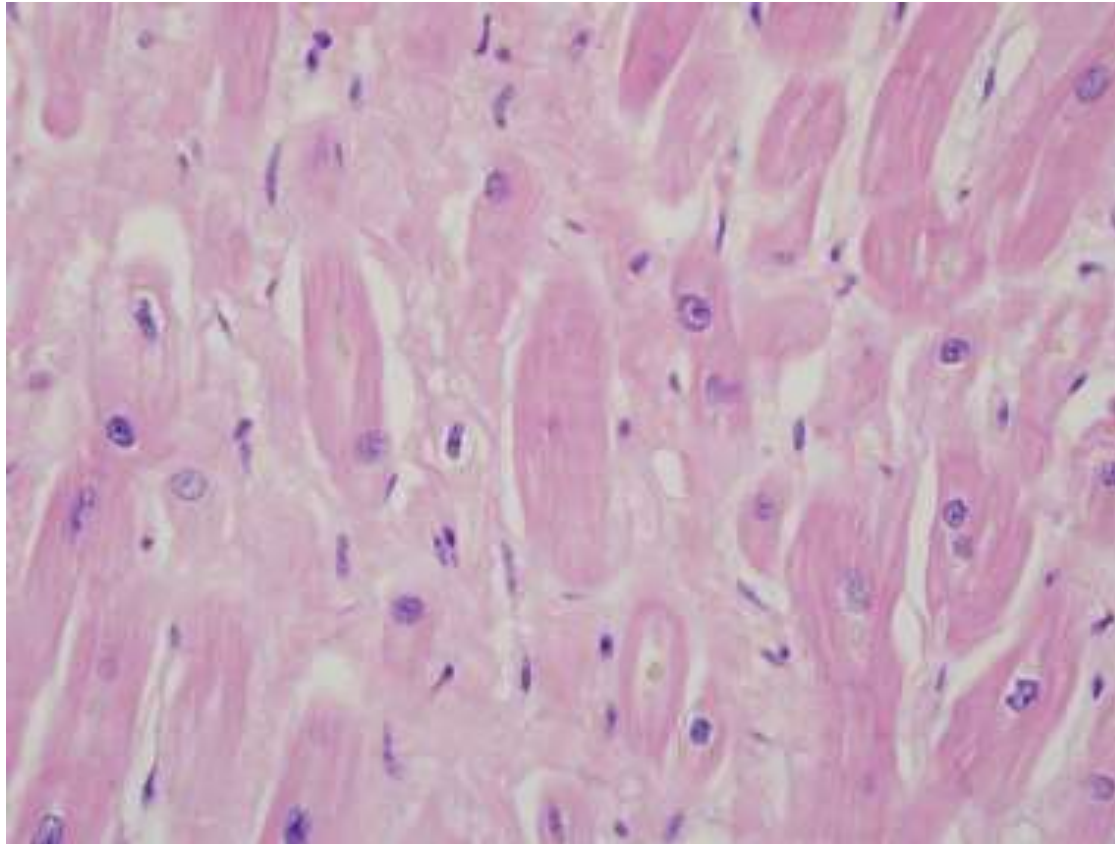
# Mechanisms

## (Dilated Cardiomyopathy: Microscopic Findings)

- The histologic features of DCM are nonspecific; therefore, it is a microscopic diagnosis of exclusion.
- In biopsies, the findings range from minimal variation in myocyte size to typical features of myofiber loss, interstitial fibrosis, and marked variation in myofiber size.
- Transmural scars may also occur in dilated cardiomyopathy.
- Quantitation of collagen has shown up to 4 times the normal collagen concentration, with a decrease in mature cross-linked collagen, correlating with an increase in neutrophil-type collagenase activity.
- The volume density of myofibrils is reduced, and mitochondrial density is normal, but the mitochondria are more numerous and small.

# Mechanisms

## (Dilated Cardiomyopathy: Microscopic Findings)



Heart section from a cardiac explant in a patient with end-stage DCM. There is focal interstitial fibrosis. The change is nonspecific and can be seen in heart failure from any cause.

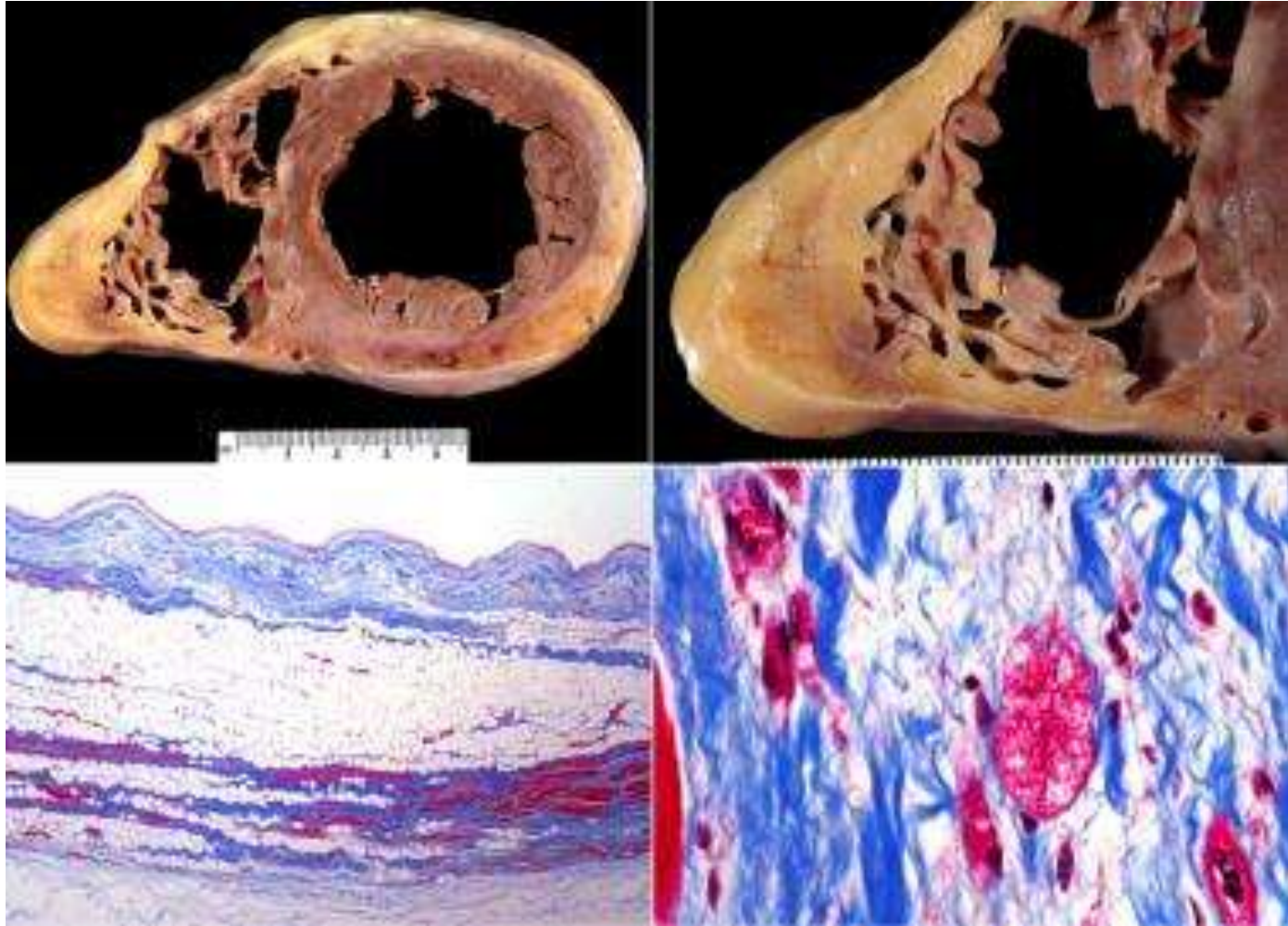
# Mechanisms

## (Dilated Cardiomyopathy: Immunohistochemistry)

- Immunolocalization of sarcomeric and cytoskeletal proteins have demonstrated abnormal distribution in explanted hearts from patients with DCM.
- Tubulin and desmin are increased in amount and irregularly distributed.
- Titin, a member of the sarcomeric skeleton family, is reduced, usually in areas where contractile material is lacking.
- Connexin-43 is also decreased.
- Increased myocyte cell death and apoptosis is found.
- In cases of dystrophin-related dilated cardiomyopathy (up to 6% in males with dilated cardiomyopathy), immunohistochemical and molecular studies are essential to identify protein and gene defects.

# Mechanisms

(Dilated Cardiomyopathy: Immunohistochemistry)



Arrhythmogenic right ventricular cardiomyopathy (ARVC).

# Mechanisms

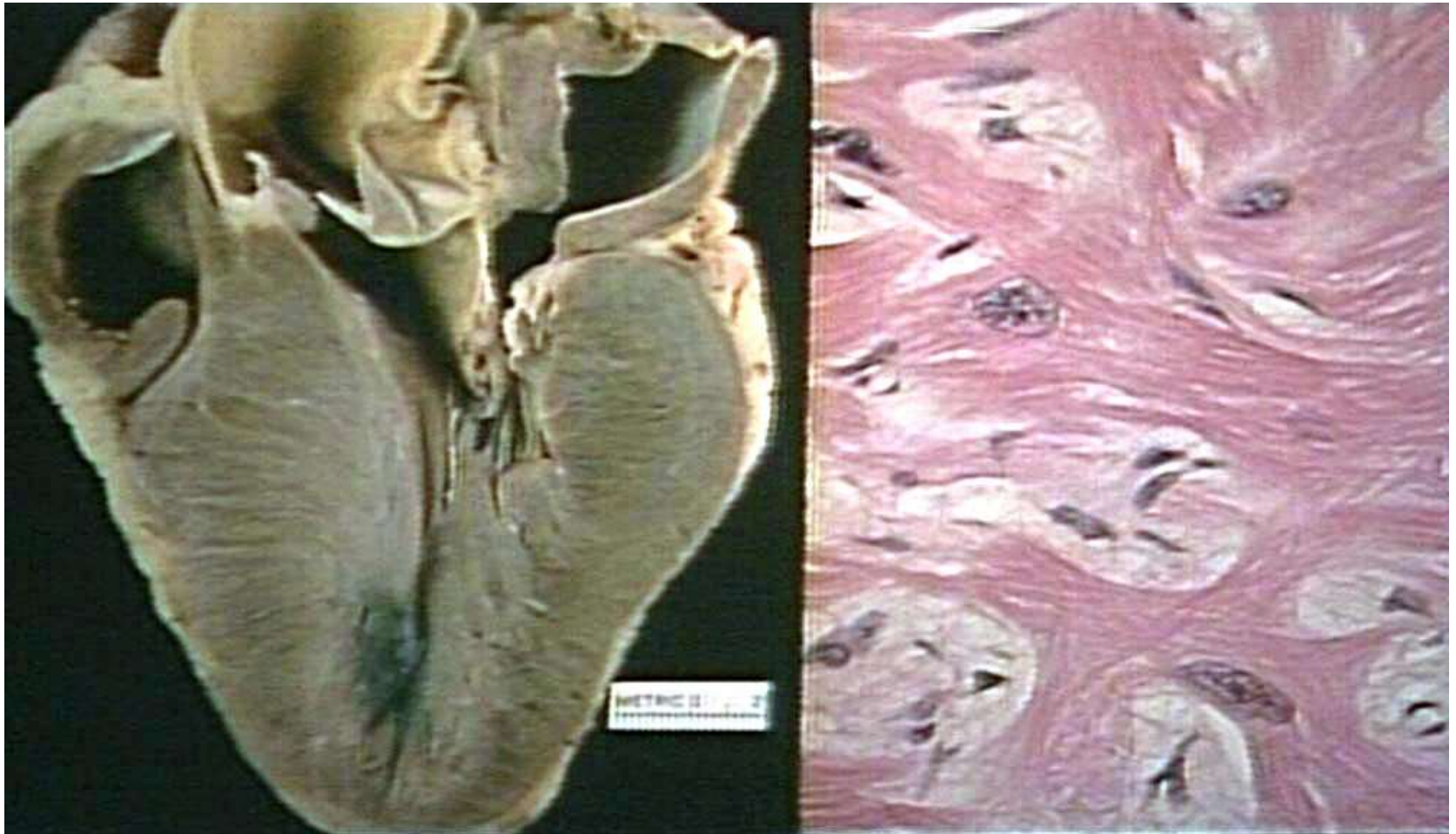
## (Hypertrophic Cardiomyopathy: Gross Findings)

- About 1/4 individuals with HCM demonstrate an obstruction to the outflow of blood from the LV during rest and in 70% of patients, obstruction can be provoked under certain conditions (dynamic outflow obstruction).
- Myocardial hypertrophy and extracellular fibrosis predispose to increased LV stiffness which in concert with compromised cellular energetics and abnormal calcium handling lead to diastolic dysfunction manifested as dyspnea and exercise intolerance
- The altered structure of the coronary vessels and increased diastolic pressure (reduced blood supply), with the hypertrophy and outflow tract obstruction (increased demand), may cause myocardial ischemia manifested as angina, and may trigger ventricular arrhythmias.



# Mechanisms

## (Hypertrophic Cardiomyopathy: Gross Findings)





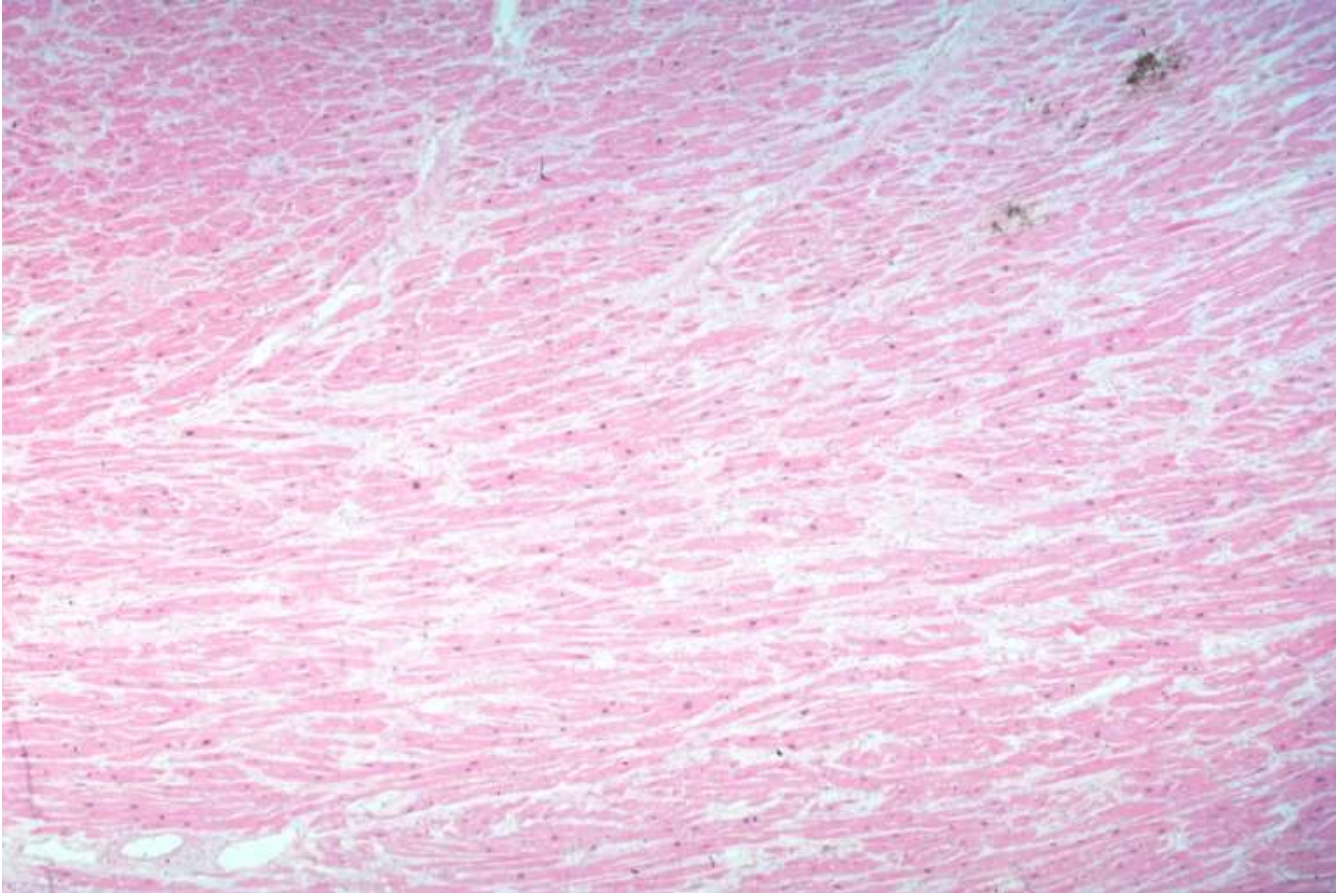
# Mechanisms

## (Hypertrophic Cardiomyopathy: Microscopic Findings)

- The earliest histological changes are myocyte disorganization / disarray which is widespread throughout the ventricles.
- The interventricular septum demonstrates myocyte disarray, the hallmark of HCM.
- The abnormal arrangement of large hypertrophied muscle bundles crossing each other.
- The most sensitive and specific change is circular arrays of myocytes around central foci of connective tissue .
- Cross sections of the sarcomere show a highly organized orthohexagonal array, with six thin actin filaments surrounding one thick myosin filament.
- The abnormal myosin interferes with the normal spatial arrangement of the myofibril.

# Mechanisms

## (Hypertrophic Cardiomyopathy: Microscopic Findings)



Interstitial fibrosis with many fibroblastic cells.

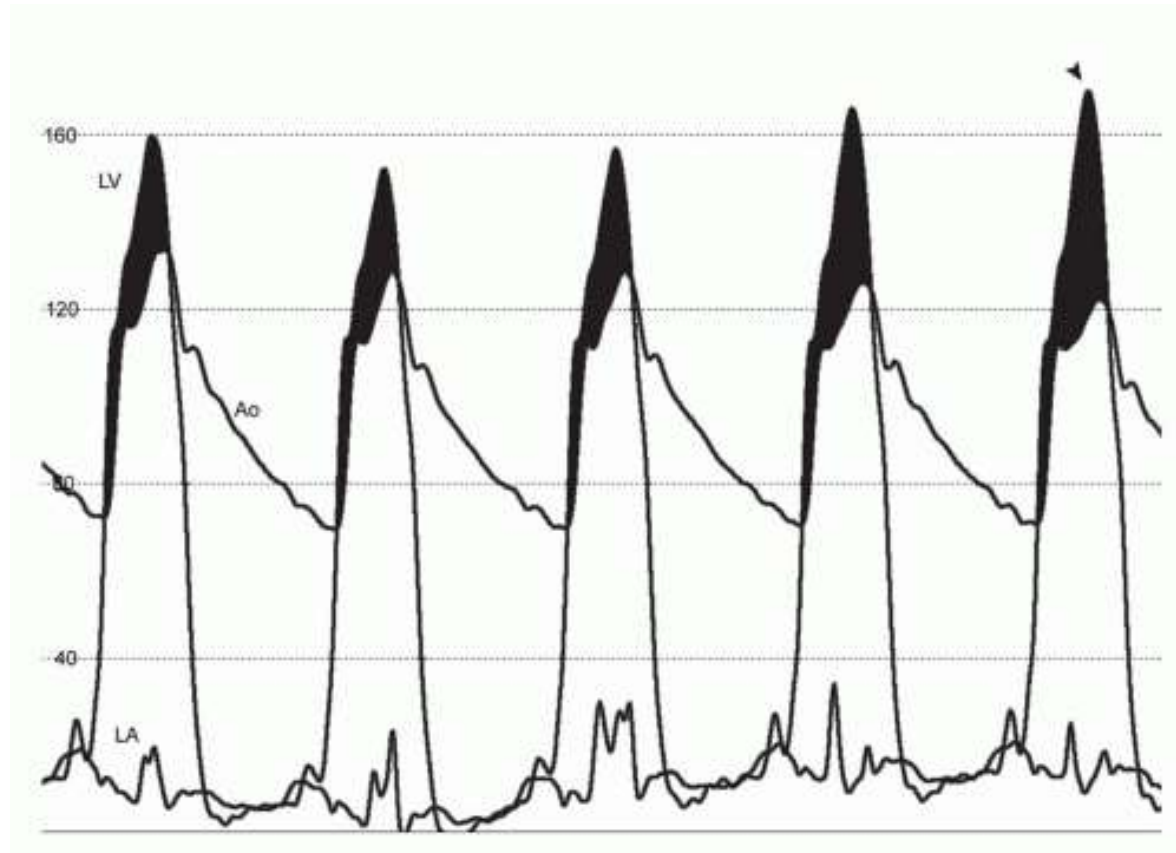
# Mechanisms

## (Hypertrophic Cardiomyopathy: Pathophysiology)

- The greatest factor in HCM is the dynamic pressure gradient across the LV outflow tract.
- Three explanations for the systolic anterior motion of the mitral valve (MV) have been offered: (1) the MV is pulled against the septum by contraction of the papillary muscles, which occurs because of the valve's abnormal location and septal hypertrophy altering the orientation of the papillary muscles; (2) the MV is pushed against the septum because of its abnormal position in the outflow tract; (3) the MV is drawn toward the septum because of the lower pressure that occurs as blood is ejected at high velocity through a narrowed outflow tract (Venturi effect).
- Most patients with HCM have abnormal diastolic function (whether or not a pressure gradient is present), which impairs ventricular filling and increases filling pressure, despite a normal or small ventricular cavity.

# Mechanisms

## (Hypertrophic Cardiomyopathy: Pathophysiology)



Dynamic changes in left ventricular outflow tract obstruction. Ao, ascending aorta; LA, left atrium; LV, left ventricle.

# Classification

## (International Classification of Diseases (ICD): 1)

142 Cardiomyopathy

142.0 Dilated (congestive)  
cardiomyopathy

142.1 Obstructive hypertrophic  
cardiomyopathy (hypertrophic  
subaortic stenosis)

142.2 Other (nonobstructive)  
hypertrophic cardiomyopathy

142.3 Endomyocardial (eosinophilic)  
disease

142.4 Endocardial fibroelastosis  
(congenital cardiomyopathy)

142.5 Other restrictive  
cardiomyopathy

142.6 Alcoholic cardiomyopathy

142.7 Cardiomyopathy due to drugs  
and other external agents

142.8 Other cardiomyopathies

142.9 Cardiomyopathy, unspecified

143\* Cardiomyopathy in diseases  
classified elsewhere

143.0\* Cardiomyopathy in infectious  
and parasitic diseases classified  
elsewhere

143.1\* Cardiomyopathy in metabolic  
diseases

143.2\* Cardiomyopathy in nutritional  
diseases

143.8\* Cardiomyopathy in other  
diseases classified elsewhere

# Classification

## (Primary and Secondary)

- Primary/intrinsic cardiomyopathies
  - Genetic (HCM, arrhythmogenic right ventricular cardiomyopathy (ARVC), left ventricle (LV) non-compaction, Ion Channelopathies, DCM, restrictive cardiomyopathy (RCM))
  - Acquired (stress cardiomyopathy, myocarditis, ischemic cardiomyopathy)
- Secondary/extrinsic cardiomyopathies: metabolic/storage (Fabry's disease, hemochromatosis), endomyocardial (endomyocardial fibrosis, hypereosinophilic syndrome), endocrine (diabetes mellitus, hyperthyroidism, acromegaly), cardiofacial (noonan syndrome), neuromuscular (muscular dystrophy, Friedreich's ataxia), other (obesity-associated cardiomyopathy).

# Classification

## (World Health Organization Classification)

Type	Features	Causative Factors
Dilated	Dilated left or both ventricle(s), with impaired contraction	Ischemic, idiopathic, familial-genetic, immune, alcoholic, toxic, valvular
Hypertrophic	Left or right ventricular hypertrophy, or both	Familial, with autosomal dominant inheritance
Restrictive	Restrictive filling and reduced diastolic filling of one or both ventricles	Idiopathic, amyloidosis, endomyocardial fibrosis
Arrhythmogenic right ventricular cardiomyopathy	Fibrofatty replacement of right ventricular myocardium, Uhl's anomaly (parchment heart)	Unknown; familial, with incomplete penetrance; possible autosomal recessive inheritance; rare forms (eg, Naxos disease)
Unclassified	Not typical for previous four groups	Fibroelastosis, noncompacted myocardium, systolic dysfunction with minimal dilation, mitochondrial disease

# Clinical Investigation

## (Signs and Symptoms)

### Dilated Cardiomyopathy

- Some patients remain asymptomatic throughout life.
- Some patients have severe symptoms of heart failure; arrhythmias; systemic embolism; angina, but only in the presence of ischemic heart disease.

### Hypertrophic Cardiomyopathy

- Some patients remain asymptomatic throughout life.
- Some patients have severe symptoms of heart failure, arrhythmias, systemic embolism.
- Some patients die suddenly, often in the absence of previous symptoms.



# Diagnosis

## (Dilated Cardiomyopathy)

- DCM is characterized by enlargement of the heart with a decreased shortening fraction (usually less than 25%), sinus tachycardia or atrial fibrillation, left bundle-branch block (LBBB).
- Genetic testing can help understand the underlying cause of the DCM.
- DCM is usually identified when limiting symptoms are severe, but arrhythmias or sudden death are uncommonly early manifestations.
- In contrast to arrhythmogenic and hypertrophic cardiomyopathy, arrhythmias in DCM are typically prominent only after the onset of significant heart failure.
- A family history of DCM is present in over 50% of patients.

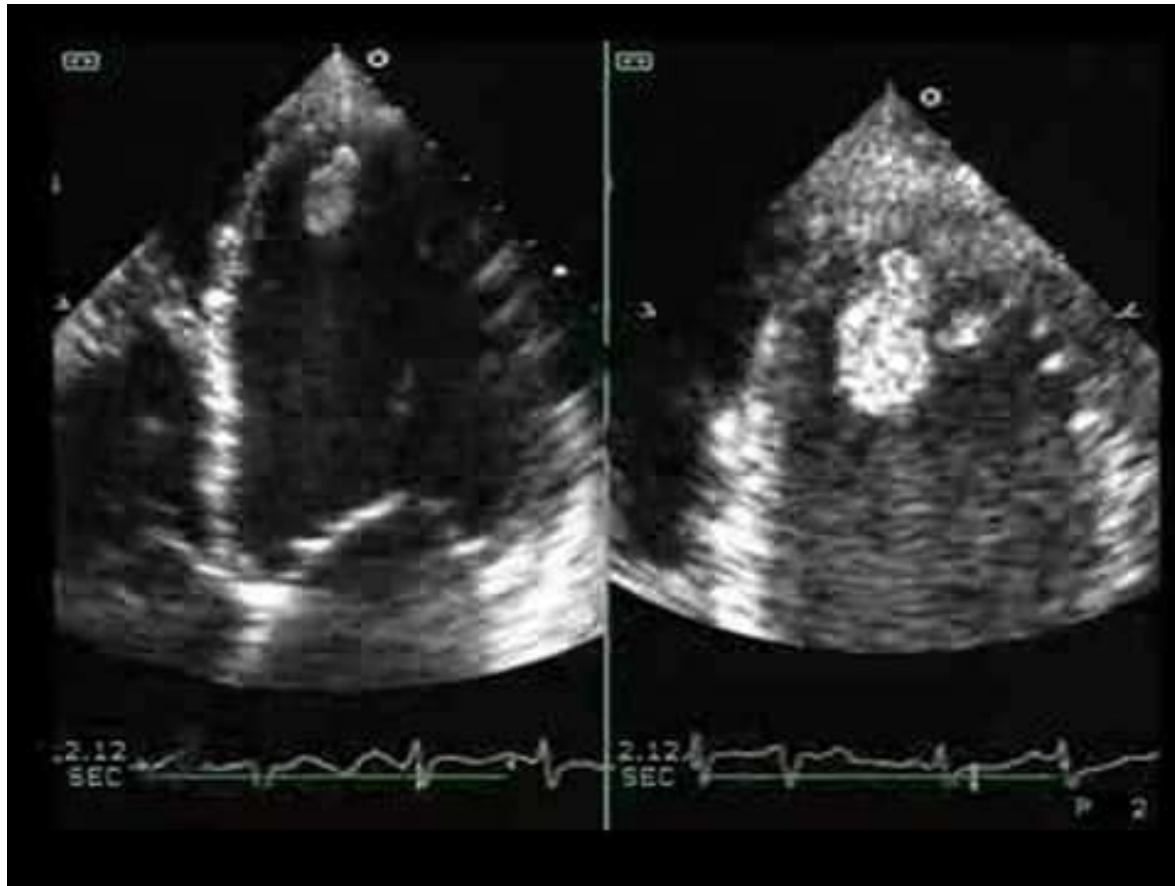
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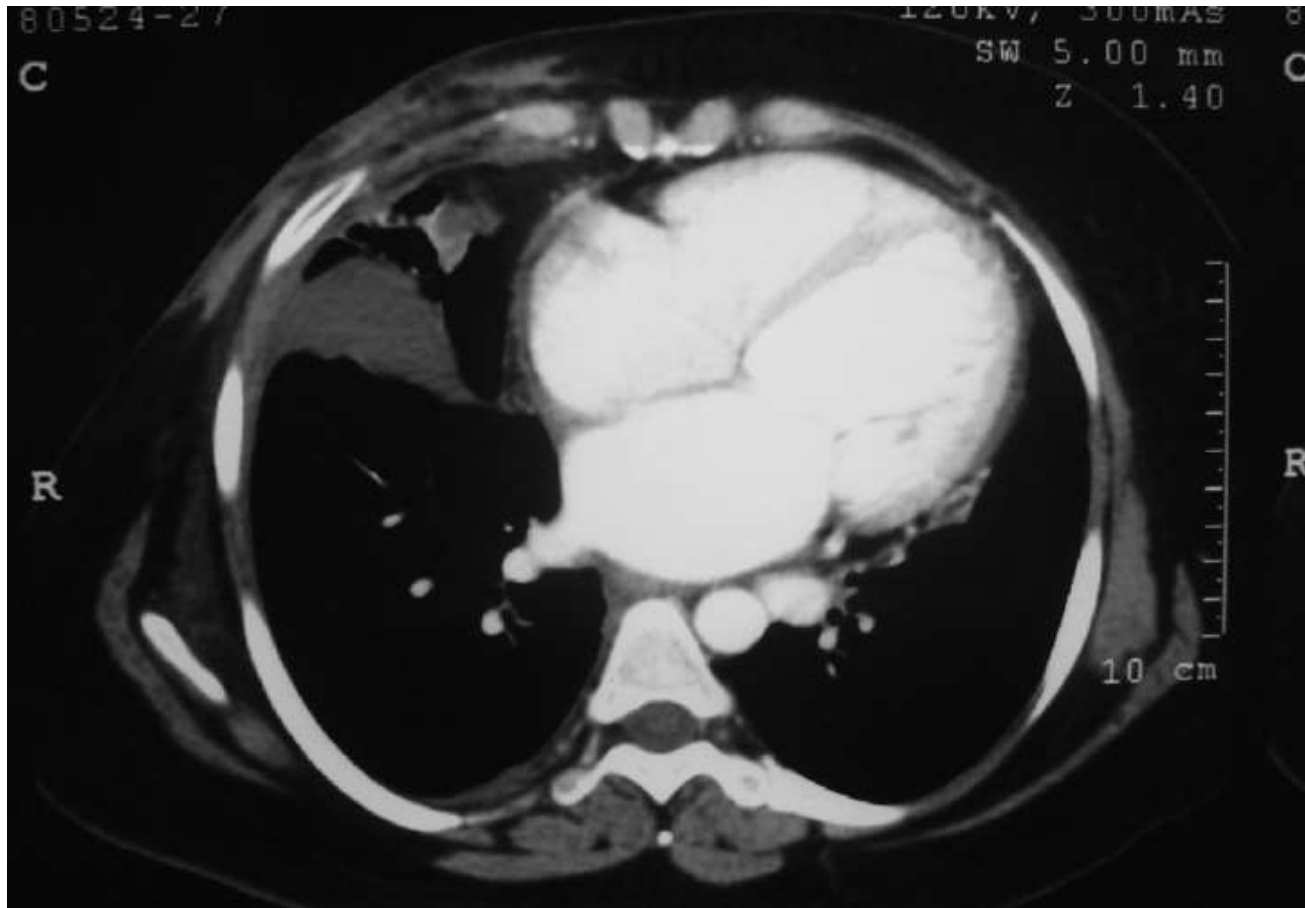
# Diagnosis

## (Dilated Cardiomyopathy with Mural Thrombus)



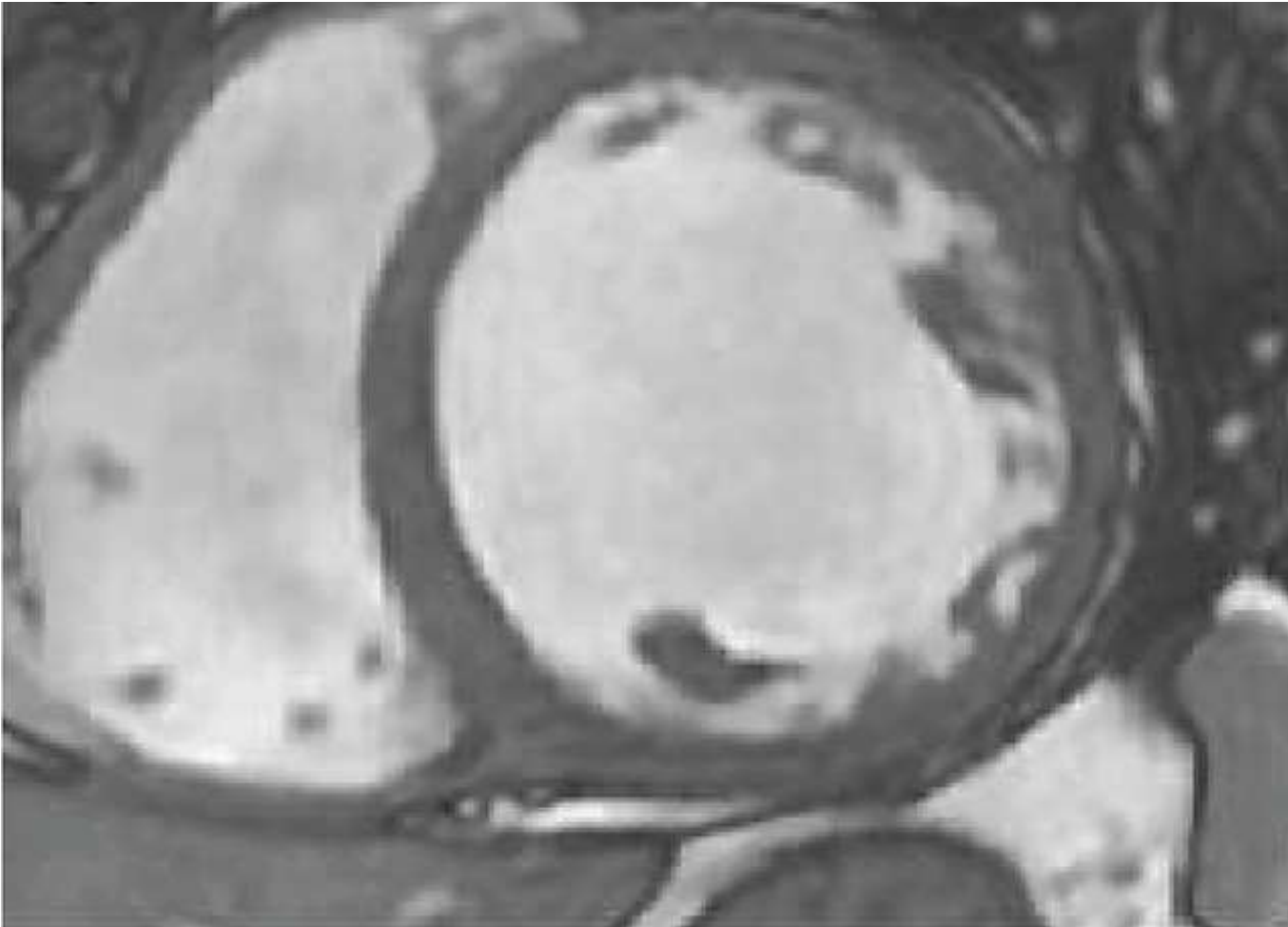
# Diagnosis

(Dilated Cardiomyopathy following Trastuzumab Chemotherapy)



# Diagnosis

(Dilated Cardiomyopathy: The Veteran Athlete's Heart)



# Diagnosis

## (Dilated Cardiomyopathy: Chest Radiograph)



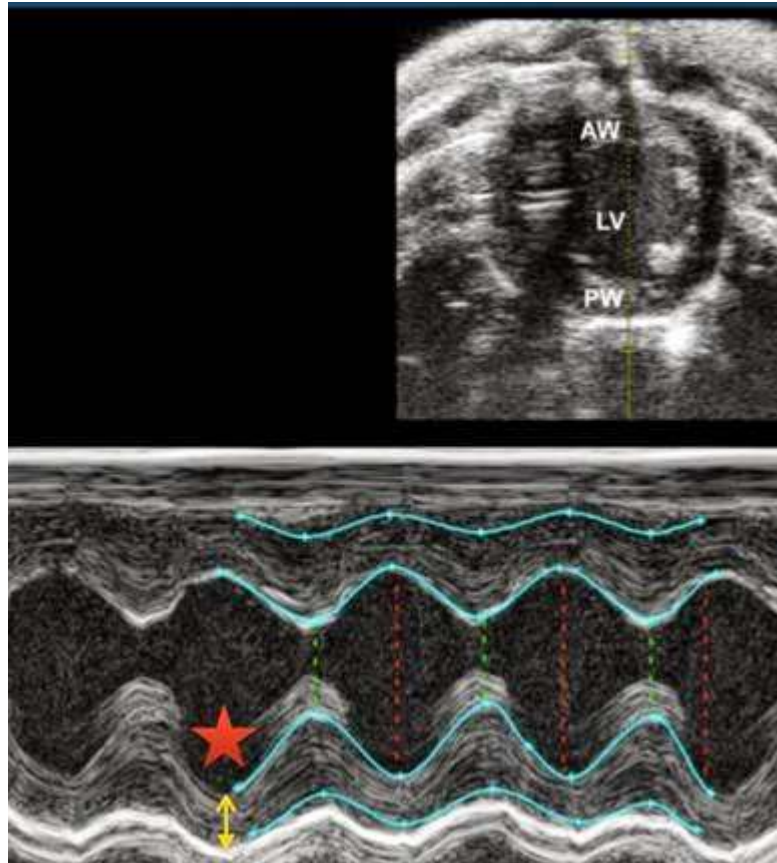
# Diagnosis

## (Hypertrophic Cardiomyopathy)

- No specific laboratory blood tests are required in the workup.
- Genetic testing is not yet widely available.
- Imaging modalities data: abnormal systolic anterior leaflet motion of the mitral valve, LV hypertrophy, left atrial enlargement, small ventricular chamber size, septal hypertrophy with septal-to-free wall ratio greater than 1.4:1, mitral valve prolapse and mitral regurgitation, decreased midaortic flow, partial systolic closure of the aortic valve in midsystole.
- Electrocardiography (ECG): ST-T wave abnormalities and LVH, axis deviation, conduction abnormalities, sinus bradycardia with ectopic atrial rhythm, atrial enlargement, abnormal and prominent Q wave in the anterior precordial and lateral limb leads, atrial fibrillation, etc.

# Diagnosis

## (Hypertrophic Cardiomyopathy)





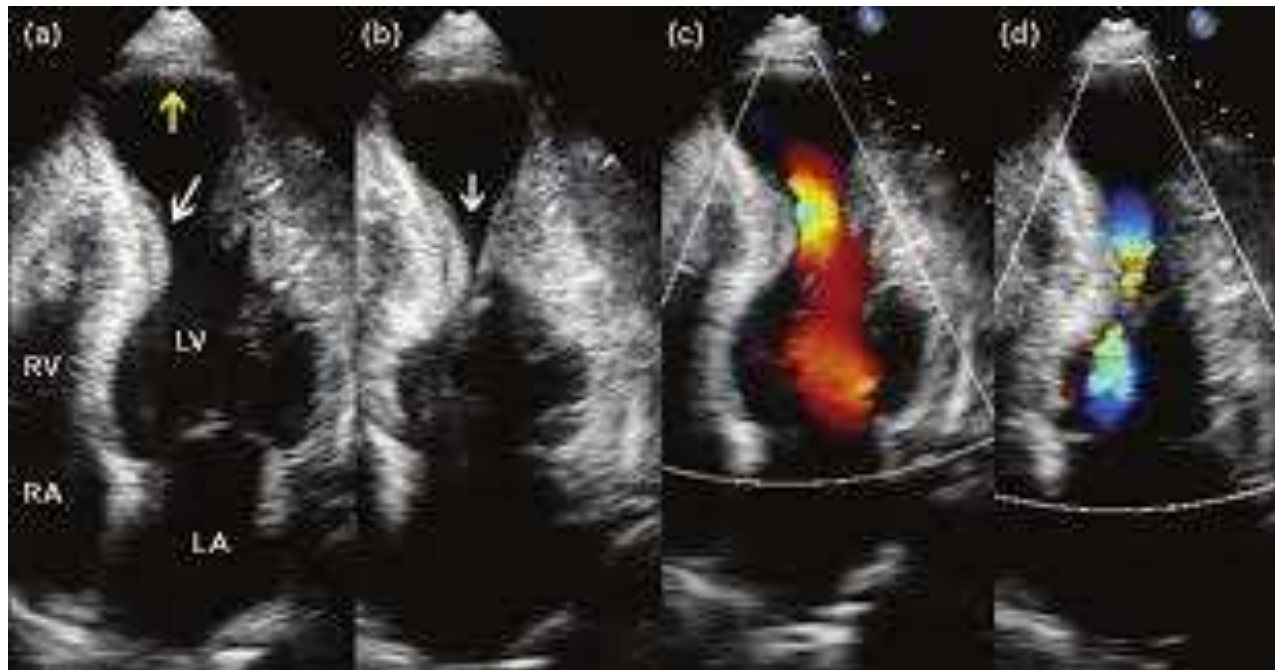
# Diagnosis

## (Hypertrophic Cardiomyopathy)



# Diagnosis

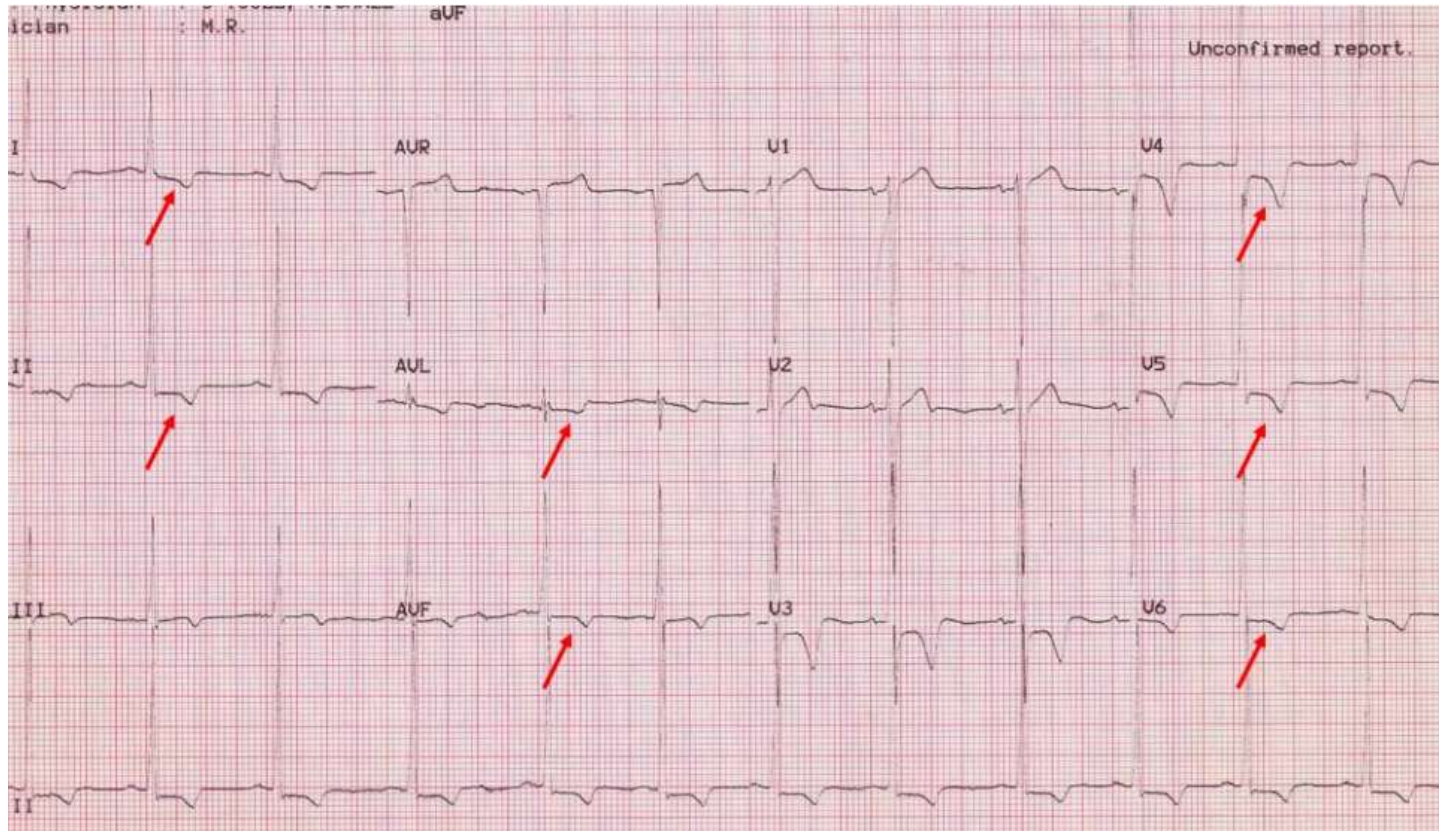
## (Hypertrophic Cardiomyopathy: Midventricular Obstructive)



Abnormal ECG in a patient with hypertrophic cardiomyopathy. Note the T wave inversion and ST depression in the inferolateral leads (arrows)

# Diagnosis

## (Hypertrophic Cardiomyopathy in Athletes)



Abnormal ECG in a patient with hypertrophic cardiomyopathy. Note the T wave inversion and ST depression in the inferolateral leads (arrows)

# Treatment

## (Dilated Cardiomyopathy)

- Essentially the same as treatment of chronic heart failure (HF).
- Drug therapy can slow down progression and in some cases even improve the heart condition and may include salt restriction, angiotensin converting enzyme (ACE) inhibitors, diuretics, anticoagulants.
- Surgery: artificial pacemakers; implantable cardioverter-defibrillators; ventricular remodeling, heart transplantation may be considered.

# Treatment

## (Hypertrophic Cardiomyopathy)

- A significant number of patients do not have any symptoms and will have normal life expectancies, though they should be counseled to avoid particularly strenuous activities or competitive athletics.
- In patients with resting or inducible outflow obstructions, situations that will cause dehydration or vasodilation should be avoided.
- The primary goal of medications is to relieve symptoms, and first-line agents include beta blockers and calcium channel blockers (verapamil).
- Surgery: septal myectomy, septal ablation, implantable pacemaker or defibrillator, cardiac transplantation.

# Prognosis

- DCM: survival rate of less than 50% at 10 years; there is a negative association survival with frequent ventricular tachyarrhythmias that require antiarrhythmic treatment or automated implantable cardioverter-defibrillator (AICD) placement.
- HCM: annual mortality rates of up to 6% , important independent predictors of mortality are mutations in the  $\beta$ -MHC, occurrence of atrial fibrillation, stroke, presence of basal outflow obstruction of at least 30 mm Hg and marked left ventricular wall thickness of more than 25 mm.

# Prophylaxis

- Cardiomyopathy may be due to an underlying diseases or conditions.
- Treating that conditions early enough may help prevent cardiomyopathy complications.
- Sudden cardiac arrest (SCA) may be prevented in patients at high risk if they are treated with an implantable cardioverter defibrillator.

# Abbreviations

ACE – angiotensin converting enzyme

Ao -ascending aorta

ARVC - arrhythmogenic right ventricular cardiomyopathy

DCM - dilated cardiomyopathy

ECG – electrocardiography

HCM - hypertrophic cardiomyopathy

HF - chronic heart failure

LA - left atrium

LBBB - left bundle-branch block

LV - left ventricle

MV - mitral valve

SCA - sudden cardiac arrest



# Diagnostic and treatment guidelines

[2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy](#)

[Hypertrophic Cardiomyopathy](#)

[Dilated Cardiomyopathy](#)