

Internal Medicine

Lecture 6. Cardiomyopathies and Myocarditis

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Cardiomyopathies

The *cardiomyopathies* are diseases that involve the myocardium primarily and are not the result of hypertension or congenital, valvular, coronary, arterial, or pericardial abnormalities.

When the cardiomyopathies are classified on an etiologic basis, two fundamental forms are recognized:

- (1) a primary type, consisting of heart muscle disease of unknown cause, and
- (2) a secondary type, consisting of myocardial disease of known cause or associated with a disease involving other organ systems

WHO Classification

- **Unknown cause (primary)**
 - Dilated
 - Hypertrophic
 - Restrictive
 - Unclassified (dysrhythmic right ventricular cardiomyopathy)
- **Specific heart muscle disease (secondary)**
 - Infective
 - Metabolic
 - Systemic disease
 - Heredofamilial
 - Sensitivity
 - Toxic

Clinical Classification Of Cardiomyopathies

1. Dilated:

Left and/or right ventricular enlargement, impaired systolic function, congestive heart failure, arrhythmias, emboli.

2. Hypertrophic:

Disproportionate left ventricular hypertrophy, typically involving septum more than free wall, with or without an intraventricular systolic pressure gradient; usually of a nondilated left ventricular cavity.

3. Restrictive:

Endomyocardial scarring or myocardial infiltration resulting in restriction to left and/or right ventricular filling.

Idiopathic Dilated Cardiomyopathy

IDC - Definition

- **a disease of unknown etiology that principally affects the myocardium**
- **LV dilatation and systolic dysfunction**
- **pathology**
 - **increased heart size and weight**
 - **ventricular dilatation, normal wall thickness**
 - **heart dysfunction out of proportion to fibrosis**

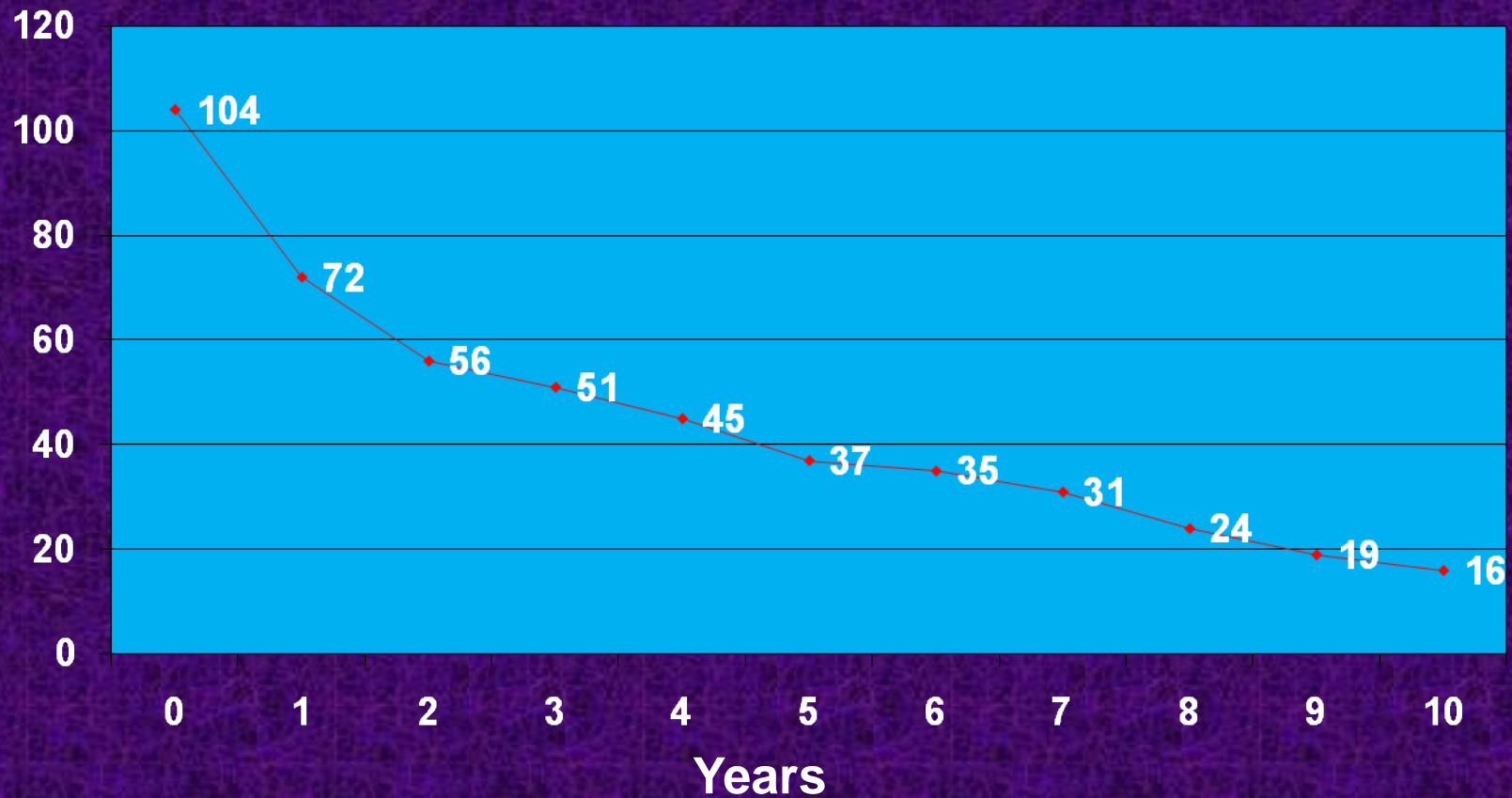
Incidence and Prognosis

- 3-10 cases per 100,000
- 20,000 new cases per year in the U.S.A.
- death from progressive pump failure

1-year	25%
2-year	35-40%
5-year	40-80%
- stabilization observed in 20-50% of patient
- complete recovery is rare

Idiopathic Dilated Cardiomyopathy

Observed Survival of 110 Patients



Am J Cardiol 2009; 67:521

Predicting Prognosis in IDC

	Predictive	Possible	Not Predictive
Clinical factors	symptoms	alcoholism peripartum family history	age duration viral illness
Hemodynamics	LVEF Cardiac index	LV size atrial pressure	
Dysarrhythmia	LV cond delay complex VPC	AV block atrial fibrillation	simple VPC
Histology		myofibril volume	other findings
Neuroendocrine	hyponatremia plasma norepinephrine atrial natriuretic factor		

Clinical Manifestations

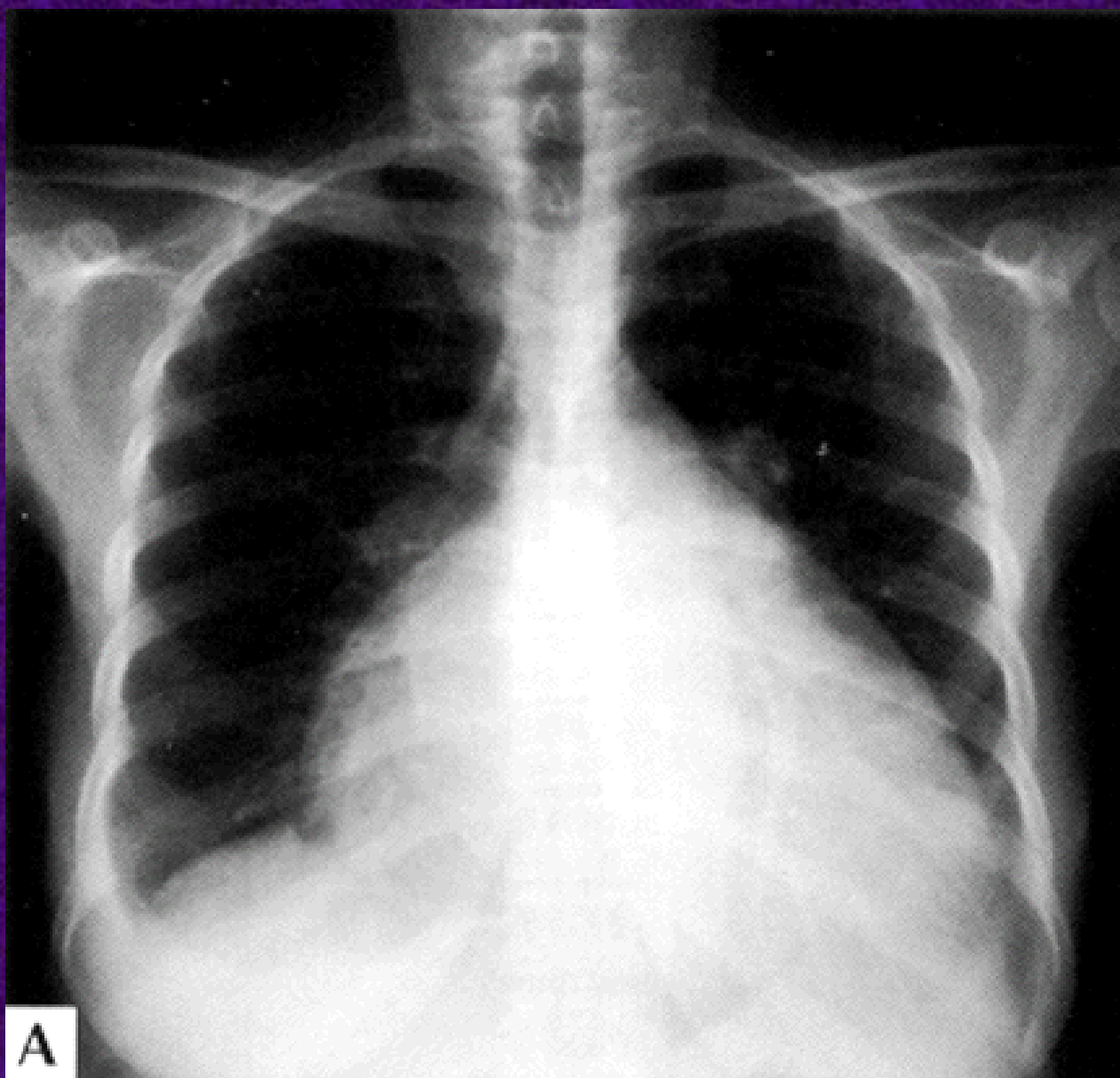
- **Highest incidence in middle age**
 - blacks 2x more frequent than whites
 - men 3x more frequent than women
- **symptoms may be gradual in onset**
- **acute presentation**
 - misdiagnosed as viral URI in young adults
 - uncommon to find specific myocardial disease on endomyocardial biopsy

History and Physical Examination

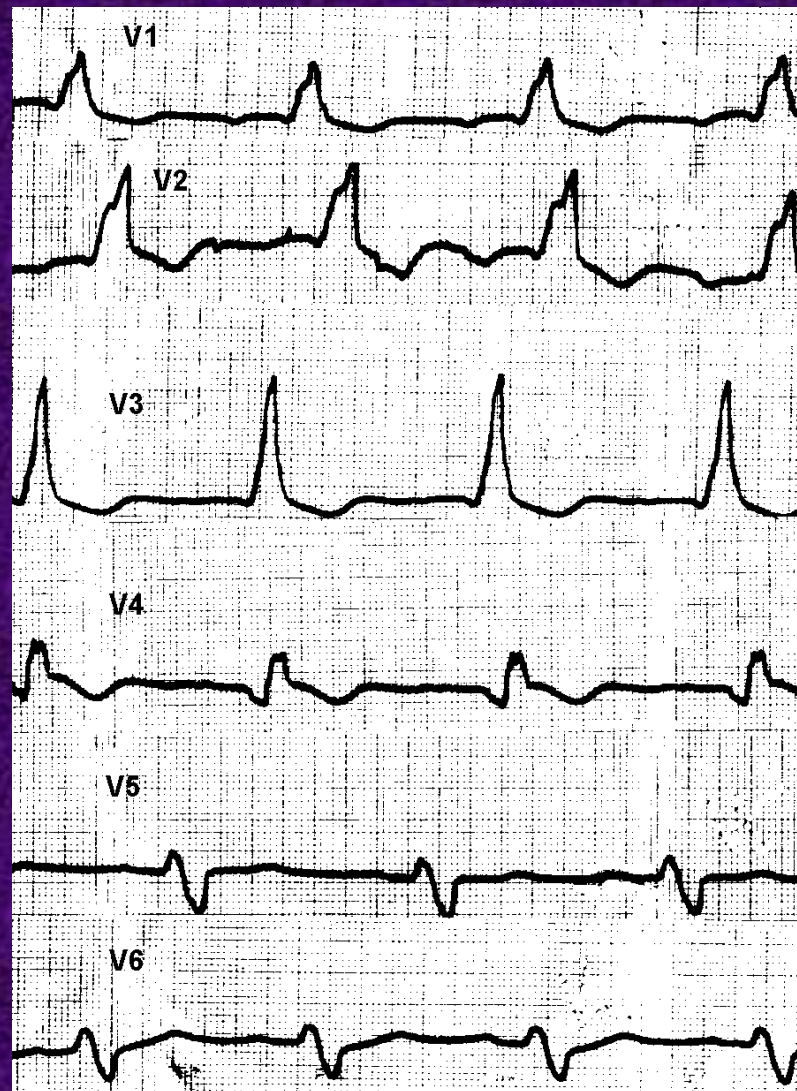
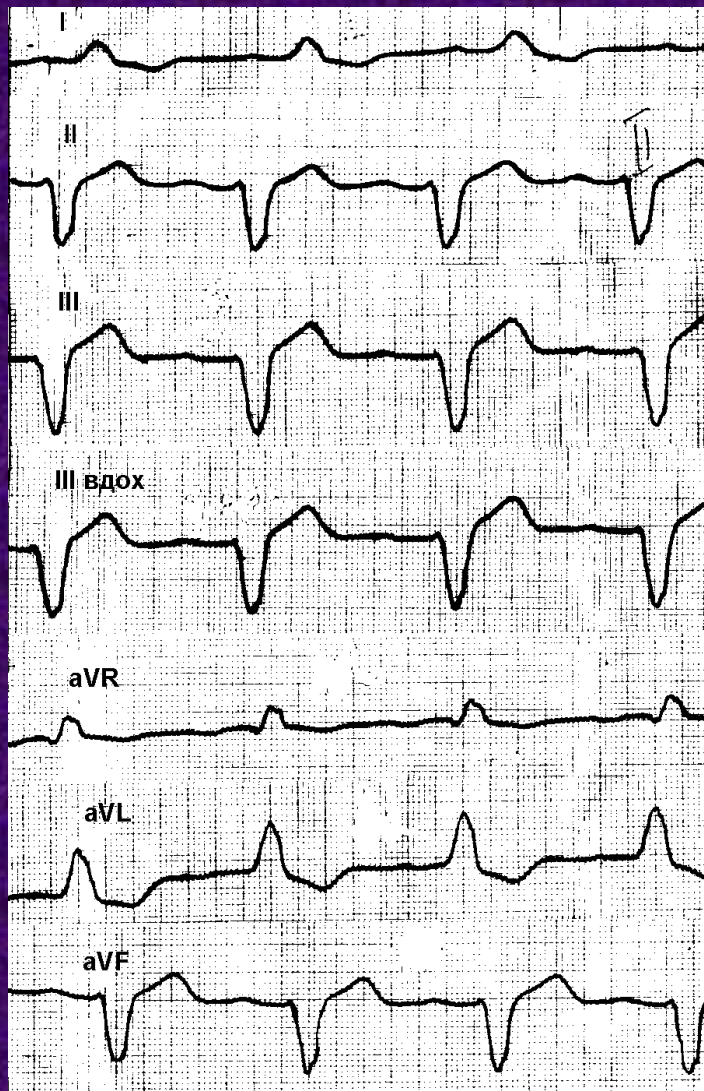
- Symptoms of heart failure
 - pulmonary congestion (left HF)
dyspnea (rest, exertional, nocturnal), orthopnea
 - systemic congestion (right HF)
edema, nausea, abdominal pain, nocturia
 - low cardiac output
fatigue and weakness
- hypotension, tachycardia, tachypnea, JVD

Cardiac Imaging

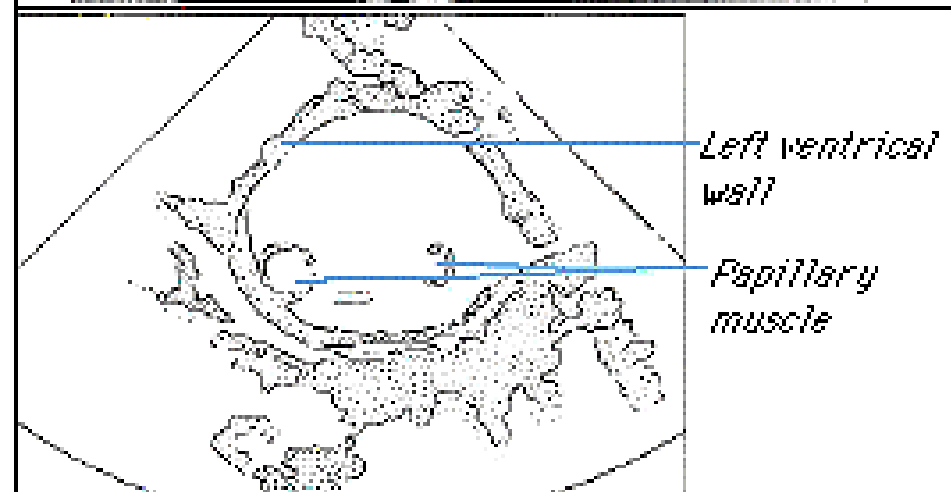
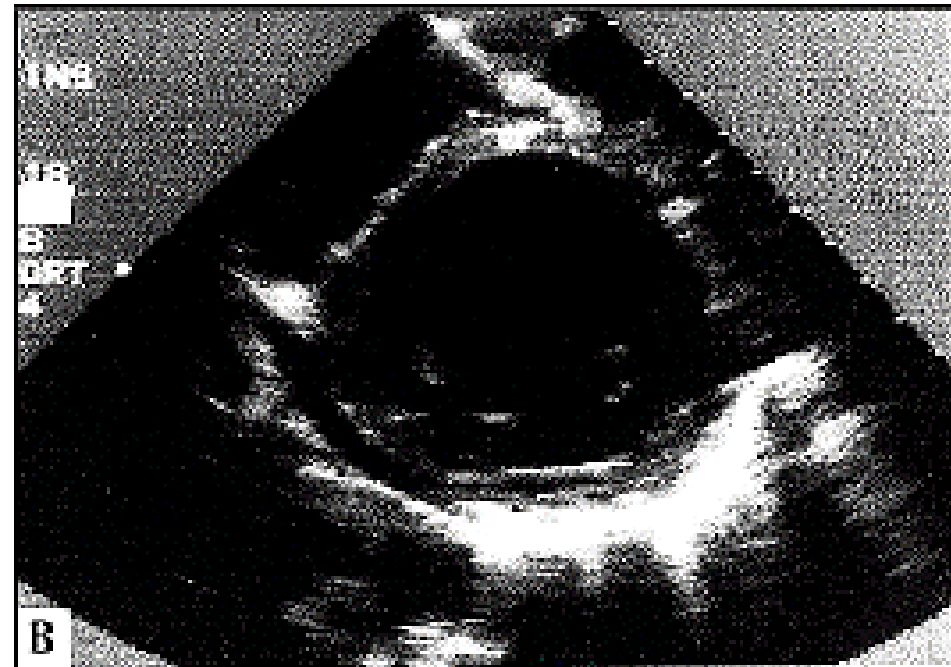
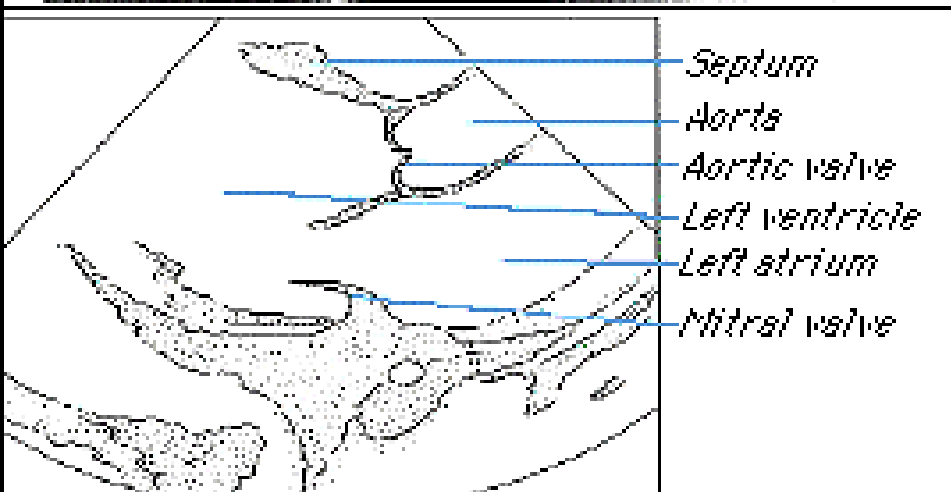
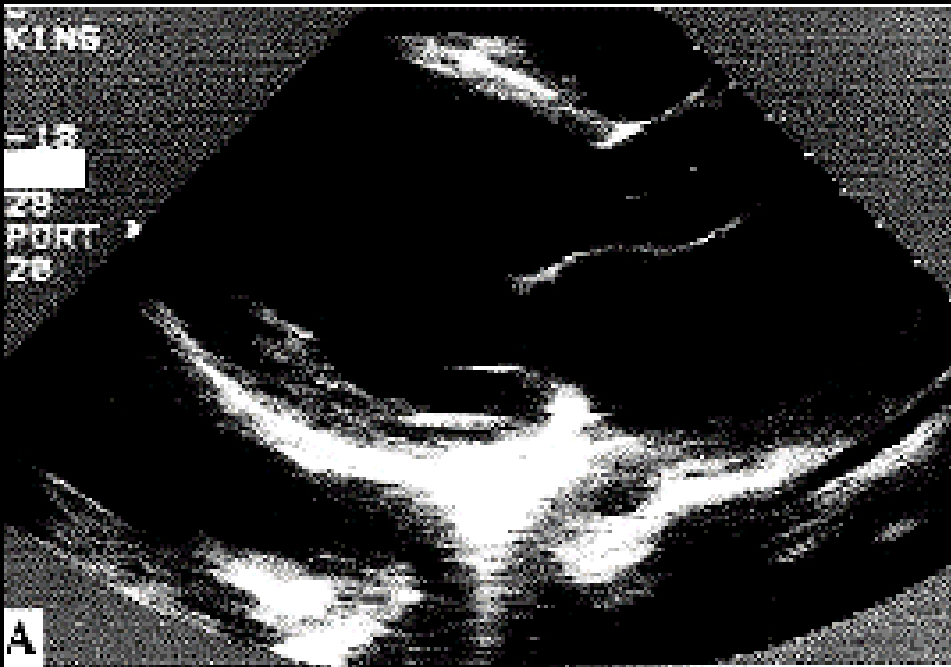
- Chest radiogram
- Electrocardiogram
- 24-hour ambulatory ECG (Holter)
 - lightheadedness, palpitation, syncope
- Two-dimensional echocardiogram
- Radionuclide ventriculography
- Cardiac catheterization
 - age >40, ischemic history, high risk profile, abnormal ECG



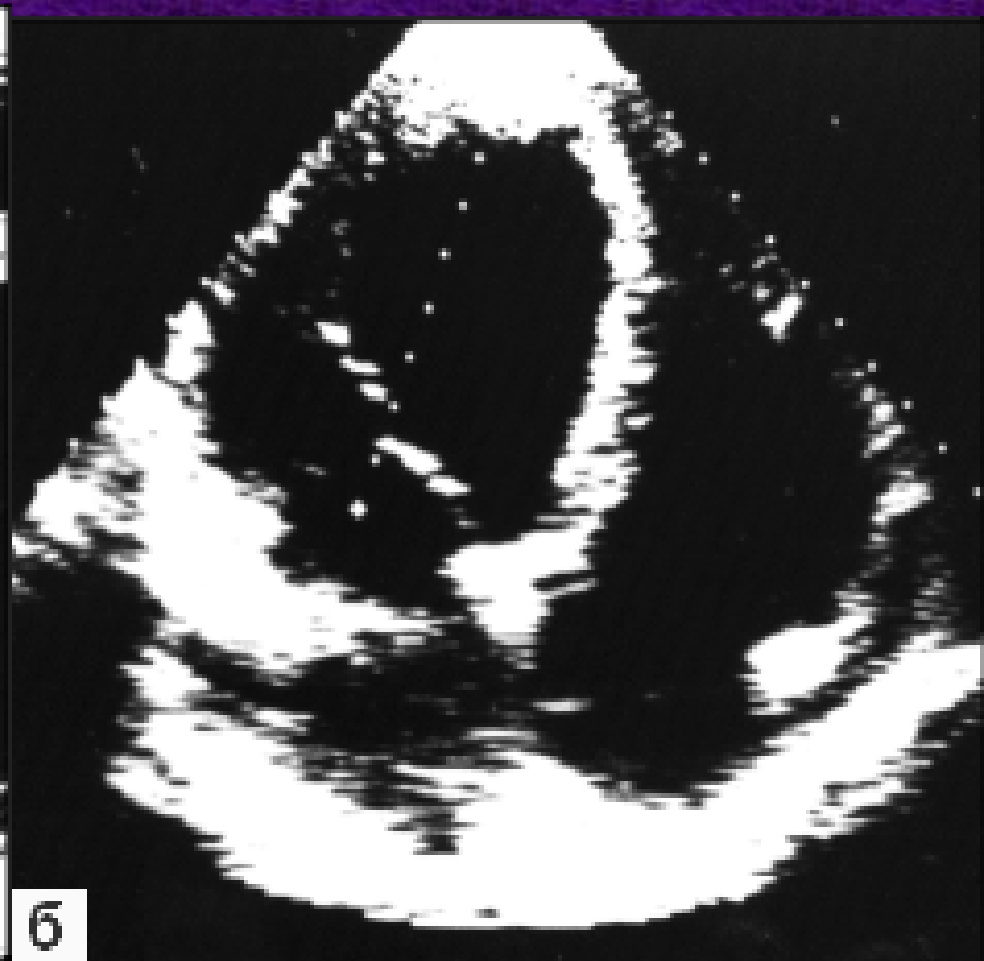
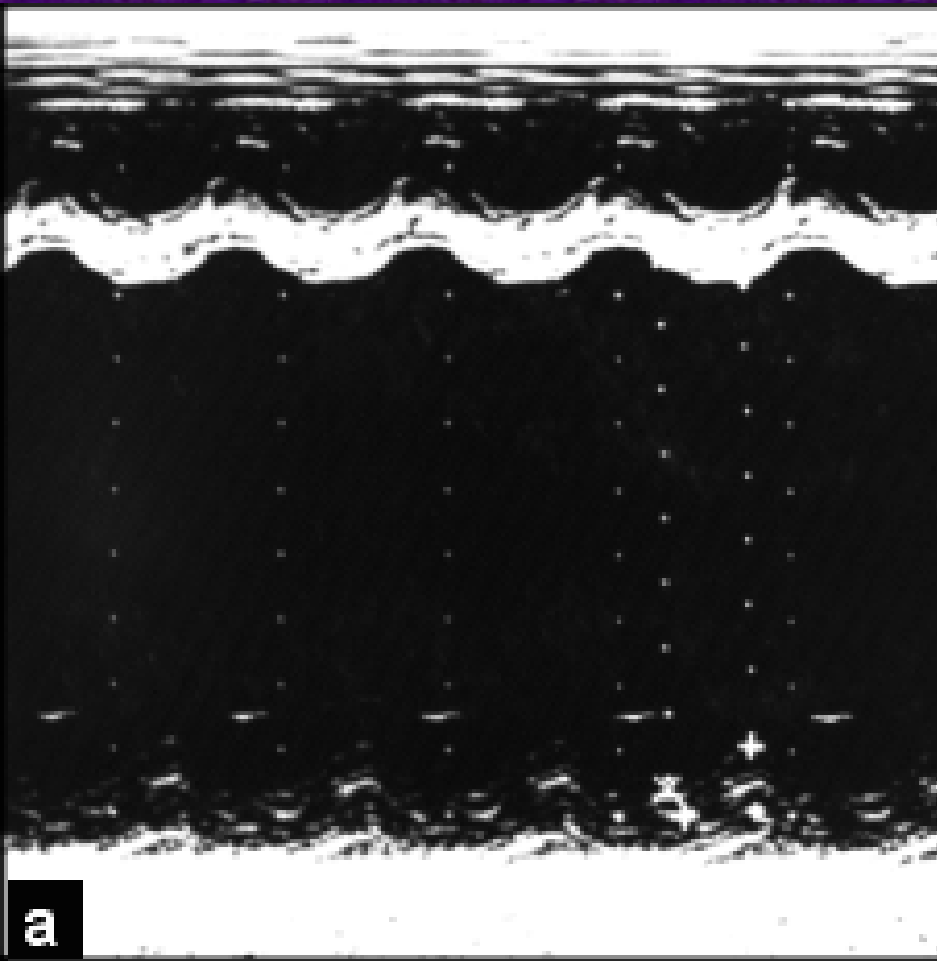
Chest roentgenogram of patient with severe heart failure. This roentgenogram demonstrates cardiomegaly (cardiothoracic ratio 0.77), pulmonary congestion, and bilateral pleural effusions (note blunted costophrenic angles).



The electrocardiogram shows atrial enlargement, ventricular hypertrophy, *bifascicular block* including right bundle branch block with left anterior fascicular block and diffuse nonspecific ST-T wave abnormalities.



Echocardiographic parasternal long-axis (A) and short-axis (B) views in a 26-year-old patient with idiopathic dilated cardiomyopathy. The chambers are dilated and the walls are thin.



Echocardiography shows left ventricular dilatation, with normal or minimally thickened or thinned walls, and systolic dysfunction (reduced ejection fraction).

Clinical Indications for Endomyocardial Biopsy

- **Definite**
 - monitoring of cardiac allograft rejection
 - monitoring of anthracycline cardiotoxicity
- **Possible**
 - detection and monitoring of myocarditis
 - diagnosis of secondary cardiomyopathies
 - differentiation between restrictive and constrictive heart disease

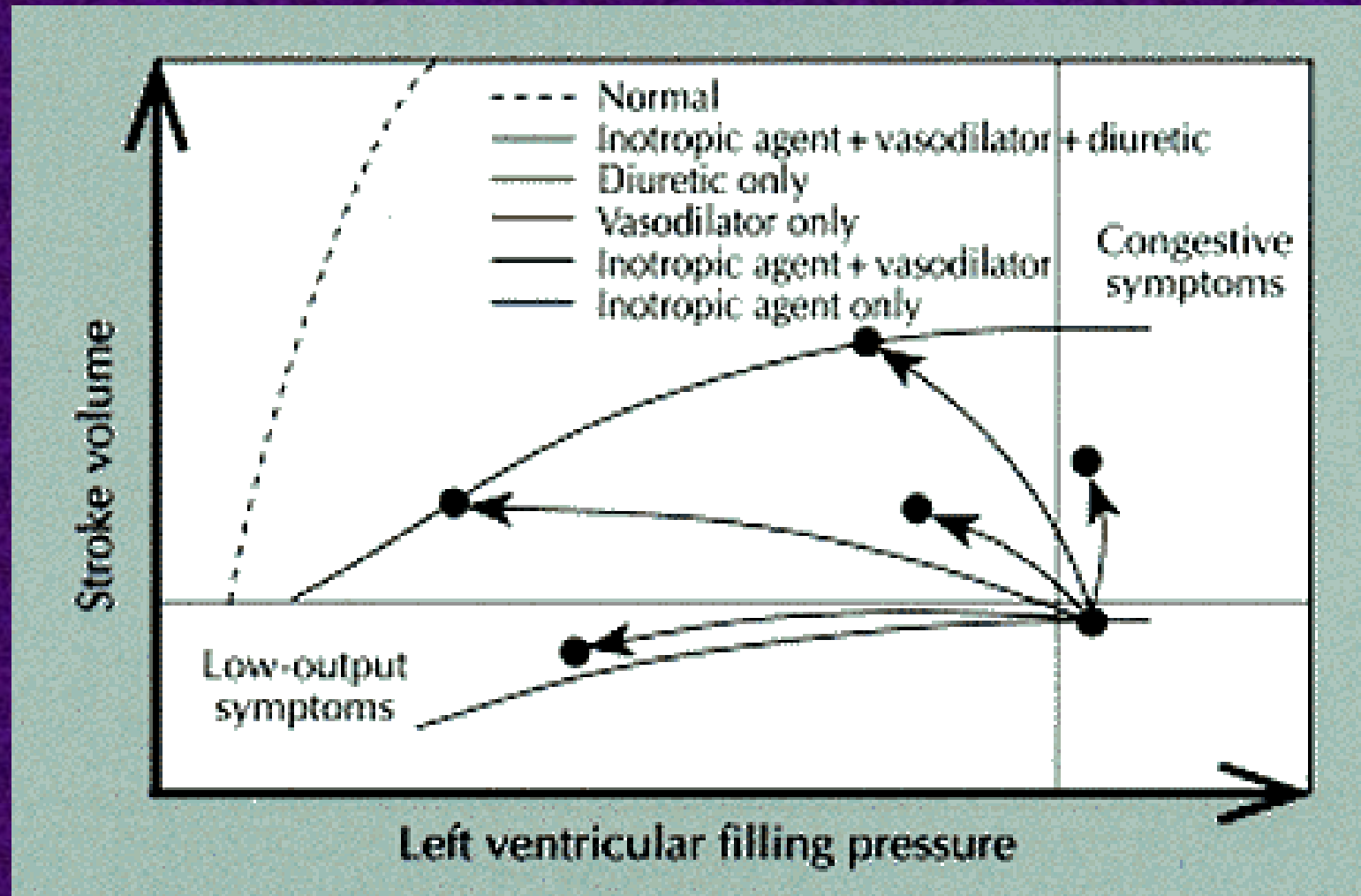
Management of DCM

- Limit activity based on functional status
- salt restriction of a 2-g Na⁺ (5g NaCl) diet
- fluid restriction for significant low Na⁺
- initiate medical therapy
 - ACE inhibitors, diuretics
 - digoxin, carvedilol
 - hydralazine / nitrate combination

Management of DCM

- consider adding β -blocking agents if symptoms persists
- anticoagulation for EF <30%, history of thromboemoli, presence of mural thrombi
- intravenous dopamine, dobutamine and/or phosphodiesterase inhibitors
- cardiac transplantation

Physiologic Response To Pharmacologic Intervention In Heart Failure



The curves represent the relationship between left ventricular end-diastolic filling pressure and stroke volume for a normal heart and for the patient with heart failure symptoms resulting from predominant systolic dysfunction before and after treatment with digoxin or diuretics, alone or in combination with a vasodilator. Positive inotropic agents, such as digoxin, and vasodilators shift the patient's hemodynamic profile upward and leftward to a more favorable ventricular function curve, resulting in an improvement in cardiac output despite a reduction in ventricular filling pressure. Diuretics reduce heart failure symptoms by lowering ventricular filling pressures, but they may cause a reduction in cardiac output.

Alcoholic Cardiomyopathy

Individuals who consume large quantities of alcohol over many years may develop a clinical picture identical to idiopathic dilated cardiomyopathy; indeed, alcoholic cardiomyopathy is the major form of secondary dilated cardiomyopathy in the western world. Ceasing alcohol consumption before severe heart failure has developed may halt the progression or even reverse the course of this disease, unlike the idiopathic variety, which is marked by progressive deterioration. Alcoholic patients with advanced heart failure have a poor prognosis, particularly if they continue to drink; fewer than one-quarter survive 3 years. The key to the treatment of alcoholic cardiomyopathy is total and permanent abstinence. The toxic effect of alcohol on striated muscle often extends beyond the heart to cause myopathy in skeletal muscles. A second presentation of alcoholic cardiotoxicity may be found in individuals without overt heart failure and consists of recurrent supraventricular or ventricular tachyarrhythmias. Termed the *holiday heart syndrome*, it typically appears after a drinking binge; atrial fibrillation is seen most frequently, followed by atrial flutter and ventricular premature depolarizations. Other patients develop left ventricular hypertrophy, perhaps related to concomitant systemic hypertension; they may present with symptoms of pulmonary congestion due to abnormal diastolic stiffness (diminished compliance) of the left ventricle.

Peripartum Cardiomyopathy

Cardiac dilatation and congestive heart failure of unexplained cause may develop during the last trimester of pregnancy or within 6 months after delivery; most women develop symptoms in the month before or immediately after delivery. The cause of this disorder is unknown, but in some patients endomyocardial biopsy has shown evidence of a myocarditis. Necropsy shows cardiac enlargement, often with mural thrombi, along with histologic evidence of myocardial degeneration and fibrosis. The symptoms, signs, and treatment are similar to those in patients with idiopathic dilated cardiomyopathy. The mortality rate is quite variable but may be as high as 25 to 50 percent. The prognosis in these patients appears to be closely related to whether the heart size returns to normal after the first episode of congestive heart failure. If it does, subsequent pregnancies may sometimes be well tolerated; if the heart remains enlarged, however, further pregnancies frequently produce increasing myocardial damage, ultimately leading to refractory congestive heart failure and death. Those who recover should be encouraged to avoid further pregnancies, particularly if cardiomegaly persists.

Hypertrophic Cardiomyopathy

Hypertrophic Cardiomyopathy

- **First described by the French and Germans around 1900**
- **uncommon with occurrence of 0.02 to 0.2%**
- **a hypertrophied and non-dilated left ventricle in the absence of another disease**
- **small LV cavity, asymmetrical septal hypertrophy (ASH), systolic anterior motion of the mitral valve leaflet (SAM)**

Hypertrophic Cardiomyopathy

This disease is characterized by left ventricular hypertrophy, typically of a nondilated chamber, without obvious cause such as hypertension or aortic stenosis. Two features of the disease have attracted the greatest attention:

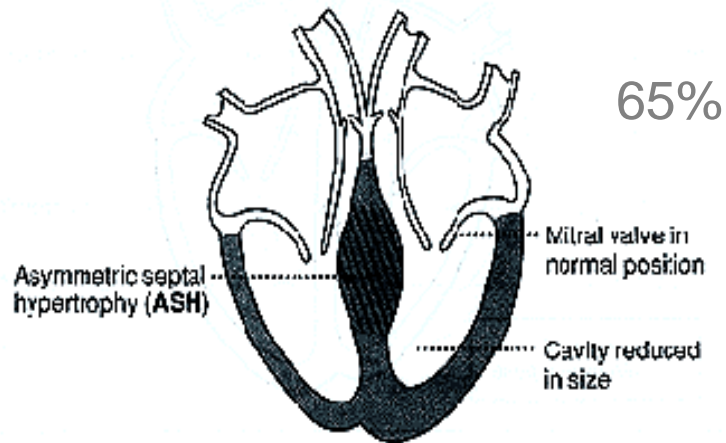
- 1). heterogeneous left ventricular (LV) hypertrophy, often with preferential hypertrophy of the interventricular septum resulting in asymmetric septal hypertrophy (ASH);
- 2). a dynamic left ventricular outflow tract pressure gradient, related to a narrowing of the subaortic area as a consequence of the midsystolic apposition of the anterior mitral valve leaflet against the hypertrophied septum, i.e., systolic anterior motion (SAM) of the mitral valve.

Initial studies of this disease emphasized the dynamic "obstructive" features, and it has been termed *idiopathic hypertrophic subaortic stenosis* (IHSS), *hypertrophic obstructive cardiomyopathy* (HOCM), and *muscular subaortic stenosis*. It has become clear, however, that only about one-quarter of patients with hypertrophic cardiomyopathy demonstrate an outflow tract gradient.

The ubiquitous pathophysiologic abnormality is not systolic but rather *diastolic* dysfunction, characterized by increased stiffness of the hypertrophied muscle.

Hypertrophic Cardiomyopathy

Asymmetric septal hypertrophy without obstruction



Hypertrophic Cardiomyopathy

Symmetric hypertrophy

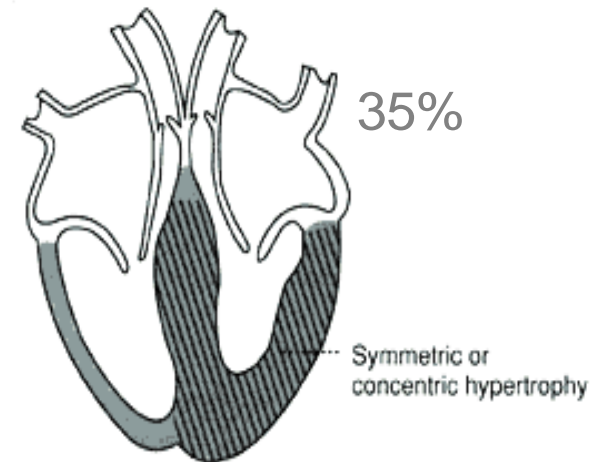
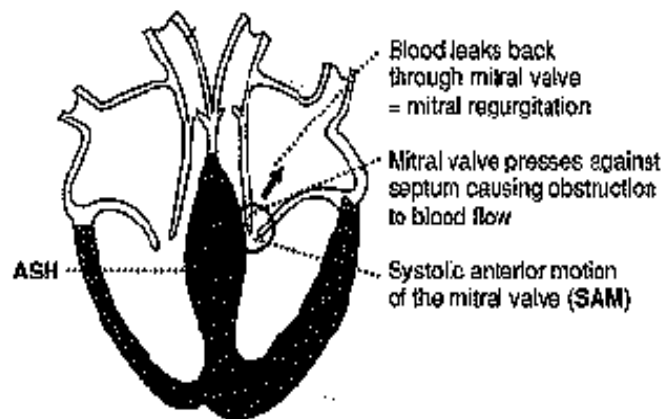


FIGURE 7

Hypertrophic Cardiomyopathy

Asymmetric septal hypertrophy with obstruction



Hypertrophic Cardiomyopathy

Apical hypertrophy

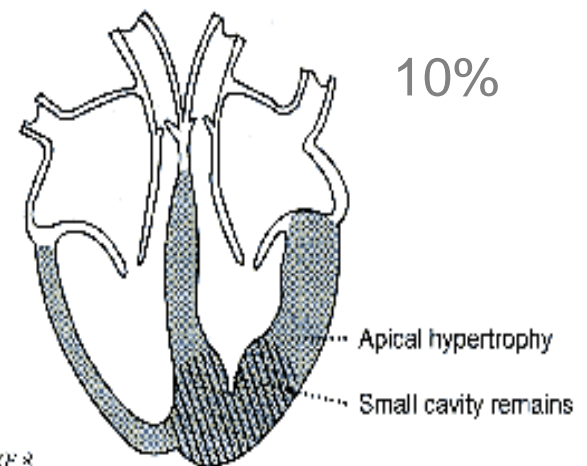


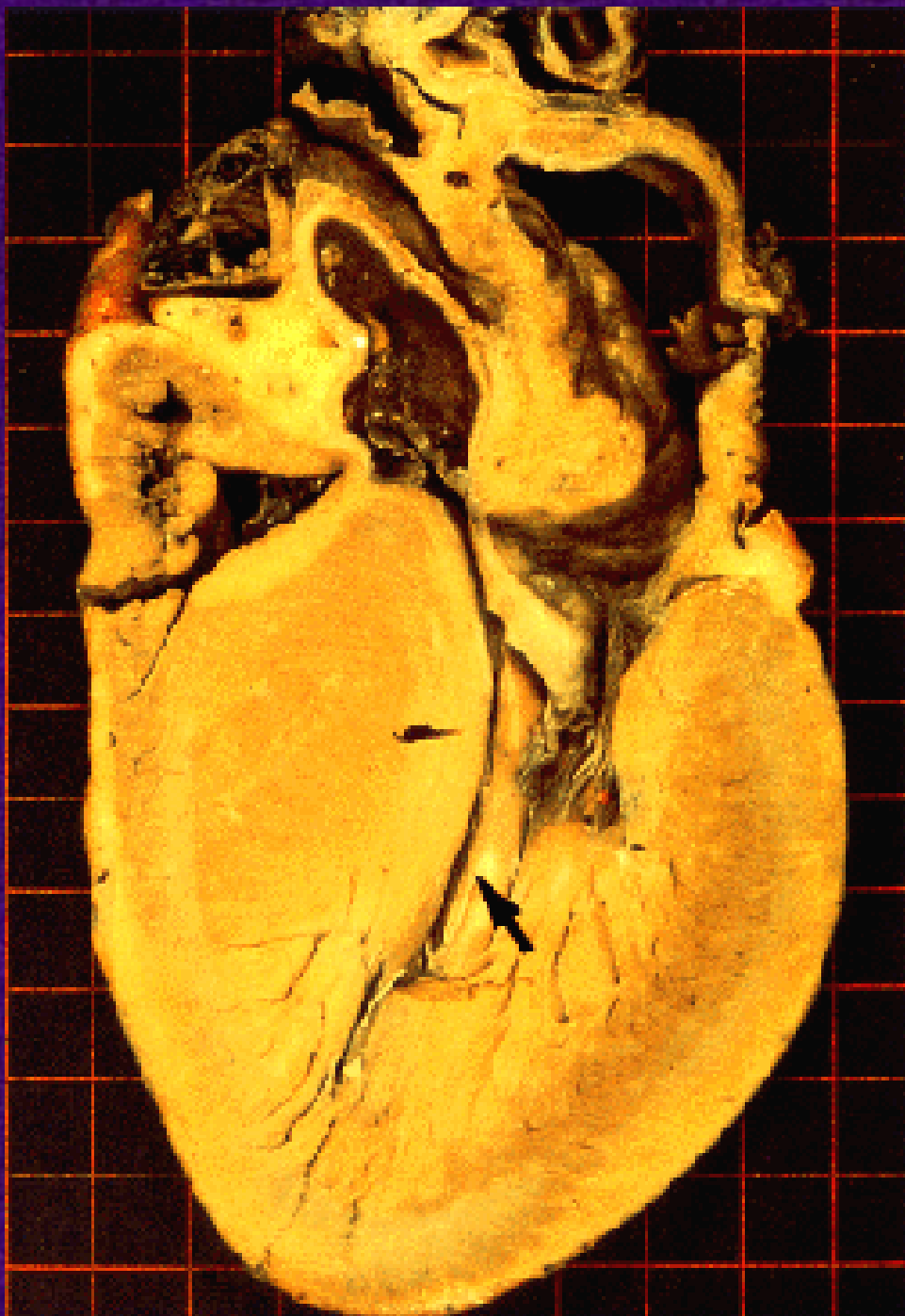
FIGURE 8

Familial HCM

- **First reported by Seidman et al in 1989**
- **occurs as autosomal dominant in 50%**
- **5 different genes on at least 4 chromosome with over 3 dozen mutations**
 - **chromosome 14 (myosin)**
 - **chromosome 1 (troponin T)**
 - **chromosome 15 (tropomyosin)**
 - **chromosome 11 (?)**

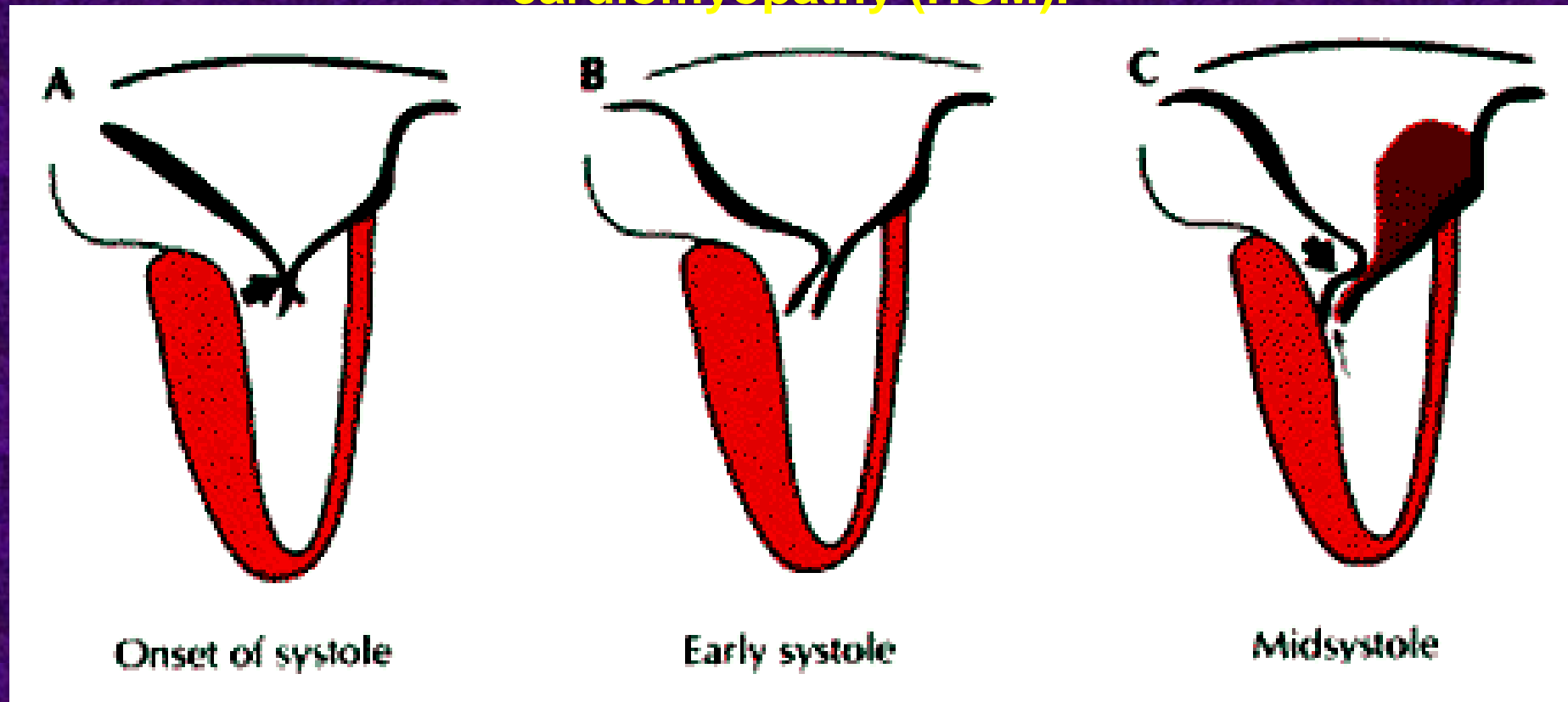
Pathophysiology

- **Systole**
 - dynamic outflow tract gradient
- **Diastole**
 - impaired diastolic filling,
 - ↑ filling pressure
- **Myocardial ischemia**
 - ↑ muscle mass, filling pressure, O_2 demand
 - ↓ vasodilator reserve, capillary density
 - abnormal intramural coronary arteries
 - systolic compression of arteries



Asymmetric septal hypertrophy. Longitudinal section of the heart of a 32-year-old woman with subaortic obstructive HCM who died suddenly. Hemodynamic investigation confirmed subaortic obstruction as well as mitral regurgitation. The regurgitation was partially due to an abnormal mitral valve [insertion of an anomalous papillary muscle (arrow) onto the ventricular surface of the anterior mitral leaflet]. There is asymmetric hypertrophy with a grossly thickened ventricular septum. A narrowed outflow tract between the upper septum and the anterior mitral leaflet, which is very thickened and fibrosed from repeated contact with the septum, can also be seen.

Functional anatomy of mitral leaflet systolic anterior motion and mitral regurgitation in subaortic obstructive hypertrophic cardiomyopathy (HCM).



Drawing of a transesophageal echocardiogram demonstrating the anterior and superior motion of the anterior mitral leaflet to produce mitral leaflet-septal contact and failure of leaflet coaptation in midsystole. A. At the onset of systole, the coaptation point (arrow) is in the body of the anterior and posterior leaflets rather than at the tip of the leaflets, as in normal subjects. During early systole (B) and midsystole (C) there is anterior and superior movement of the residual length of the anterior mitral leaflet (thick arrow in C), with septal contact and failure of leaflet coaptation (thin arrow in C) with consequent mitral regurgitation directed posteriorly into the left atrium (dotted area).

Clinical Manifestation

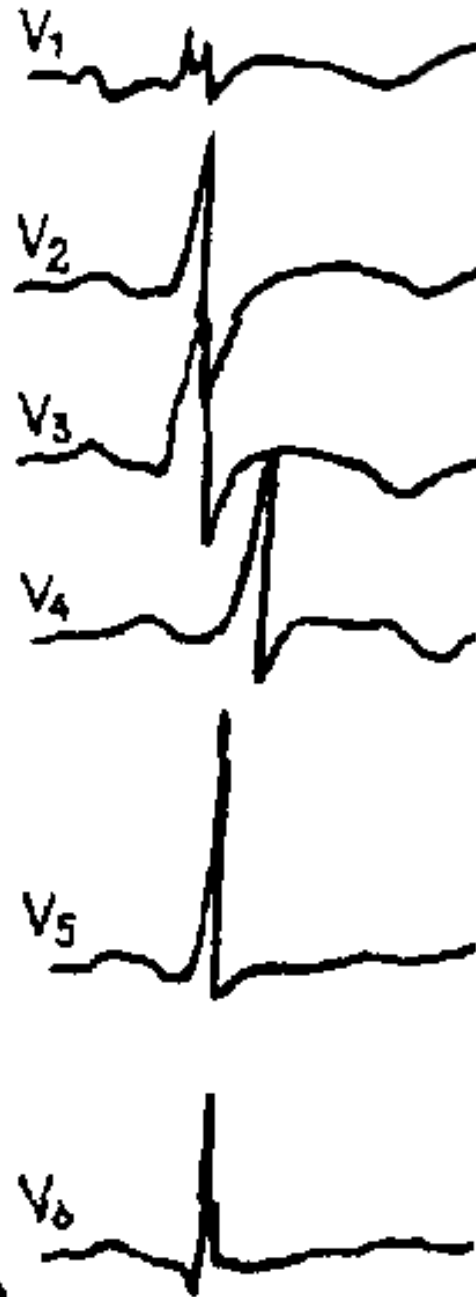
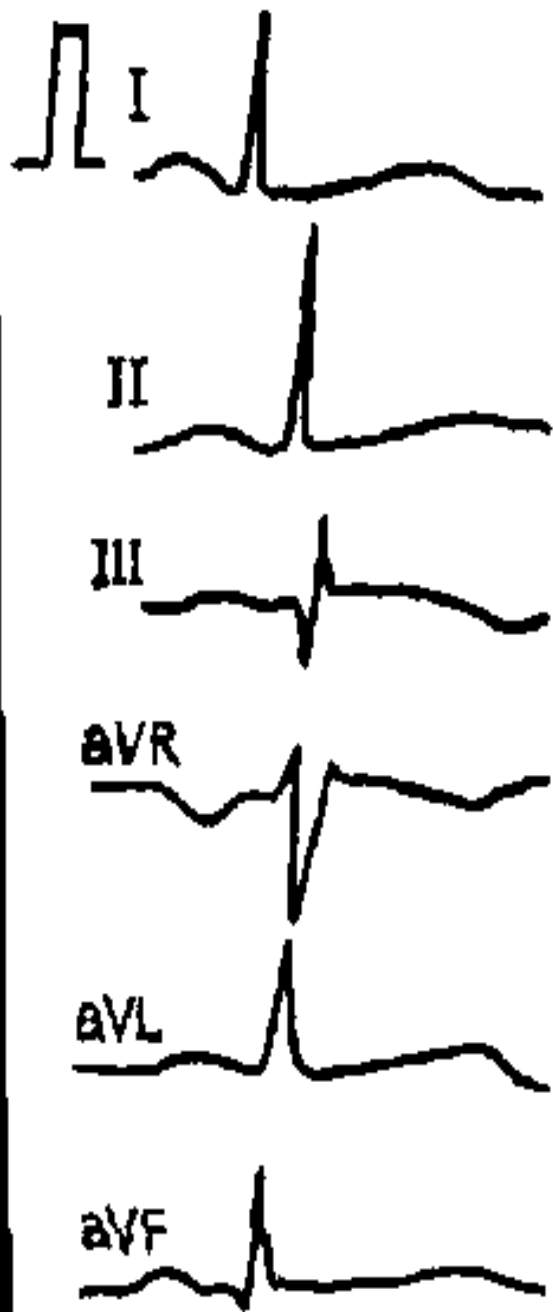
- Asymptomatic, echocardiographic finding
- Symptomatic
 - dyspnea in 90%
 - angina pectoris in 75%
 - fatigue, pre-syncope, syncope
 - ↑ risk of SCD in children and adolescents
 - palpitation, PND, CHF, dizziness less frequent

Increase in Gradient and Murmur

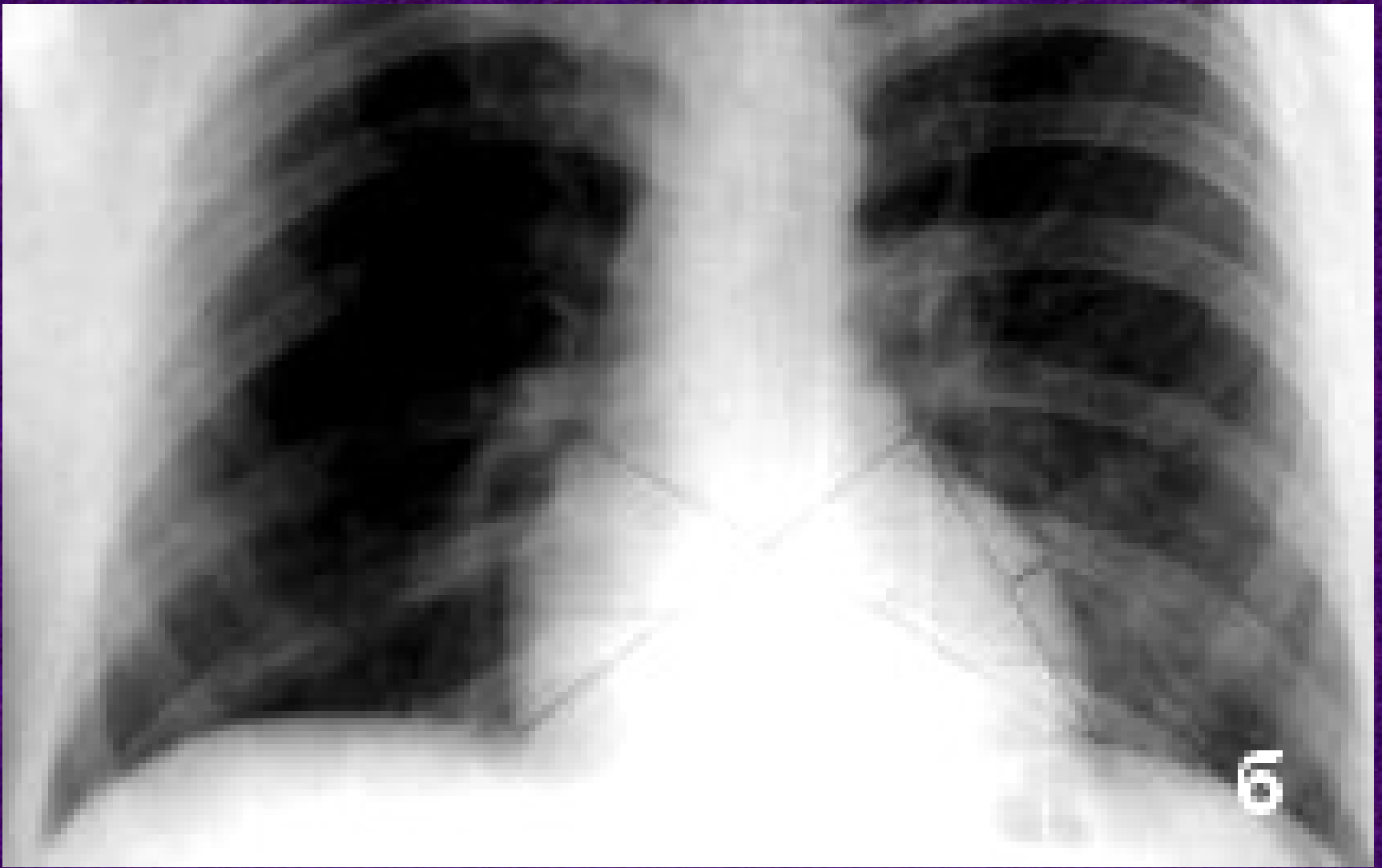
	Contractility	Preload	Afterload
valsalva (strain)	---	↓	↑
standing	---	↓	---
postextrasystole	↑	↑	--
isoproterenol	↑	↓	↓
digitalis	↑	↓	--
amyl nitrite	-- ↑	↓ ↑	↓
nitroglycerine	---	↓	↓
exercise	↑	↑	↑
tachycardia	↑	↓	--
hypovolemia	↑	↓	↓

Decrease in Gradient and Murmur

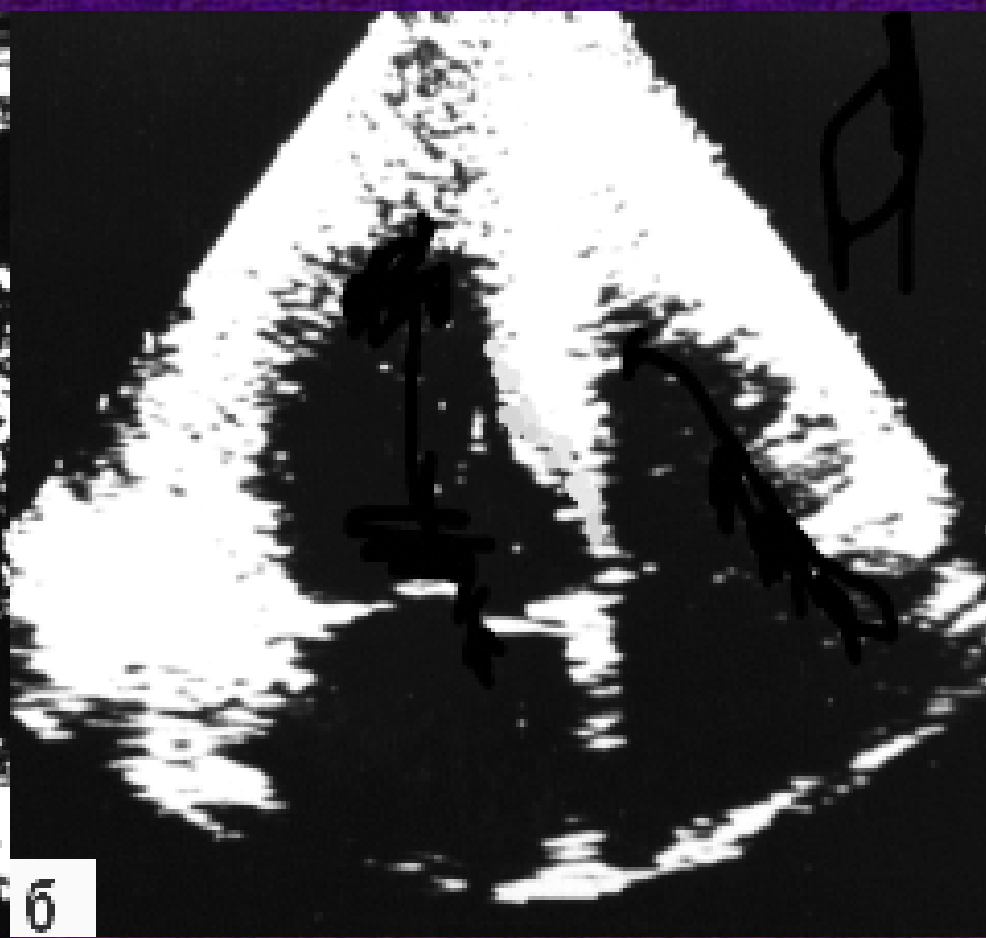
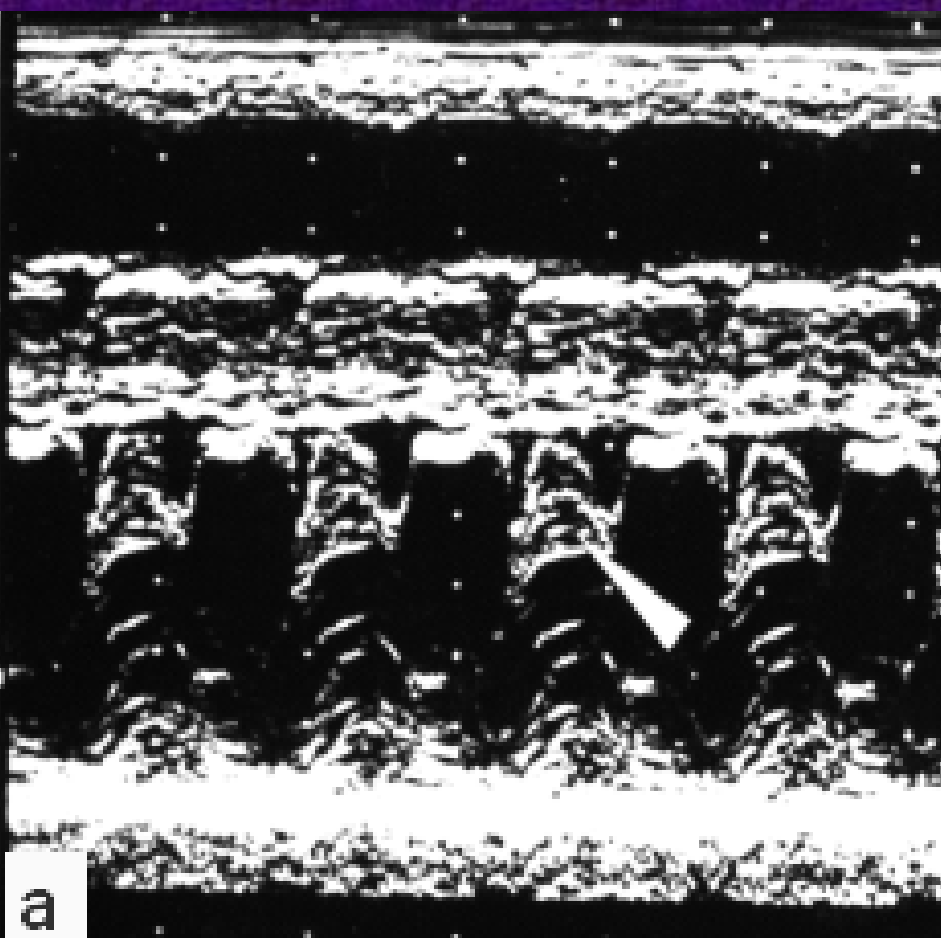
	Contractility	Preload	Afterload
Mueller meneuver	---	↑	↑
valsalva (overshoot)	---	↑	↑
squatting	---	↑	↑
passive leg elevation	---	↑	--
phenylephrine	---	--	↑
beta-blocker	↓	↑	--
general anesthesia	↓	--	--
isometric grip	---	--	↑



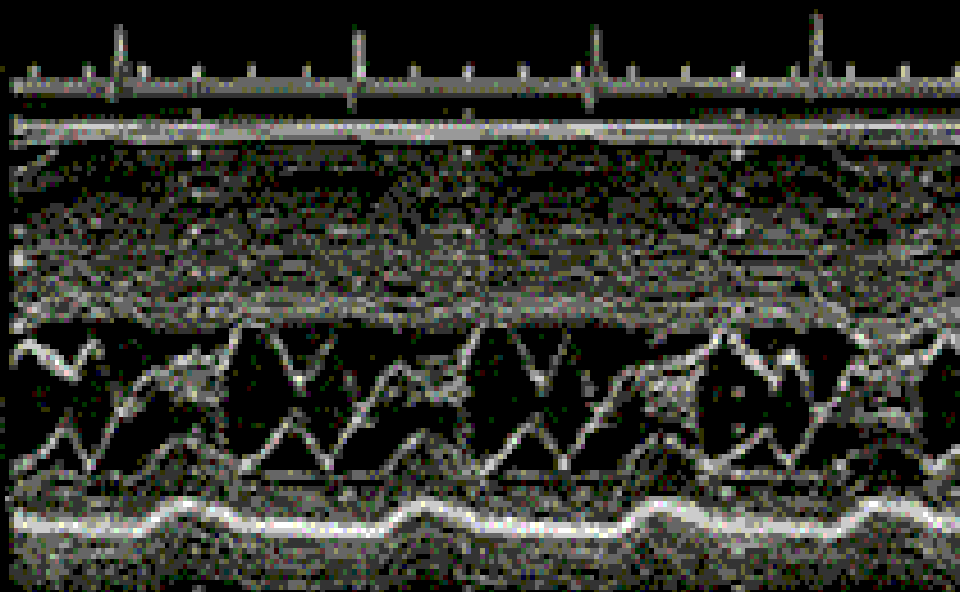
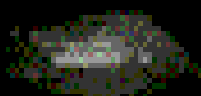
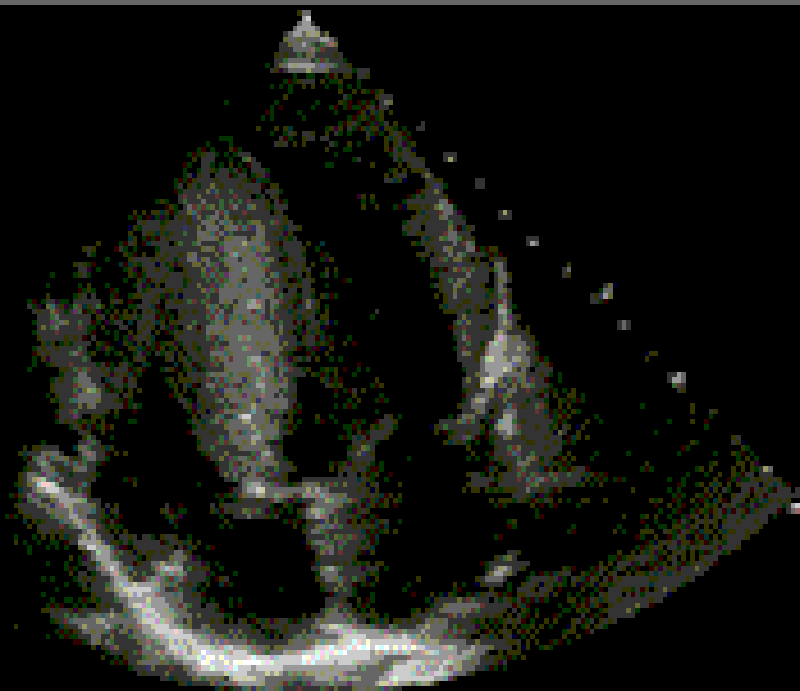
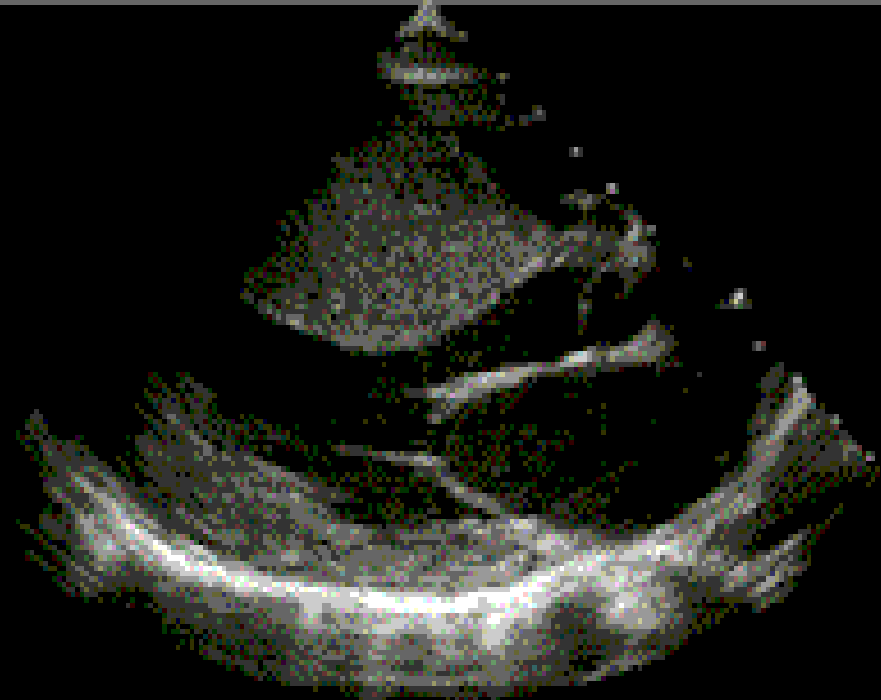
The *electrocardiogram* shows left ventricular hypertrophy and widespread, deep, broad Q waves that suggest an old myocardial infarction.

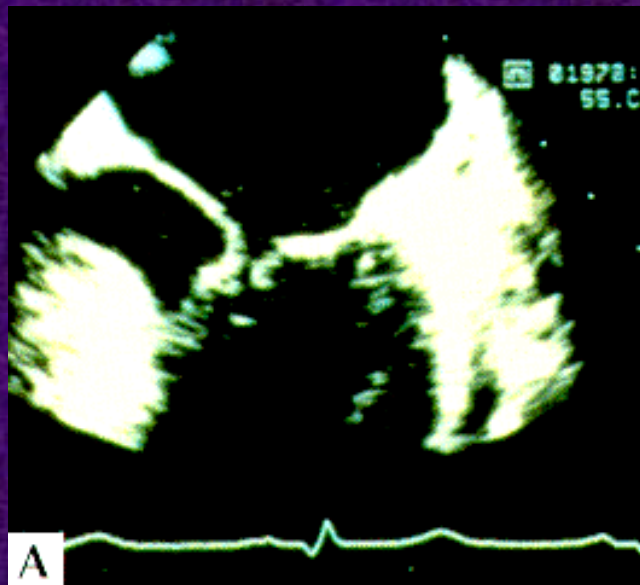


Chest roentgenography: moderate increase in the cardiac silhouette owing to left ventricular hypertrophy.

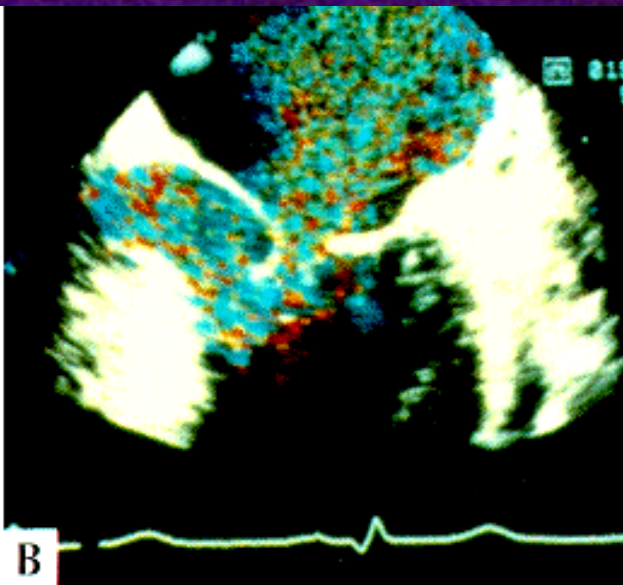


Echocardiogram demonstrates left ventricular hypertrophy, with the septum 1.5 the thickness of the high posterior left ventricular free wall. The septum demonstrates an unusual ground glass appearance, probably related to its abnormal cellular architecture and myocardial fibrosis. The left ventricular cavity typically is small, with vigorous posterior wall motion but reduced septal excursion.

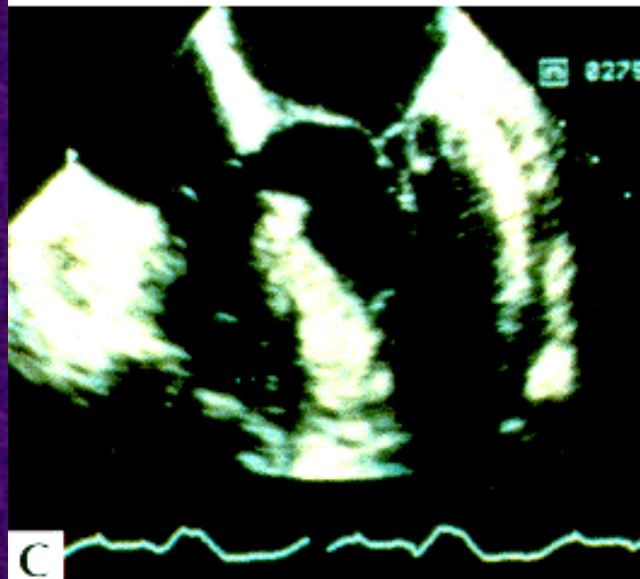




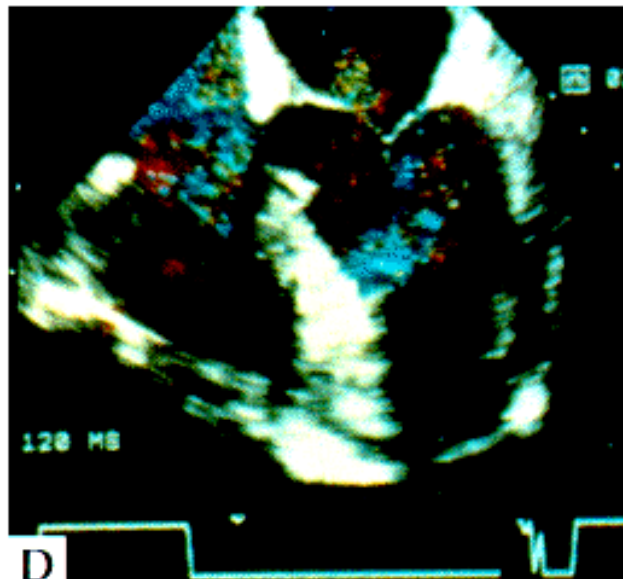
A



B



C



D

myectomy demonstrating a widened left ventricular outflow tract and abolition of systolic anterior motion. Panel D is the same frame with Doppler color-flow imaging demonstrating nonturbulent left ventricular outflow with a marked reduction in the severity of the mitral regurgitation (which is now reflected only by a small residual central jet).

Obstruction and mitral regurgitation in subaortic obstructive HCM before and after myectomy. [Showing intraoperative transesophageal echocardiographic and Doppler study (frontal long-axis plane) before (A and B) and after (C and D) myectomy.] Panel A shows a two-dimensional systolic frame demonstrating systolic anterior motion of the residual length of the anterior mitral leaflet, with mitral leaflet-septal contact and failure of coaptation between the mitral leaflets. Panel B shows the same frame with Doppler color-flow imaging demonstrating turbulent left ventricular outflow as a result of the subaortic obstruction and a large jet of posteriorly directed mitral regurgitation arising from the funnel-shaped gap between the two mitral leaflets due to their failure to coapt. There is no evidence of left ventricular cavity obliteration at the time of subaortic obstruction and concomitant regurgitation. Panel C is a two-dimensional systolic frame following

Drugs Used in Treatment of Hypertrophic Cardiomyopathy

Drug	Mode of Administration
Propranolol	Oral, 10-200 mg q 6 h
Metoprolol	Oral, 25-100 mg bid
Verapamil	Oral, 80-120 mg q 6-8 h
Diltiazem	Oral, 180-360 mg qd or in divided dosages
Amiodarone	IV, 5-10 mg/kg Oral, load 800-1400 mg/d for 1-2 weeks Maintenance. 100-600 mg/d
Sotalol	Oral, 80-160 mg q 12 h for atrial fibrillation; up to 320 mg q 12 h for ventricular arrhythmias.
Propafenone	Oral, 450-900 mg q 8 h
Disopyramide	Oral, 100-150 mg q 6 h

Natural History

- annual mortality 3% in referral centers probably closer to 1% for all patients
- risk of SCD higher in children may be as high as 6% per year majority have progressive hypertrophy
- clinical deterioration usually is slow
- progression to DCM occurs in 10-15%

Risk Factors for SCD

- **Young age (<30 years)**
- **“Malignant” family history of sudden death**
- **Gene mutations prone to SCD (ex. Arg403Gln)**
- **Aborted sudden cardiac death**
- **Sustained VT or SVT**
- **Recurrent syncope in the young**
- **Nonsustained VT (Holter Monitoring)**
- **Brady arrhythmias (occult conduction disease)**

Recommendations for Athletic Activity

- **Avoid most competitive sports (whether or not symptoms and/or outflow gradient are present)**
- **Low-risk older patients (>30 yrs) may participate in athletic activity if all of the following are absent**

Recommendations for Athletic Activity

- **Low-risk older patients (>30 yrs) may participate in athletic activity if all of the following are absent**
 - ventricular tachycardia on Holter monitoring
 - family history of sudden death due to HCM
 - history of syncope or episode of impaired consciousness
 - severe hemodynamic abnormalities, gradient ≥ 50 mmHg
 - exercise induced hypotension
 - moderate or severe mitral regurgitation
 - enlarged left atrium (≥ 50 mm)
 - paroxysmal atrial fibrillation
 - abnormal myocardial perfusion

Management

- **beta-adrenergic blockers**
- **calcium antagonist**
- **disopyramide**
- **amiodarone, sotalol**
- **DDD pacing**
- **myotomy-myectomy**
- **plication of the anterior mitral leaflet**

HCM vs Aortic Stenosis

	HCM	Fixed Obstruction
carotid pulse	spike and dome	parvus et tardus
murmur		radiate to carotids
	↑ valsalva, standing	
	↓ squatting, handgrip	
	↓ passive leg elevation	
systolic thrill	4th left interspace	2nd right interspace
systolic click	absent	present

Other Causes of Hypertrophy

- **Clinical mimics**
 - glycogen storage, infants of diabetic mothers, amyloid
- **Genetic**
 - Noonan's, Friedreich's ataxia, Familial restrictive cardiomyopathy with disarray
- **Exaggerated physiologic response**
 - Afro-Caribbean hypertension, old age hypertrophy, athlete's heart

HCM vs Athlete's Heart

HCM

Athlete

+	Unusual pattern of LVH	-
+	LV cavity <45 mm	-
-	LV cavity >55 mm	+
+	LA enlargement	-
+	Bizarre ECG patterns	-
+	Abnormal LV filling	-
+	Female gender	-
-	↓ thickness with deconditioning	+
+	Family history of HCM	-

Hypertensive HCM of the Elderly

- **Characteristics**
 - modest concentric LV hypertrophy (<22 mm)
 - small LV cavity size
 - associated hypertension
 - ventricular morphology greatly distorted with reduced outflow tract
 - sigmoid septum and “grandma SAM”

Restrictive Cardiomyopathy

Restrictive Cardiomyopathies

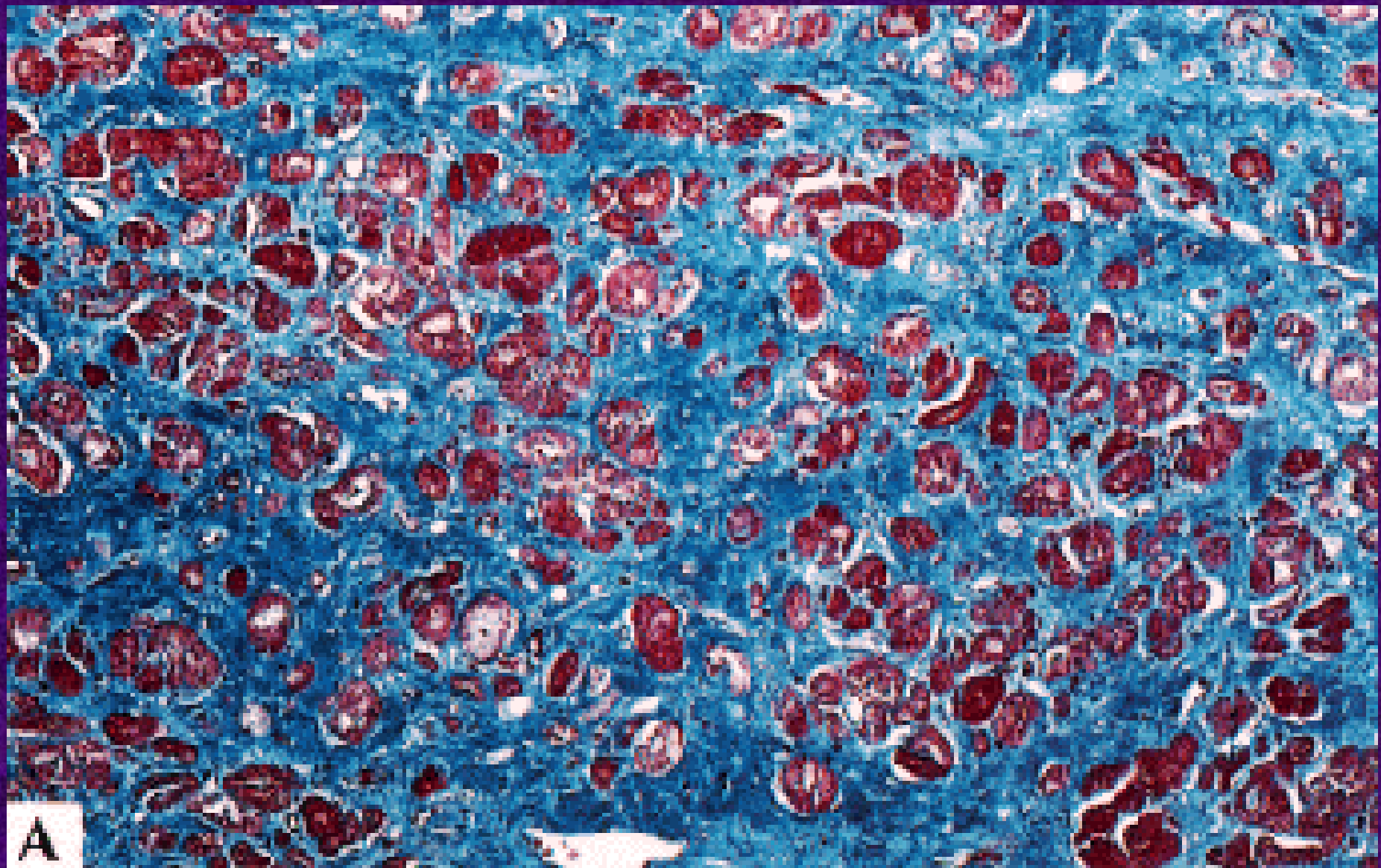
- Hallmark: abnormal diastolic function
- rigid ventricular wall with impaired ventricular filling
- bear some functional resemblance to constrictive pericarditis
- importance lies in its differentiation from operable constrictive pericarditis

Exclusion “Guidelines”

- LV end-diastolic dimensions ≥ 7 cm
- Myocardial wall thickness ≥ 1.7 cm
- LV end-diastolic volume ≥ 150 mL/m²
- LV ejection fraction $< 20\%$

Classification

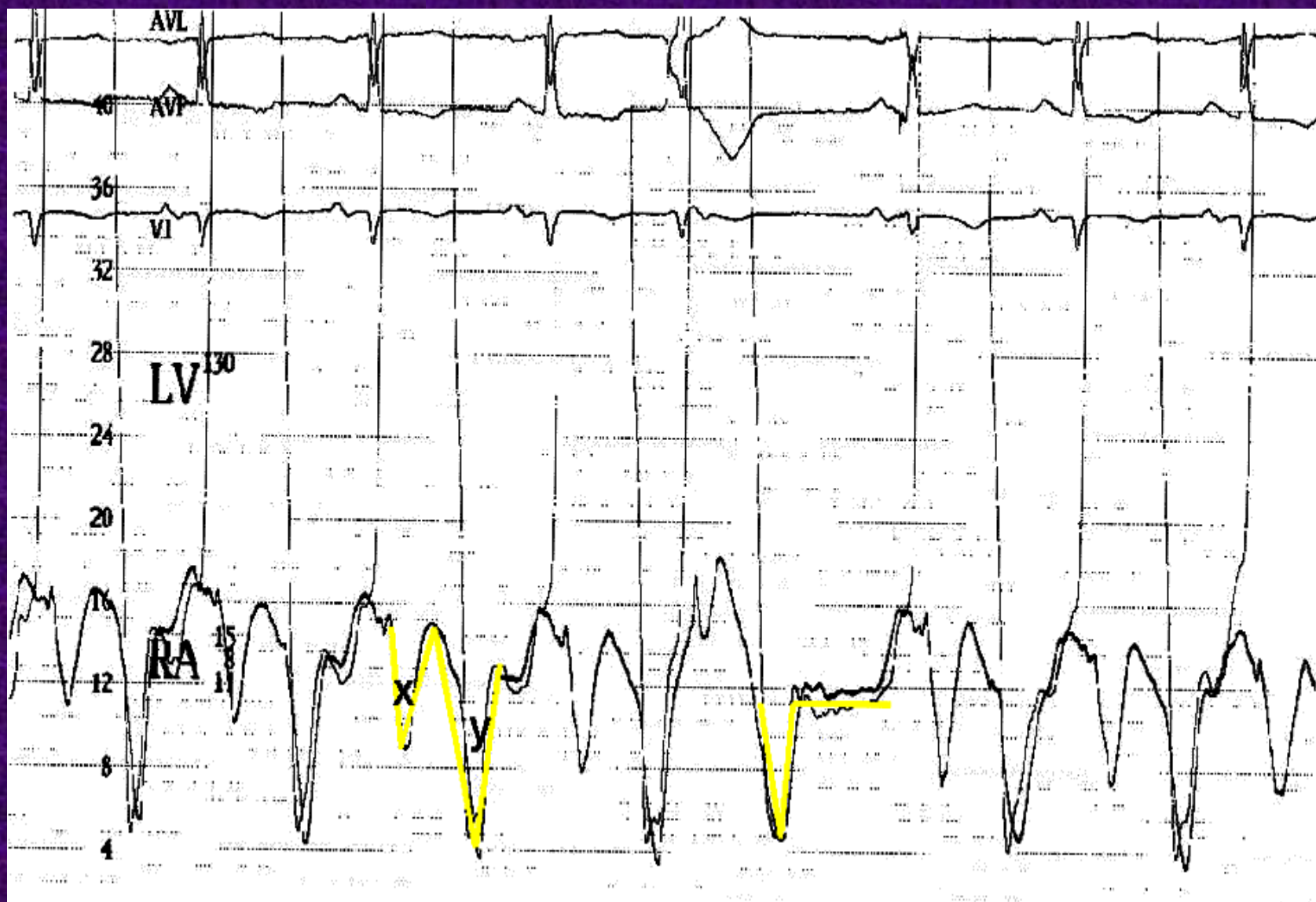
- **Idiopathic**
- **Myocardial**
 - 1. Noninfiltrative**
 - Idiopathic
 - Scleroderma
 - 2. Infiltrative**
 - Amyloid
 - Sarcoid
 - Gaucher disease
 - Hurler disease
 - 3. Storage Disease**
 - Hemochromatosis
 - Fabry disease
 - Glycogen storage
- **Endomyocardial**
 - endomyocardial fibrosis
 - Hyperesinophilic synd
 - Carcinoid
 - metastatic malignancies
 - radiation, anthracycline



Idiopathic restrictive cardiomyopathy. Cross-sectional view of myocytes surrounded by fibrous tissue (Mallory-azan stain). Severe interstitial fibrosis is present with fibrous tissue surrounding each myocyte.

Clinical Manifestations

- Symptoms of right and left heart failure
- Jugular Venous Pulse
 - prominent x and y descents
- Echo-Doppler
 - abnormal mitral inflow pattern
 - prominent E wave (rapid diastolic filling)
 - reduced deceleration time (↑ LA pressure)



Restriction vs Constriction

History provide can important clues

- **Constrictive pericarditis**
 - history of TB, trauma, pericarditis, collagen vascular disorders
- **Restrictive cardiomyopathy**
 - amyloidosis, hemochromatosis
- **Mixed**
 - mediastinal radiation, cardiac surgery

Treatment

- **No satisfactory medical therapy**
- **Drug therapy must be used with caution**
 - **diuretics for extremely high filling pressures**
 - **vasodilators may decrease filling pressure**
 - **? Calcium channel blockers to improve diastolic compliance**
 - **digitalis and other inotropic agents are not indicated**

Myocarditis

Myocarditis

- **Definition: Myocarditis is an inflammatory disease of cardiac muscle**
- **It can be acute, subacute, or chronic, and there may be either focal or diffuse involvement of the myocardium**

Etiology

- **Myocarditis may be caused by infectious organisms, such as viruses, bacteria, fungi, protozoa, or helminths, or by a toxin, such as cocaine.**
- **Myocarditis can also be associated with a systemic illness, including granulomatous, collagen-vascular, and autoimmune diseases.**

Important Causes of Myocarditis

- **Infection**
 - Viral
 - Bacterial, rickettsial, spirochetal
 - Protozoal, Metazoal
 - Fungal
- **Toxic**
 - anthracyclines, catecholamines, Interleukin-2, α_2 -interferon
 - cocaine
- **Rheumatic myocarditis**
- **Myocarditis in mixed to connective tissue disease**
- **Hypersensitivity (Allergic myocarditidis)**

Viral Infection

- Coxsackie (A, B)
- Echo
- Influenza (A, B)
- Polio
- Herpes simplex
- Varicella-zoster
- Epstein-Barr
- Cytomegalovirus
- Mumps
- Rubella
- Rubeola
- Vaccinia
- Coronavirus
- Rabies
- Hepatitis B
- Arbovirus
- Junin virus
- Human immunodeficiency

Incidence

- The true incidence of myocarditis is unknown because the majority of cases are asymptomatic
- Involvement of the myocardium has been reported in one to five percent of patients with acute viral infections
- Autopsy studies have revealed varying estimates of the incidence of myocarditis. A five percent prevalence of active myocarditis was reported in a high-risk group of 186 sudden, unexpected medical deaths in children

Risk factors

- **Certain groups appear to be at increased risk of virus-induced myocarditis, and the course may be hyperacute**
 - **Young males**
 - **pregnant women**
 - **children (particularly neonates)**
 - **immunocompromised patients**

Pathogenesis

- Both direct viral-induced myocyte damage and post-viral immune inflammatory reactions contribute to myocyte damage and necrosis
- Inflammatory lesions and the necrotic process may persist for months, although the viruses only replicate in the heart for at most two or three weeks after infection
- Evidence from experimental models has incriminated cytokines such as interleukin-1 and TNF, oxygen free radicals and microvascular changes as contributory pathogenic factors

Clinical Manifestations

- Most cases of acute myocarditis are clinically silent
- 60% of pts had antecedent flulike symptoms
- Large number identified by heart failure symptoms
- 35% of pts with myocarditis and HF have chest pain
- May mimic an acute MI with ventricular dysfunction, ischemic chest pain, ECG evidence of injury or Q waves

Clinical Manifestations

- May present with syncope, palpitation with AV block or ventricular arrhythmia
- May cause sudden death
 - myocarditis found at autopsy in 20% of Air Force recruits with sudden death*
- May present with systemic or pulmonary thromboembolic disease

- **A variety of cardiac symptoms can be induced by myocarditis**
 - **Chest pain may occur, usually due to concomitant pericarditis**
 - **Excessive fatigue or decreased exercise ability may be the initial sign of myocardial dysfunction**
 - **Since both ventricles are generally involved, patients develop biventricular failure**
 - **Patients present with signs of right ventricular failure such as increased JVP, hepatomegaly, and peripheral edema**
 - **If there is predominant left ventricular involvement, the patient may present with the symptoms of pulmonary congestion: dyspnea, orthopnea, rales, and, in severe cases, acute pulmonary edema**

Physical examination

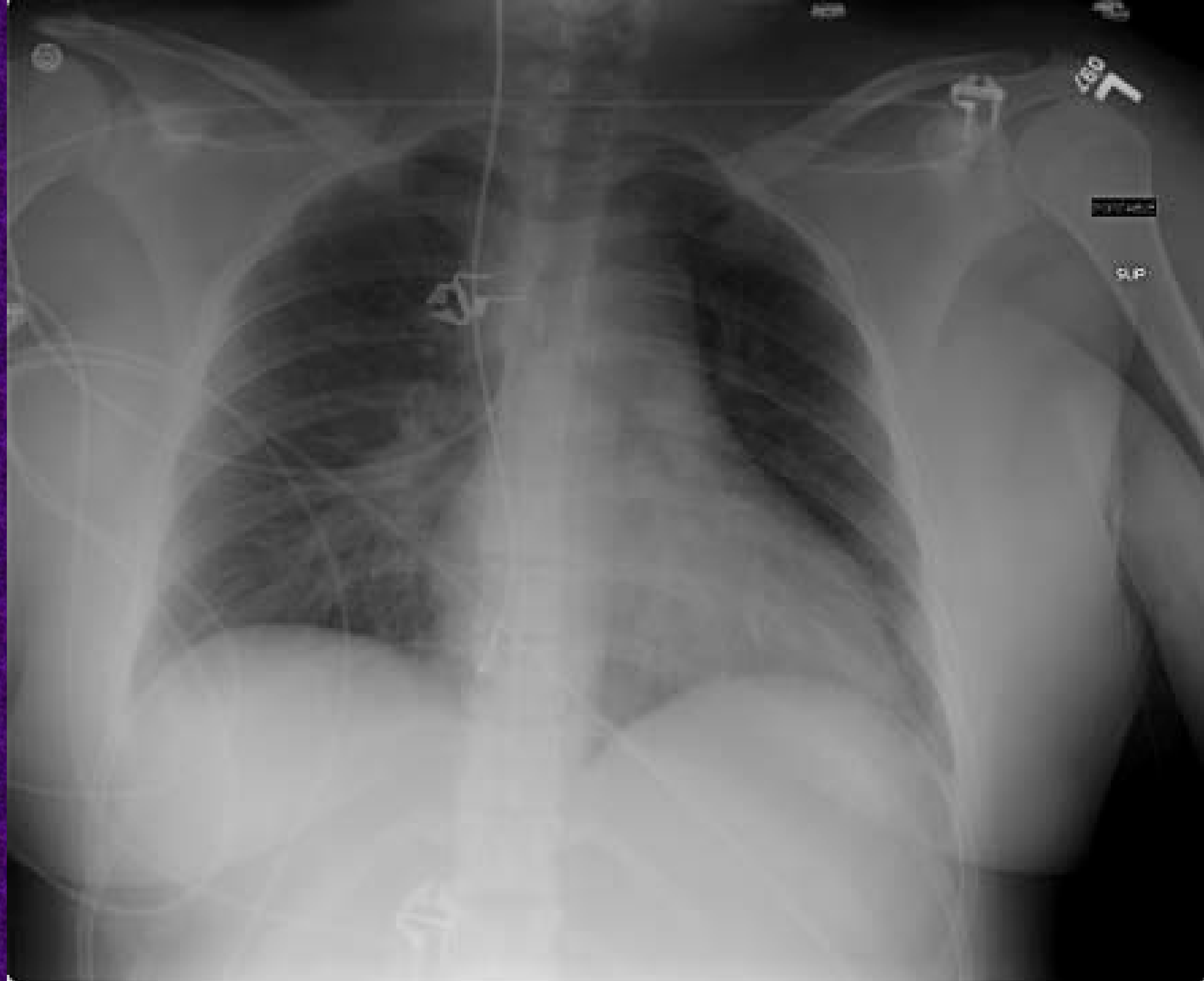
- In addition to the signs of fluid overload, the physical examination often reveals direct evidence of cardiac dysfunction in symptomatic patients
- S3 and S4 gallops are important signs of impaired ventricular function
- If the right or left ventricular dilatation is severe, auscultation may reveal murmurs of functional mitral or tricuspid insufficiency
- A pericardial friction rub and effusion may become evident in patients with myopericarditis

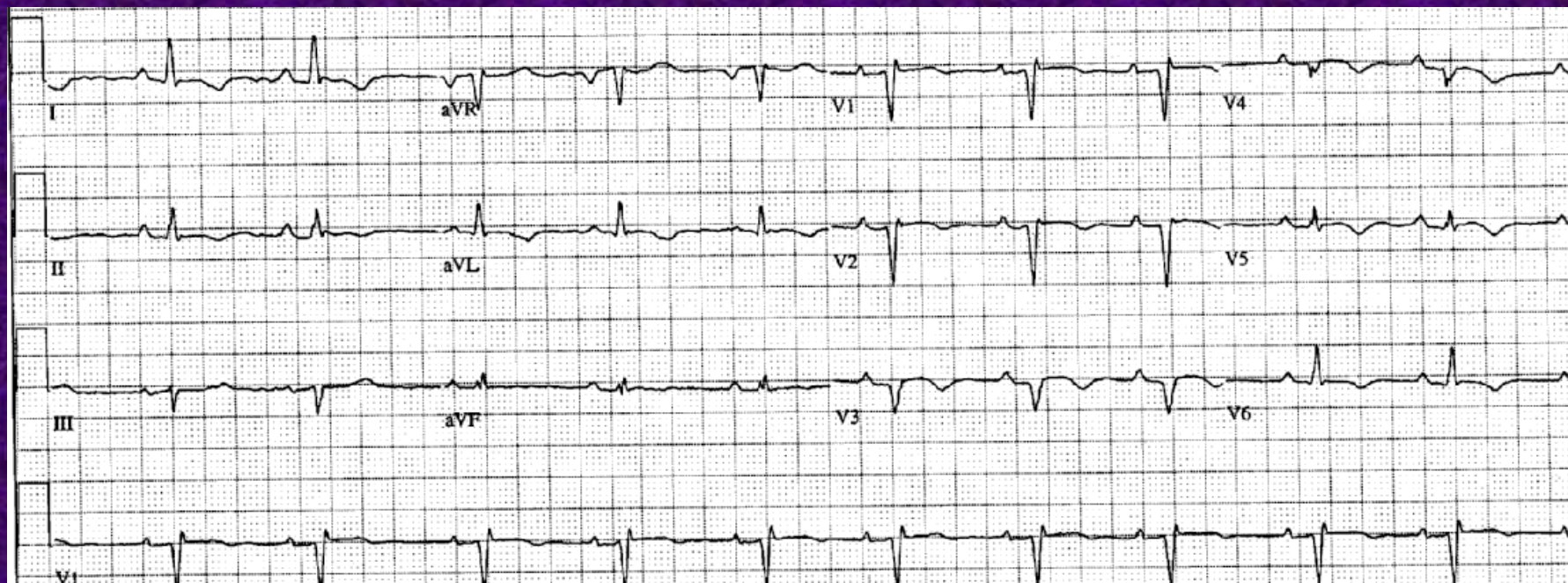
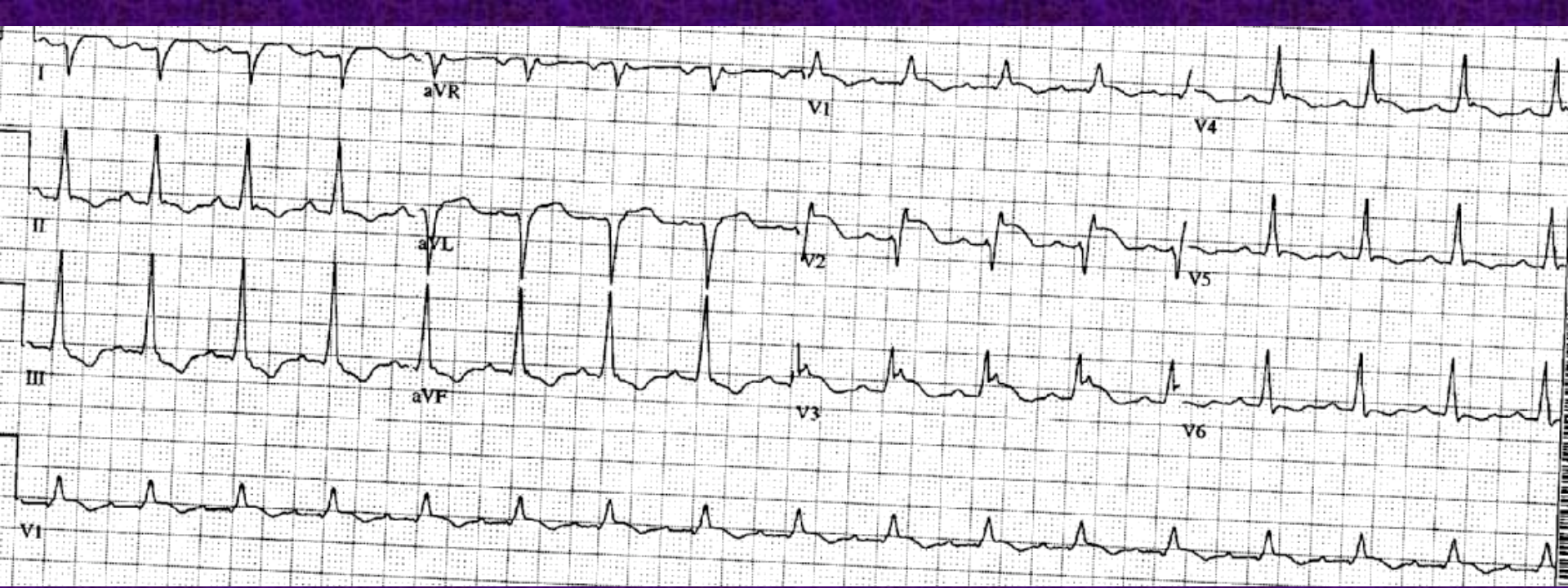
Blood studies

- Sedimentation rate elevation 60%
- White count elevation 25%
- CK-MB elevation 12%
- a 4 fold rise in IgG titer over a 4-6 wk period is required to document an acute viral infection
- Heart specific antibodies are nonspecific for myocarditis; also found in dilated cardiomyopathy

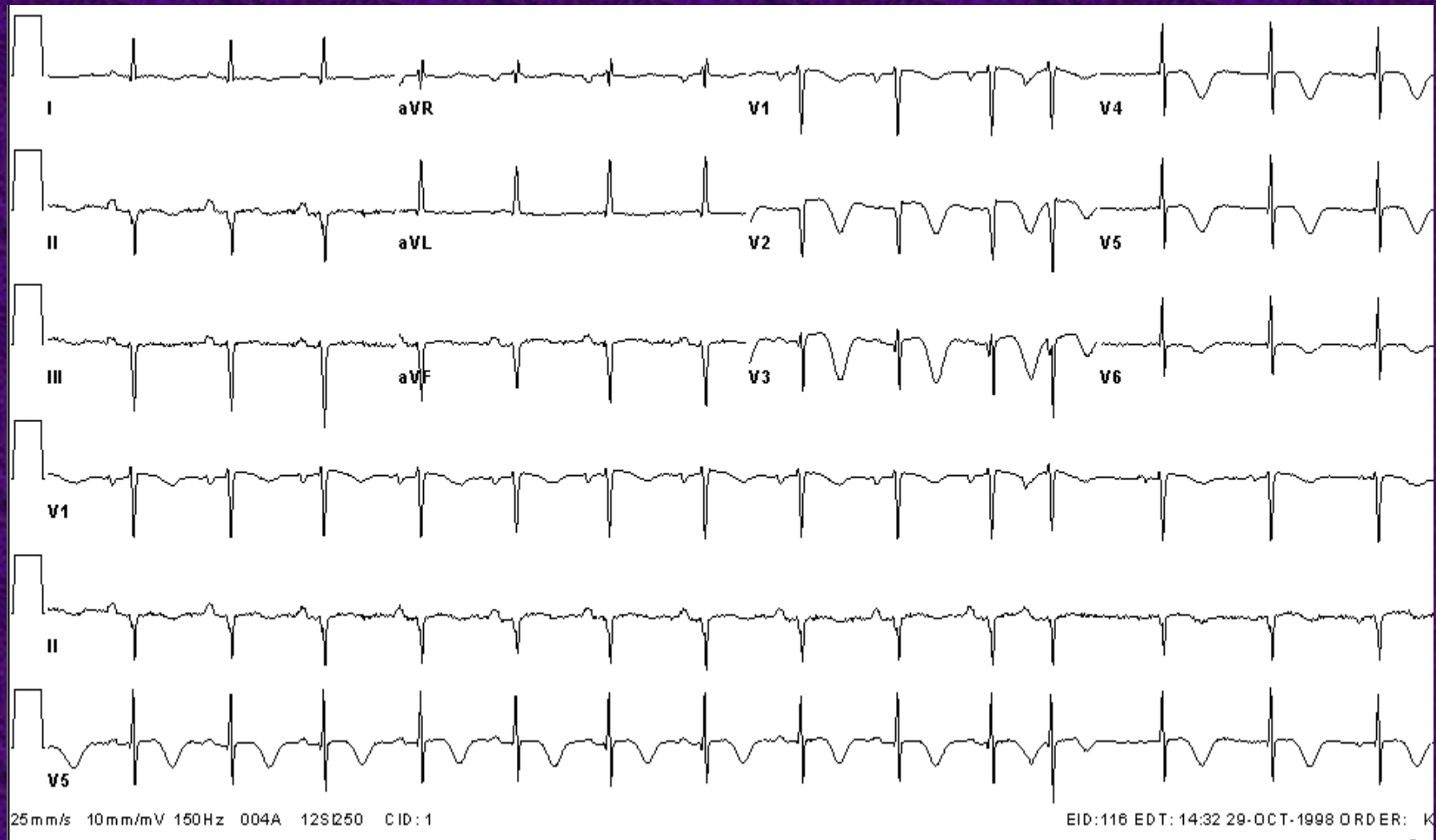
Electrocardiogram

- sinus tachycardia is most common
- diffuse ST-T wave changes
- myocardial infarction pattern
- conduction delay and LBBB in 20%
- complete heart block causing Stokes-Adams attacks (particularly in Japan), but rarely require a permanent pacer
- supraventricular and ventricular arrhythmias



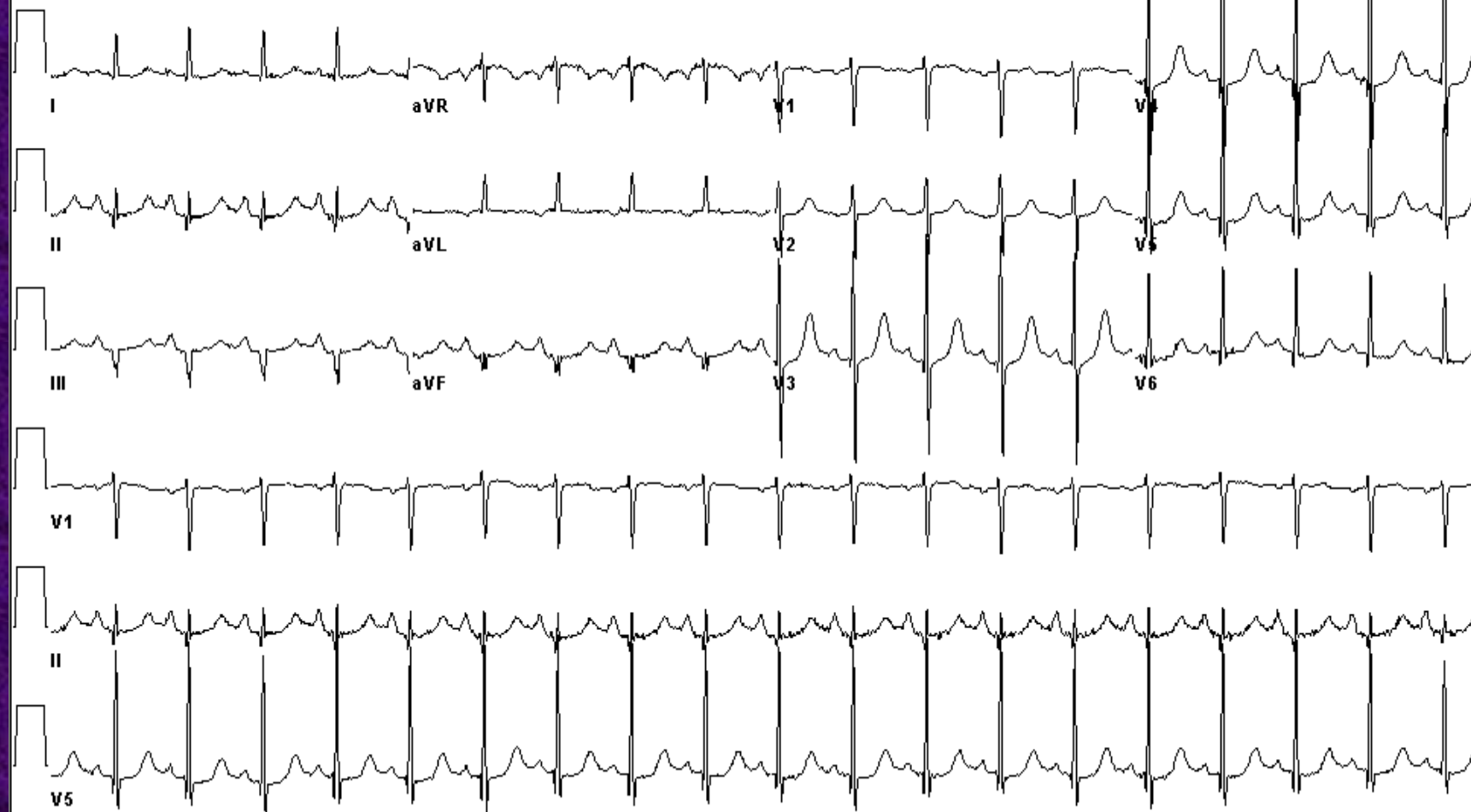


Myocarditis



Referred by:

Confirmed by: NOT READ BY

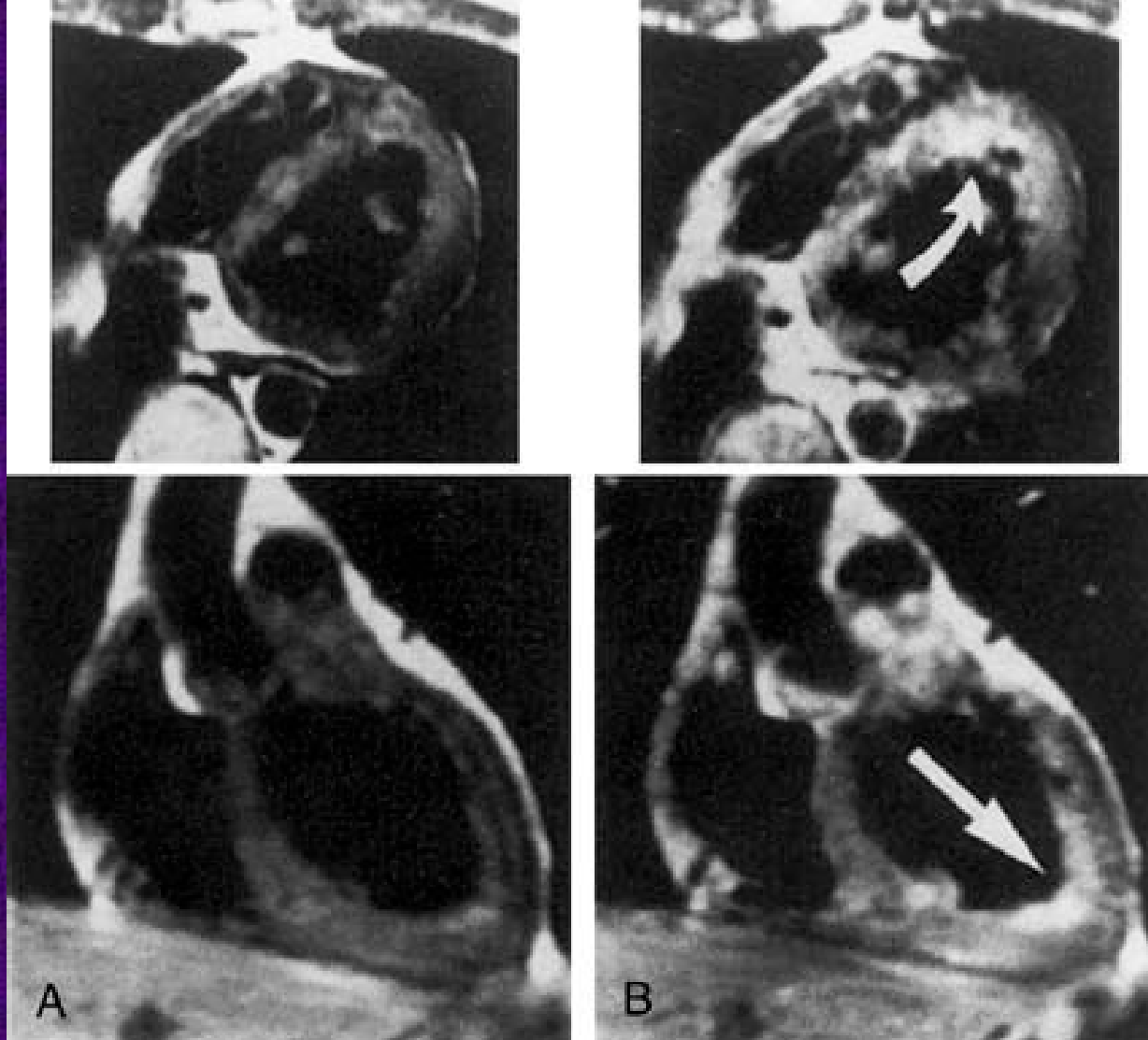


25mm/s 10mm/mV 150Hz 004A 12S1250 CID:1

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Echocardiography

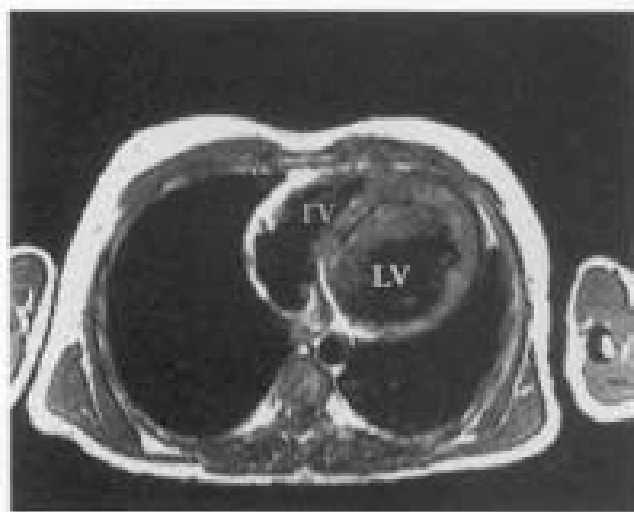
- **Useful tool in managing patients with acute myocarditis**
 - **LV systolic dysfunction is common with segmental wall motion abnormalities**
 - **LV size is typically normal or mildly dilated**
 - **wall thickness may be increased**
 - **ventricular thrombi detected in 15%**



A. Precontrast T1-weighted transaxial (**upper**) and coronal (**lower**) magnetic resonance images through the left ventricle in a patient with **myocarditis**.

B. Postcontrast magnetic resonance images at the same levels after contrast injection. Note enhancement of the myocardial signal in the septum and apical region (arrows)

Matsouka H, Hamada M, Honda T, et al: Evaluation of acute myocarditis and pericarditis by Gd-DTPA enhanced magnetic resonance imaging. Eur Heart J 15:283, 1994



A



B

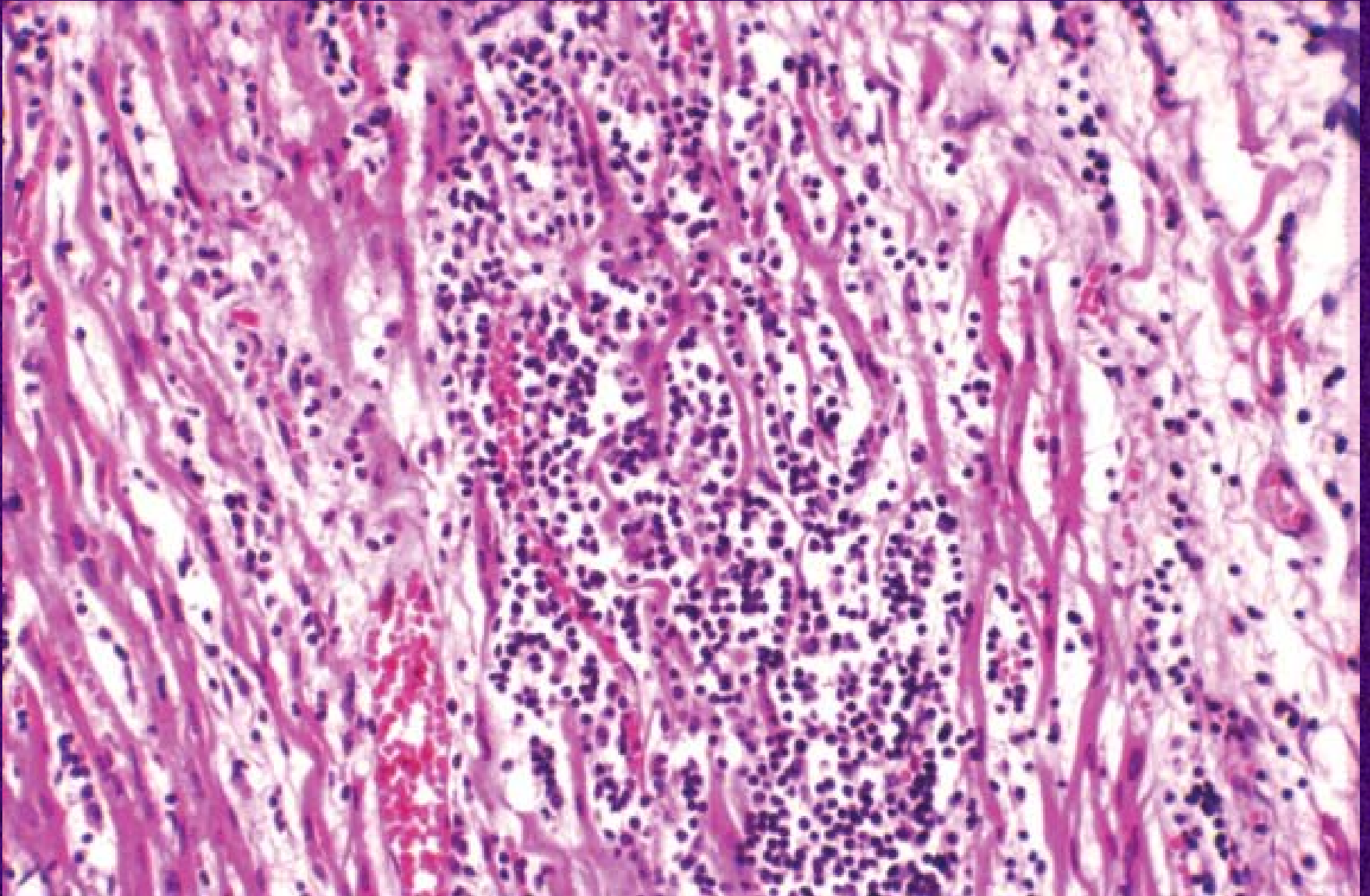


C

Endomyocardial Biopsy

- RV bioptome permit repetitive sampling
- biopsy should be applied early after onset of symptoms to maximize yield - resolution may be seen in four days on serial biopsies
- Dallas criteria for active myocarditis
 - “an inflammatory infiltrate of the myocardium with necrosis and/or degeneration of adjacent myocytes not typical of the ischemic changes associated with coronary artery disease”

Endomyocardial Biopsy



Lymphocytic infiltrates in myocardium

- **Viral titers**
 - Acute and convalescent antibody titers may indicate an active or recent viral infection; they do not necessarily indicate the etiology of the cardiac abnormalities
- **Electrocardiogram**
 - May be normal or abnormal in myocarditis
 - However, the abnormalities are nonspecific unless there is pericardial involvement
 - The changes that may be seen include nonspecific ST abnormalities, atrial or ventricular ectopic beats, high grade ventricular arrhythmias, atrial tachycardia or atrial fibrillation
- **Chest radiograph**
 - ranges from normal to cardiomegaly with or without pulmonary congestion

- **Echocardiography**
 - Most valuable means of detecting decreased ventricular function in myocarditis, even when subclinical
 - The dysfunction is generally global
 - Mild impairments in myocardial contractility may be evident only when the study is performed at rest and during exercise
 - The echocardiogram can also detect coexistent pericardial involvement
- **Magnetic resonance imaging**
 - Contrast-enhanced MRI, using gadopentate dimeglumine which accumulates in inflammatory lesions, can detect the degree and extent of inflammation
 - The extent of relative myocardial enhancement correlates with clinical status and left ventricular function

Diagnosis

- **Acute myocarditis should be suspected whenever a patient, especially a young male, presents with otherwise unexplained cardiac abnormalities of new onset, such as heart failure, arrhythmias, or conduction disturbances**
- **A history of recent upper respiratory infection or enteritis may also be present**
- **A presumptive diagnosis of cardiomyopathy generally requires that congenital, valvular, ischemic, and pulmonary heart disease be ruled out.**

- **A presumptive diagnosis of myocarditis may be made on the basis of the clinical and laboratory presentations**
- **This presumption may be strengthened if an echocardiogram is characteristic and does not reveal evidence of other forms of heart disease**
- **A number of other tests have been used in selected cases but their general utility is relatively limited:**
 - **Gallium scanning**
 - **Antimyosin scans**
 - **Magnetic resonance imaging**

- **Cardiac catheterization does not yield any specific information but may be valuable in ruling out other cardiac disease, such as congenital, or ischemic heart disease**
- **The definitive diagnosis of myocarditis can be made only by endomyocardial biopsy**
- **A negative biopsy does not rule out focal myocarditis because of sampling error. This problem is minimized by multiple biopsies**
- **Endomyocardial biopsy is of greatest value in myocarditis when performed early in the course of the disease**

- **Histopathologic diagnosis of a specific cause of myocarditis is occasionally possible in patients with toxoplasmosis, Chagas' disease, Lyme carditis, and trichinosis**
- **Electron microscopic examination is only rarely contributory as with the characteristic intranuclear inclusion bodies that may be seen in CMV carditis**

Natural history

- The majority of cases of acute myocarditis have a benign course. In these patients, the inflammatory process is self-limited without clinically overt sequelae
- Some patients, however, develop heart failure, serious arrhythmias, disturbances of conduction, or even circulatory collapse
- The illness may be fatal due to myocardial failure or sudden, unexpected death

Treatment

- majority of patients have a self-limited disease
- management of LV dysfunction similar to other forms of congestive heart failure
- ? exercise may intensify inflammatory response
- consider anticoagulation to prevent thromboemboli
- consider temporary pacer for complete AV block
- ? prednisone and azathioprine - no apparent benefit seen in the Myocarditis Treatment Trial

Specific therapy

- There are a number causes (primarily infectious) of myocarditis for which there is specific therapy, such as Mycoplasma or Lyme disease
- Viral infection is the most common cause of myocarditis, with Coxsackievirus B being most frequently implicated
- Antiviral therapy with ribavirin or alpha-interferon has been shown to reduce the severity of myocardial lesions as well as mortality in experimental murine myocarditis due to Coxsackievirus B3

- **However, this beneficial effect is seen only if therapy is started prior to inoculation or soon thereafter**
- **The applicability of these findings to humans is therefore uncertain**
- **Nevertheless, antiviral therapy may be considered in acute, fulminant myocarditis, in institutional outbreaks (eg, in neonates), and in laboratory-acquired cases**

Specific therapy

- A number of therapeutic trials in humans, mostly uncontrolled, have suggested clinical benefit from immunosuppressive therapy with corticosteroids, azathioprine, or cyclosporine
- However, both corticosteroids and cyclosporine have been shown to exacerbate murine myocarditis

Nonspecific therapy

- **Avoidance of exercise**
 - 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
- **Electrocardiographic monitoring**
 - Electrocardiographic monitoring can permit early detection of asymptomatic yet potentially life-threatening arrhythmias and/or conduction defects

Nonspecific therapy

- **Antiarrhythmic drugs**
 - Most antiarrhythmic drugs have negative inotropic activity and may therefore aggravate heart failure. They should therefore be used only when the expected benefit exceeds the risk
 - Supraventricular arrhythmias, may induce or aggravate heart failure; these arrhythmias should be converted
 - High-grade ventricular ectopy should be treated cautiously with antiarrhythmic drugs
 - Complete heart block is an indication for transvenous pacing. This conduction abnormality is often transient; as a result, use of a temporary pacemaker should be the first step

Nonspecific therapy

- Congestive heart failure should be treated with a low sodium diet and cautiously with digoxin, diuretics, and ACE inhibitors
- The threshold for digitalis toxicity may be low
- Excessive reduction of preload by diuresis may reduce ventricular filling pressures below the level needed to maintain cardiac output, possibly converting heart failure into cardiogenic shock

Nonspecific therapy

- Anticoagulation is recommend in patients who fulfill the following criteria:
 - Symptomatic heart failure with a LVEF below 20 percent
 - Minimal risk factors for hemorrhage
 - A stable hemodynamic profile without evidence of liver synthetic dysfunction
- The optimal degree of anticoagulation has not been established
- INR between 1.5 and 2.5 is generally recommended

Diphtheritic Myocarditis

Diphtheritic myocarditis develops in over one-quarter of the patients with diphtheria, is one of the most serious complications, and is the most common cause of death due to diphtheria. Cardiac damage is due to the liberation of a toxin that inhibits protein synthesis and leads to a dilated, flabby, hypocontractile heart; the conducting system is frequently involved as well. Myocarditis may present during the acute phase of illness, develop as local disease is resolving, or begin insidiously after several weeks. *Cardiomegaly* and severe *congestive heart failure* typically appear after the first week of illness. Clinical signs include diminished heart sounds, gallop rhythm, systolic murmurs, and (less commonly) acute or insidiously progressive congestive heart failure. Electrocardiographic abnormalities include ST-T-wave changes, varying degrees of heart block, and arrhythmias, including atrial fibrillation, ventricular premature beats, ventricular tachycardia, and ventricular fibrillation. Serum levels of aspartate aminotransferase reflect the intensity of myocardial damage and can be used to monitor its course. Prompt therapy with antitoxin is crucial; antibiotic therapy is also indicated but is of less urgency.

Drugs

A variety of pharmacologic agents may damage the myocardium acutely, producing a pattern of inflammation (myocarditis), or they may lead to chronic damage of the type seen with idiopathic dilated cardiomyopathy.

The anthracycline derivatives, particularly *doxorubicin* (Adriamycin), are powerful antineoplastic agents that, when given in high doses (more than 550 mg/m² for doxorubicin), may produce fatal heart failure. Recent efforts to modify the dose schedule by giving the drug more slowly have further reduced the risk of cardiotoxicity.

High-dose *cyclophosphamide* may produce congestive heart failure acutely or within 2 weeks of administration; a characteristic histopathologic feature is myocardial edema and hemorrhagic necrosis.

Rarely, patients treated with *5-fluorouracil* will develop chest pain and electrocardiographic changes of myocardial ischemia or infarction.

Electrocardiographic changes and arrhythmias may result from treatment with tricyclic antidepressants, the phenothiazines, emetine, lithium, and various aerosol propellants.

Cocaine abuse is associated with a variety of life-threatening cardiac complications, including sudden death, myocarditis, dilated cardiomyopathy, and acute myocardial infarction (resulting from coronary spasm and/or thrombosis with or without underlying coronary artery stenosis). Nitrates and calcium antagonists have been used as well to treat a variety of cocaine-induced cardiotoxicities; beta-adrenergic blockers should be avoided.

Prevention

- **As a result of the widespread use of vaccination in developed countries, myocarditis secondary to measles, rubella, mumps, poliomyelitis, and influenza is now rare**
- **Similarly, the elimination of trichinosis by meat inspection has all but eliminated this infection**
- **It is possible that vaccines against other cardiotropic viruses may prevent viral myocarditis**