

# CARDIOMYOPATHY

**By:**

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**Physician/ Cardiologist**

# Cardiomyopathies

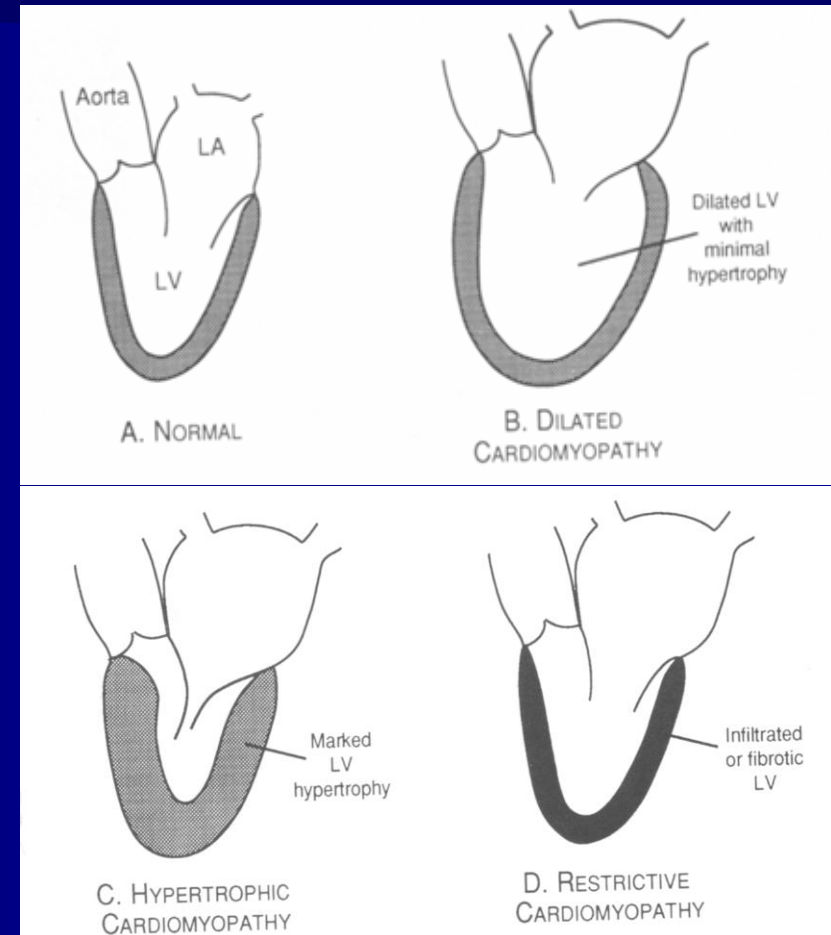
- Definition: diseases of heart muscle
- 1980 WHO: unknown causes
  - Not clinically relevant
- 1995 WHO: “diseases of the myocardium associated with cardiac dysfunction”
  - pathophysiology
  - each with multiple etiologies

# Cardiomyopathy

## WHO Classification

anatomy & physiology of the LV

1. Dilated
  - Enlarged
  - Systolic dysfunction
2. Hypertrophic
  - Thickened
  - Diastolic dysfunction
3. Restrictive
  - Diastolic dysfunction
4. Arrhythmogenic RV dysplasia
  - Fibrofatty replacement
5. Unclassified
  - Fibroelastosis
  - LV noncompaction



# CM: Specific Etiologies

- Ischemic
- Valvular
- Hypertensive
- Inflammatory
- Metabolic
- Inherited
- Toxic reactions
- Peripartum

Ischemic: thinned, scarred tissue



# Dilated Cardiomyopathy

- Dilation *and* impaired contraction of ventricles:
  - Reduced *systolic* function with or without heart failure
  - Characterized by myocyte damage
  - Multiple etiologies with similar resultant pathophysiology
- Majority of cases are **idiopathic**
  - incidence of idiopathic dilated CM 5-8/100,000
  - incidence likely higher due to mild, asymptomatic cases
  - 3X more prevalent among males and African-Americans

# DCM: Etiology

**Ischemic**  
**Valvular**  
**Hypertensive**

**Familial**  
**Idiopathic**  
**Inflammatory**

**Infectious**

**Viral – picornovirus, Cox B, CMV, HIV**

**Rickettsial - Lyme Disease**

**Parasitic - Chagas' Disease, Toxoplasmosis**

**Non-infectious**

**Collagen Vascular Disease (SLE, RA)**

**Peripartum**

**Toxic**

**Alcohol, Anthracyclins (adriamycin), Cocaine**

**Metabolic**

**Endocrine –thyroid dz, pheochromocytoma, DM, acromegaly,**

**Nutritional**

**Thiamine, selenium, carnitine**

**Neuromuscular (Duchene's Muscular Dystrophy--x-linked)**

# DCM: Infectious

## Acute viral myocarditis

- Coxsackie B or echovirus
- Self-limited infection in young people
- Mechanism?:
  - Myocyte cell death and fibrosis
  - Immune mediated injury
  - BUT:
    - No change with immunosuppressive drugs

# DCM: toxic

## Alcoholic cardiomyopathy

- Chronic use
- Reversible with abstinence
- Mechanism?:
  - Myocyte cell death and fibrosis
  - Directly inhibits:
    - mitochondrial oxidative phosphorylation
    - Fatty acid oxidation



# DCM: inherited

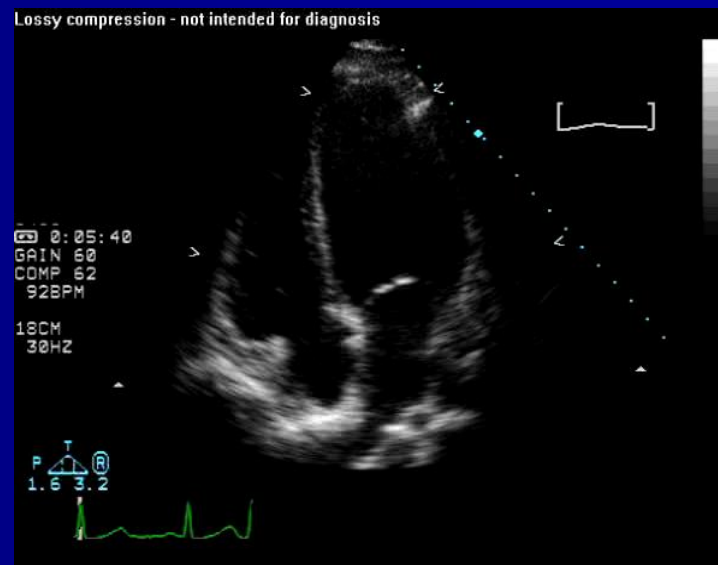
## Familial cardiomyopathy

- 30% of 'idiopathic'
- Inheritance patterns
  - Autosommal dom/rec, x-linked, mitochondrial
- Associated phenotypes:
  - Skeletal muscle abn, neurologic, auditory
- Mechanism:
  - Abnormalities in:
    - Energy production
    - Contractile force generation
  - Specific genes coding for:
    - Myosin, actin, dystophin...

# DCM: Peripartum

## Diagnostic Criteria

- 1 mo pre, 5 mos post
- Echo: LV dysfunction
  - LVEF < 45%
  - LVEDD > 2.7 cm/m<sup>2</sup>
- Epidemiology/Etiology
- 1:4000 women
  - JAMA 2000;283:1183
- Proposed mechanisms:
  - Inflammatory Cytokines:
    - TNF $\alpha$ , IL6, Fas/AP01
    - JACC 2000 35(3):701.



# MECHANISMS IN HEART FAILURE

Ischemic injury

Myocardial disease

Genetics

Neurohormones

Cytokines

Oxidative stress



Altered molecular expression

Ultrastructural changes

Myocyte hypertrophy

Myocyte contractile dysfunction

Apoptosis

Fibroblast proliferation

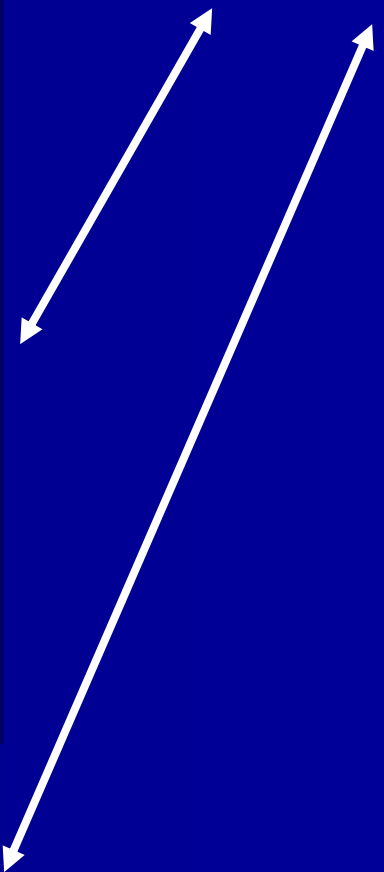
Collagen deposition

Ventricular remodeling

Hemodynamic Derangement

Clinical Heart Failure

Arrhythmia



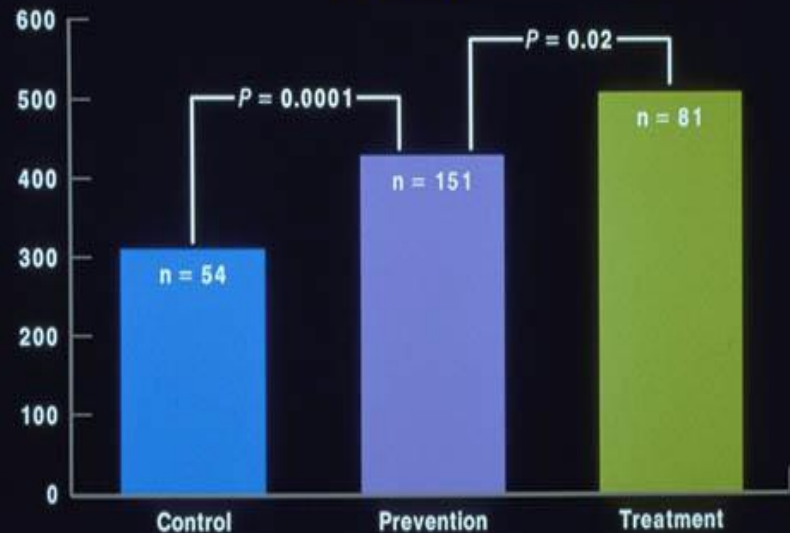
# Pathophysiology

- Initial Compensation for impaired myocyte contractility:
  - Frank-Starling mechanism
  - Neurohumoral activation
  - ↑ intravascular volume
- Eventual decompensation
  - ventricular remodeling
  - myocyte death/apoptosis
  - valvular regurgitation

# Pathophysiology: Neurohumoral

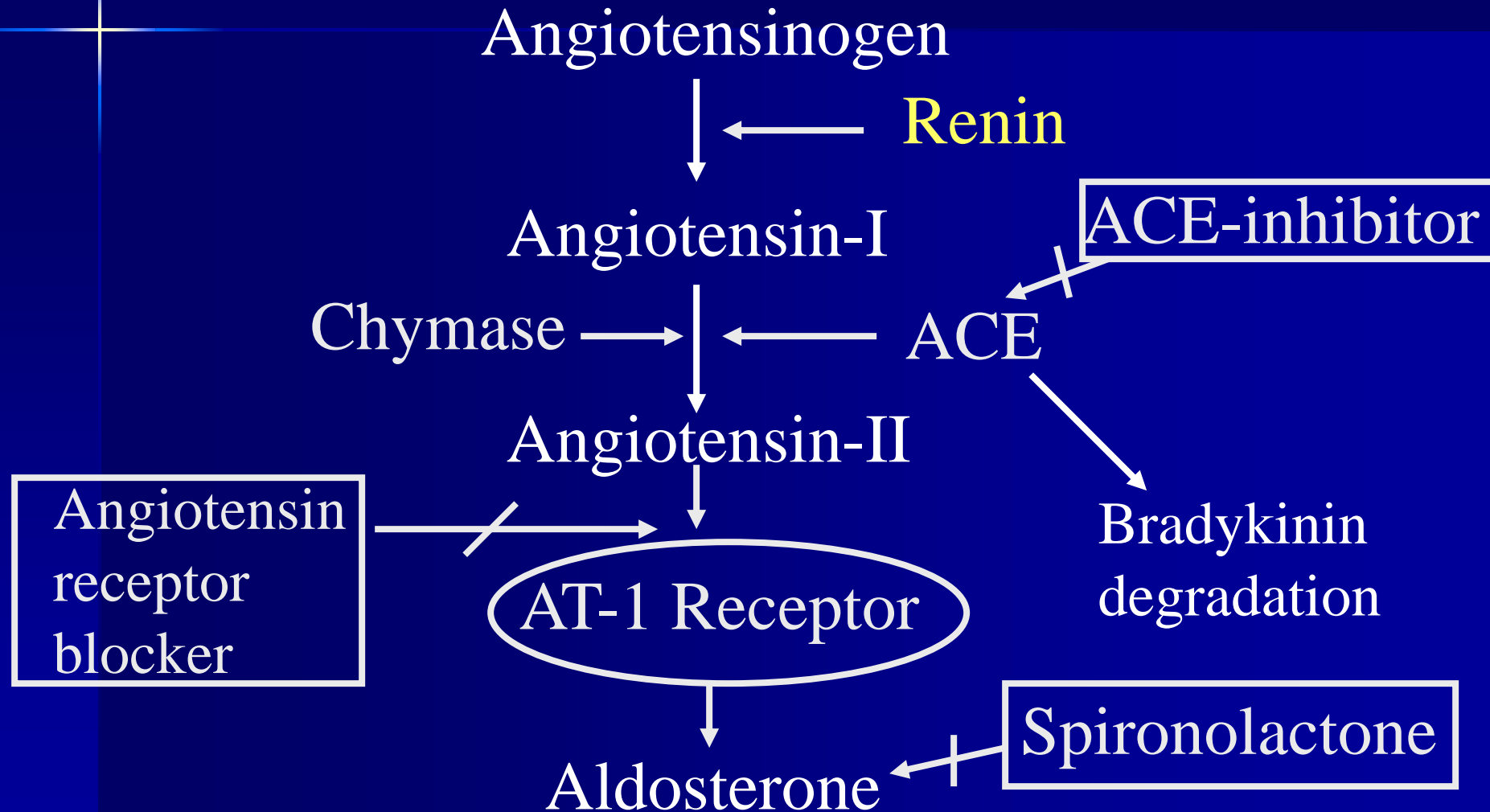
- Adrenergic nervous system
- Renin-angiotensin-aldosterone axis
- Vasopressin
- Natriuretic peptides
- Endothelin

**MEDIAN PLASMA NOREPINEPHRINE LEVELS (pg/mL)**



From: Francis. *Circulation*. 1990;82:1724-1729.

# Renin-Angiotensin-Aldosterone Pathways



# Angiotensin-II Effects

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- Vasoconstriction
- Aldosterone production
- Myocyte hypertrophy
- Fibroblast proliferation
- Collagen deposition
- Apoptosis
- Pro-thrombotic
- Pro-oxidant
- Adrenergic stimulation
- Endothelial dysfunction

# The Kidney in Heart Failure

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- Reduced renal blood flow
- Reduced glomerular filtration rate
- Increased renin production
- Increased tubular sodium reabsorption
- Increased free water retention (vasopressin)



# Clinical Findings

## Biventricular Congestive Heart Failure

### -Low forward Cardiac Output

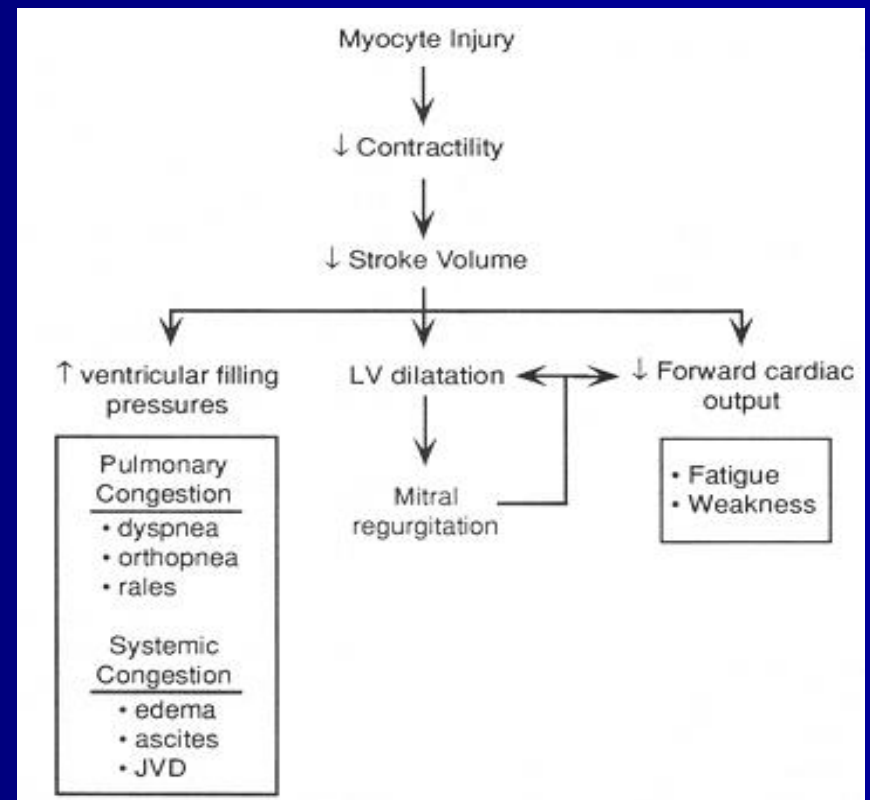
-fatigue, lightheadedness, hypotension

### -Pulmonary Congestion

-Dyspnea,  
-orthopnea, & PND

### -Systemic Congestion

-Edema  
-Ascites  
-Weight gain



# Physical Exam

Decreased C.O.

Tachycardia

↓ BP and pulse pressure

cool extremities (vasoconstriction)

Pulsus Alternans (end-stage)

Pulmonary venous congestion:

rales

pleural effusions

Cardiac:

laterally displaced PMI

S3 (acutely)

mitral regurgitation murmur

Systemic congestion

↑ JVD

hepatosplenomegaly

ascites

peripheral edema

# Diagnostic Studies

**CXR** -enlarged cardiac silhouette,  
vascular redistribution interstitial edema,  
pleural effusions

**EKG** –normal  
tachycardia, atrial and ventricular  
enlargement, LBBB, RBBB, Q-waves

Blood Tests

(ANA,RF, Fe<sup>2+</sup>, TFT's,ferritin,)

**Echocardiography**

LV size, wall thickness function  
valve dz, pressures

**Cardiac Catheterization**

hemodynamics

LVEF

angiography

**Endomyocardial Biopsy**

# Criteria for NYHA Functional Classification

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**Class 1: No limitation of physical activity.**

Ordinary physical activity w/o fatigue, palpitation, or dyspnea.

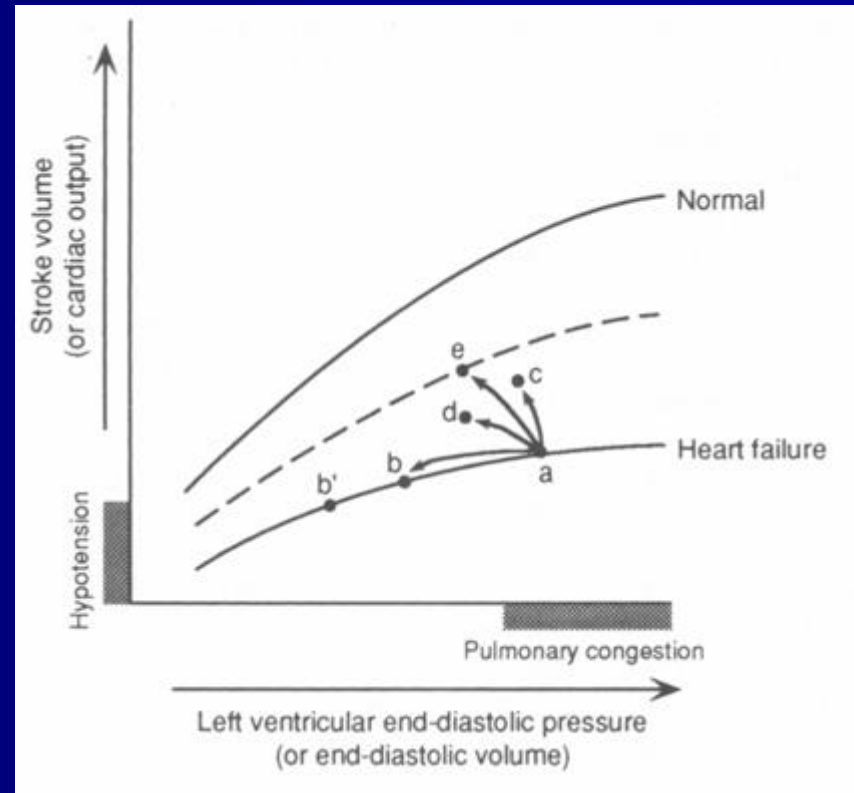
**Class 2: Slight limitation of physical activity. Comfortable at rest, but symptoms w/ ordinary physical activity**

**Class 3: Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes fatigue, palpitation, or dyspnea.**

**Class 4: Unable to carry out any physical activity without discomfort. Symptoms include cardiac insufficiency at rest. If any physical activity is undertaken, discomfort is increased.**

# Aim of Treatment

- Preload reduction
  - Diuretics
  - venodilators
- Vasodilators
  - ACEI
- Inotropes
  - Acutely
  - Chronically
    - mortality



# Vasodilator Agents in Heart Failure

<u>Drug</u>	<u>Mechanism</u>	<u>Action</u>	<u>Use</u>
Nitroglycerin and long-acting nitrates*	Direct via nitric oxide	Veno / arteriolar	Hemodynamic; anti-ischemic; long term
Nitroprusside	Direct via nitric oxide	Arteriolar > venodilation	Hemodynamic
Hydralazine*	Direct	Arteriolar	?long term*
ACE inhibitors#	Reduced A-II Incr. bradykinin	Veno / arteriolar	Long-term

\*Hydralazine and a long-nitrate shown to reduce mortality long-term

# Other actions (aside from vasodilation) likely to be important

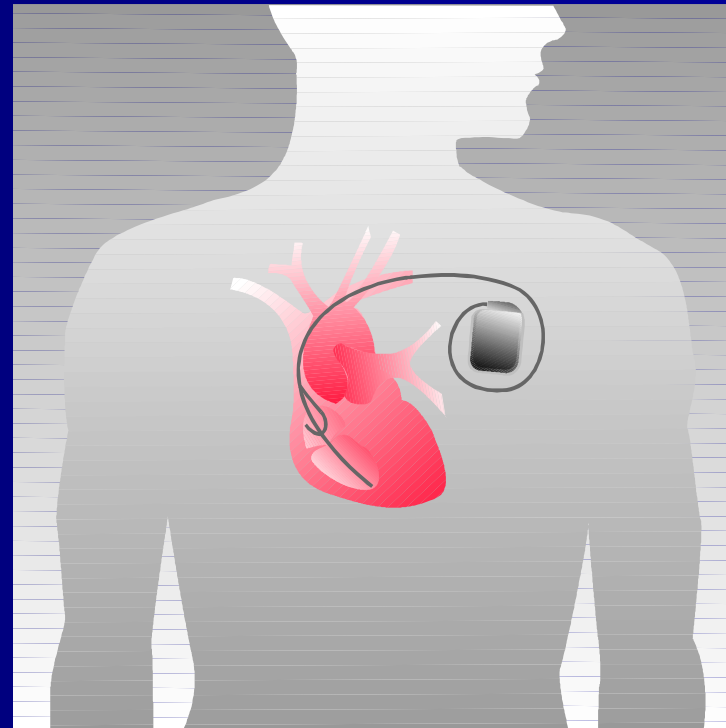
# CRT: Cardiac Resynchronization Therapy

## 1. Improved hemodynamics

- Increased CO
- Reduced LV filling pressures
- Reduced sympathetic activity
- Increased systolic function w/o MVO<sub>2</sub>

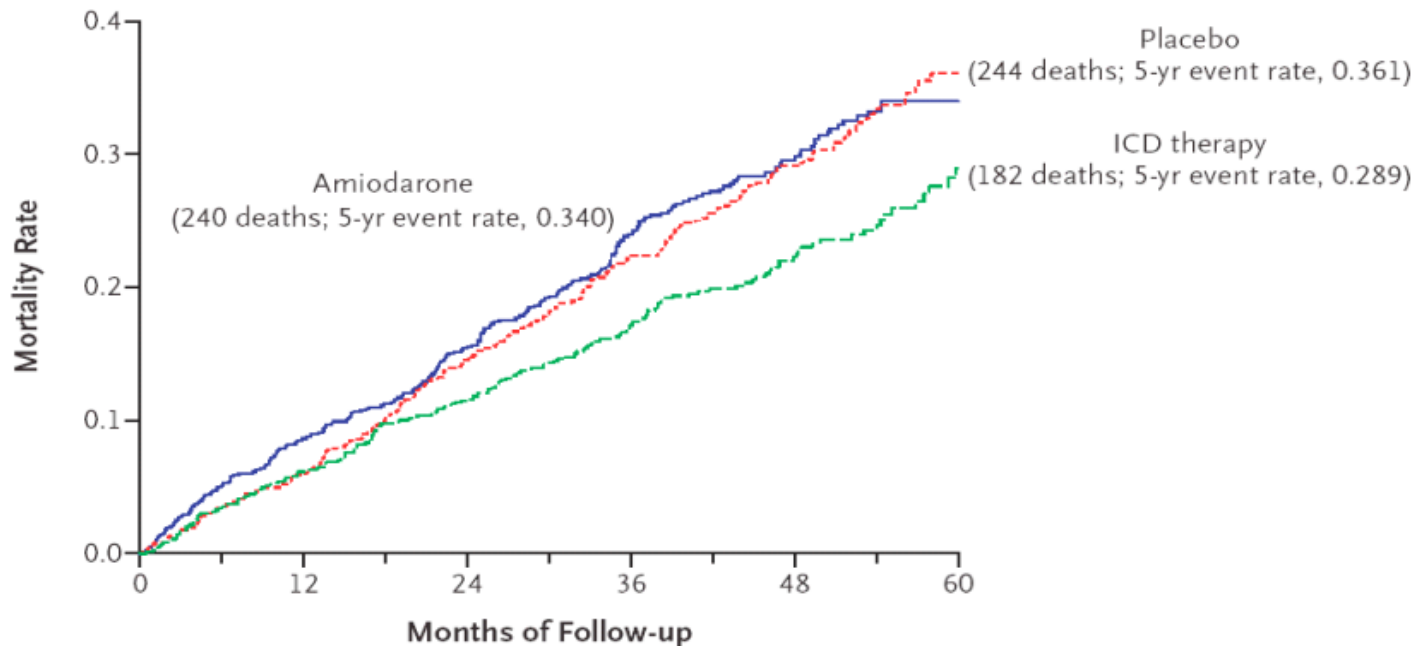
## 2. Reverse LV remodeling/architecture

- Decreased LVES/ED volumes
- Increased LVEF
  - Circ '02, JACC '02, JACC '02, NEJM'02



# Anti-arrhythmic drugs, ICD placebo and Death

	Hazard Ratio (97.5% CI)	P Value
Amiodarone vs. placebo	1.06 (0.86–1.30)	0.53
ICD therapy vs. placebo	0.77 (0.62–0.96)	0.007



## No. at Risk

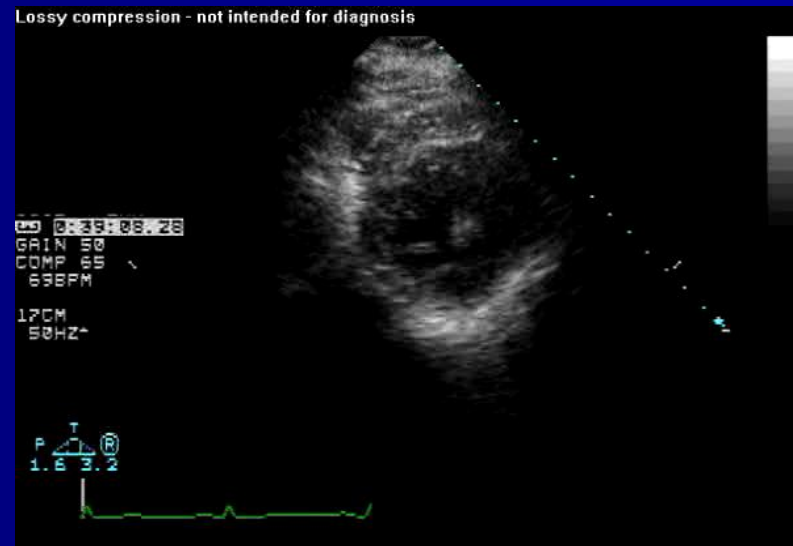
Amiodarone	845	772	715	484	280	97
Placebo	847	797	724	505	304	89
ICD therapy	829	778	733	501	304	103

Bardy G et al.  
NEJM 2005; 352:3



# Diastolic Dysfunction

- 40-50% of pts w/ CHF have nml LVEF
  - Vasan JACC '99
  - Grossman Circ '00
- Prevalence:
  - increases with age
  - higher in women
- Etiology: HTN & LVH
- Diagnosis:
  - MV& PV Doppler
  - TDI, Color m-mode



# Hypertrophic Cardiomyopathy

Left ventricular hypertrophy not due to pressure overload

Hypertrophy is variable in both severity and location:

- asymmetric septal hypertrophy
- symmetric (non-obstructive)
- apical hypertrophy

Vigorous systolic function, but impaired diastolic function  
impaired relaxation of ventricles  
elevated diastolic pressures

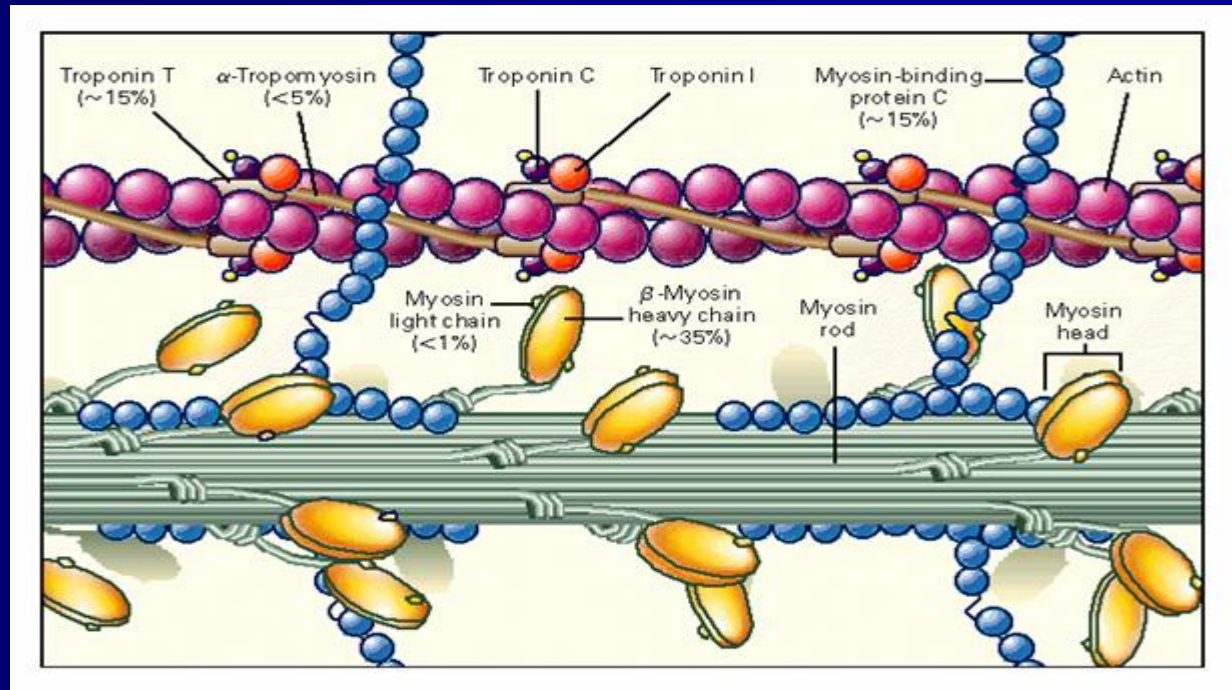
prevalence as high as 1/500 in general population  
mortality in selected populations 4-6% (institutional)  
probably more favorable ( $\leq 1\%$ )

# Etiology

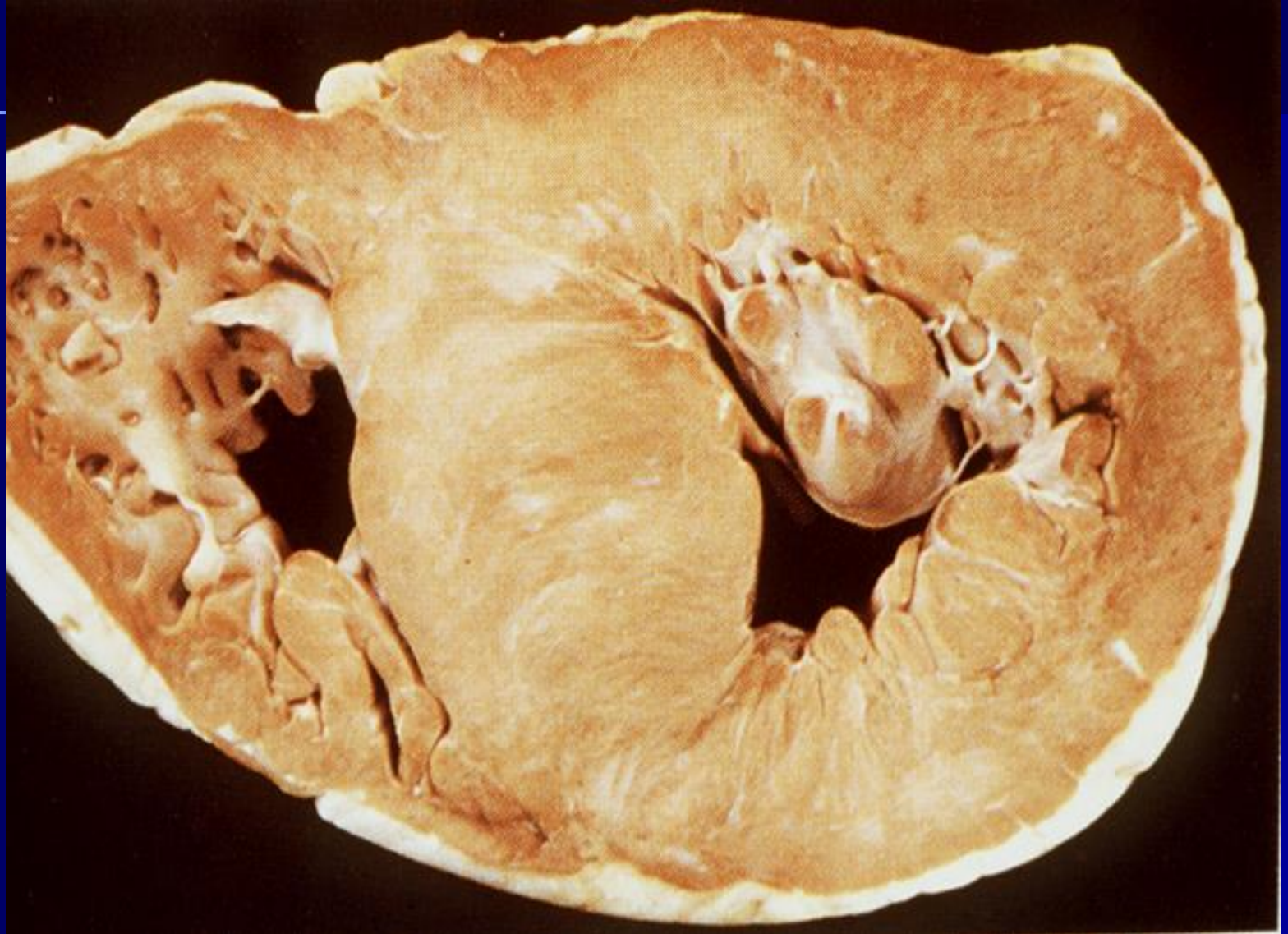
Familial in ~ 55% of cases with autosomal dominant transmission  
Mutations in one of 4 genes encoding proteins of cardiac sarcomere  
account for majority of familial cases

$\beta$ -MHC  
cardiac troponin T  
myosin binding protein C  
 $\alpha$ -tropomyosin

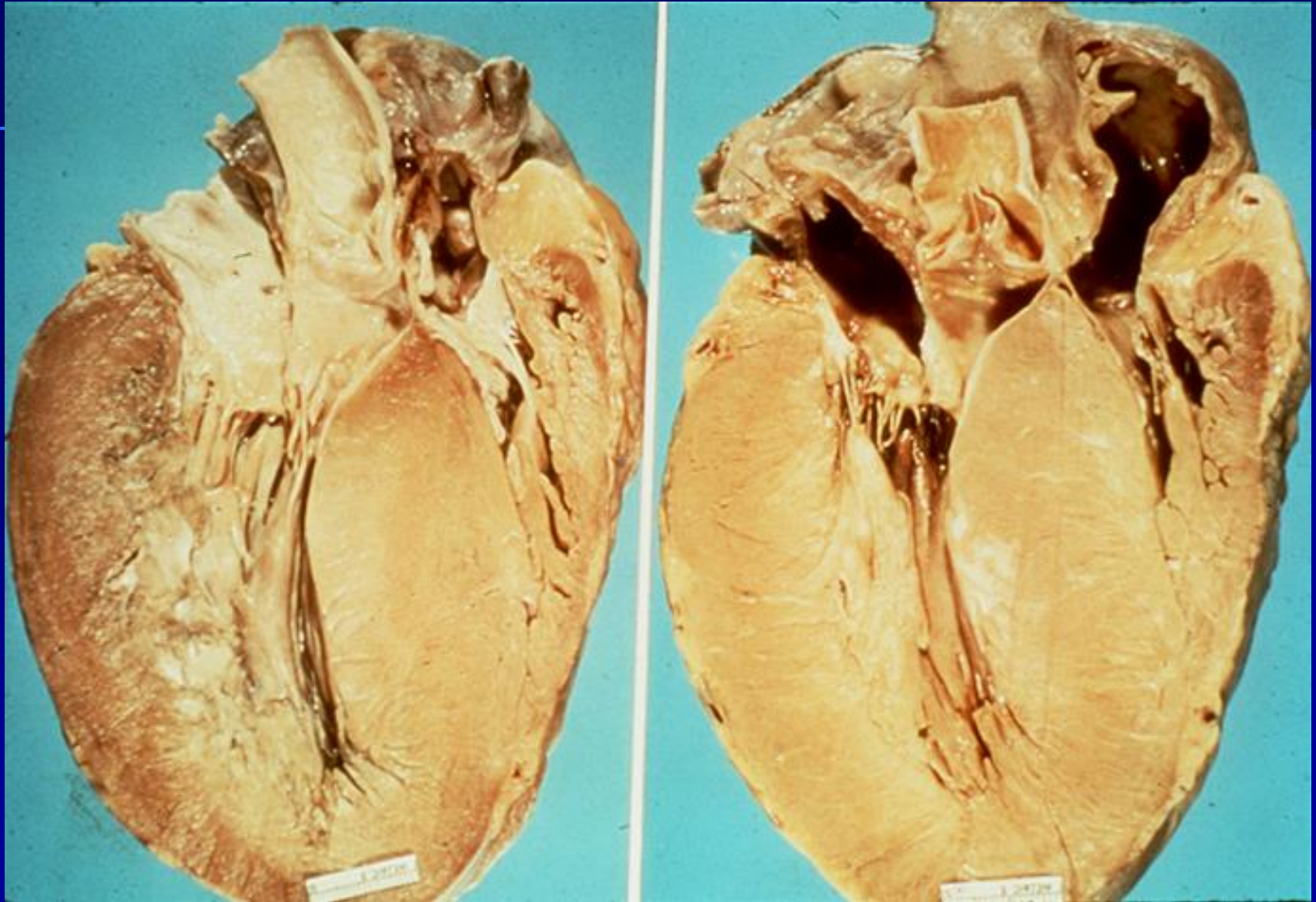
Remainder are  
spontaneous  
mutations.



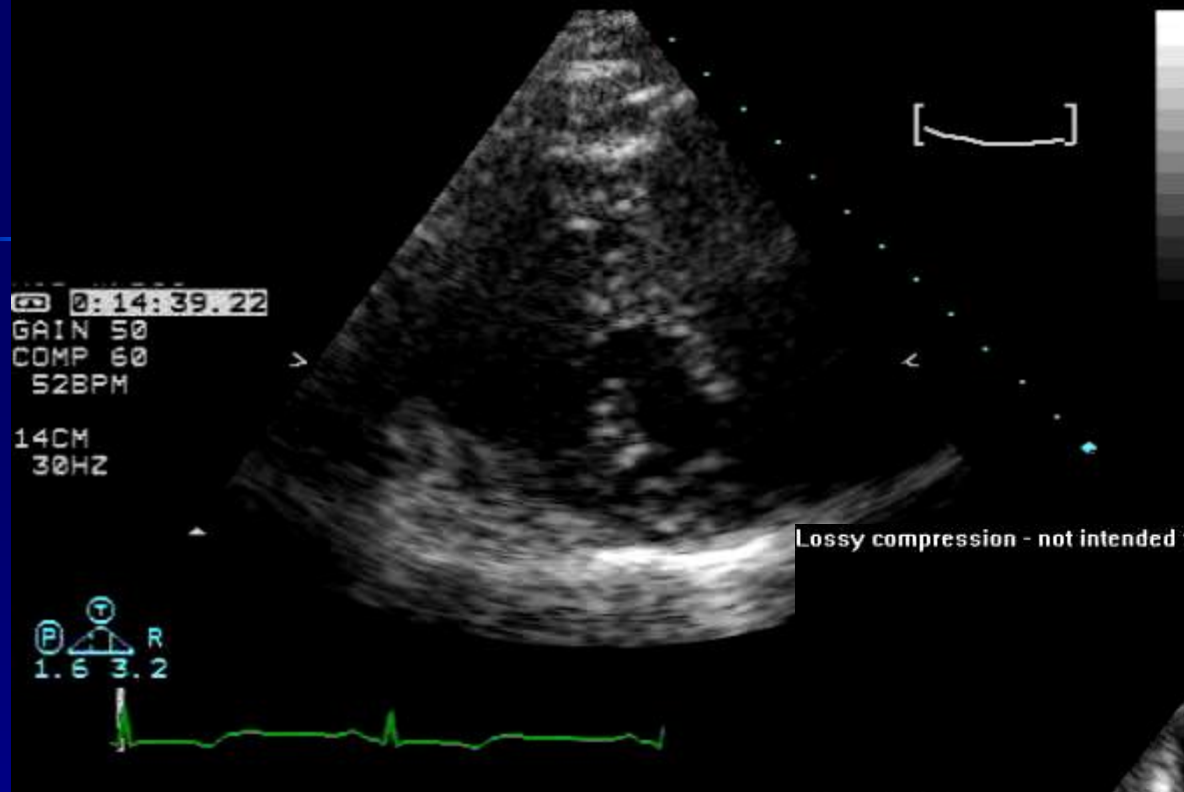
# Hypertrophic Cardiomyopathy



# Hypertrophic Cardiomyopathy

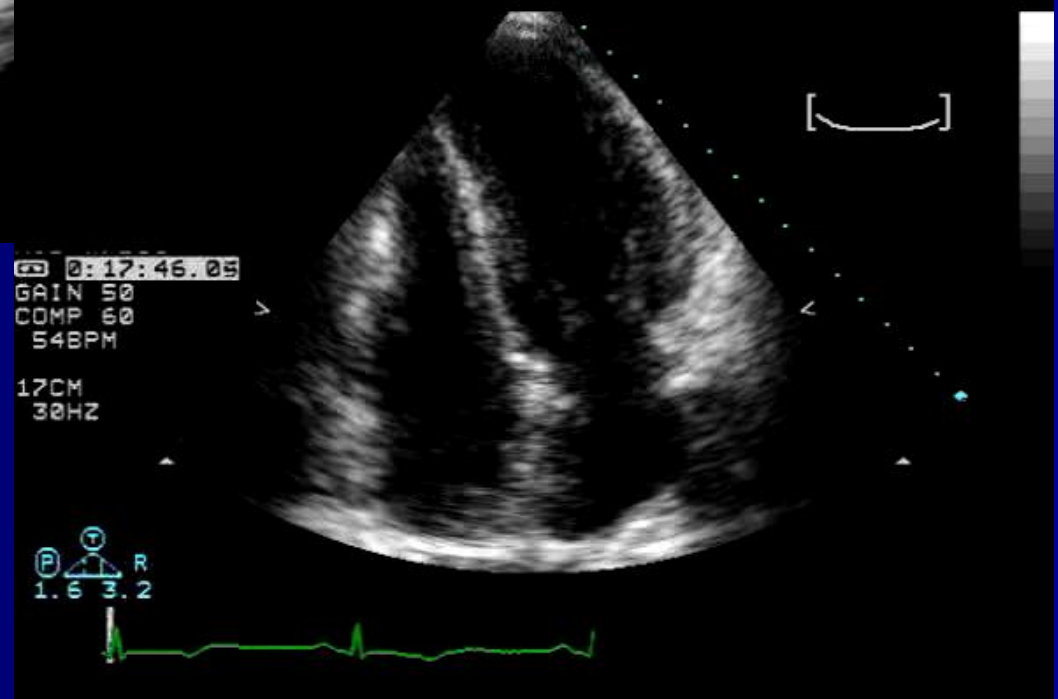


Lossy compression - not intended for diagnosis



Hypertrophic  
cardiomyopathy

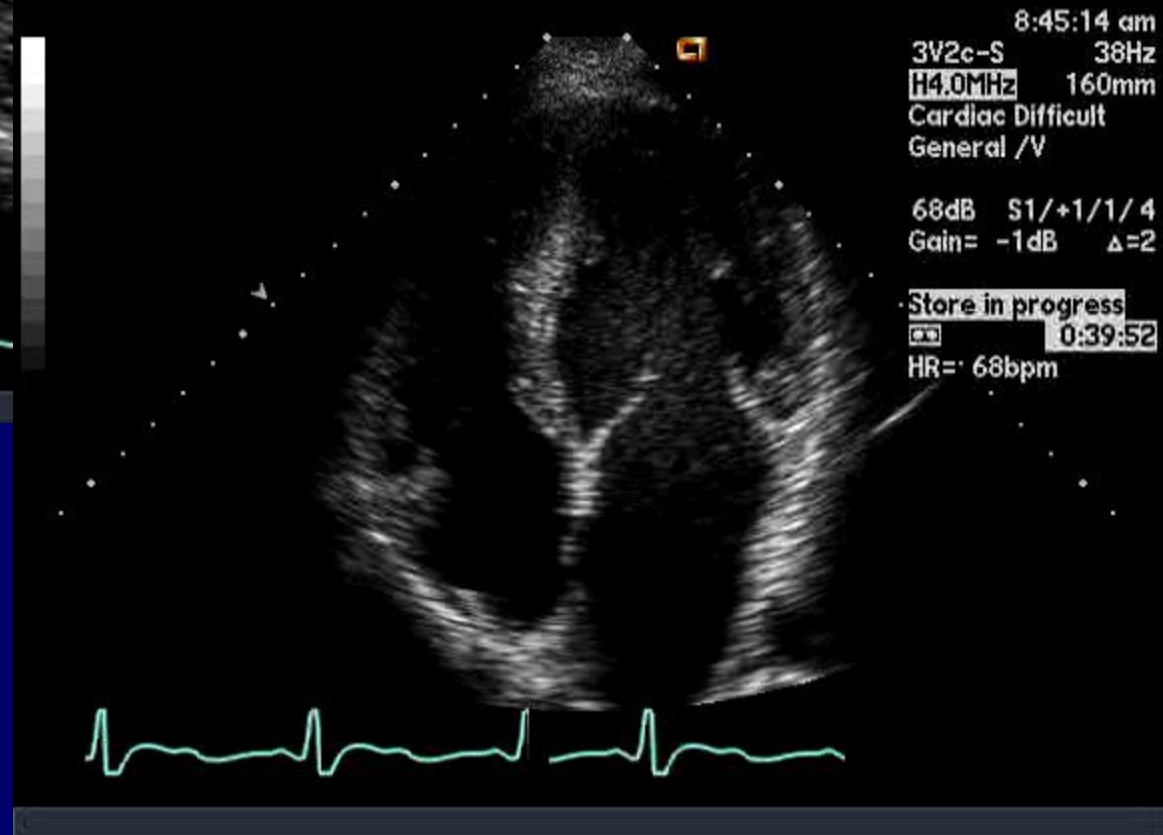
Lossy compression - not intended for diagnosis



Lossy compression - not intended for diagnosis

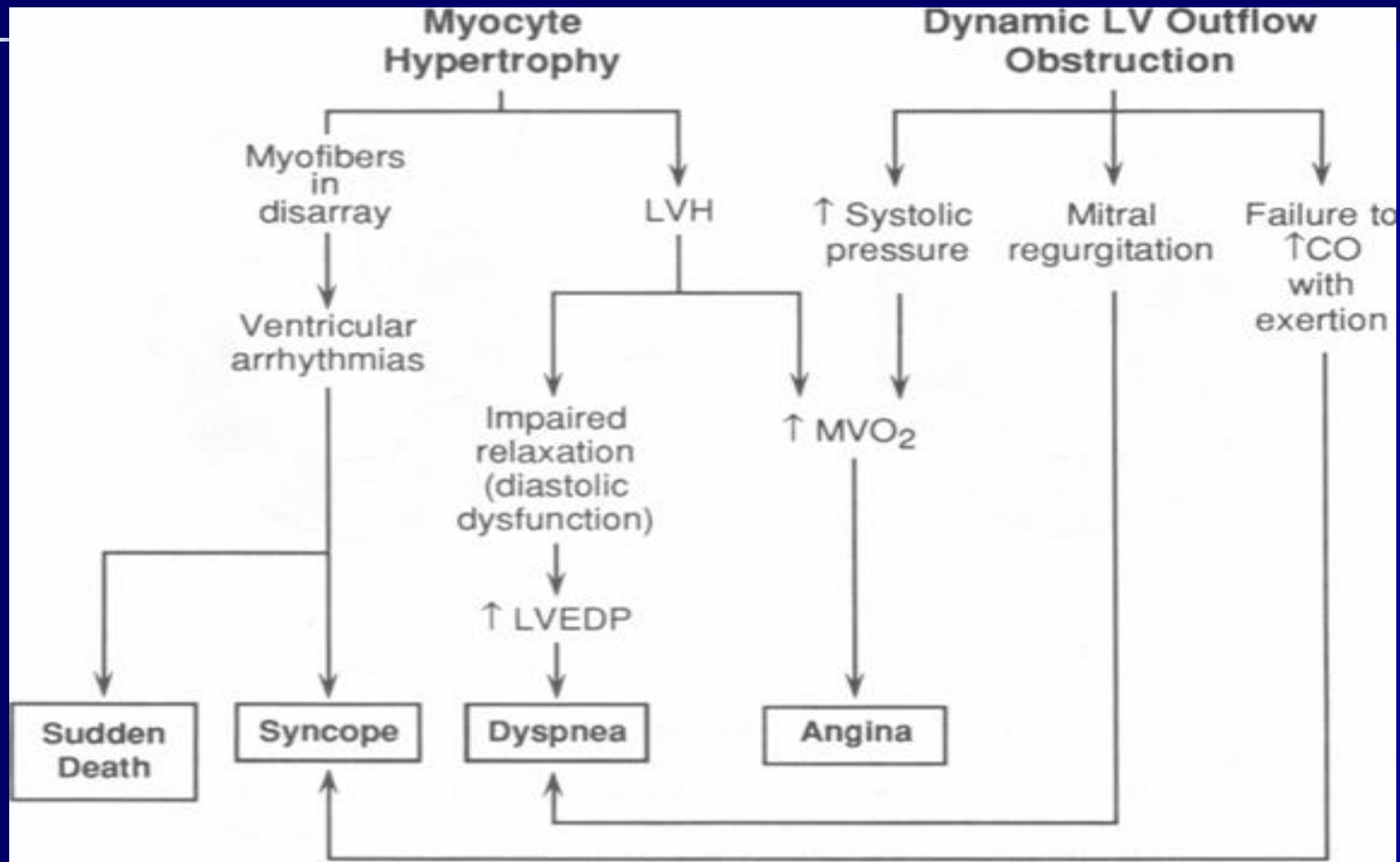


Lossy compression - not intended for diagnosis



## Apical Hypertrophic Cardiomyopathy

# Pathophysiology





# HCM with outflow obstruction

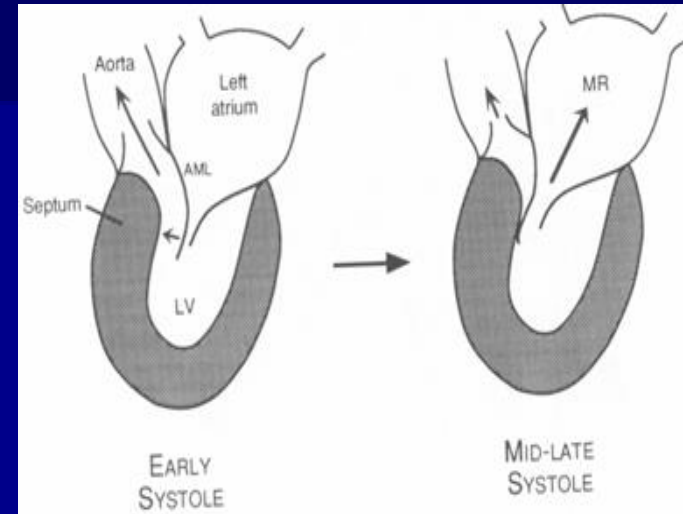
Dynamic LVOT obstruction (may not be present at rest)

SAM (systolic anterior motion of mitral valve)

LVOT Obstruction  $\Rightarrow$  LVOT gradient  
 $\Rightarrow$   $\uparrow$  wall stress  $\Rightarrow$   $\uparrow$  MVO<sub>2</sub>  $\Rightarrow$  ischemia/angina

$\uparrow$  LVOT gradient:  $\uparrow$  HR (DFP),  $\downarrow$  preload (LVEDV),  
 $\downarrow$  afterload (BP).

$\downarrow$  LVOT gradient:  $\uparrow$  BP (Afterload),  $\uparrow$  LVEDV (preload)



Symptoms of dyspnea and angina more related to diastolic dysfunction than to outflow tract obstruction

Syncope: LVOT obstruction (failure to increase CO during exercise or after vasodilatory stress) or arrhythmia.

# Physical Exam

Bisferiens pulse (“spike and dome”)

S4 gallop

Crescendo/Decrescendo systolic ejection murmur

## HOCM vs. Valvular AS

## Intensity of murmur

Valsalva (↓preload, ↓ afterload)

Squatting (↑ preload, ↑ afterload)

Standing (↓preload, ↓ afterload)

### HOCM

↑

↓

↑

### AS

↓

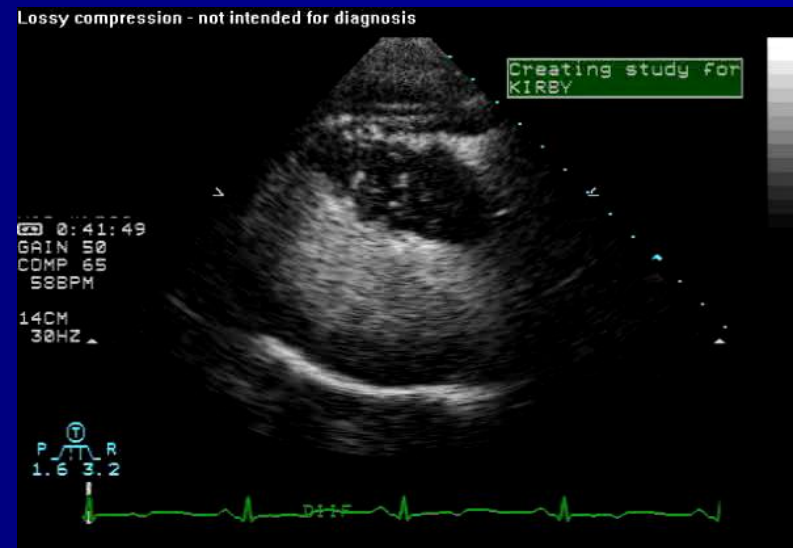
↑

↓

Holosystolic apical blowing murmur of mitral regurgitation

# Diagnostic Studies

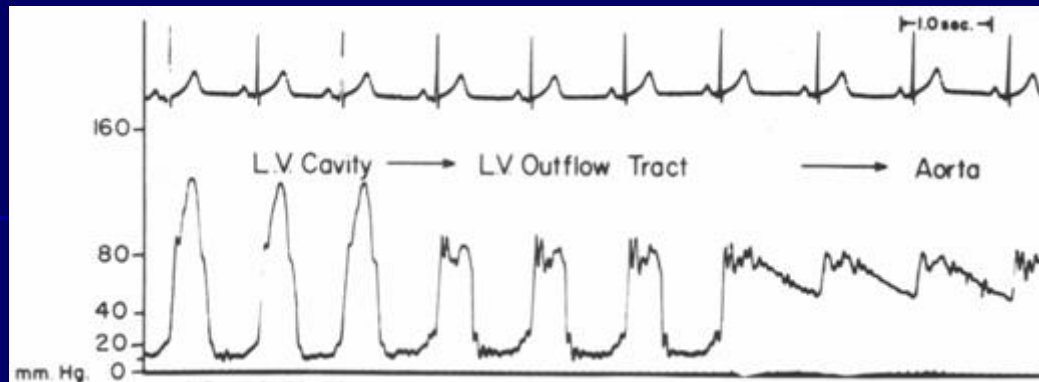
- EKG
  - NSR
  - LVH
  - septal Q waves
- 2D-Echocardiography
  - LVH; septum  $>1.4x$  free wall
  - LVOT gradient by Doppler
  - Systolic anterior motion of the mitral valve regurgitation
- Cardiac Catheterization
  - LVOT gradient and pullback
  - provocative maneuvers
  - Brockenbrough phen



HCM-ASH using contrast

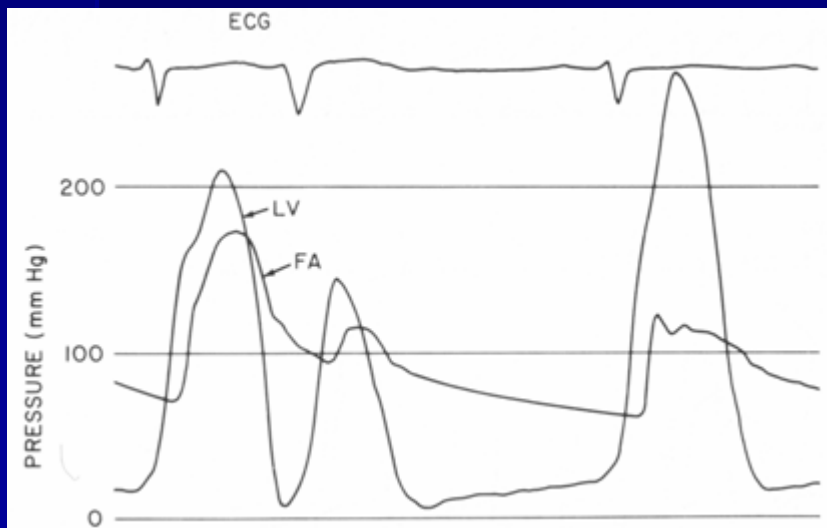
# Cardiac Catheterization

LV pullback



Brockenbrough-Braunwald Sign

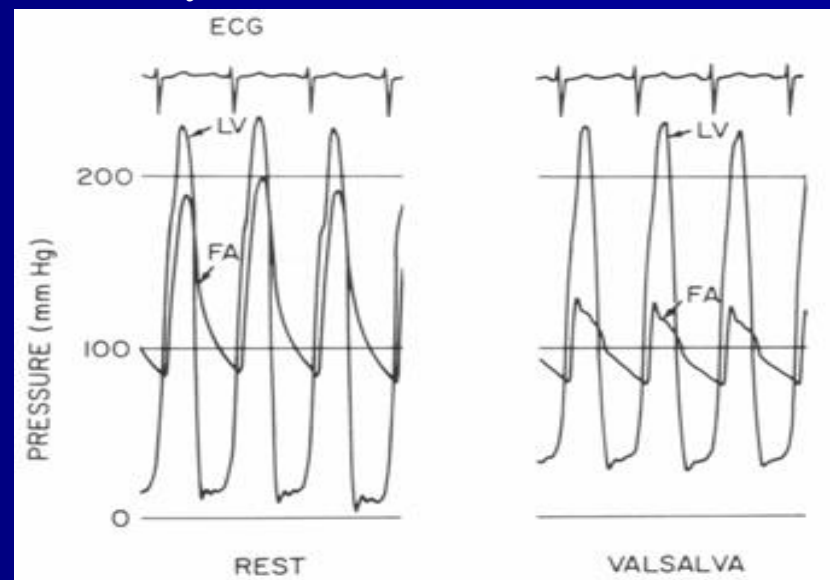
failure of aortic pulse pressure to rise post PVC



Provocative maneuvers:

Valsalva

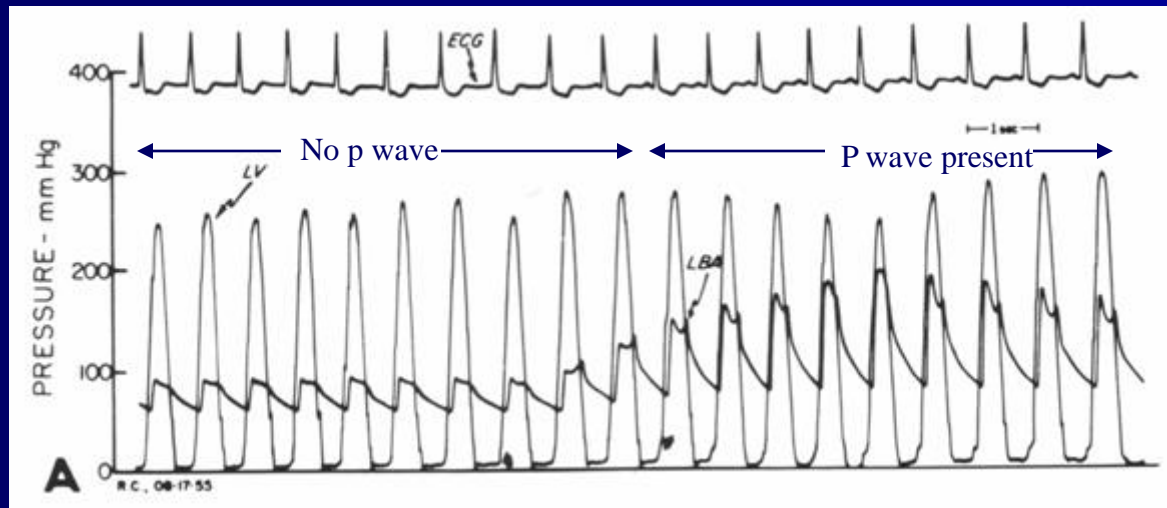
amyl nitrate inhalation



# Atrial Fibrillation

Acute A. Fib is poorly tolerated - Acute Pulmonary Edema and Shock  
Chronic a fib - Fatigue, dyspnea and angina

Rapid HR - decreased time for diastolic filling and LV relaxation  
Loss of atrial “Kick” – decreased LV filling  
- decreased SV and increased outflow tract obstruction



Rate slowing with  $\beta$ -blockers and  $\text{Ca}^{2+}$  channel blockers  
Digitalis is relatively contra-indicated- positive inotrope  
DC Cardioversion

# Treatment

For symptomatic benefit

$\beta$ -blockers

↓ mvO<sub>2</sub>

↓ gradient (exercise)

arrhythmias

Calcium Channel blockers

Anti-arrhythmics

afib

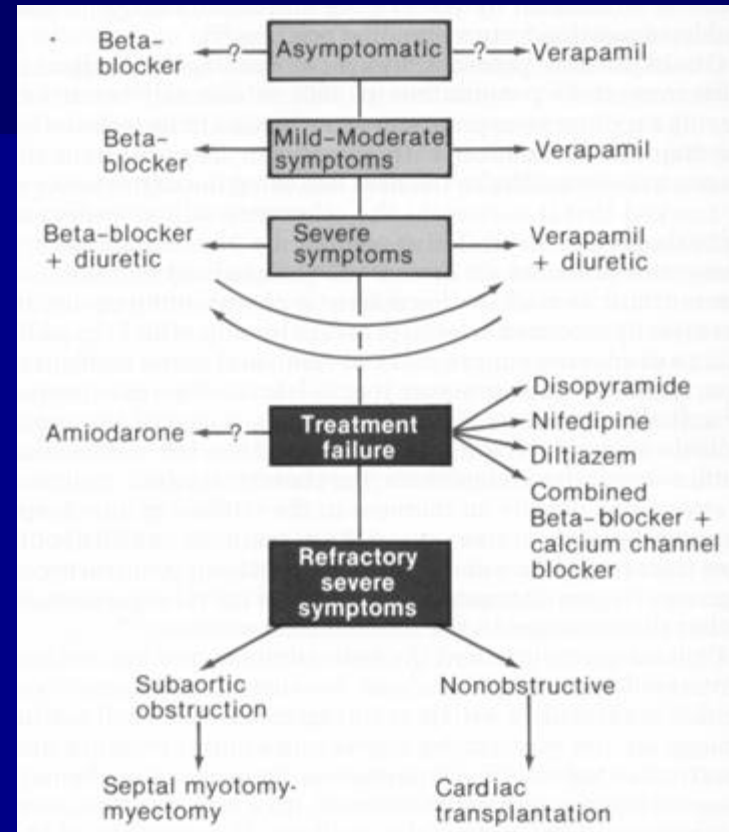
amiodorone

Disopyramide

AICD for sudden death

antibiotic prophylaxis for endocarditis

No therapy has been shown to improve mortality



# HCM: Surgical Treatment

For severe symptoms with large outflow gradient ( $>50\text{mmHg}$ )

*Does not prevent Sudden Cardiac Death*

## Myomyectomy

removal of small portion of upper IV septum

+/- mitral valve replacement

5 year symptomatic benefit in ~ 70% of patients

## Dual Chamber (DDD pacemaker) pacing

decreases LVOT gradient (by ~25%)

randomized trials have shown little longterm benefit

possible favorable morphologic changes

## ETOH septal ablation

AICD to prevent sudden death

# Hypertrophic CM

- Most common cause of death in young people.
- The magnitude of left ventricular hypertrophy is directly correlated to the risk of SCD.
- Young pts with extreme hypertrophy and few or no symptoms are at substantial long-term risk of SCD.

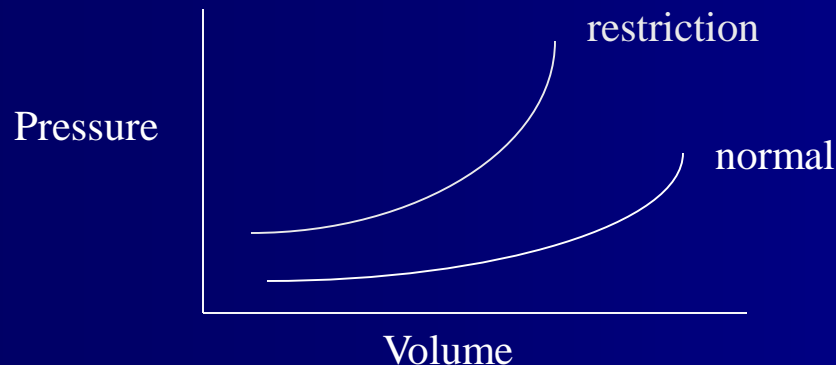




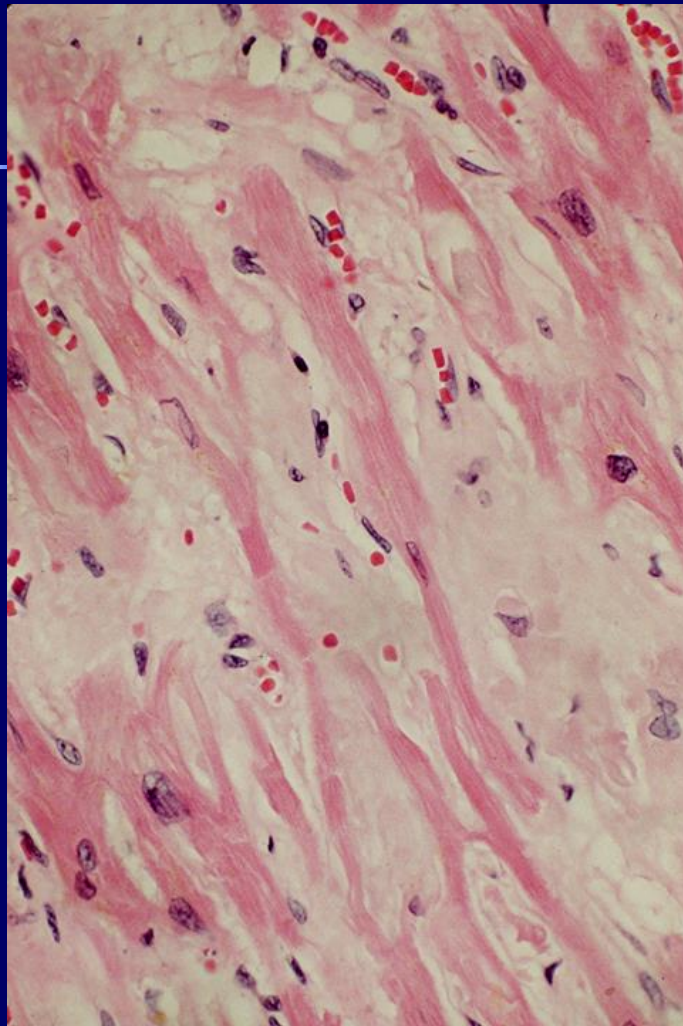
# Restrictive Cardiomyopathy

## Characterized by:

- impaired ventricular filling due to an abnormally stiff (rigid) ventricle
- normal systolic function (early on in disease)
- intraventricular pressure rises precipitously with small increases in volume



Causes : infiltration of myocardium by abnormal substance  
fibrosis or scarring of endocardium



Amyloid infiltrative CM

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**TABLE 4. CAUSES OF RESTRICTIVE  
CARDIOMYOPATHY.**

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**Myocardial**

Noninfiltrative disorders

- Idiopathic disease
- Familial disease
- Hypertrophy
- Scleroderma
- Diabetes mellitus
- Pseudoxanthoma elasticum

Infiltrative disorders

- Amyloidosis
- Sarcoidosis
- Gaucher's disease
- Hurler's syndrome
- Fatty infiltration

Storage disorders

- Hemochromatosis
- Fabry's disease
- Glycogen storage disease

**Endomyocardial**

- Endomyocardial fibrosis
  - Hyper eosinophilic (Löffler's) syndrome
  - Carcinoid syndrome
  - Metastatic cancer
  - Exposure to radiation
  - Toxins
    - Anthracycline (doxorubicin or daunorubicin)
    - Serotonin
    - Methysergide
    - Ergotamine
    - Mercurial agents
    - Busulfan
-

# Amyloidosis

## Primary Amyloidosis

immunoglobulin light chains -- multiple myeloma

## Secondary Amyloidosis

deposition of protein other than immunoglobulin

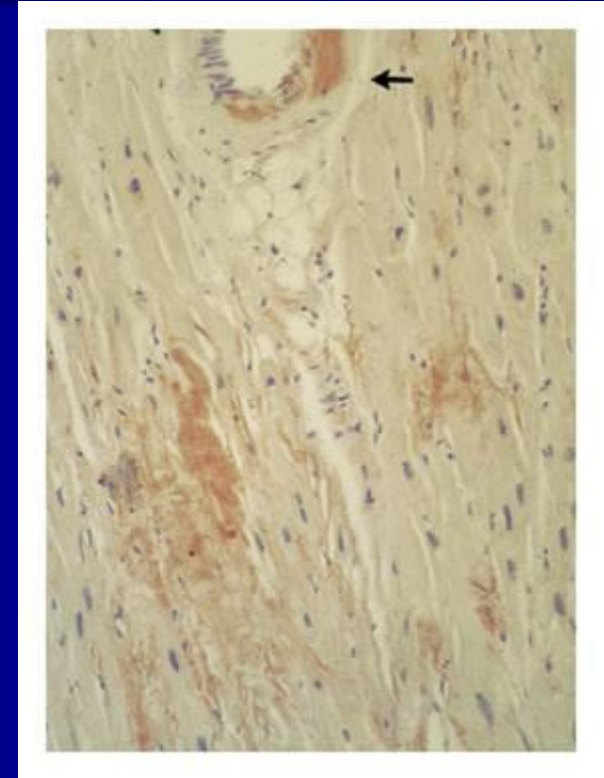
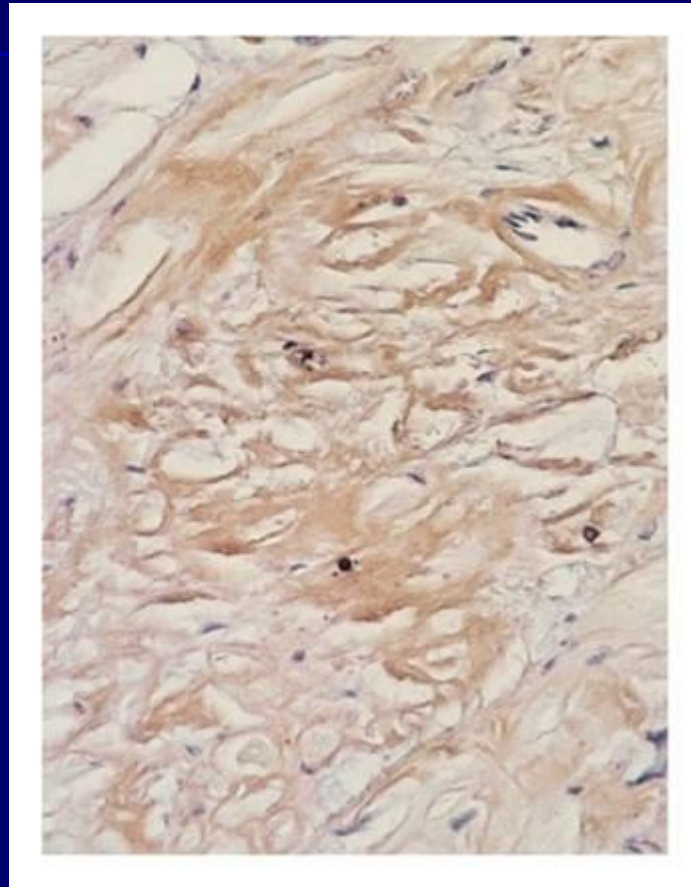
senile

familial

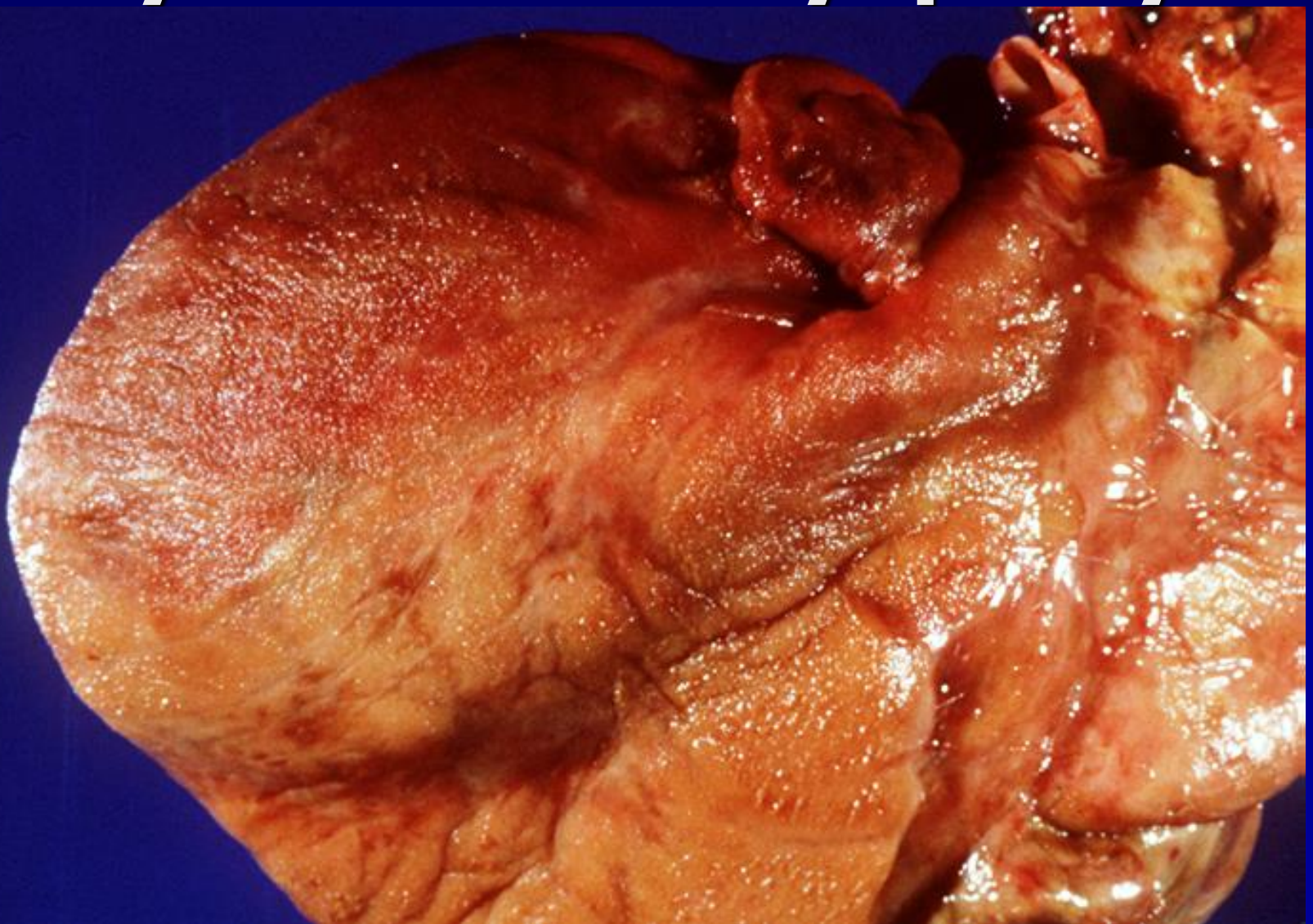
chronic inflammatory process

restriction caused by replacement of normal myocardial contractile elements by infiltrative interstitial deposits

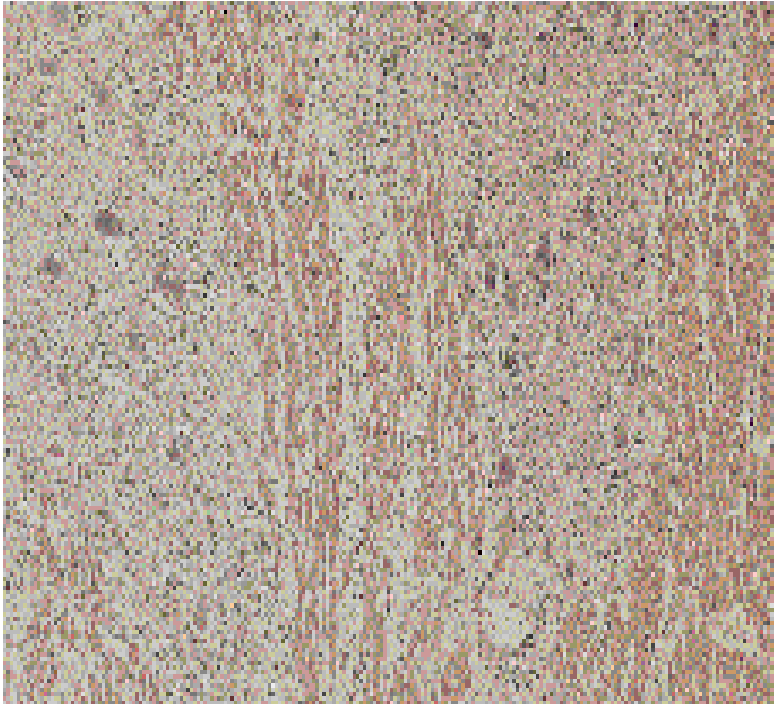
# Amyloidosis



# Amyloid Cardiomyopathy



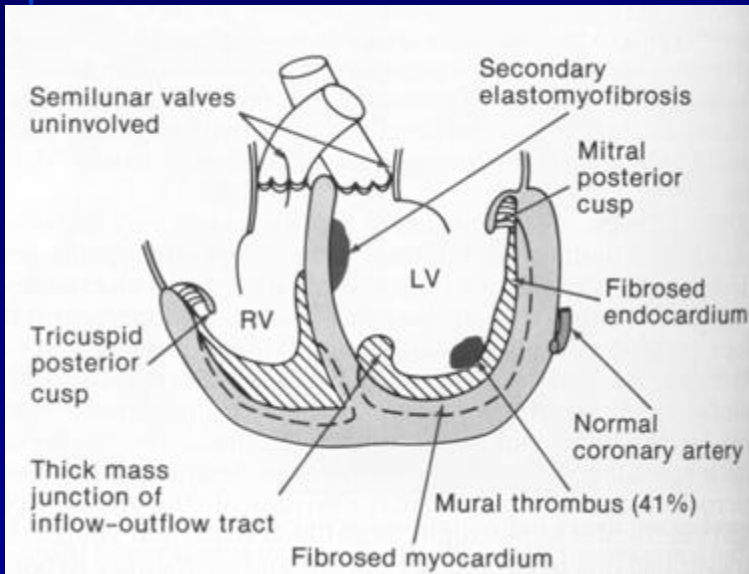
# Sarcoidosis



Restriction  
Conduction System Disease  
Ventricular Arrhythmias  
(Sudden Cardiac Death)

# Endomyocardial Fibrosis

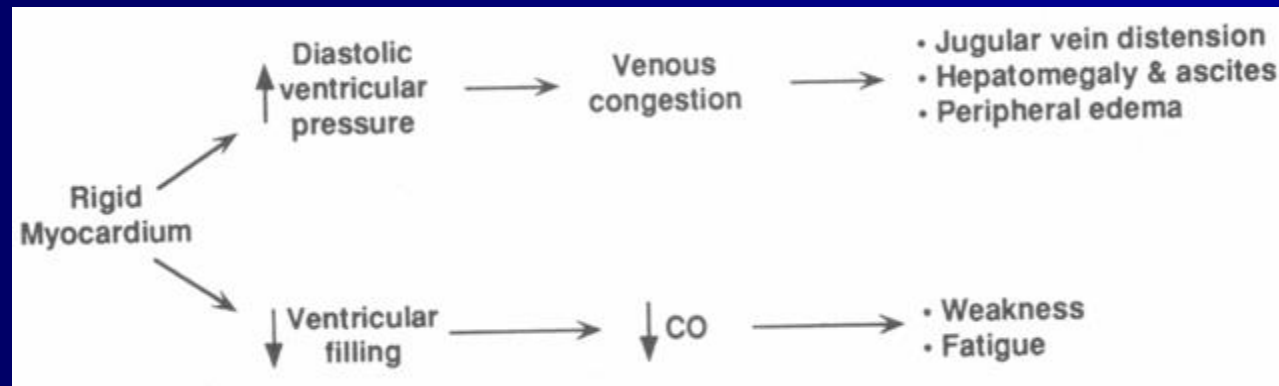
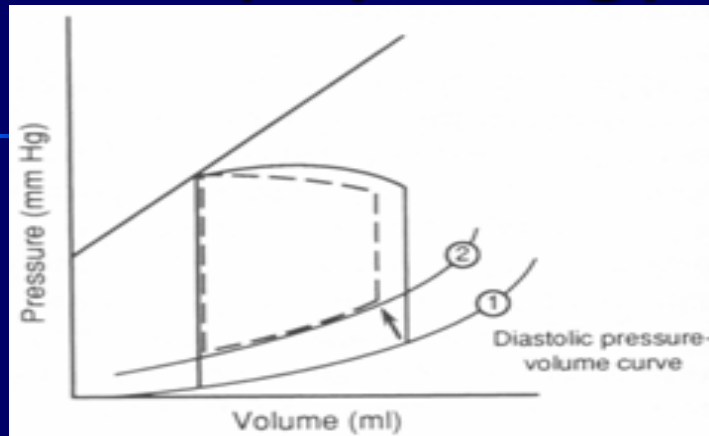
Endemic in parts of Africa, India, South and Central America, Asia  
15-25% of cardiac deaths in equatorial Africa  
hypereosinophilic syndrome (Loffler's endocarditis)



Thickening of basal inferior wall  
endocardial deposition of thrombus  
apical obliteration  
mitral regurgitation  
80-90% die within 1-2 years



# Pathophysiology of Restriction



Elevated systemic and pulmonary venous pressures  
right and left sided congestion  
reduced ventricular cavity size with  $\downarrow$ SV and  $\downarrow$ CO

# Clinical Findings

Right > Left heart failure

Dyspnea

Orthopnea/PND

Peripheral edema

Ascites/Hepatomegaly

Fatigue/ ↓exercise tolerance

Clinically mimics constrictive Pericarditis

# Diagnostic Studies

2D-Echo/Doppler-

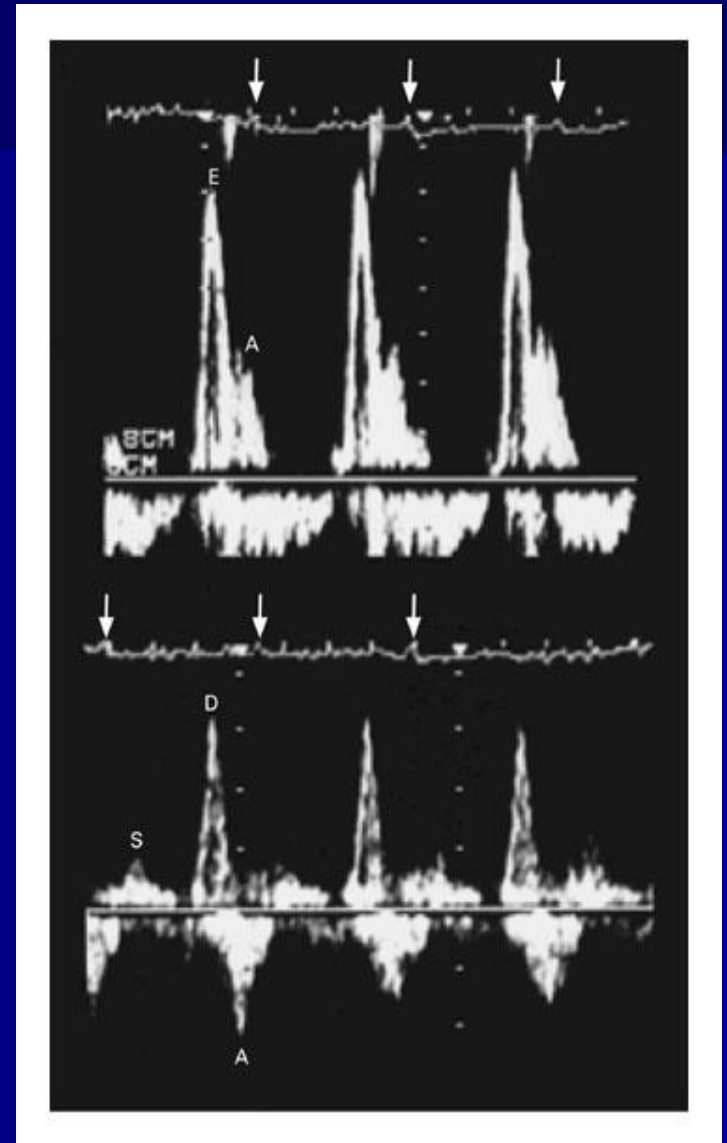
mitral in-flow velocity  
rapid early diastolic filling

Catheterization –

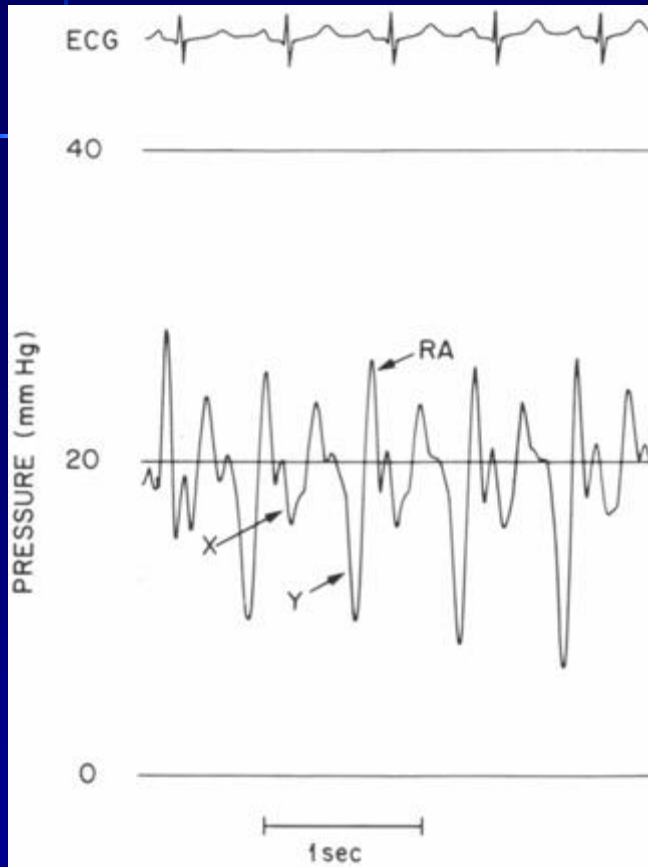
diastolic pressure equilibration  
restrictive vs constrictive  
hemodynamics

Endomyocardial biopsy-

definite Dx of restrictive pathology



# Cardiac Catheterization



Prominent y descent  
rapid atrial emptying  
then abrupt cessation of blood flow due to non-compliant myocardium

“dip and plateau”  
rapid ventricular filling

# Constriction vs. Restrictive CM

**TABLE 2. THE DIFFERENTIAL DIAGNOSIS OF RESTRICTIVE CARDIOMYOPATHY AND CONSTRICTIVE PERICARDITIS.\***

TYPE OF EVALUATION	RESTRICTIVE CARDIOMYOPATHY	CONSTRICTIVE PERICARDITIS
Physical examination	Kussmaul's sign may be present Apical impulse may be prominent S3 may be present, rarely S4 Regurgitant murmurs common	Kussmaul's sign usually present Apical impulse usually not palpable Pericardial knock may be present Regurgitant murmurs uncommon
Electrocardiography	Low voltage (especially in amyloidosis), pseudoinfarction, left-axis deviation, atrial fibrillation, conduction disturbances common	Low voltage (<50 percent)
Echocardiography	Increased wall thickness (especially thickened interatrial septum in amyloidosis) Thickened cardiac valves (amyloidosis) Granular sparkling texture (amyloid)	Normal wall thickness Pericardial thickening may be seen Prominent early diastolic filling with abrupt displacement of interventricular septum
Doppler studies	Decreased RV and LV velocities with inspiration Inspiratory augmentation of hepatic-vein diastolic flow reversal Mitral and tricuspid regurgitation common	Increased RV systolic velocity and decreased LV systolic velocity with inspiration Expiratory augmentation of hepatic-vein diastolic flow reversal
Cardiac catheterization	LVEDP often >5 mm Hg greater than RVEDP, but may be identical	RVEDP and LVEDP usually equal RV systolic pressure <50 mm Hg RVEDP >one third of RV systolic pressure
Endomyocardial biopsy	May reveal specific cause of restrictive cardiomyopathy	May be normal or show nonspecific myocyte hypertrophy or myocardial fibrosis
CT/MRI	Pericardium usually normal	Pericardium may be thickened

\*LV denotes left ventricular, RV right ventricular, LVEDP left ventricular end-diastolic pressure, RVEDP right ventricular end-diastolic pressure, CT computed tomography, and MRI magnetic resonance imaging.

# Treatment

## Treat underlying cause

r/o constriction which is treatable (restriction poor prognosis)  
amyloid (melphalan/prednisone/colchicine)  
Endomyocardial Fibrosis (steroids, cytotoxic drugs, MVR)  
Hemochromatosis (chelation, phlebotomy)  
Sarcoidosis (steroids)

## Diuretics

For congestive symptoms, but  $\downarrow$  LV/RV filling  $\Rightarrow$   $\downarrow$  CO

Digoxin (avoid in amyloidosis)

Antiarrhythmics for afib

amiodorone

Pacemaker for conduction system disease

Anticoagulation for thrombus (esp in atrial appendages)

# Arrhythmogenic RV Dysplasia

- Myocardium of RV free wall replaced:
  - Fibrofatty tissue
  - Regional wall motion/function is reduced
- Ventricular arrhythmias
  - SCD in young

# MRI: RV Dysplasia





# LV Noncompaction

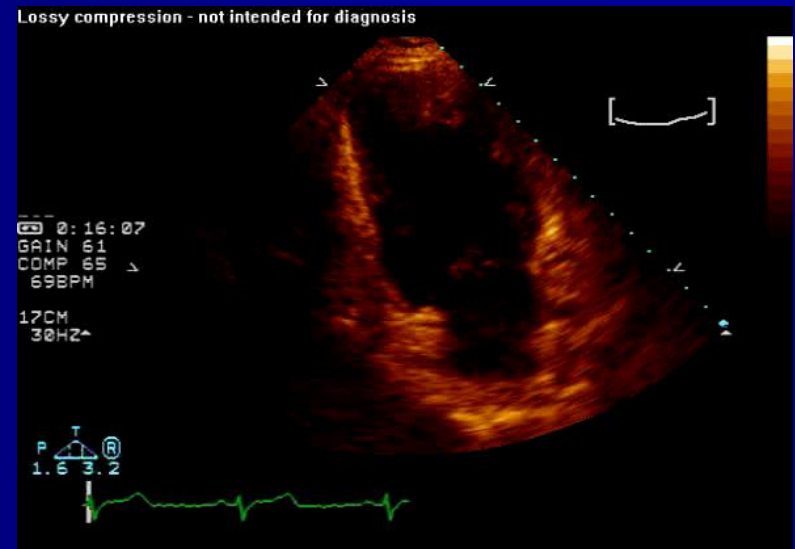
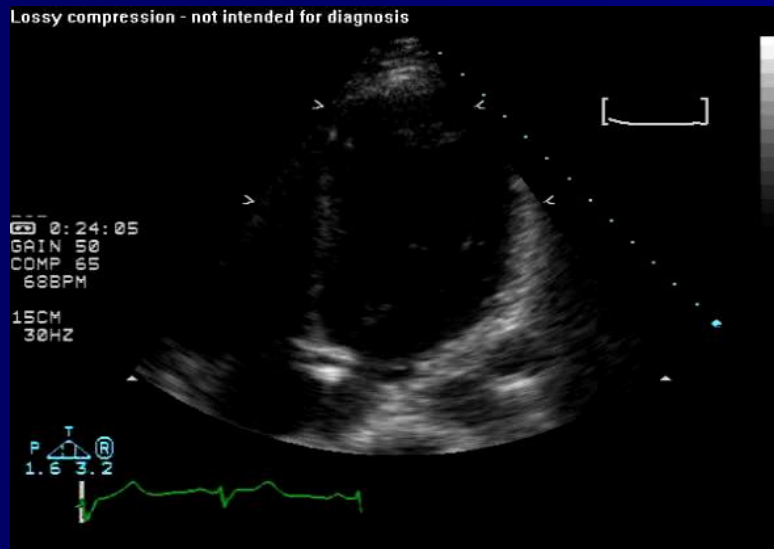
## Diagnostic Criteria

- Prominent trabeculations, deep recesses in LV apex
- Thin compact epicardium, thickened endocardium
  - Stollberger C, JASE '04
- Other phenotypic findings

## Prognosis and Treatment

- Increased risk of CHF, VT/SCD, thrombosis
  - Oechslin EN, JACC '00
- Hereditary risk
  - Screening of offspring
- Pregnancy: case report

# Echo: LV Noncompaction



# Cardiomyopathy

## WHO Classification

anatomy & physiology of the LV

1. Dilated
  - Enlarged
  - Systolic dysfunction
2. Hypertrophic
  - Thickened
  - Diastolic dysfunction
3. Restrictive
  - Myocardial stiffness
  - Diastolic dysfunction
4. Arrhythmogenic RV dysplasia
  - Fibrofatty replacement
5. Unclassified
  - Fibroelastosis
  - LV noncompaction

