

Myocardial Diseases

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Columbia University
New York, USA*

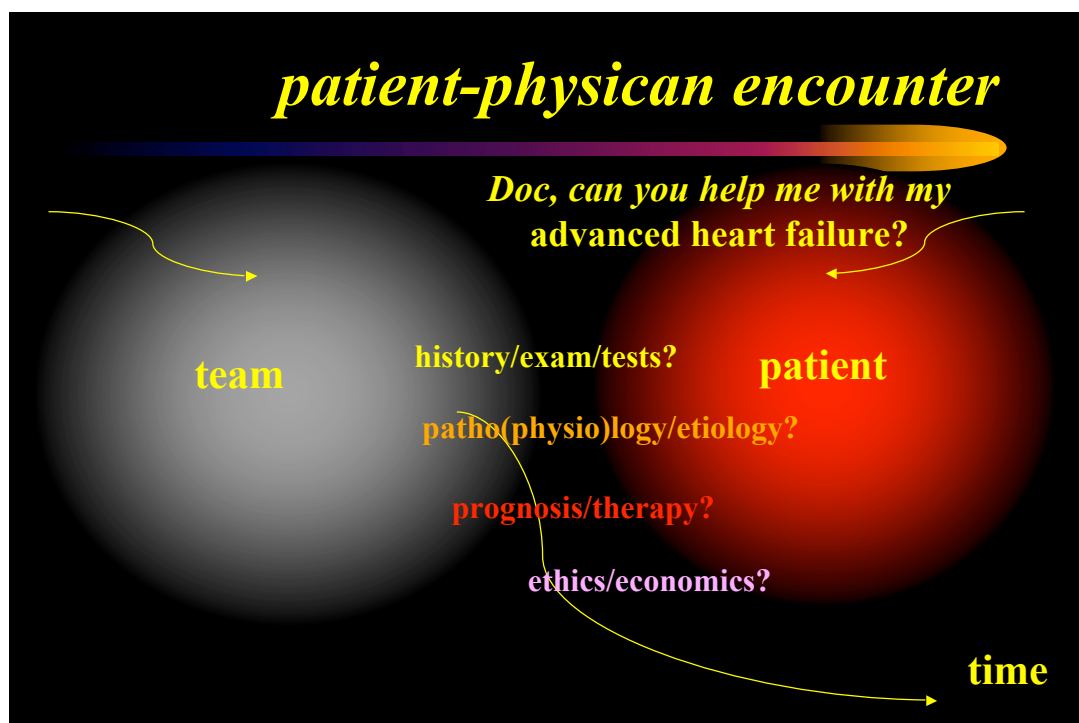
context

- **Cardiac cycle**
- **Valvular heart diseases**
- **Ischemic heart diseases**
- **Congenital heart diseases**
- **Myocardial diseases**

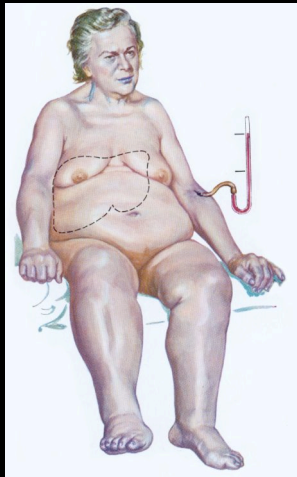
objectives

- **classify myocardial diseases into three major phenotypes**
- **describe their clinical presentation during the initial encounter**
- **delineate the diagnostic process and the role of different tests**
- **interpret these results in the context of pathophysiology**
- **employ the stages of heart failure to delineate therapeutic steps**

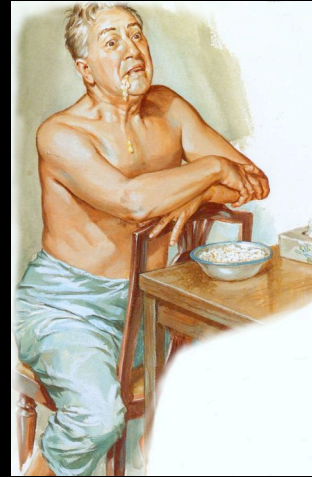
patient-physician encounter



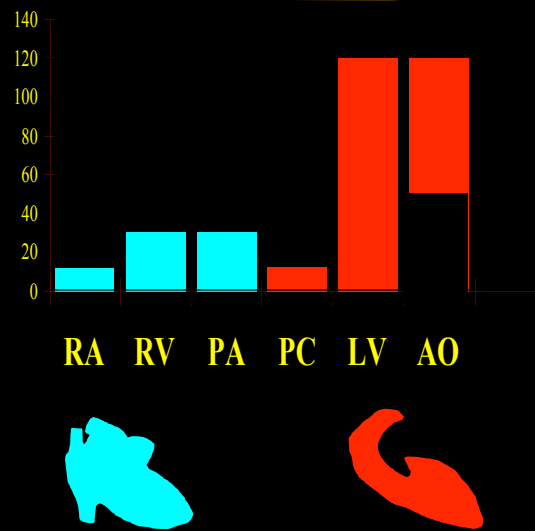
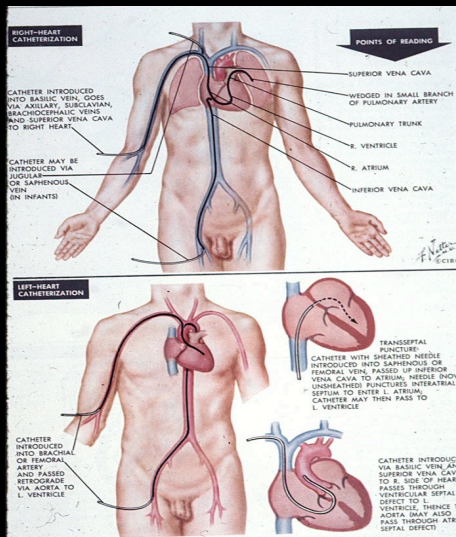
advanced heart failure



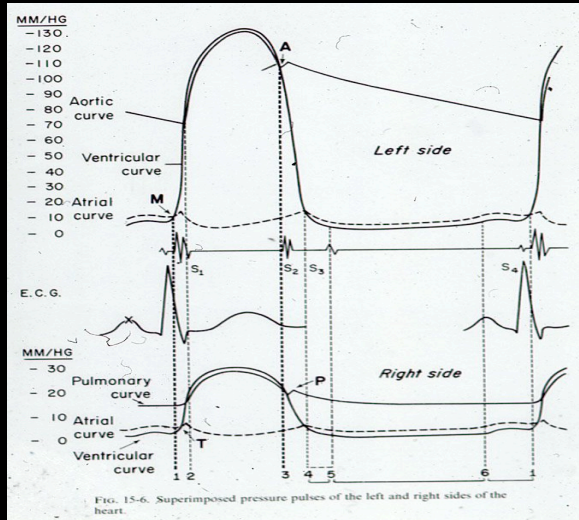
- low ejection fraction
- cardiac dilatation
- ventricular arrhythmia
- inotrope requirement
- chronic hyponatremia
- organ dysfunction
- severe symptoms
- frequent hospitalization



right & left heart catheter

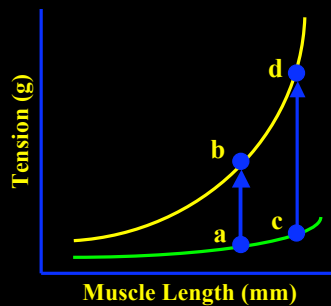


cardiac cycle - ECG & pressures



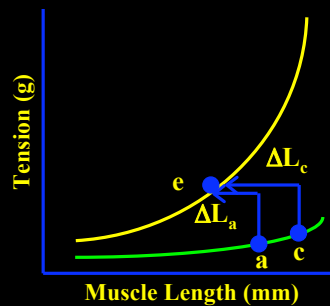
cardiac muscle function

Preload



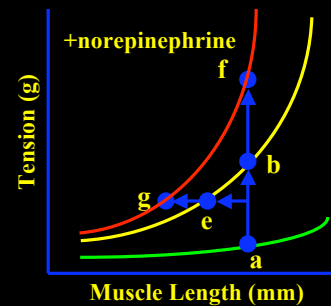
- The length of a cardiac muscle fiber prior to the onset of contraction.
- Frank Starling

Afterload



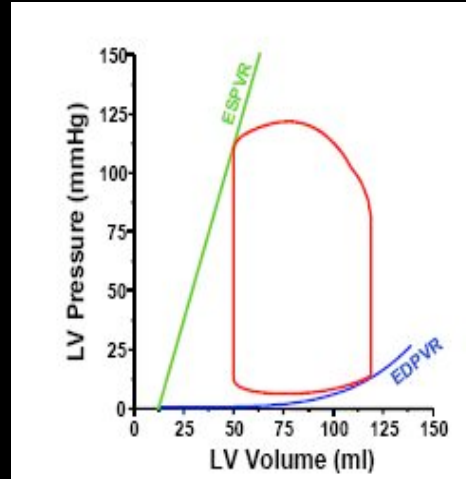
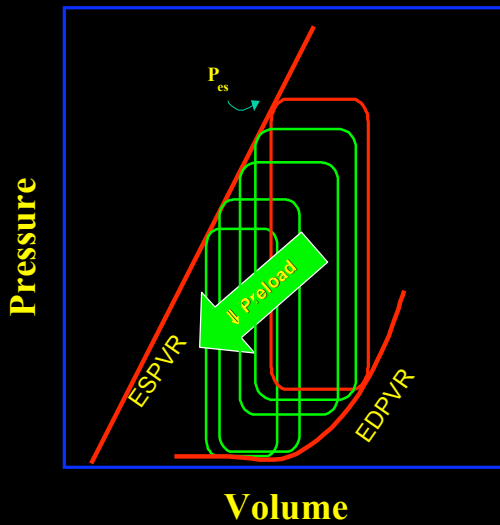
- The force against which a cardiac muscle fiber must shorten.
- Isotonic Contraction

Contractility



- The force of contraction independent of preload and afterload.
- Inotropic State

the pressure volume loop



<http://www.columbia.edu/itc/hs/medical/heartsim/>

AHF pathophysiology & therapy

adrenergic system
renin-angiotensin
endothelin system

natriuretic system
cytokine system
growth hormone

+ organ failure -
+ cachexia -
+ congestion -
+ hypoperfusion -

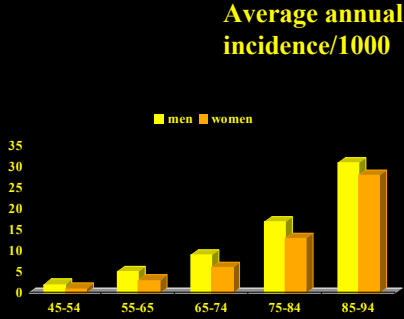
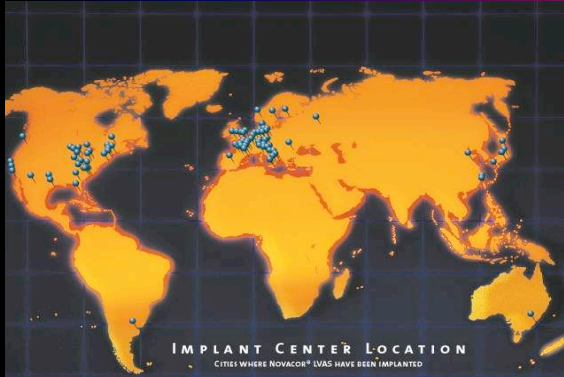
+ afterload -
+ preload -
+ contractility -
+ heart rate -
+ remodeling -
+ ischemia -
+ arrhythmia -





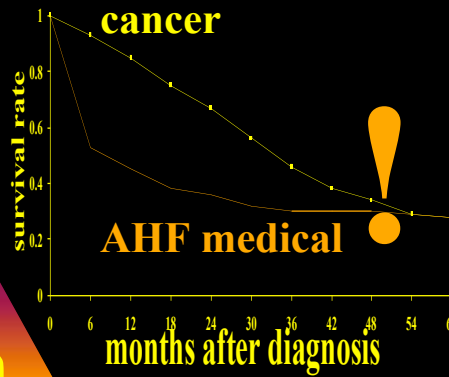
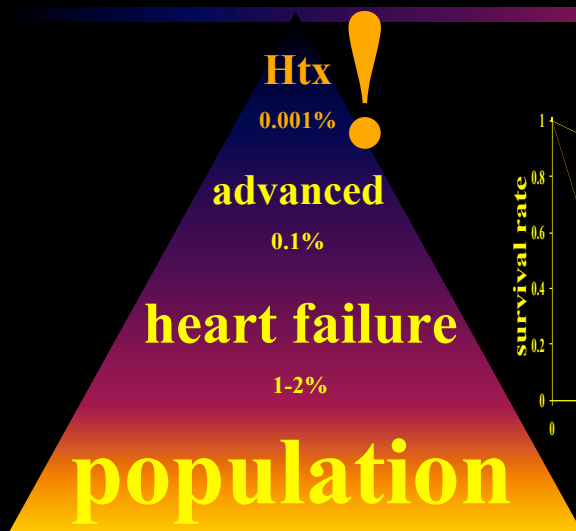
*Columbia
University
Medical
Center*

age, sex & heart failure



Kannel et al. Br Heart J 1994;72:53

epidemiology



macroscopic pathology

**hypertrophic
cardiomyopathy**

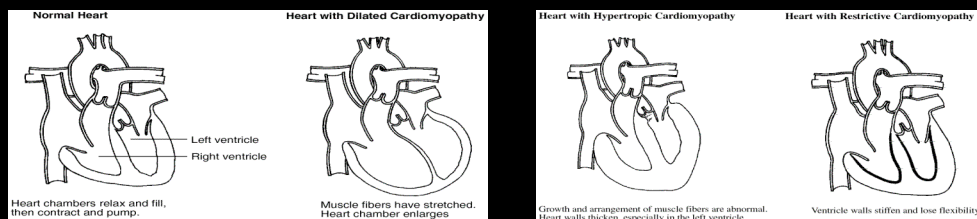
normal

**dilated
cardiomyopathy**

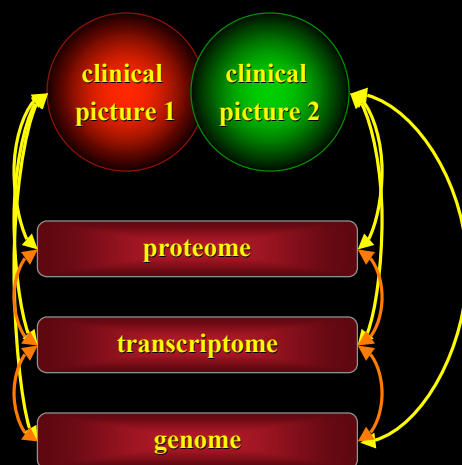


cardiomyopathy phenotypes

- dilated cardiomyopathy
- hypertrophic cardiomyopathy
- restrictive cardiomyopathy



systems biology strategy



- level distinction
- relationships within levels
- relationships between levels
- iterative strategy

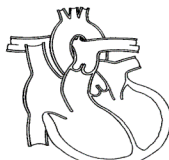


NYPH Hammer Health Sciences Building

cardiomyopathy phenotypes

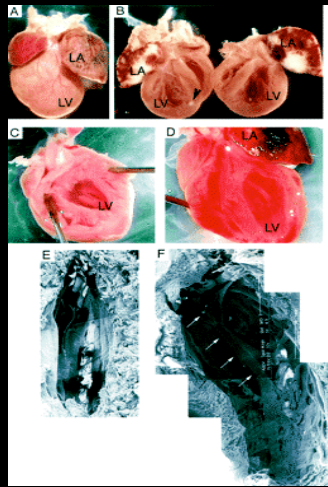
- **dilated cardiomyopathy**
- **hypertrophic cardiomyopathy**
- **restrictive cardiomyopathy**

Heart with Dilated Cardiomyopathy



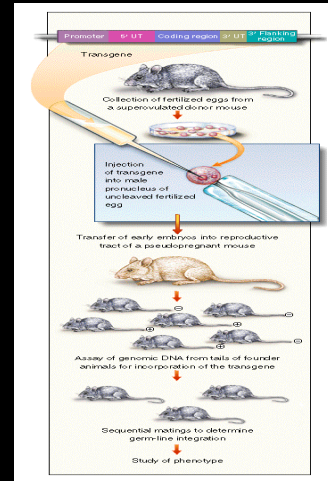
Muscle fibers have stretched.
Heart chamber enlarges

transgenic animals



**Cardiac
Compartment-
specific
Overexpression
of a Modified
Retinoic Acid
Receptor
Produces Dilated
Cardiomyopathy
and Congestive
Heart Failure in
Transgenic Mice**

Colbert CM...Robbins J



Shuldiner AR. NEJM 1996;334:653

specific cardiomyopathies

- Ischemic
- Valvular
- Hypertensive
- Inflammatory (Idiopathic, Autoimmune, Infectious)
- Metabolic (Endocrine, Amyloid)
- General system Disease (Connective Tissue Disorders)
- Muscular Dystrophies
- Neuromuscular Disorders
- Sensitivity and Toxic Reactions
- Peripartum

ischemic dilated cardiomyopathy

team

patient

initial presentation

- 55 y male
- married, 2 kids
- large anterolat wall AMI
- 10/31/04 Impella pump
- 11/03/04 HeartMate 1 MCS
- evaluation for heart transplant
- 2/17/05 heart transplant

follow-up

- stable post-transplant course
- back to work and normal life

teaching points

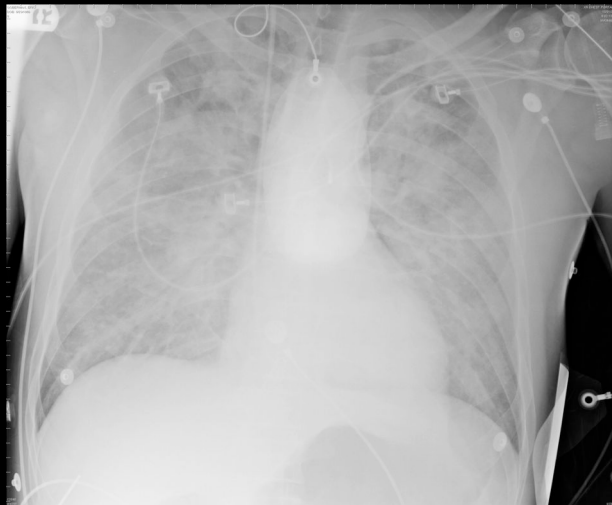
- benefits of hi-tech medicine

GE #4734815 *1950 m

Xray ischemic cardiomyopathy

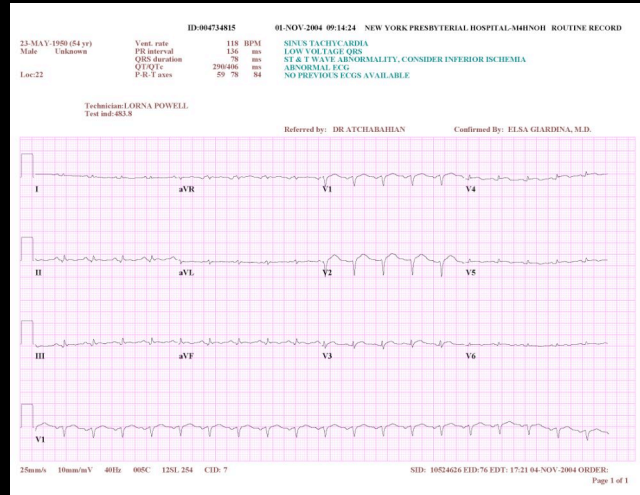
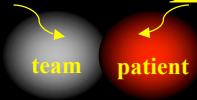
team

patient



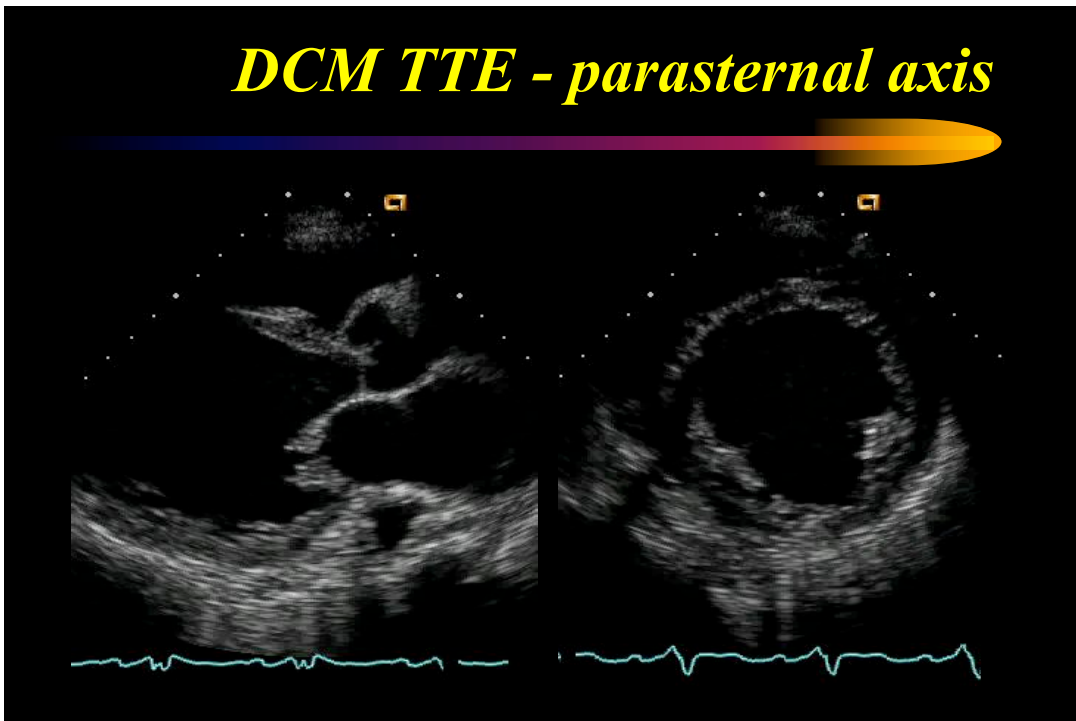
GE #4734815 *1950 m

ECG ischemic cardiomyopathy

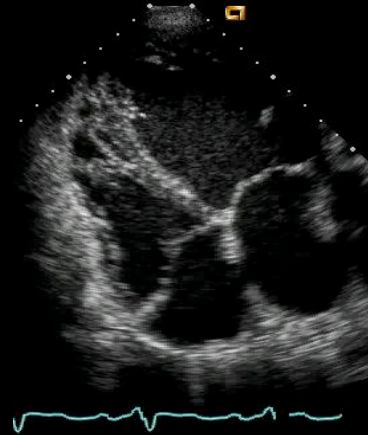
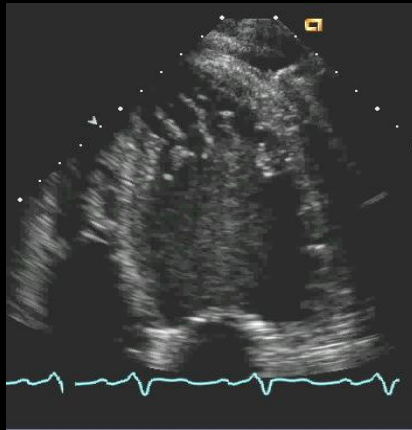


GE #4734815 *1950 m

DCM TTE - parasternal axis

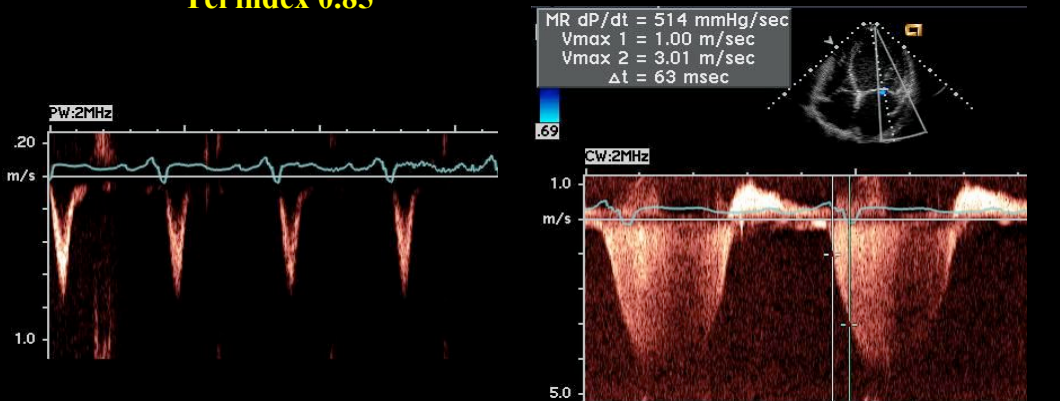


DCM TTE – apical 2/4 chamber view

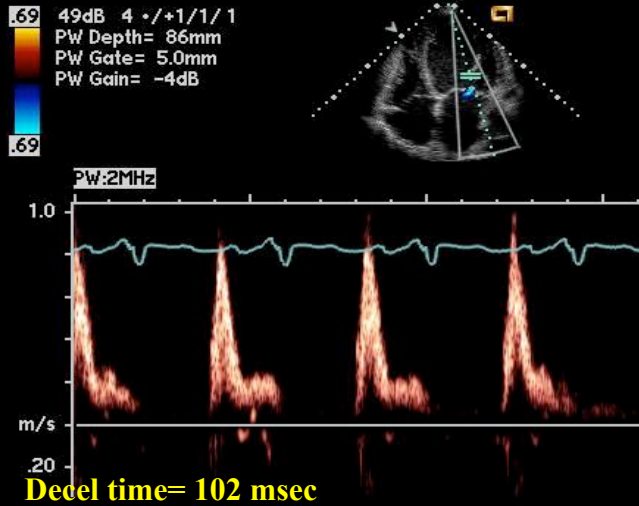


DCM TTE – AV/MV velocity

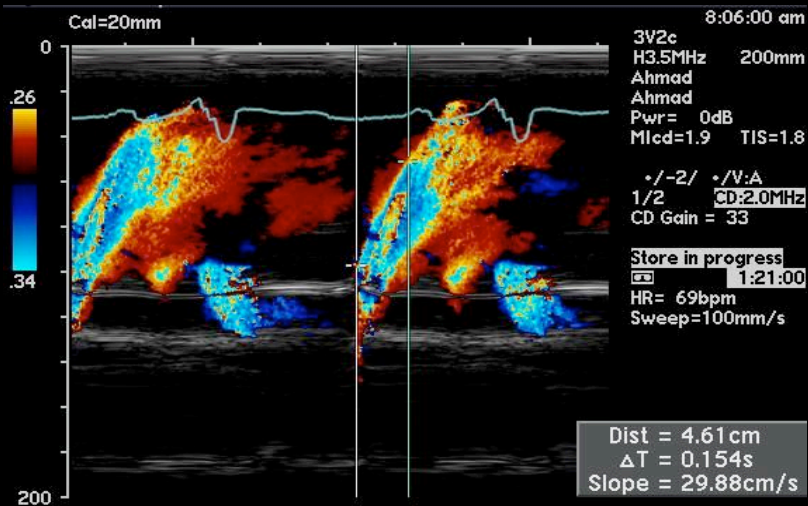
Calculated CO= 2.1 L/min
Tei index 0.85



DCM TTE – E deceleration time

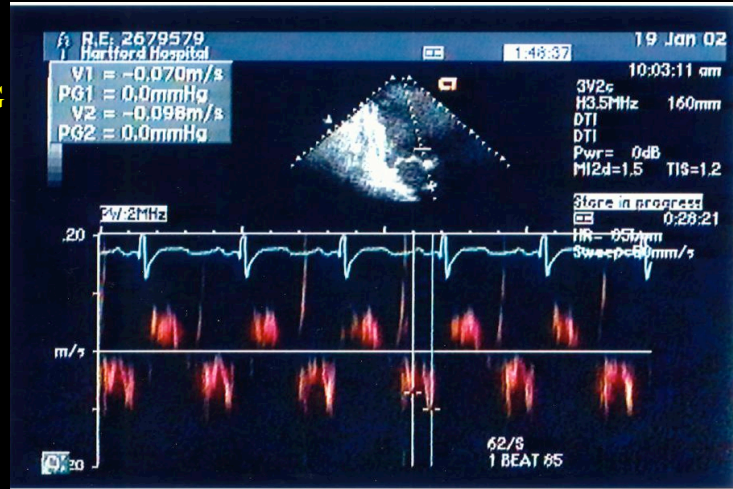


DCM TTE – early mitral flow

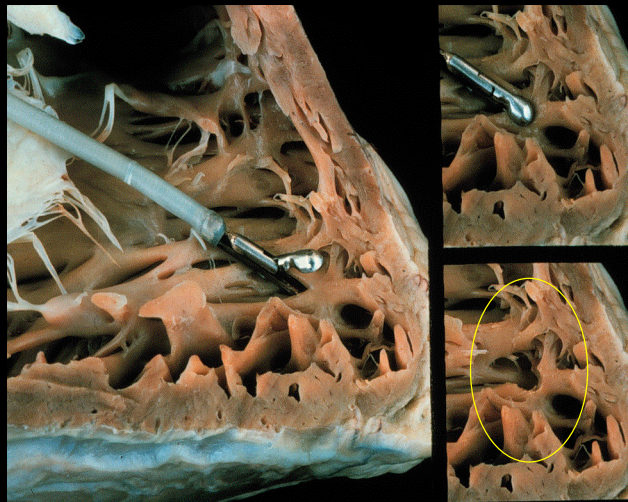


DCM TTE – PA pressure

E/prop vel = 2.7
E/Ea = 16
PASP= 56mmHG



endomyocardial biopsy



NYPH - South West View



macroscopic pathology

normal

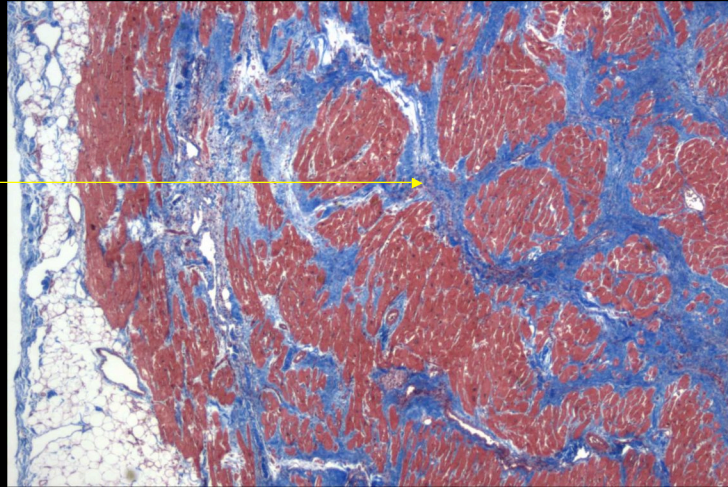
**dilated
cardiomyopathy**



idiopathic dilated cardiomyopathy

Masson
trichrome
stain

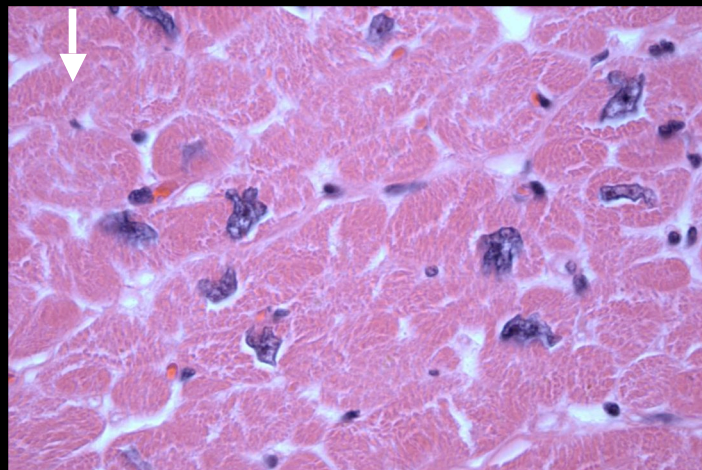
extensive
interstitial
fibrosis
(blue) with
myocytes in
red and
epicardial
fat/pericard
ium to the
left



idiopathic dilated cardiomyopathy

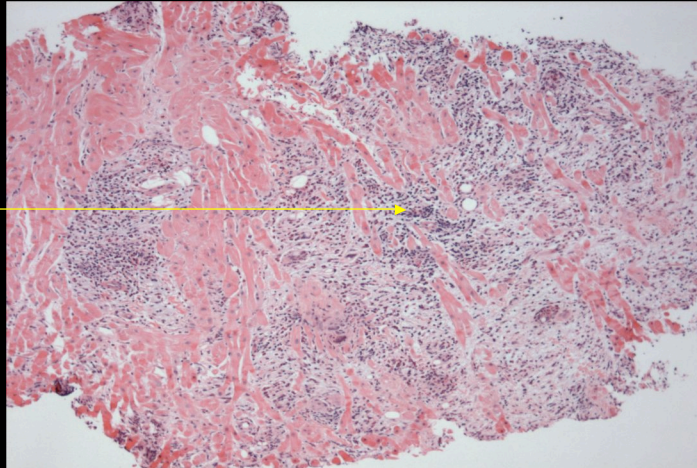
Hematoxylin
& eosin
stain:

Myocyte
hypertrophy
(very
enlarged and
irregular
nuclei)



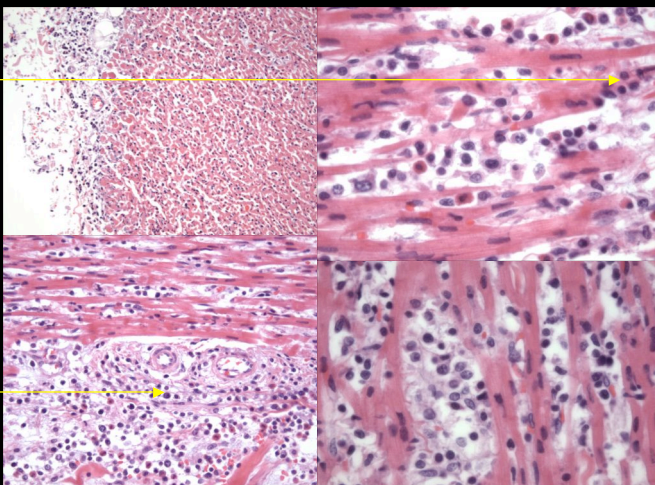
myocarditis

**inflammatory
infiltrate in
the
myocardium
associated
with myocyte
damage**



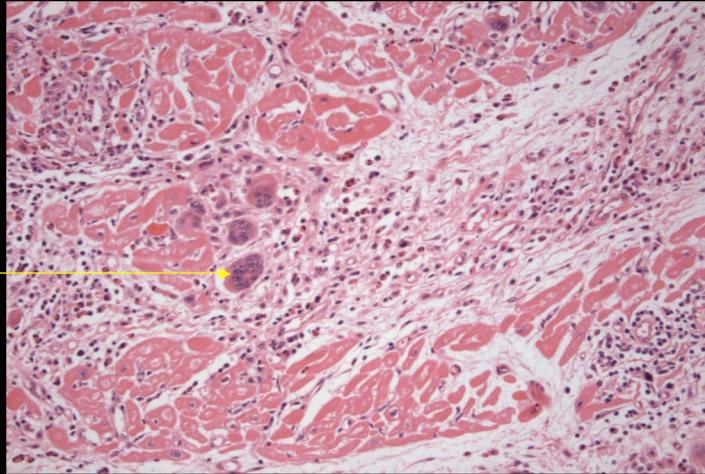
myocarditis

**inflammatory
infiltrate in
the
myocardium
associated
with myocyte
damage**



giant cell myocarditis

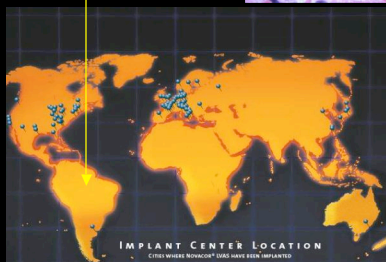
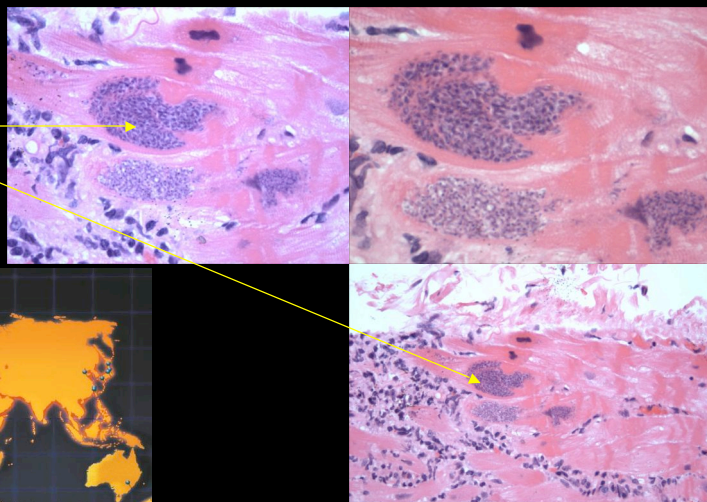
**multinucleated
giant cells**



chagas disease

***Trypanosom
a cruzi***

Amastigotes



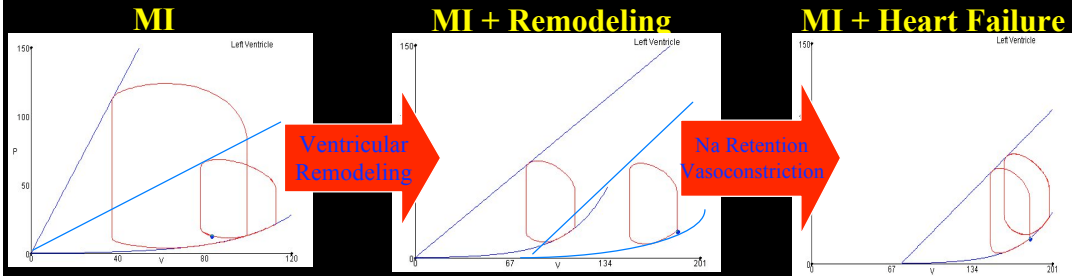


*Columbia
University
College of
Physicians &
Surgeons*

dilated cardiomyopathy

- **pathology**
 - enlargement of all four chambers, mild hypertrophy, interstitial fibrosis
- **pathophysiology**
 - Frank-Starling mechanism, neurohormonal activation, myocardial remodeling
- **etiology**
 - genetic, infectious, inflammatory, toxic, metabolic, neuromuscular

decreased contractility

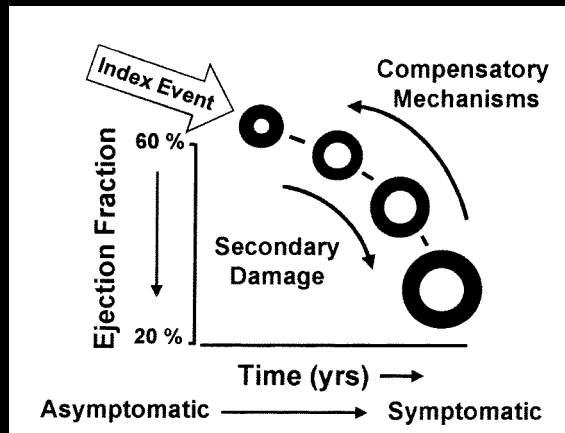


Etiologies

- Ischemic Cardiomyopathy
 - Myocardial Infarction
 - Myocardial Ischemia
- Myocarditis
- Toxins
 - Anthracycline
 - Alcohol
 - Cocaine

Parameter	Normal	MI	MI + Remodeling	MI + HF
BP (mm Hg)	124/81	68/46	68/45	80/50
SV (ml)	61	35	34	38
Cardiac Output (L/min)	3.7	2.1	2.0	2.3
PCWP (mm Hg)	10	16	18	33

heart failure & remodeling



Mann DL et al. Circulation 1999;100:999-1008

transcriptome>proteome>phenotype

• gene

- Ca⁺⁺, K⁺-channel ↑↓
- Na⁺/H⁺ antiporter ↑
- SERCA2 ↓
- Phospholamban ↓
- Ryanodine receptor ↓
- β₁-adrenoceptors ↓
- M₂ muscarinic receptors ↓
- G_{qi-2} subunit ↑
- ATII-R1 ↓
- myosin heavy chain V3 ↑
- Atrial natriuretic peptide ↓
- endothelin ↓
- iNOS ↑
- TNFα, IL6 ↓
- titin, desmin, vinculin ↑
- type I,III,V collagen ↑
- MMP1,9, TIMP1-4 ↑
- Fibronectin, laminin ↑

• cell

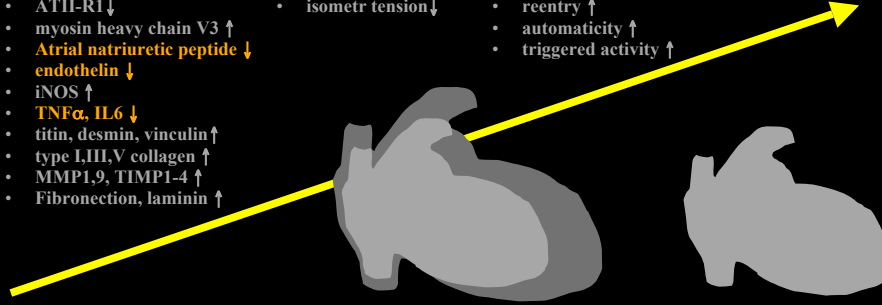
- cell size ↓
- cell # ↑
- cell nucleus # ↑
- DNA repair ↑
- mitochondr mass ↑
- apoptosis ↓
- SR Ca²⁺ release ↓
- peak Ca²⁺_i ↓
- isometr tension ↓

• organ

- cardiac mass ↓
- LVEDP ↓
- LVEDV ↓
- wall stress ↑
- ejection fraction ↓
- force-time integral ↓
- shortening velocity ↓
- fibrosis ↓
- reentry ↑
- automaticity ↑
- triggered activity ↑

• organism

- neurohormoes ↓
- cytokines ↓
- oxygen uptake ↑
- body weight ↓
- endothelial function ↓
- immune competence ↑



dilated cardiomyopathy

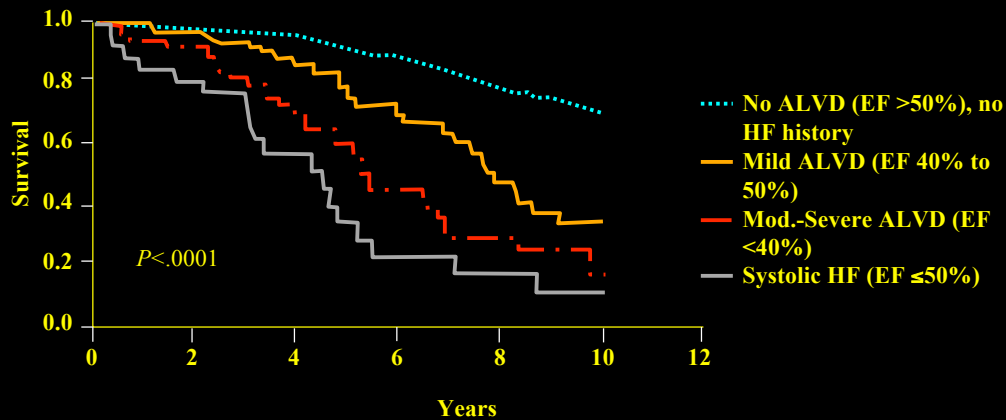
• prognosis

- 1-year survival 10-90%, 5-year survival 50%
- Improved with active therapy

• therapy

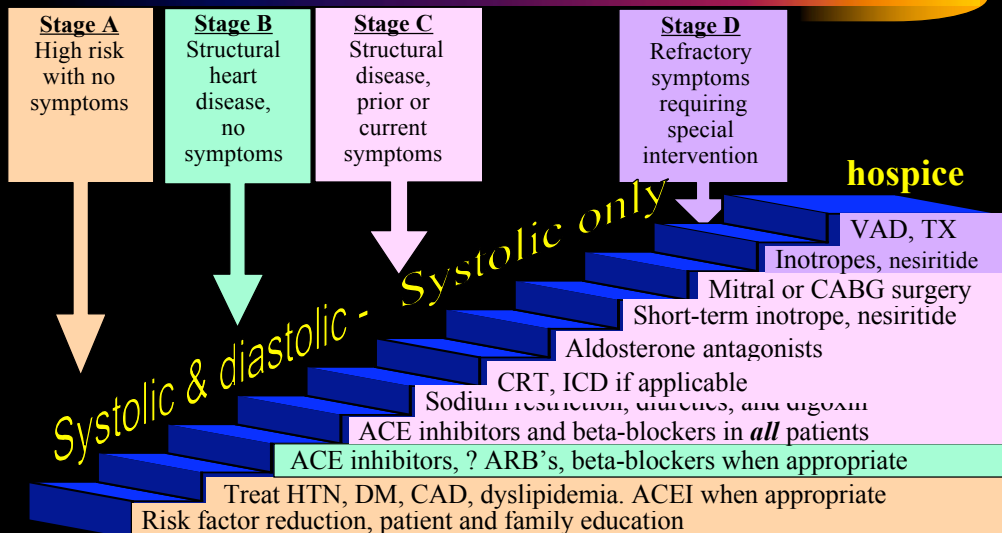
- underlying cause, relief of congestion, augmentation of cardiac output, prevention of arrhythmias and thromboemboli

Framingham Study - mortality



Wang TJ et al. *Circulation*. 2003;108:977

CHF stages and steps of treatment



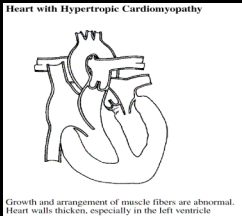
Hunt SA et al. *J Am Coll Cardiol* 2001;38:2101



NYPH Garden

cardiomyopathy phenotypes

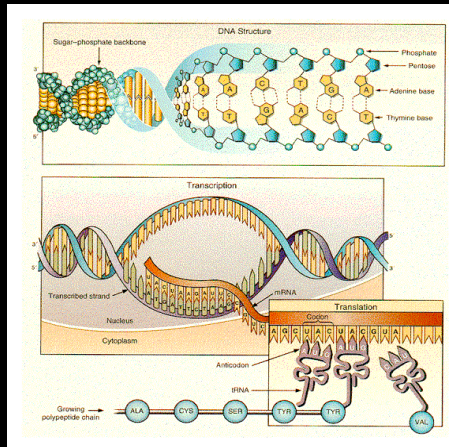
- dilated cardiomyopathy
- **hypertrophic cardiomyopathy**
- restrictive cardiomyopathy



Growth and arrangement of muscle fibers are abnormal. Heart walls thicken, especially in the left ventricle.

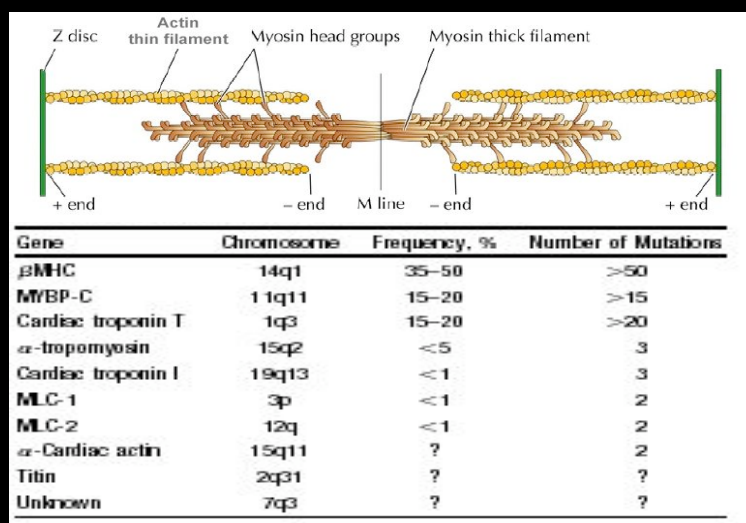
hypertrophic cardiomyopathy genetics

- **autosomal dominant trait**
 - 2/3 of patients have family history
 - more than 200 mutations in 10 genes encoding contractile sarcomeric proteins
 - two genes for non-sarcomeric proteins and mitochondrial genome



Rosenthal N. NEJM 1994;331:39

HCM mutation frequencies



hypertrophic cardiomyopathy

team

patient

initial presentation

- 44 y female
- heart murmur since childhood
- married ,4 kids
- 3/6/06 mitral valve repair & myectomy
- 3/8/06 mitral valve replacement
- complicated postoperative course

follow-up

- good longterm recovery

teaching points

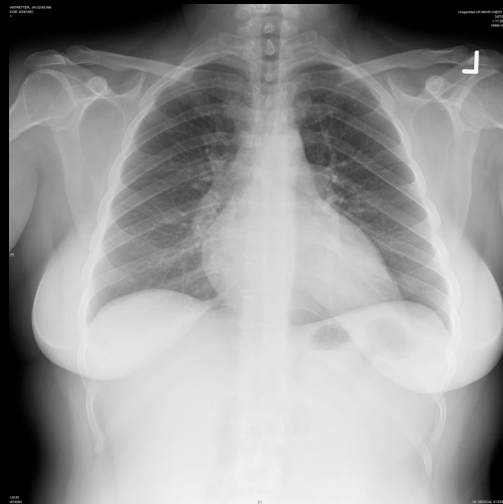
- HOCM surgically challenging

AJ #5015860 *1962 f

Xray hypertrophic cardiomyopathy

team

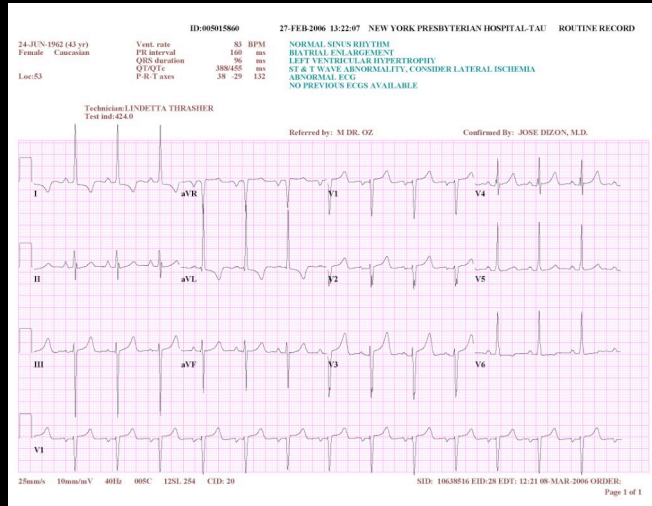
patient



AJ #5015860 *1962 f

ECG hypertrophic cardiomyopathy

team patient

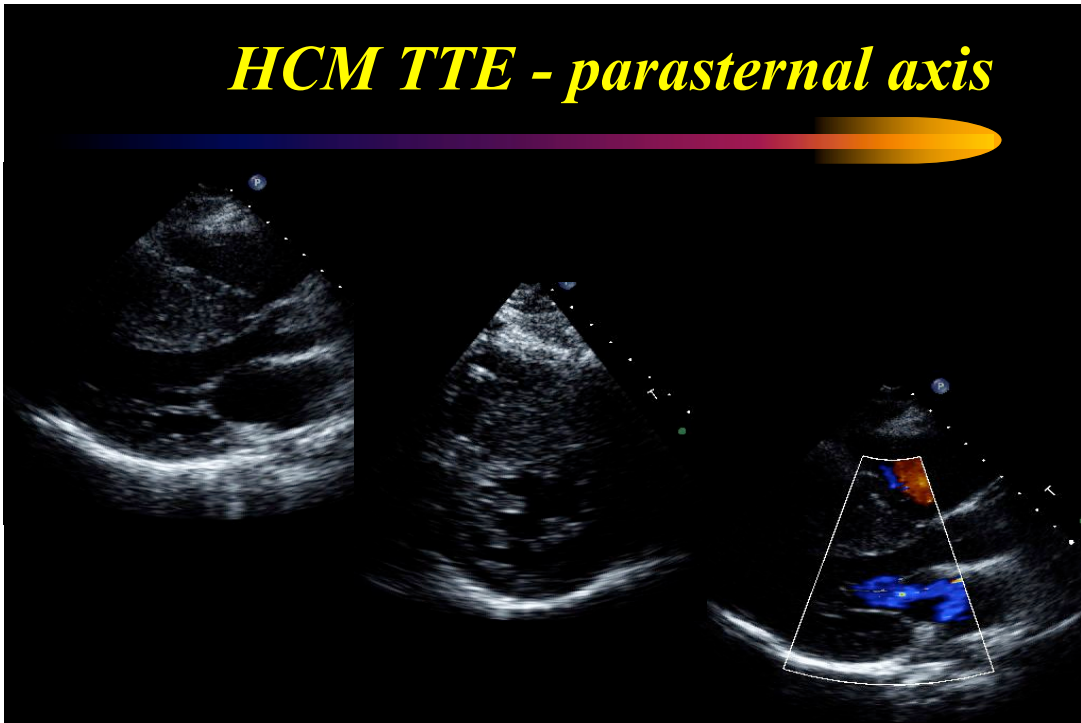


AJ #5015860 *1962 f

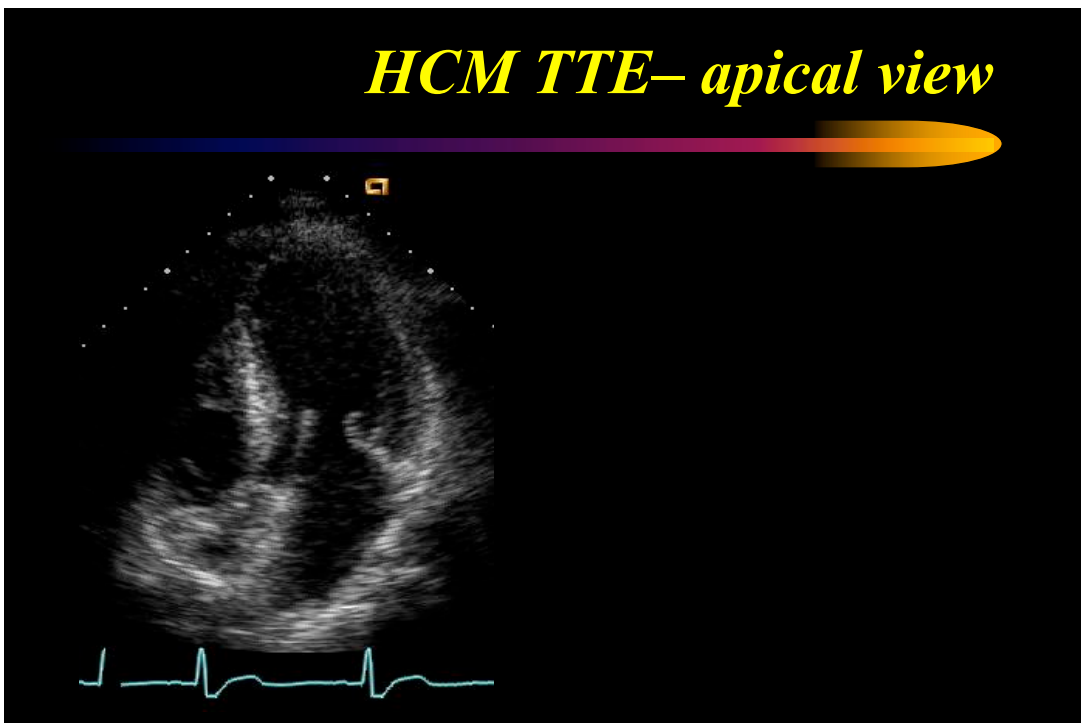
hypertrophic cardiomyopathy

- **history**
 - sudden death during vigorous exercise 1/500, syncope, angina, dyspnea
- **physical exam**
 - S4, systolic murmur (LVOT obstruction – increased by Valsalva, MR)
- **diagnostic tests**
 - X-ray
 - ECG (LAH, LVH)
 - Echocardiogram (asymmetric hypertrophy)
 - Catheterization (LVOT gradient)
 - Genetic testing

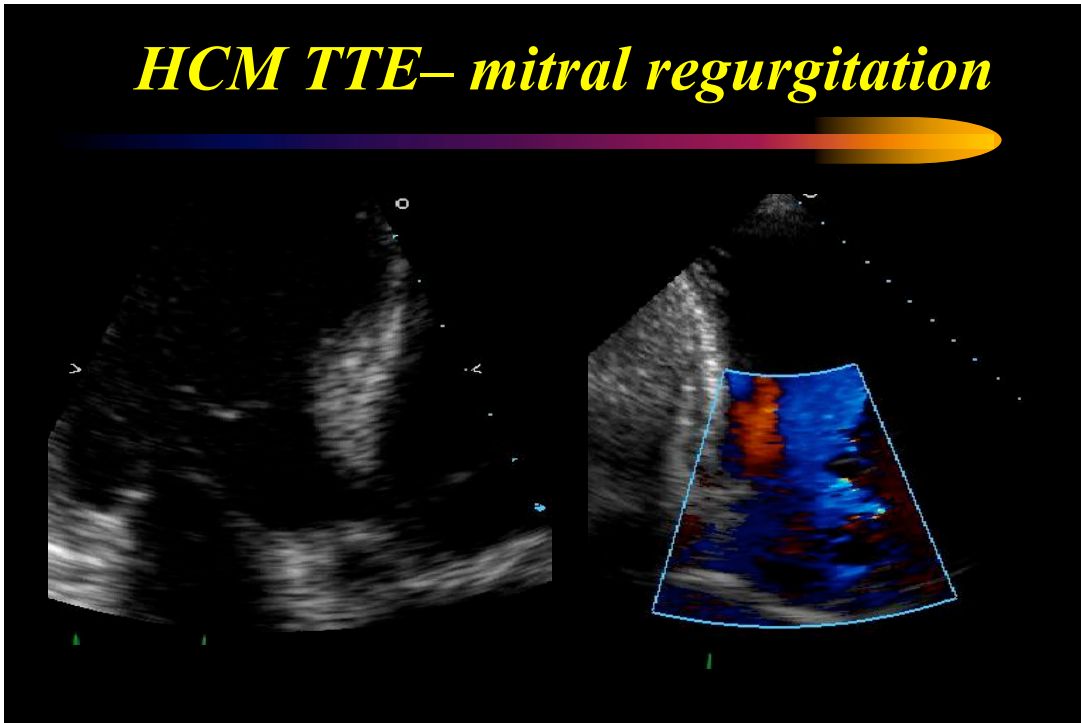
HCM TTE - parasternal axis



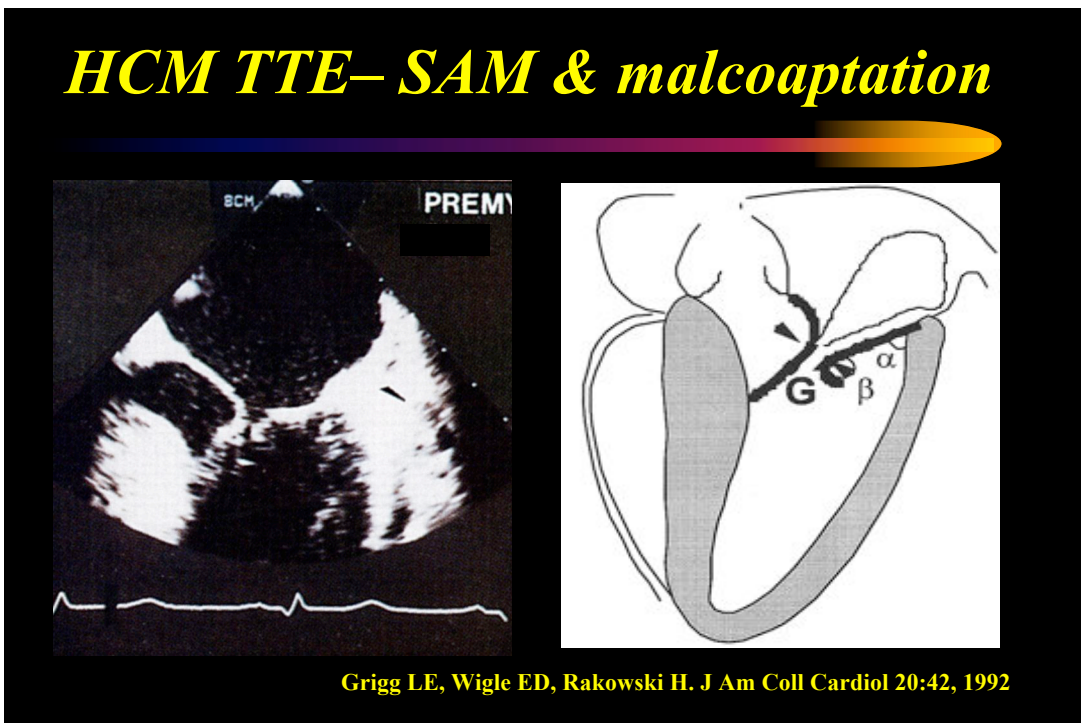
HCM TTE - apical view



HCM TTE– mitral regurgitation

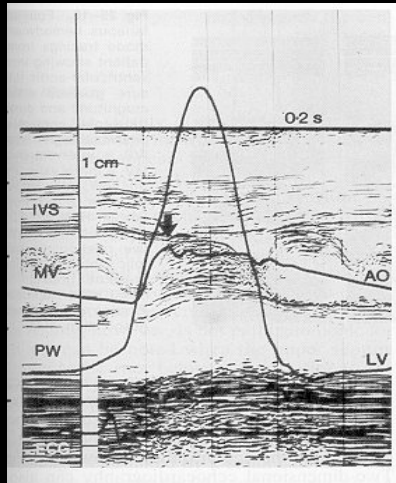


HCM TTE– SAM & malcoaptation



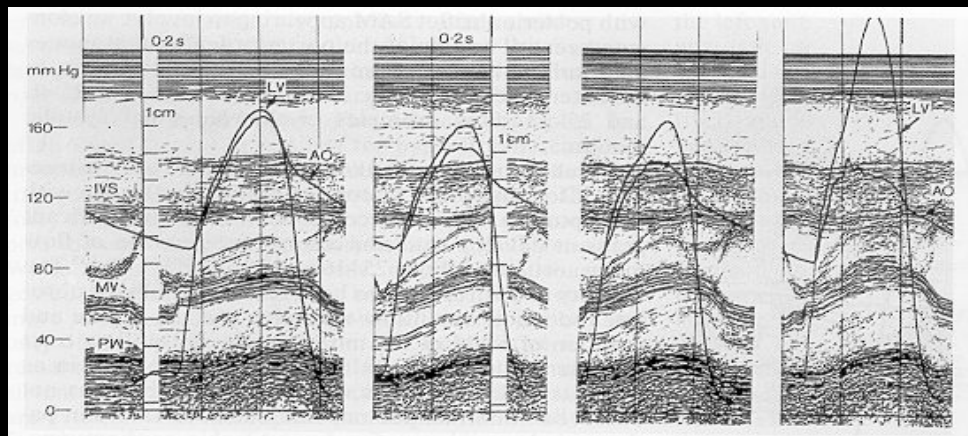
Grigg LE, Wigle ED, Rakowski H. J Am Coll Cardiol 20:42, 1992

HCM TTE– SAM & obstruction



Pollick C, Rakowski H, Wigle ED. *Circulation* 66:1087, 1982

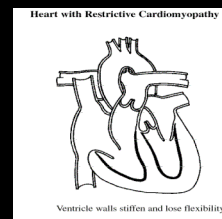
HCM TTE– LVOT obstruction



Pollick C, Rakowski H, Wigle ED. *Circulation* 69:43, 1984

cardiomyopathy phenotypes

- dilated cardiomyopathy
- hypertrophic cardiomyopathy
- restrictive cardiomyopathy



amyloidosis cardiomyopathy

PRIMARY: amyloid light chain (AL)

lambda: kappa = 2:1

SECONDARY: serum amyloid A (AA)

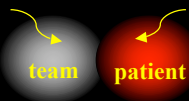
SENILE CARDIAC: (SCA); transthyretin

FAMILIAL: autosomal dominant with mutations in transthyretin, gelsolin, apolipoprotein A-I, lysozyme, or fibrinogen genes.

iron storage disorders

- **Iron overload – Hemosiderosis – following multiple blood transfusions.**
- **Hereditary Hemochromatosis**
 - Autosomal recessive**
 - HFE* gene on chromosome 6**
 - Increased intestinal absorption of dietary iron**

restrictive cardiomyopathy



initial presentation

- 51 y male
- banker, 2 kids
- rapidly progressive heart failure
- heart transplant evaluation
- heart transplantation 2003
- autologous stem cell transplantation (CAMP9)

follow-up

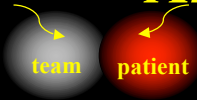
- successful post-heart/stemcell transplant course

teaching points

- amyloid-related cardiomyopathy DD challenging

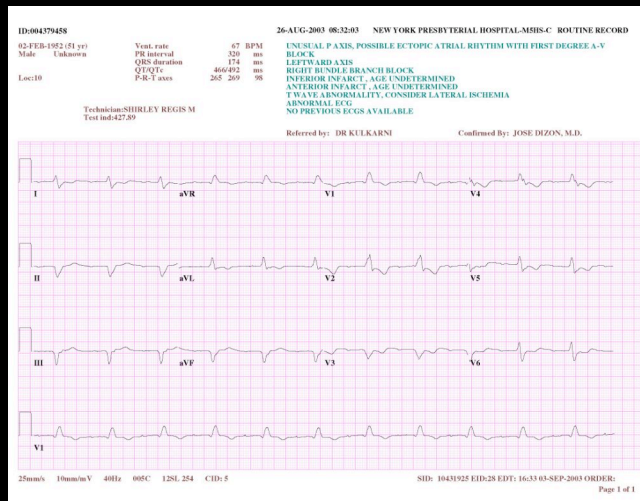
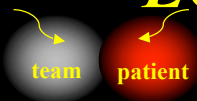
LD #4379458 *1952 m

Xray restrictive cardiomyopathy



LD #4379458 *1952 m

ECG restrictive cardiomyopathy

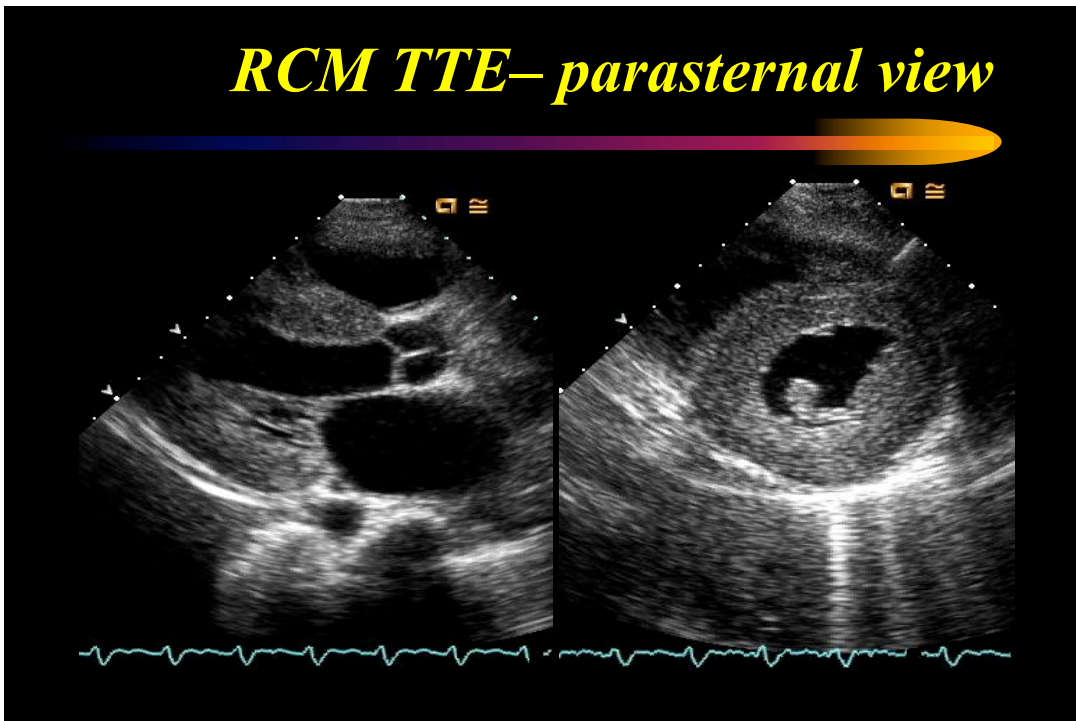


LD #4379458 *1952 m

restrictive cardiomyopathy

- **history**
 - Fatigue, exercise tolerance ↓
- **physical exam**
 - rales, neck veins ↑, ascites, peripheral edema, KUSSMAUL SIGN
- **diagnostic tests**
 - Xray: normal sized heart, congestion
 - ECG: ST/T-changes, a-fib, AB-block, BBB
 - echocardiography
 - endomyocardial biopsy

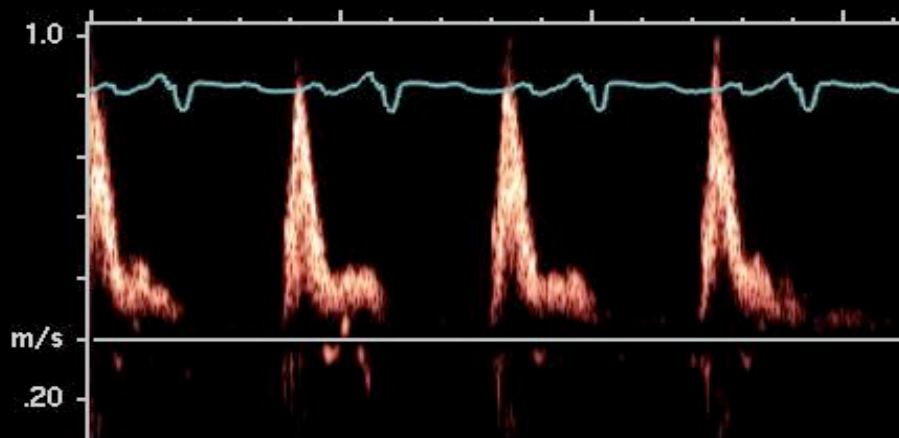
RCM TTE— parasternal view



RCM TTE– apical view



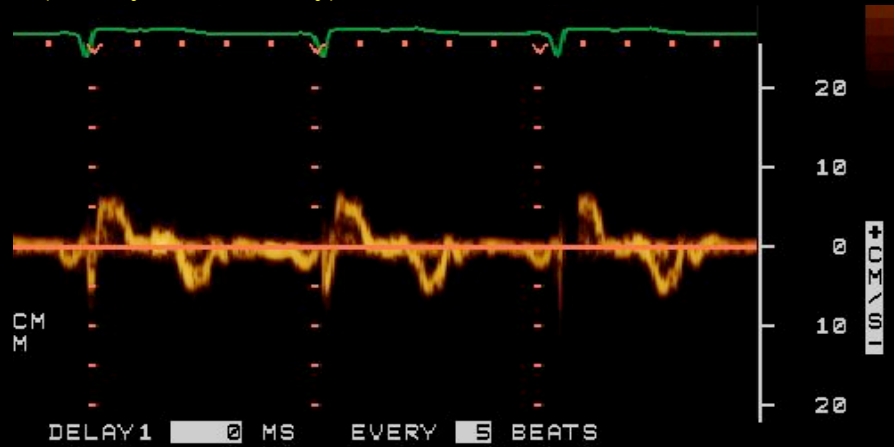
RCM TTE– restrictive mitral filling



Decel time= 102 msec

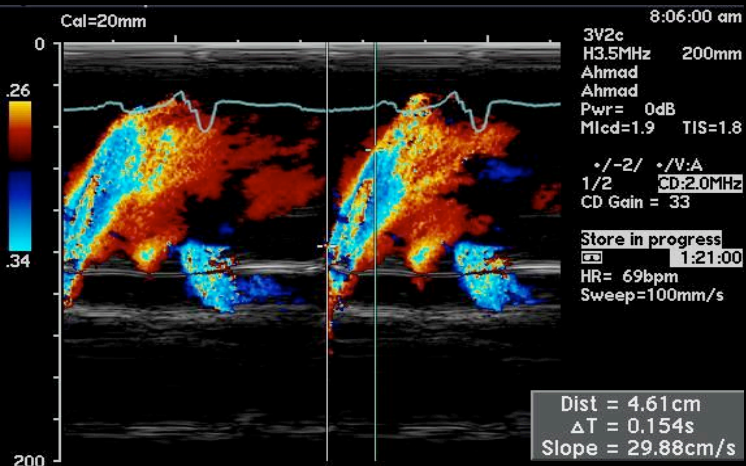
RCM TTE- tissue doppler

- Abnormally low E'
- (Atrial mechanical failure)
- (Low systolic velocity)



RCM TTE- tissue doppler

Impaired relaxation- reduced propagation velocity

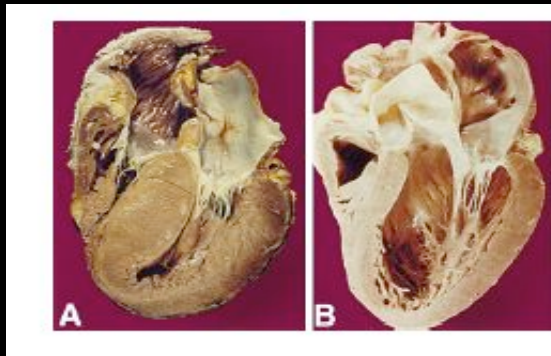




macroscopic pathology

**hypertrophic
cardiomyopathy**

normal



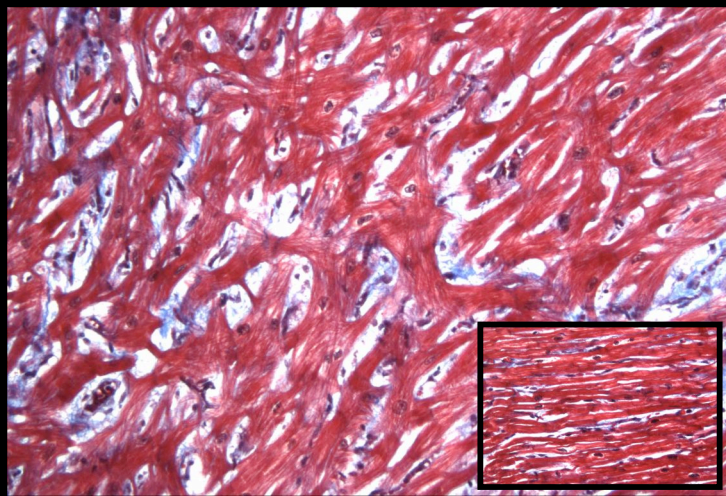
macroscopic pathology

**concentric
hypertrophy**



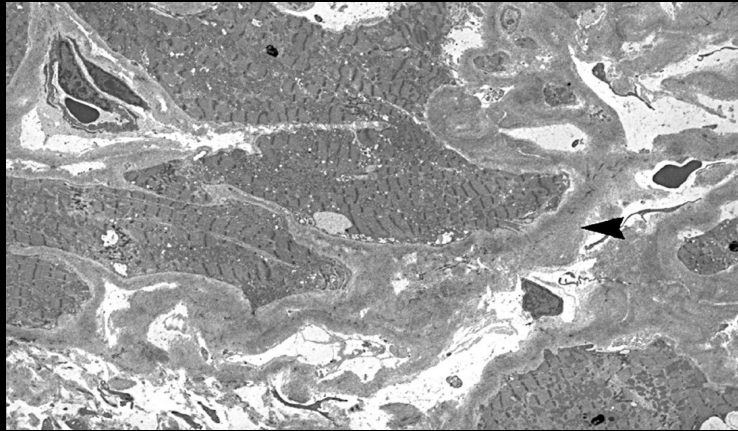
microscopic pathology HCM

**myocyte
disarray**



microscopic pathology amyloid

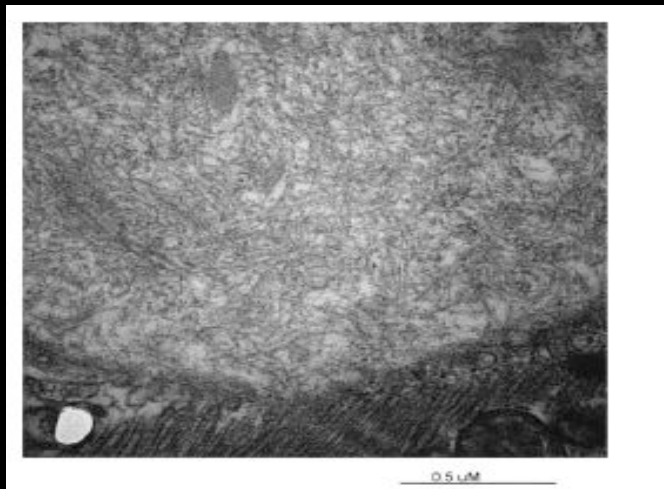
Amyloid encircling
a myocyte
(original
magnification,
x1890)



Mudhar, H S et al. J Clin Pathol 2001;54:321-325

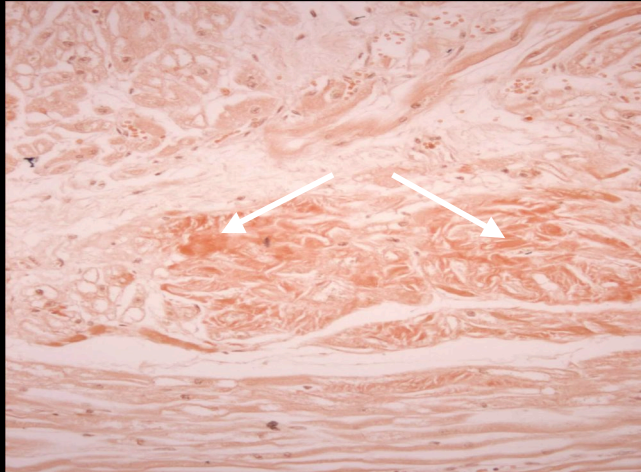
microscopic pathology amyloid

Amyloid: 7-10
nm fibrils
haphazardly
arranged



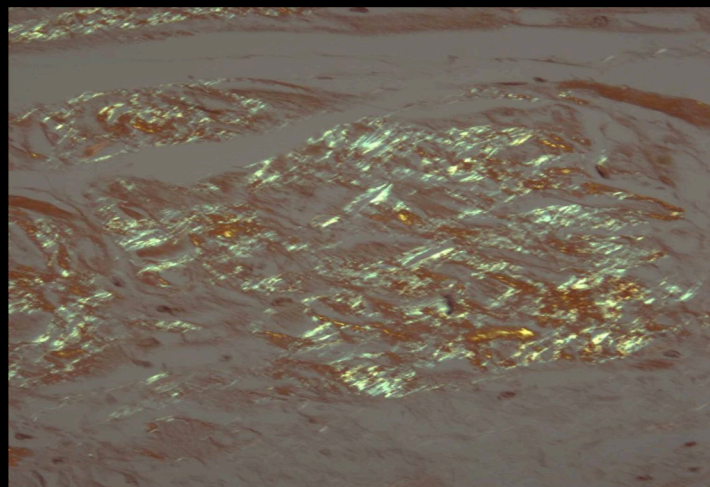
microscopic pathology amyloid

Congo Red stain of amyloid deposits in the heart



microscopic pathology amyloid

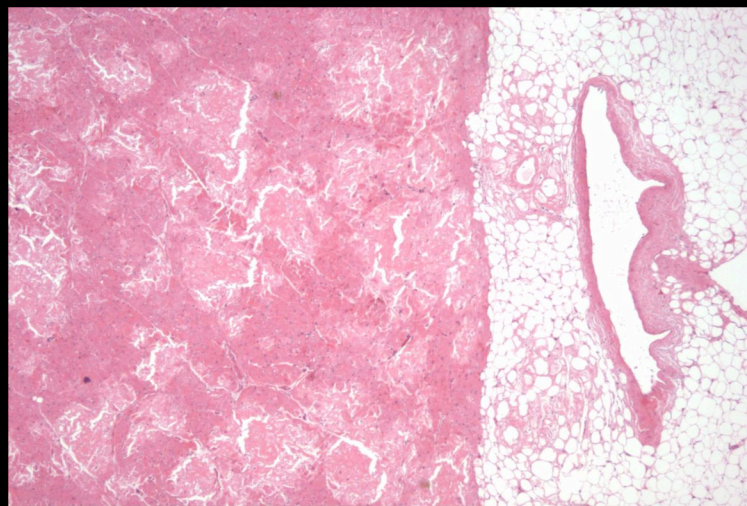
Congo Red stain under polarized light: Amyloid deposits are birefringent.



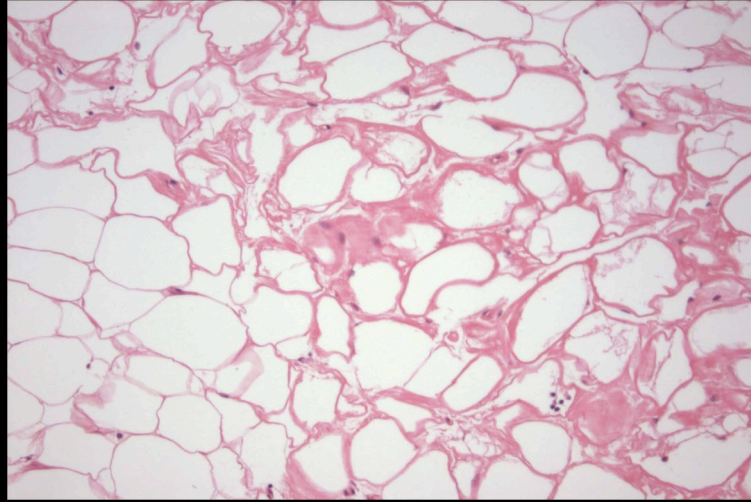
macroscopic pathology amyloid



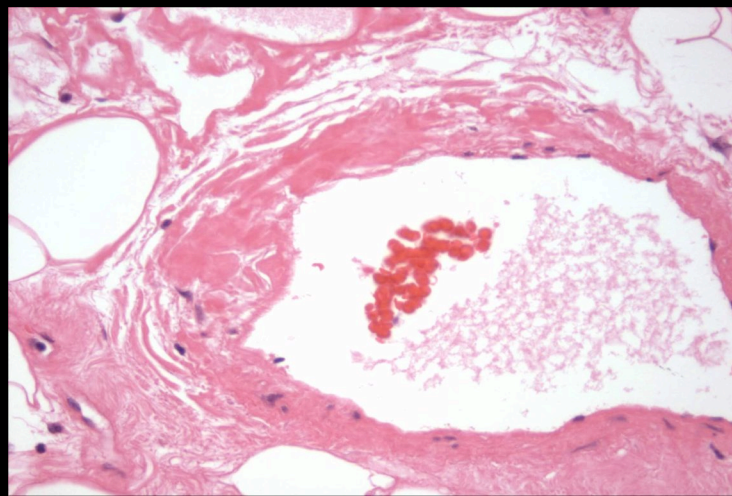
microscopic pathology amyloid



microscopic pathology amyloid

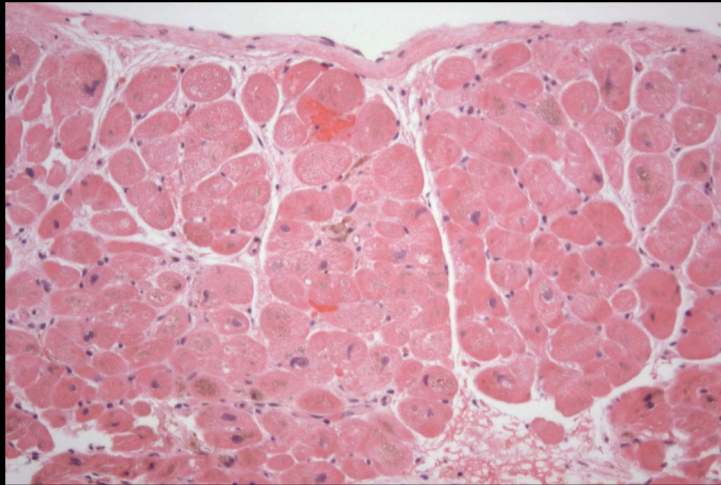


microscopic pathology amyloid



iron storage disease

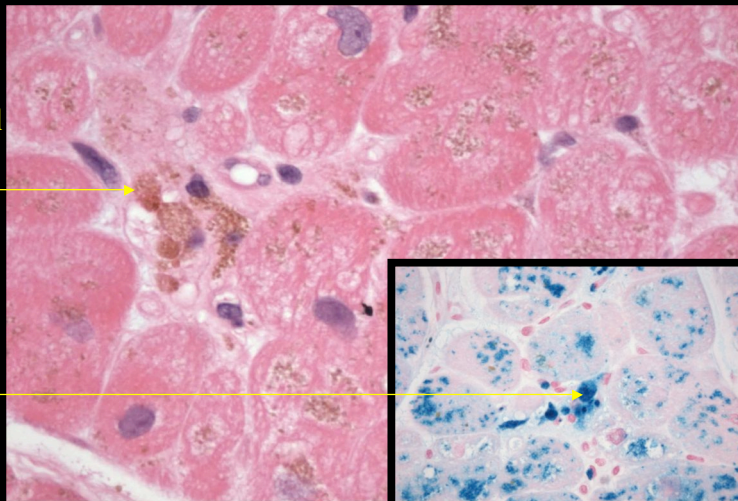
**Endomyocardial Biopsy:
Iron storage disease in the heart**



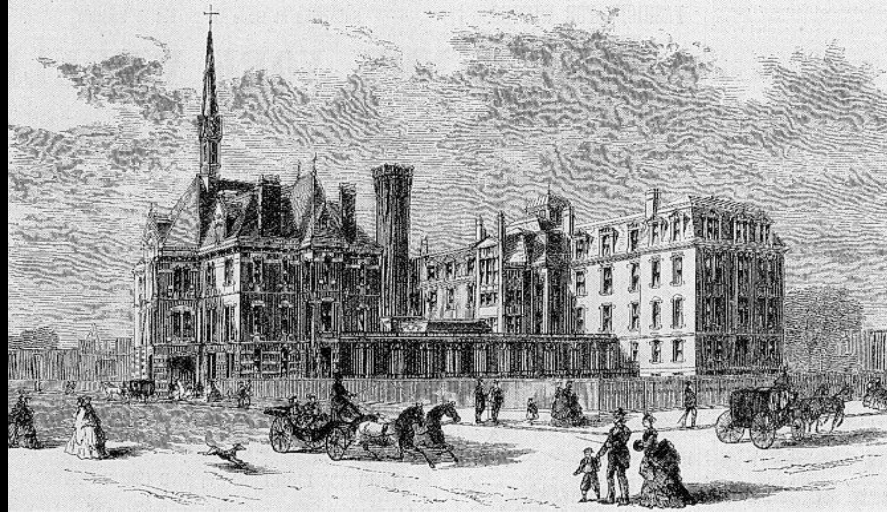
iron storage disease

**Iron deposits
in myocytes
and interstitial
macrophages**

**Prussian Blue
stain: Iron is
blue**



Columbia Presbyterian 1872



hypertrophic cardiomyopathy

- **pathology**
 - asymmetric septal hypertrophy, myocardial fibers in disarray, compensatory hypertrophy and fibroblast proliferation
- **pathophysiology**
 - compliance and relaxation reduced, dynamic LV outflow tract obstruction, abnormal motion of the anterior mitral leaflet
- **etiology**
 - sarcomere complex mutations (β -myosin heavy chain, cardiac trop T, myosin-binding protein C (autosomal dominant mechanism))

restrictive cardiomyopathy

- **pathology**

- abnormally rigid ventricles (not necessarily hypertrophied), endocardial fibrosis or scarring or myocardial infiltration

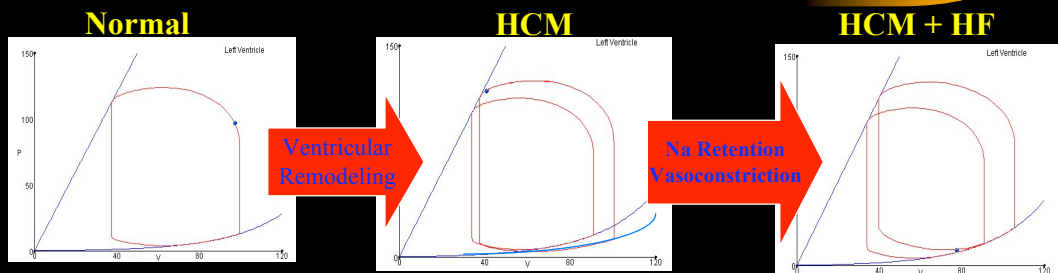
- **pathophysiology**

- upward shift of passive ventricular filling curve > elevated pulmonary and systemic venous pressures
- reduced cavity size > stroke volume/cardiac output ↓

- **etiology**

- infiltrative: amyloidosis, sarcoidosis
- storage disease: hemochromatosis, glycogen storage diseases
- endocardial fibrosis
- hypereosinophilic syndrome
- metastatic tumors
- radiation therapy
- noninfiltrative: scleroderma, idiopathic

decreased filling

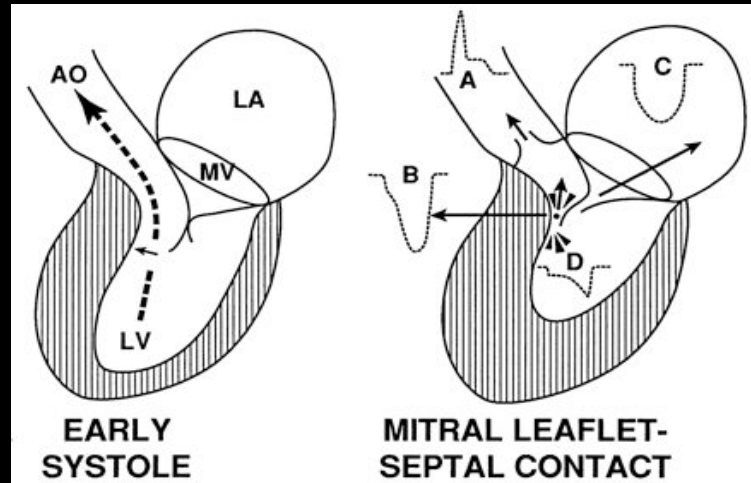


Etiologies

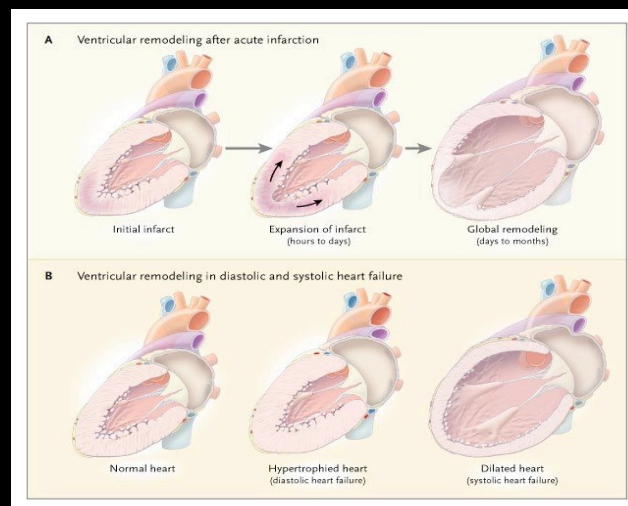
- Mitral Stenosis
- Constriction
- Restrictive Cardiomyopathy
- Cardiac Tamponade
- Hypertrophic Cardiomyopathy
- Infiltrative Cardiomyopathy

Parameter	Normal	HCM	HCM + HF
BP (mm Hg)	124/81	112/74	131/87
SV (ml)	61	57	66
Cardiac Output (L/min)	3.7	3.4	4.0
PCWP (mm Hg)	10	12	27

LV outflow tract obstruction



ventricular remodeling



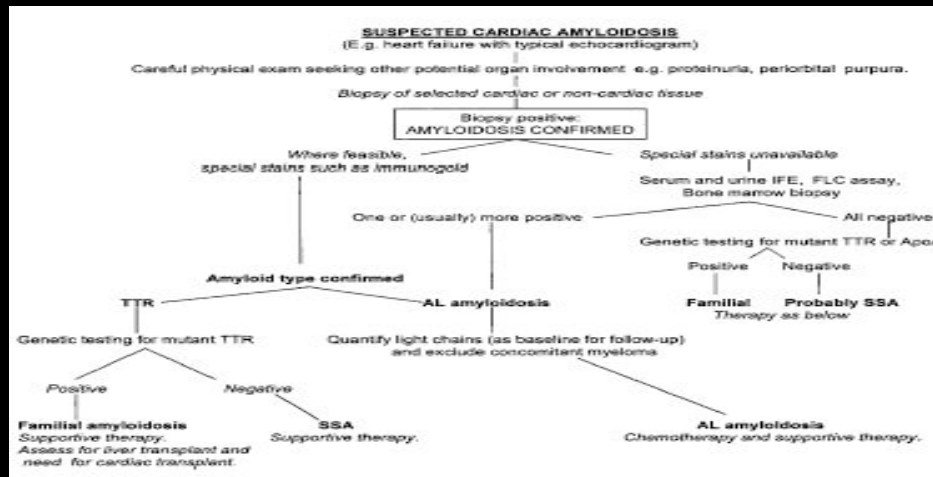
hypertrophic cardiomyopathy

- **prognosis**
 - dependent on mutation
 - Sudden death 4-6% per year (children), 2-4% (adults)
- **therapy**
 - AVOID strenuous exercise
 - B-blockers (myocardial oxygen demand↓, LVOT gradient ↓)
 - CA-channel antagonists
 - amiodarone (a-fib)
 - antibiotic prophylaxis
 - Defibrillator (patient with elevated risk)
 - dual chamber PM
 - Septal ablation with ethanol
 - myomectomy

restrictive cardiomyopathy

- **prognosis**
 - Very poor prognosis
- **therapy**
 - salt restriction
 - diuretics (cautious use)
 - Maintenance of SR
 - Intraventricular thrombus: anticoagulation

amyloidosis management

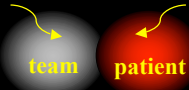


Heart-liver transplantation? Heart-autologous BM transplantation?



**NYPH
Broadway
Entrance**

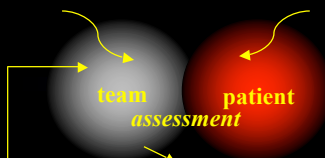
summary cardiomyopathies



<i>phenotype</i>	<i>dilated</i>	<i>hypertrophic</i>	<i>restrictive</i>
history	left heart failure	SOB, cP, syncope	right heart failure
physical exam	S3, S4, MR	S4, valsalva+ murmur	Kussmaul sign
chest Xray	LV enlargement, PVH	LA enlargement	PVH
ECG	SR↑, ST/T, IC abnorm	LVH	low volt, AV cond↓
echo	chamber dilat, regurg	asymm LVH, SAM	LV wall ↑, LVEF ok
cardiac catheter	CAD?, RA/PC↑, CO↓	compl↓, LVOT grad	RA/PC↑, square root
biopsy	r/o myocarditis	DD restrictive	r/o infiltrative
therapy	systolic HF guidelines	BB, CA, cave volume	systemic approach

Braunwald E. Heart Disease (4th Ed). Saunders, Philadelphia

top 10 controversies



end-of-life situation?
yes

comfort care
hospice

no
unsuccessful recompensation?

yes
urgent Htx/
MCSD
ICU

no
ischemia?

med
PCI
CABG

no
chronic neurohorm blockade
& evaluation for
pump failure?

med
resynch/IABP
valve OP/SVER

no
arrhythmias?

med
PM/ICD/abl
antitach OP0

potential Htx or chronic MCSD

floor/home

classification or staging

risk stratification

choice of BB/ACEI

role of added ARB

risks of aldo-antagonists

role of infusion therapy

indication for ICD

indication for CRT

timing of MCSD

selection for Htx

Columbia University Medical Center

