Cardiomyopathy

- Disease of Heart Muscle
- Multiple etiologies from intrinsic vs extrinsic factors
- 3 primary patterns
  - Dilated
  - Hypertrophic
  - Restrictive

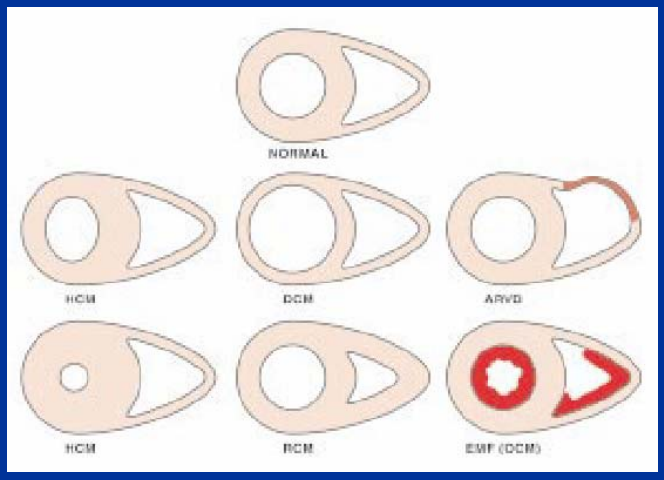
WHO Classification

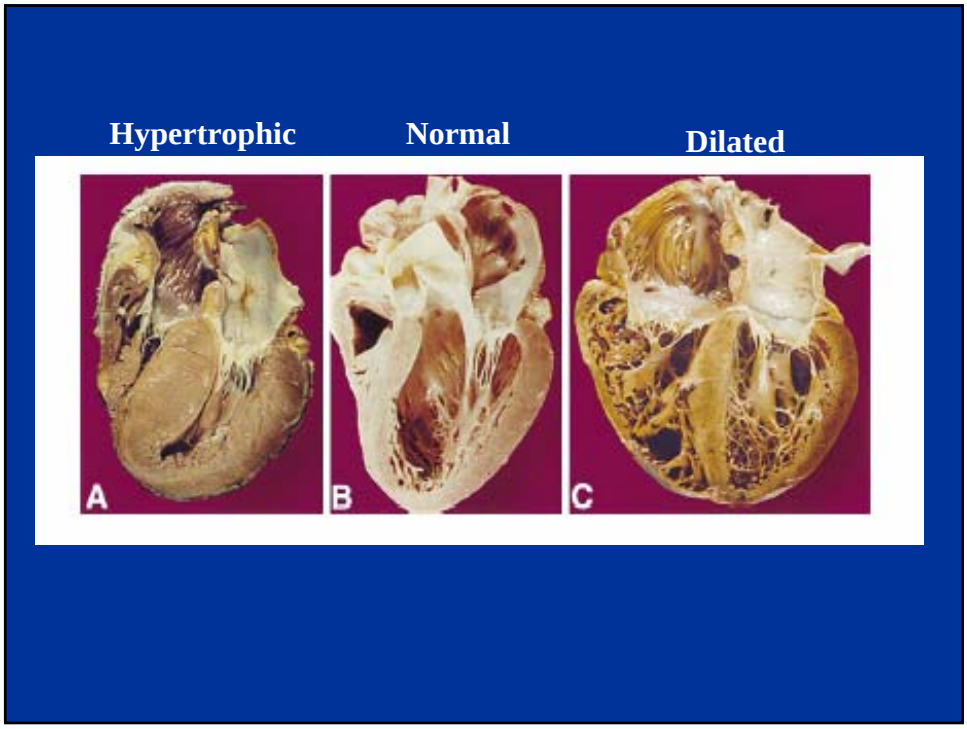
- A. Functional Classification (intrinsic to myocardium)
  - 1. Dilated Cardiomyopathy
  - 2. Hypertrophic cardiomyopathy
  - 3. Restrictive Cardiomyopathy
  - 4. RV Dysplasia
  - 5. Unclassified (Obliterative)
- B. Specific Cardiomyopathies (secondary to external diseases)

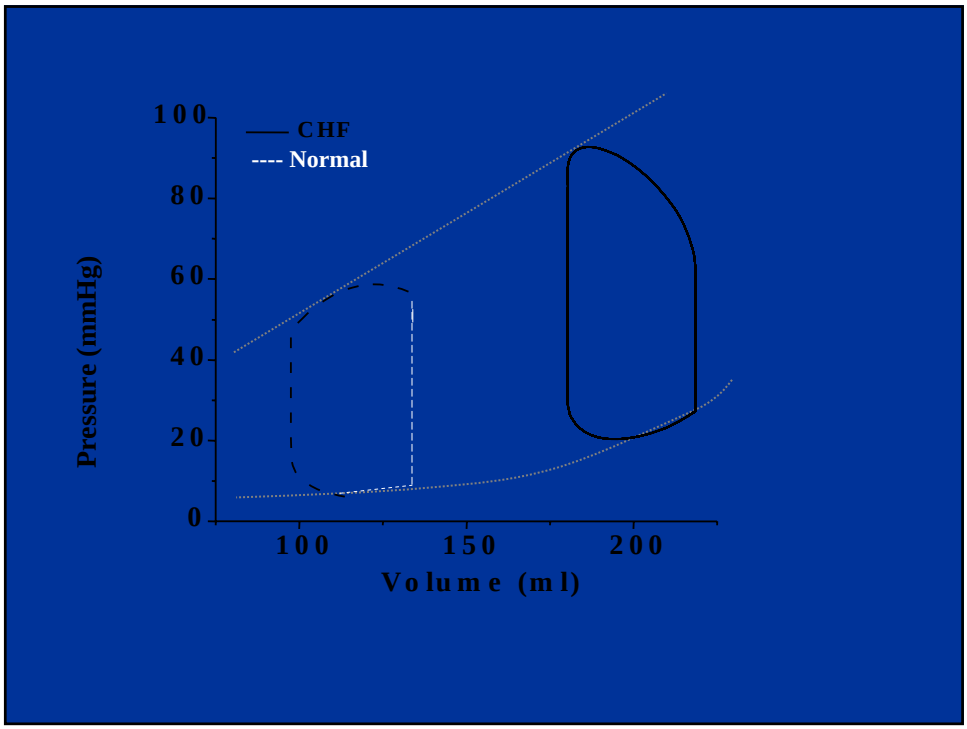
Functional Classification of Cardiomyopathies

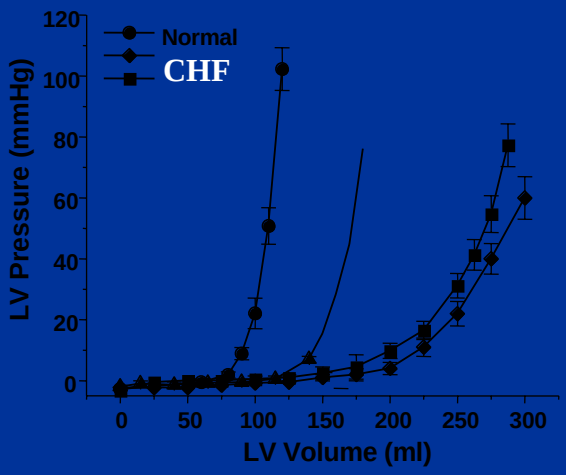
- I Cardiac Dilatation
- II Cardiac Hypertrophy
  - With Obstruction
  - Without Obstruction
- Cardiac Restriction

Normal
X section LV




Hypertrophic
Normal
Dilated
A
B
C


CHF
Normal
Pressure (mmHg)
100
80
60
40
20
0
100
150
200
Volume (ml)



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

Disease	Etiologies	Comment
Infectious Myocarditis:		
Viral	Viruses Coxsackie, Echovirus, HIV, Epstein-Barr virus, Influenza, Cytomegalovirus, Adenovirus, Hepatitis (A&B), Mumps, Poliovirus, Rabies, Respiratory Synctial Virus, Rubella, Vaccinia, Varicella-Zoster, Arbovirus	The most common etiology of infectious myocarditis in North America is viral infection by coxsackie or echo viruses. Most episodes are self-limited and asymptomatic. In patients with symptoms of CHF, acute and chronic viral titers are needed along with endomyocardial biopsy to confirm the diagnosis. In South American, the most common cause of myocarditis is Chagas' disease caused by the bite of the reduviid bug carrying the parasite T cruzi
Bacterial	Bacteria Cornyebacterium diptheriae, Streptococcus pyogene s, Staphylococcus aureus, Haemophilus pneumoniae, Salmonella spp., Neisseria gonorrhea, Leptospirosis, Lyme disease, Syphilis, Brucellosis, Tuberculosis, Actinomycosis, Chlamydia spp., Coxiella burnetti, Myocoplasma pneumoniae, Rickettsia spp.	
Fungal	Fungi Candida spp., Aspergillus spp, Histoplasmosis, Blastomycosis, Cryptococcosis, Cocciodiomyocosis	
Parasitic	Parasites Trypanosoma cruzii, Toxoplasmosis, Schistosomiasis, Trichinosis	

Disease	Etiology	Comment
Infiltrative	Amyloid Sarcoid Hemochromatosis Carcinoid Hypereosinophilic (Loefflers) Glycogen Storage	Myocardial inflammation may be present on biopsy. Routine and special stains are extremely valuable in confirming these diagnoses

Disease	*Etiology*	*Comment*
Hypersensitivity/ Eosinophilic	Antibiotics : sulphonamides, penicillins, cefaclor chloramphenicol, amphotericin B, tetracycline, streptomycin Antituberculous : isoniazide, paraaminosalicylic acid Anticonvulsants : phenindione, phenytoin, carbemazepine, Phenobarbital, Antidepressants: Amitriptyline, Desipramine Anti-inflammatories : indomethcin, phenylbutazone, Oxyphenylbutazone, Diuretics : acetazolamide, chlorthalidone, hydrochlorothiazide, spironolactone Others : methyldopa, sulphonylureas, interleukin-2, interleukin-4, tetanus toxoid	Treatment is discontinuation of the offending agent with or without steroids. Potentially reversible

	Etiology	*Comment*
Toxins	Cocaine, cyclophosphamide, emetine, lithium, methysergide, phenothiazines, interferon alpha, interleuken-2, doxorubicin, cobalt, lead, chloroquine, hydrocarbons, carbon monoxide, anabolic steroids	Potentially reversible for some toxins
Radiation	Past history of lymphoma	
Giant cell myocarditis	Unknown	Generally a fulminant disease with a high mortality. May recur after transplant
Post-Partum Cardiomyopathy	Unknown	CHF onset in last trimester or first 5 months post delivery in patient with no structural heart disease or known cause of CHF.

	Etiology	*Comment*
Genetic	Fabry, Kearns-Sayre Sndrome, Right Ventricular Dysplasia	Patients with RV dysplasia present with ventricular arrhythmias.
Endocrine	Hypothyroidism, Hyperthyroidism, Pheochromocytoma, Acromegaly, Diabetes	
Metabolic	Hypocalcemia, Hypophatemia, Uremia Carnitine	

Clinical Presentation

- Dyspnea (Asthma, unrelenting URI)
- Fatigue
- Arrhythmias (Syncope, Palpitations, Dizziness)
- Chest pain
- Edema
- Febrile illness with SOB

Diagnosis

- Physical Exam: JVD, S3, Rales, Hepatomegaly, edema,
- Labs: Elevated BNP, low serum Na,
- ECHO: key diagnostic tool to help determine etiology of CHF-myocardial disease, valvular, pericardial
- EKG: BBB, acute or old MI, arrythmia
- L heart cath/Endomyocardial Biopsy

Step I Diagnosis:

If **ALL yes** then **probable CHF** which can be admitted to NP/ ward service.

CHF Diagnostic Checklist	YES	NO
Chief Complaint		
Dyspnea		
Vital Signs		
No Symptomatic Hypotension		
No Fever		
No Respiratory Distress		
H&P		
CAD, CHF, HT, Diabetes, ETOH or IV drugs		
JVD, Rales, S3 or Edema		
EKG		
No Arrhythmia		
No Ischemia		
Labs:		
BNP>100		
Troponin normal		
Hematocrit >30		
Creatinine <3		
CXR		
No flattened diaphragms or Emphysematous changes		
Cardiomegaly		
Pulmonary vascular congestion		

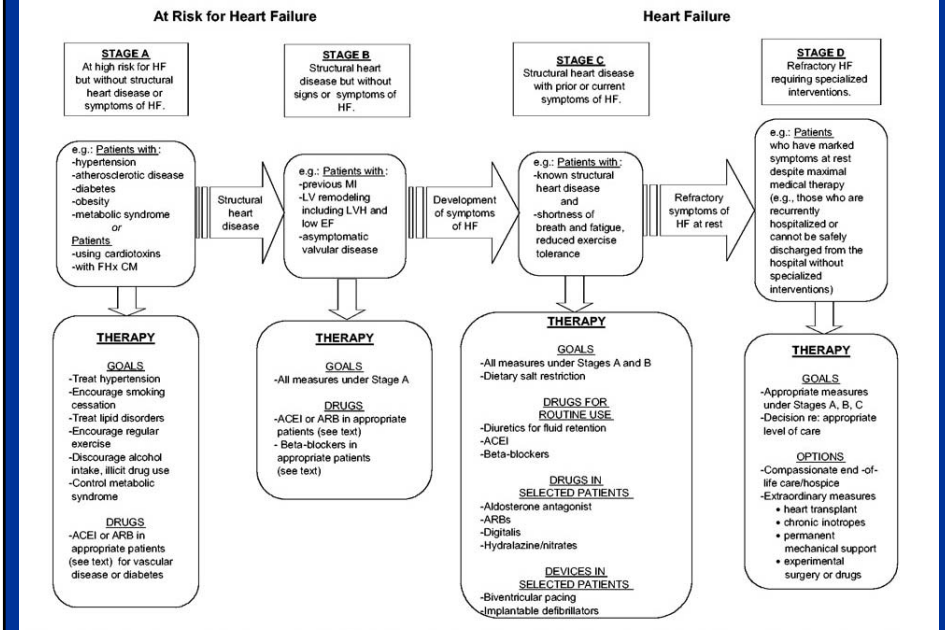
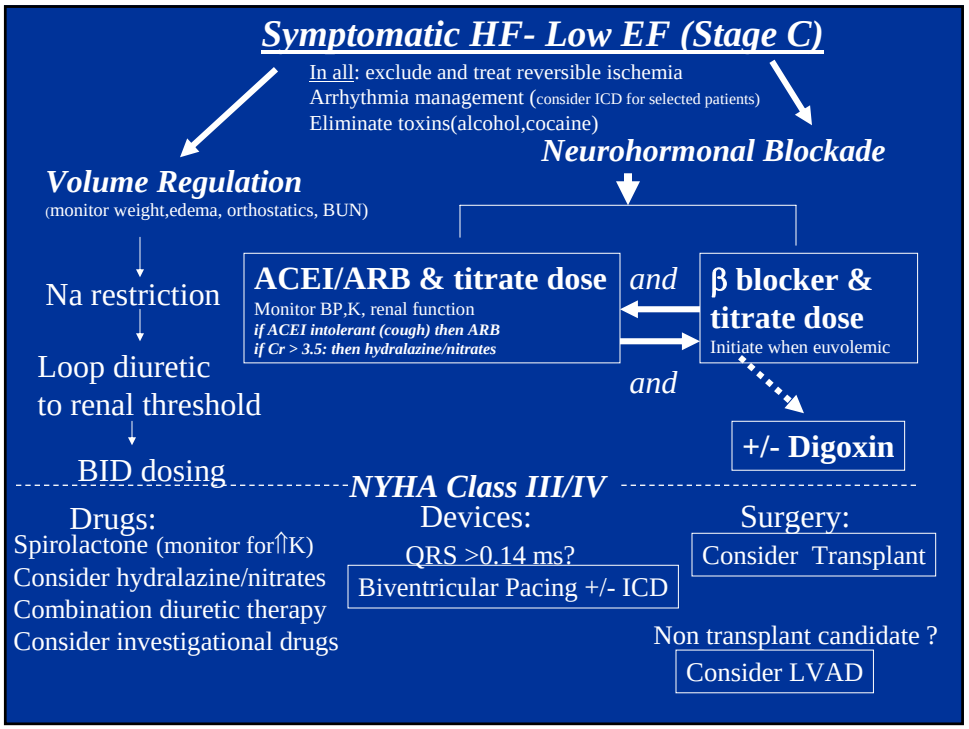


Figure 1. Stages in the development of heart failure/recommended therapy by stage. FHx CM indicates family history of cardiomyopathy; ACEI, angiotensin converting enzyme inhibitors; and ARB, angiotensin receptor blocker.



Diagnoses made by Endomyocardial Bx

1. **Myocarditis**
   - **Giant Cell**
   - **CMV**
   - **Toxo**
   - **Chagas**
   - **Rheumatic**
   - **Lyme**
3. **Toxins**
   - **Doxorubicin**
   - **Chloroquine**
   - **Radiation Injury**
2. **Infiltative**
   - **Amyloid**
   - **Sarcoid**
   - **Hemochromatosis**
   - **Carcinoid**
   - **Hypereosinophilic**
   - **Tumors**
4. **Genetic**
   - **Fabry**
   - **Kearns-Sayre Syndrome**
   - **RV Dysplasia**

Potentially Reversible Dilated Cardiomyopathies

- **Ischemic with viable myocardium**
- **Uncorrected Valvular Disease**
- **Hypersensitivity**
- **Inflammatory**
  - CMV
  - Toxo
  - Lyme
- **Toxic**
  - Alcohol
  - Cocaine
  - Cobalt
- **Endocrine**
  - Hyperthyroidism
  - Pheochromocytoma
- **Metabolic**
  - HypoCa, HypoP
  - Uremia
  - Carnitine
- **Nutritional**
  - Selenium, Thiamine
- **Infiltrative**
  - Hemochromatosis
  - Sarcoidosis

Case #1: Dilated Cardiomyopathy

SA is a 53 year old diabetic, hypertensive black male who was diagnosed with a dilated cardiomyopathy in 1998. Coronary artery catheterization revealed normal coronary vessels with an ejection fraction of 39%. Treatment with enalopril and furosemide was initiated.
The patient did well until 10/00, when he developed increasing shortness of breath and was hospitalized for decompensated heart failure. He was treated with aggressive diuresis and optimization of vasodilator therapy including beta blockade with carvediol. In 11/00, patient developed ventricular tachycardia and required AICD implantation and treatment with amiodarone for recurrent VT. He again presented 1/31/03 with decreasing exertional tolerance, increasing abdominal girth, peripheral edema, and nightly PND. The patient had been compliant with his medical regimen and diet; he denied fever, palpitations, dizziness, blood loss

Dilated cardiomyopathy continued

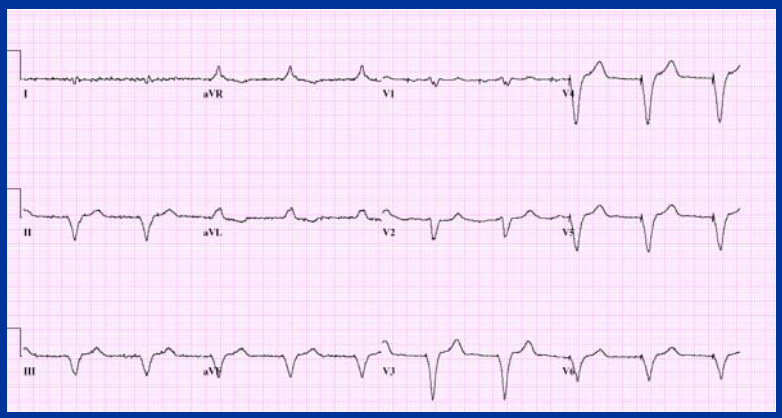
His chronic medical regimen included aldactone 25 mg daily, accupril 20 mg daily, amiodarone 200 mg BID, carvediol 3.125 mg BID, furosemide 160 mg daily, coumadin and glyburide.

Physical exam was notable for: BP of 78/48 mm Hg, pulse 60 bpm, and respirations 20/min; JVD at 15 cm, bibasilar rales, S3 and II/VI holosystolic murmur, hepatomegaly , and +3 pitting pre-tibial edema.

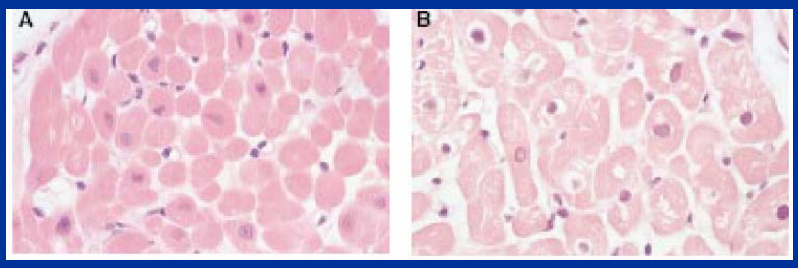
Laboratory data analysis showed a hemoglobin of 10.8 gm/dl, hematocrit 34%, BUN 36, Creatinine 1.8 mg/dl. E
EKG: NSR LVH
CXR: massive cardiomegaly, pulmonary venous redistribution, Kerley B lines, blunting of the costophrenic angles

Dilated cardiomyopathy continued

Hospital Course: He was treated acutely with Milrinone and intravenous diuretics. Right heart catheterization revealed a right atrial pressure of 20, PA 30/17, PCW 19 mm Hg, cardiac output of 1.36 L/min with a pulmonary artery saturation of 36%. Echocardiogram demonstrated 4 chamber enlargement with a left ventricular ejection fraction <20%. He diuresed approximately 20 lbs. Peak VO2 was 10.6 ml/kg/min. He was listed for cardiac transplantation. He was discharged on an increased dose of accupril 20 mg BID and furosemide 160 mg BID. Aldactone was added to the regimen.



Endomyocardial Biopsy in IDCM



Normal

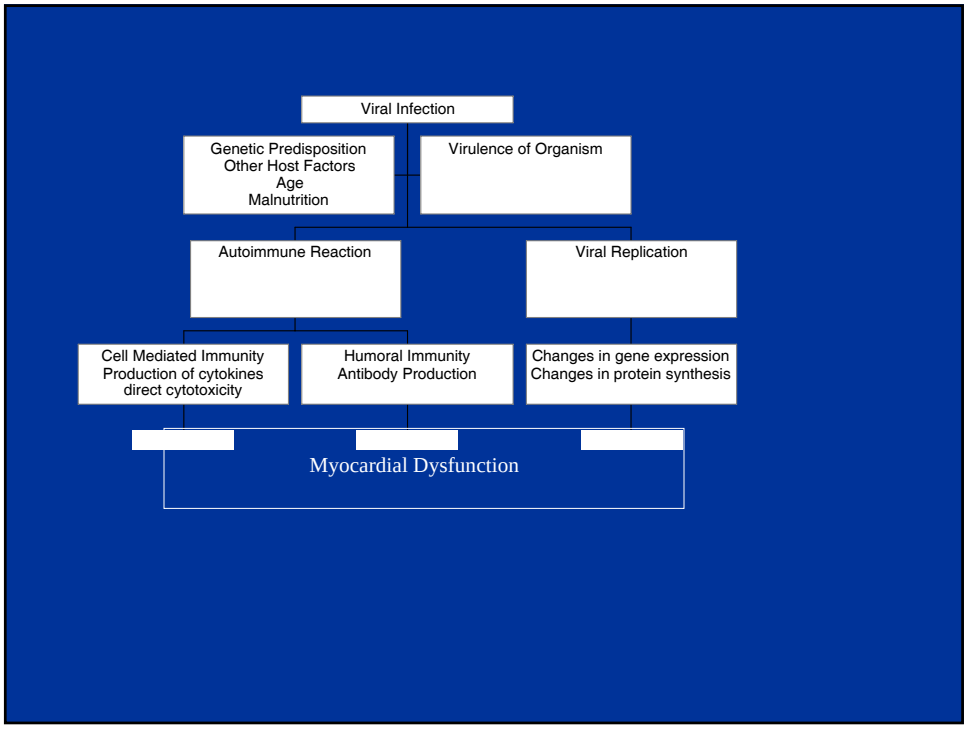
Note: Myocyte hypertrophy with interstial fibrosis

Case #2: Myocarditis

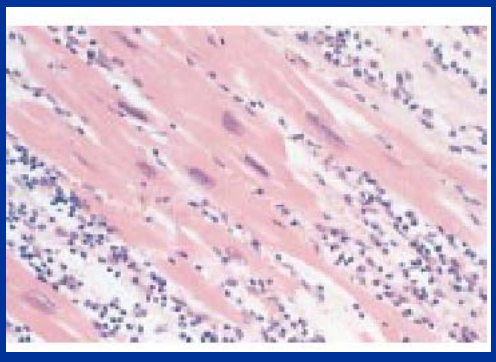
JL is a 31 year old man who presented complaining of malaise, shortness of breath, paroxysmal nocturnal dyspnea,orthopnea, nausea and vomiting. He denied any chest pain, syncope, fevers or chills. Until the day of admission he was in his usual state of very good health, and exercised daily, up to 100 miles bike riding per day.
He was found to be in pulmonary edema with a normal size heart.
Left ventricular ejection fraction was 20% by transthoracic echocardiogram.
There was no family history of heart disease,
no history of drug or alcohol abuse

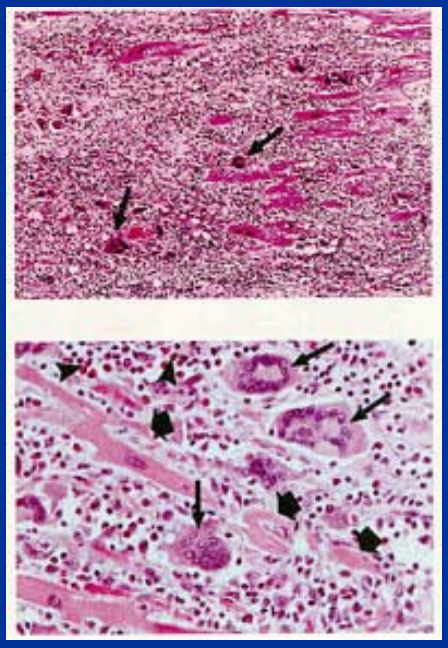
PHYSICAL EXAMINATION:
Temp 101.4 Heart rate 135, blood pressure 91/63, Respiratory rate 32 weight 170 pounds.
On physical examination he appeared pale,
had jugular venous distention,
had bilateral crackles on auscultation of his lungs.
His heart was tachycardic with a regular rhythm and S1-S2 and S3 gallop heart sounds.
He had no peripheral edema.
His abdomen was soft, nontender.
Neurologic exam wasgrossly intact and he was alert, awake and oriented times three.

A left cardiac catheterization performed showed clean coronary arteries.
An endomyocardial biopsy was done



Myocarditis





Giant Cell Myocarditis

Case #3: Restrictive Cardiomyopathy

RZ is a 48 y/o female with a past medical history of Type II diabetes now with progressive shortness of breath and fatigue. 4 months prior to admission, she noted the onset of shortness of breath with exertion. She was seen by her local doctor. Echocardiogram showed a normal ejection fraction with concentric LVH. Patient had no history of hypertension. Over next months despite treatment with diuretics and ACE inhibitors, she had increasing dyspnea on exertion, and lower extremity edema. During the past two weeks she had a severe decrease in exercise tolerance (can walk 1/2 a block and/or 3-5 steps only). She was admitted for new and progressive HF

Medications:
Lasix 40 mg po daily
Lisinopril 20 mg daily
Glucotrol 10 mg po BID

Restrictive Cardiomyopathy continued

PE: T 98.6 P 108 BP 85/70 Weight 130
Well developed female in no acute distress
Skin: multiple eccymoses
HEENT: macroglossia, peri-orbital erythema
Neck: JVD 8cm
Lungs: decreased breath sounds on R about 1/3 way up
Heart: PMI 5th ICS, MCL, S1, S2, S3
Abd; Bowel sounds normoactive, nontender 12cm liver
Ext: 1+edema

Labs:
WBC 8.5 H/H 11/33 Plt 235
Na 135 BUN 45 Cr 2.2
24 hour urine 427 g/day of protein
SPEP: Small monoclonal spike
EKG: NSR, low voltage, poor R wave progression

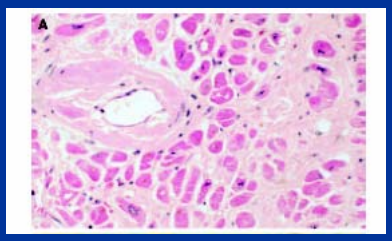
Restrictive Cardiomyopathy continued

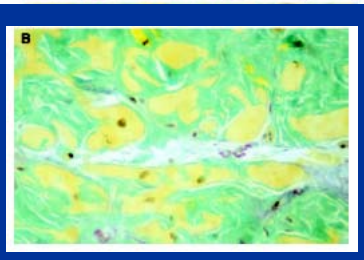
ECHO: Left ventricle is moderately hypertrophied with moderately reduced ejection fraction estimated at 30%. Right ventricle is moderately hypokinetic. Mild mitral regurgitation is seen. Trace aortic regurgitation is seen. Left atrium is moderately dilated. Right ventricular systolic pressure is estimated at 45mmHg.

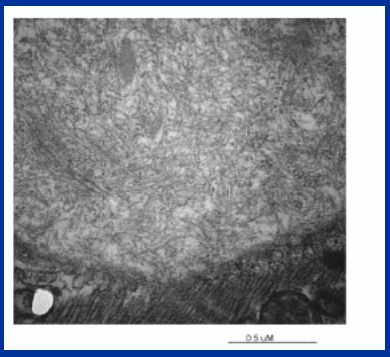
Cardiac Cath: Normal coronary arteries; Left ventriculogram: moderately reduced Lv function with an ejection fraction of 30%, trace mitral regurgitation. Abnormal right heart hemodynamics with an right atrial pressure 8, right ventricular 39/8, pulmonary prtery 40/21 with mean of 26, pulmonary capillary wedge of 21 mm Hg, PA sat 52% left ventricular diastolic pressure is 22. There was no equalization of right and left ventricular end diastolic pressures. Cardiac Output by Thermal Dilution was 2.29 L/min, Cardiac Index 1.25

Fat Pad Biopsy: negative for amyloid.
An endomyocardial biopsy showed diffuse interstitial, perimyocytic, and endocardial infiltrates of amyloid with focal vascular involvement.

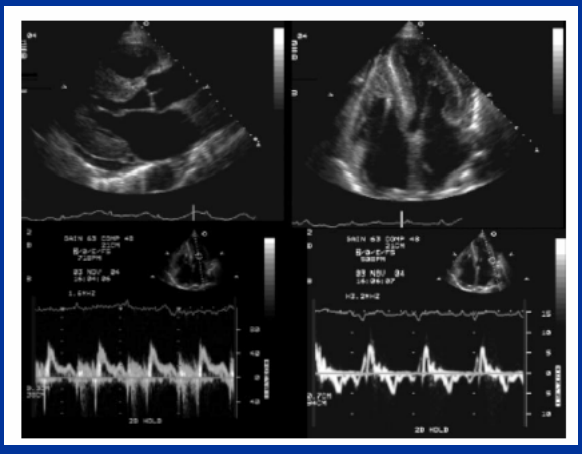
Amyloid



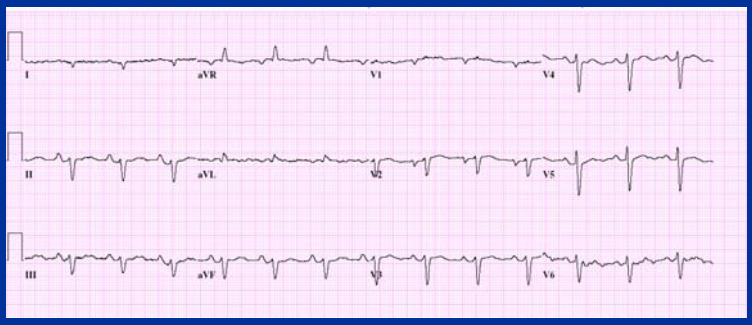




ECHO in Amyloid

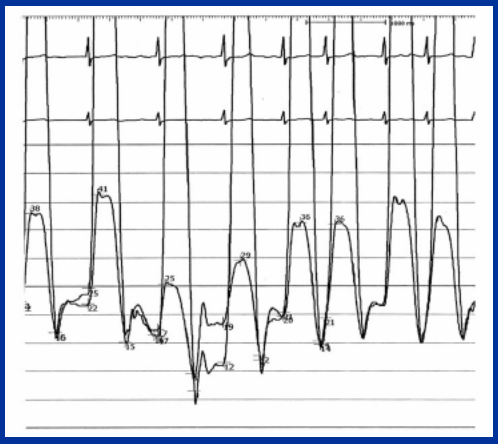


EKG in Amyloid Pt



Note: low volage, Poor R wave progression

Hemodynamic Tracing in Amyloid

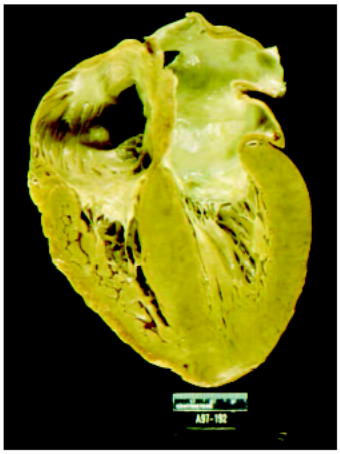


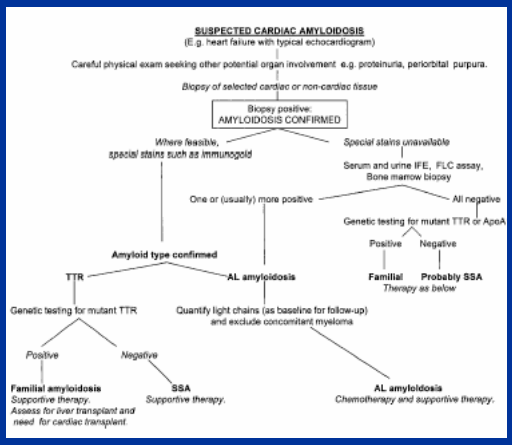
Classification of Amyloidosis

Summary of the Main Forms of Amyloidosis That Affect the Heart

Nomenclature	Precursor of Amyloid Fibril	Organ Involvement	Treatment	Comment
AL	Immunoglobulin light chain	Heart Kidney Liver	Chemotherapy	Plasma cell dyscrasia related to (but usually not associated with) multiple myeloma
		Peripheral/autonomic nerves Soft tissue Gastrointestinal system		Heart disease occurs in 1/3 to 1/2 of AL patients; heart failure tends to progress rapidly and has a very poor prognosis
ATTR (familial)	Mutant transthyretin	Peripheral/autonomic nerve Heart	Liver transplantation ? New pharmacological strategies to stabilize the TTR	Autosomal dominant; amyloid derived from a mixture of mutant and wild-type TTR; if present before, cardiac amyloid may progress despite liver transplantation
AApoA1	Mutant apolipoprotein	Kidney Heart	? Liver transplantation	Kidney disease is the commonest presentation; heart involvement rare
Senile systemic amyloid	Wild-type transthyretin	Heart	Supportive ? New pharmacological strategies to stabilize the TTR.	Almost exclusively found in elderly men; slowly progressive symptoms
AA	Serum amyloid A	Kidney Heart (rarely)	Treat underlying inflammatory process	Heart disease rare and, if present, rarely clinically significant
AANP	Atrial natriuretic peptide	Localized to the atrium	None required	Very common; may increase risk of atrial fibrillation and/or be deposited in greater amounts in the fibrillating atrium

Amyloid





Case #4: Hypertrophic Cardiomyopathy

JF is a 26 yo woman with hypertrophic cardiomyopathy, recurrent syncope and Class IV CHF symptoms admitted now with progressive dyspnea.
She was diagnosed with hypertrophic cardiomyopathy in 1987 following a syncopal event. No other family members had a history of this disorder. Over the years she was treated with calcium channel and beta blockers. A pacemaker was inserted. She was doing well until the past year when she developed increasing dyspnea on exertion and recurrent syncope. An echocardiogram showed asymmetric septal hypertrophy with normal systolic function. Left ventricular wall thickness was 2.5 cm (Nl<1.2 cm). No systolic anterior motion of the mitral valve or left ventricular outflow tract obstruction was observed. Holter monitor revealed no atrial or ventricular arrhythmias. Despite this finding an AICD was placed. Over the past 2 weeks she noted increasing dyspnea on exertion, peripheral edema, nightly PND. Though she had been compliant with her medicines, she was not adherent to a low sodium diet. She was admitted for further management.

Medications:
Lasix 40mg po qd,Toprol XL 150 mg daily

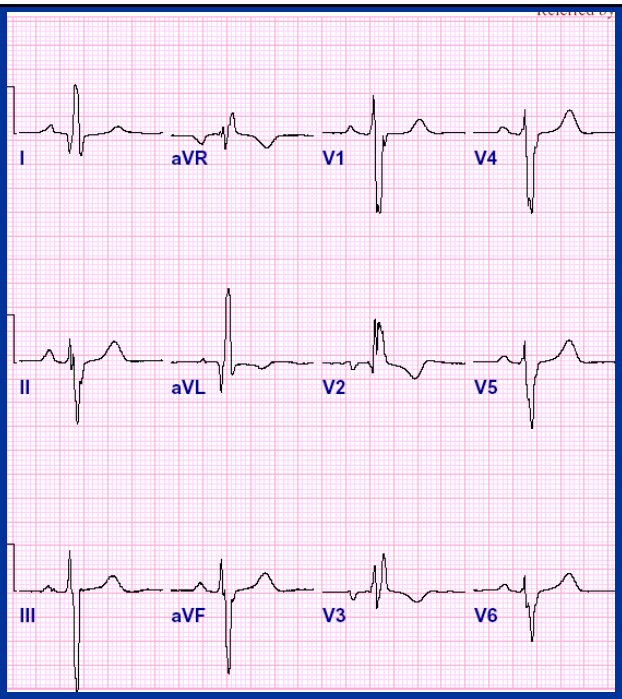
Case #2: Hypertrophic Cardiomyopathy

PE: P 60 regular BP 90/80 RR 32 T 98.6 Wght 190 lb
Well developed young woman mildly dyspneic at rest
Lungs: rales 1/2 way up bilaterally
Heart: PMI 5th ICS MCL, S4,S1,S2, III/VI holosytolic murmur at apex radiating to th e axilla
Abd: Bowel sounds normoactive, soft, mild right upper quadrant tenderness, liver 14 cm span, pulsatile
Ext: 1+ ankle edema
Neck: JVD about 10 cm with v waves

Labs:
WBC 6.5 H/H 13/39 Plt 250,000
Na 135 K 4.5 BUN 20 Cr 1.0
EKG: Predominantly paced rhythm @60; underlying rhythm NSR with LVH
CXR: normal size heart, pulmonary vasculature redistribution

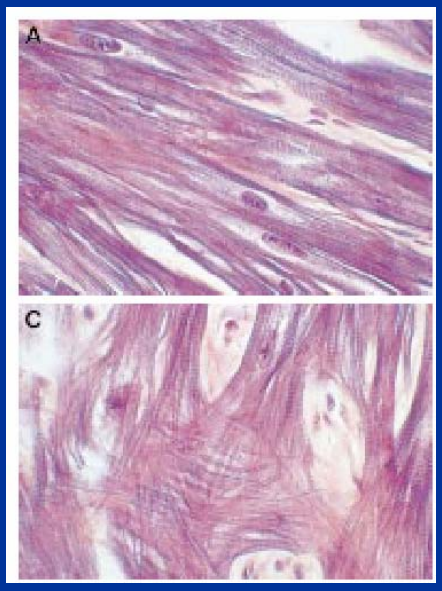
Case #4: Hypertrophic Cardiomyopathy

Hospital course
Patient was treated with IV Lasix and she had a 15 lb diuresis. With minimal exertion she had significant decline in her BP. On telemetry she was noted to have recurrent SVT with near syncope. Her Toprol XL was increased to 200 mg daily. On 4/8 she was noted to be nauseated, hypotensive with BP of 60 systolic, HR of 140 and was transferred to CCU. Her SVT degenerated into v fib. She was resuscitated (200J, 300J, lido) w/ immediate return of mental status. She was loaded w/ procainamide for suppression of atrial tachycardia. AVN ablation was scheduled. During her CCU course, the pt had multiple episodes of tachycardia with no further hemodynamic collapse. On 4/14, the patient underwent successful ablatio n of the AVN w/ stable HR post ablation.



26 yo w HCM

Myocytes aligned parallel



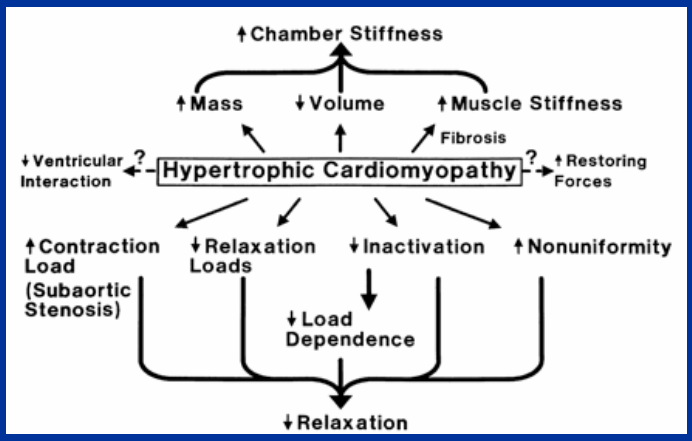
Normal

Myocyte Disarray

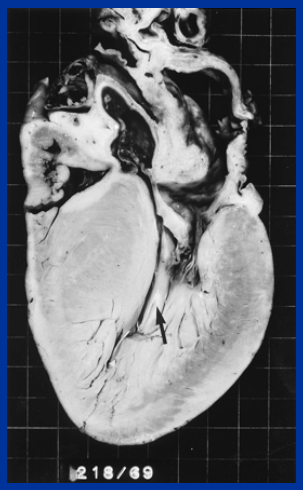
HCM

Hemodynamic Classification of Hypertrophic Cardiomyopathy

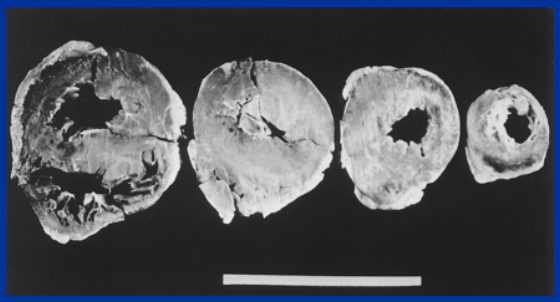
- Obstructive
  - Subaortic
  - midventricular
- Non-obstructive
- Normal or supranormal LV fn
- Impaired systolic function (end stage)



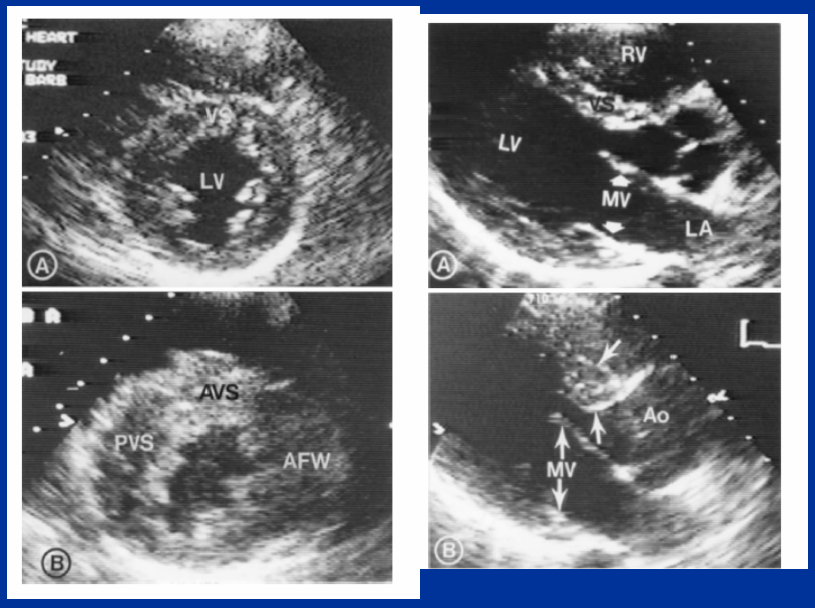
Hypertrophic Cardiomyopathy



Subaortic



Mid-ventricular


HEART
VS
LV
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RV
VS
LV
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AVS
PVS
AFW
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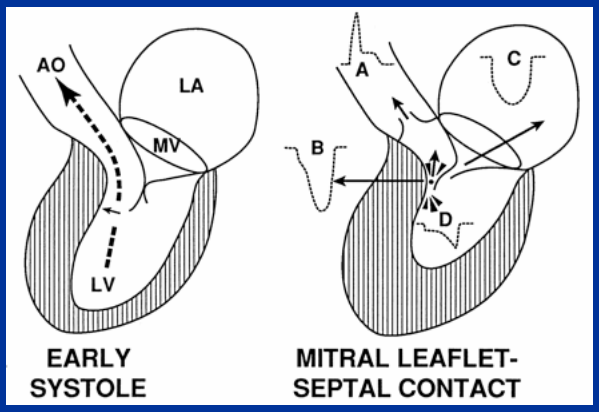
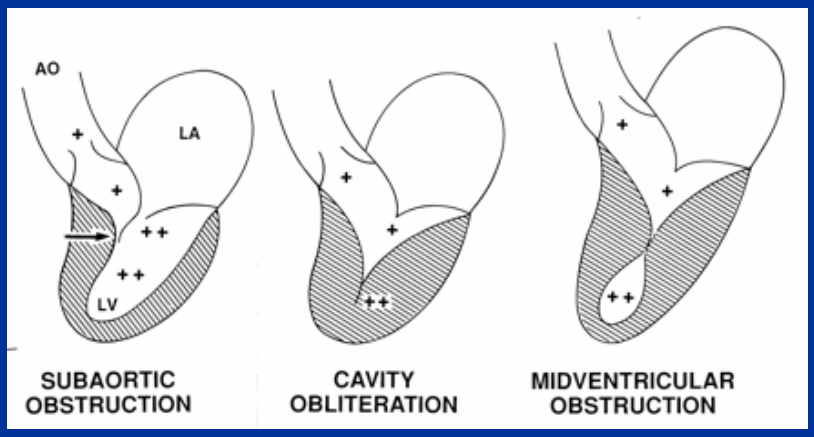
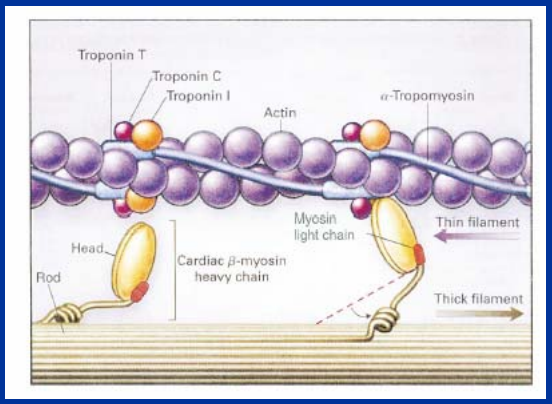
MV
B


AO
LA
MV
LV
EARLY
SYSTOLE
A
C
B
D
MITRAL LEAFLET-
SEPTAL CONTACT


AO
LA
LV
SUBAORTIC OBSTRUCTION
CAVITY OBLITERATION
MIDVENTRICULAR OBSTRUCTION

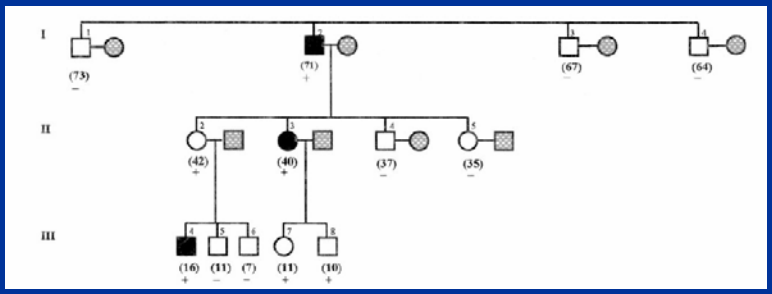

Troponin T
Troponin C
Troponin I
Actin
α-Tropomyosin
Myosin light chain
Thin filament
Head
Rod
Cardiac β-myosin heavy chain
Thick filament

Genetic Mutations in HCM

TABLE 1. HCM Genes and Their Frequencies

Gene	Chromosome	Frequency, %	Number of Mutations
βMHC	14q1	35–50	>50
MYBP-C	11q11	15–20	>15
Cardiac troponin T	1q3	15–20	>20
α-tropomyosin	15q2	<5	3
Cardiac troponin I	19q13	<1	3
MLC-1	3p	<1	2
MLC-2	12q	<1	2
α-Cardiac actin	15q11	?	2
Titin	2q31	?	?
Unknown	7q3	?	?

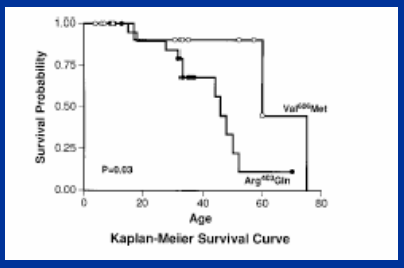
Pedigrees



Survival Curves for Different Mutations of HCM

TABLE 3. Mutations and Prognosis in HCM

	Prognosis		
Gene	Good	Intermediary	Poor
βMHC	Gly256Glu	Arg249Gln	Arg403Gln
	Leu908Val	Glu930Lys	Arg719Trp
	Val606Met	Val606Met	Arg453Cys
	Phe513Cys		Arg723Gly
	Asn232Ser		
Cardiac troponin T	Ser179Phe	Phe110Ile	Arg92Gln
			Arg92Trp
			Ile79Asn
			ΔGlu160
			Ser179Phe (homozygous)
MYBP-C	All unless listed	SASint2O	
α-Tropomyosin	Asp175Asn		
MLC		Insufficient data	



Kaplan-Meier Survival Curve

HCM

- Autosomal Dominant Disease that affects males and females equally
- 50% of the offspring of affected individuals will be at risk for inheriting the gene and developing disease
- In any one family, all members have the same mutation
- Onset of clinical symptoms is delayed until adolescence or early adulthood
- Clinical features are not predictive of Sudden Death but certain mutations are highly predictive of sudden death