Cardiomyopathy

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Magnitude of the problem

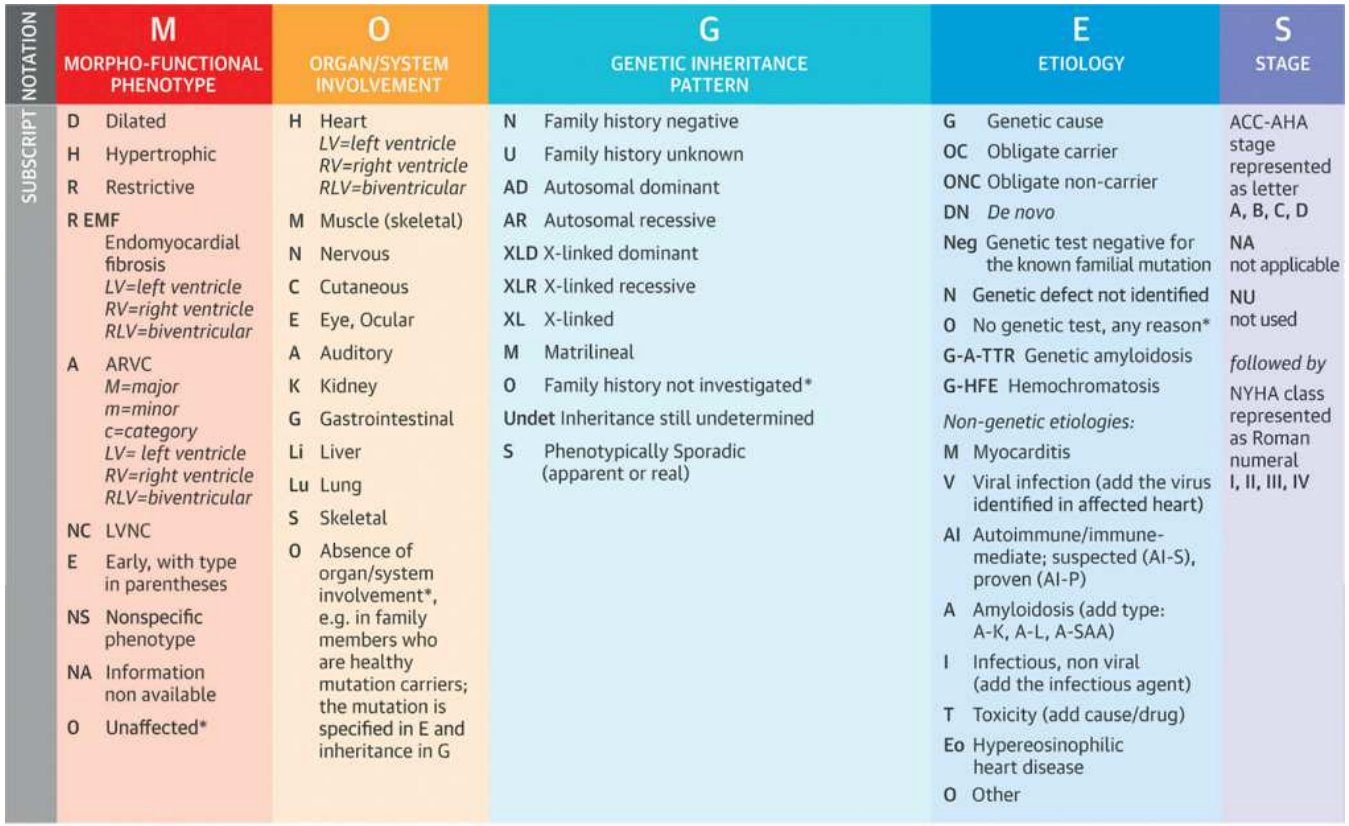
- 3.8% of hospital admissions from emergency departments in the US are for congestive heart failure
- 47% of patients visiting the emergency departments have elevated blood pressure (>140/90)
- Dilated cardiomyopathy is frequently a finding as it is a late stage of hypertensive related disease

Left ventricle function (Summary)

- Systolic dysfunction is the effect of increased preload (volume expansion) on the heart (increasing fiber length to increase tension).
- Eccentric thickening of the left ventricular wall.
- Ejection fraction diminished.
- Diastolic dysfunction is the effect of increased afterload on the heart.
- Concentric thickening of the left ventricular wall.
- Ventricular filling compromised.
- Ejection fraction may be preserved.

Change in position affects dynamics

- Standing decreases preload
- Valsalva maneuver decreases preload
- Decreases left ventricular volume
- Passive leg raising increases preload
- Squatting from a standing position increases preload AND increases afterload
- Hand grip maneuver increases afterload



NOTATION	M MORPHO-FUNCTIONAL PHENOTYPE	O ORGAN/SYSTEM INVOLVEMENT	G GENETIC INHERITANCE PATTERN	E ETIOLOGY	S STAGE
SUBSCRIPT	D Dilated H Hypertrophic R Restrictive R EMF Endomyocardial fibrosis *LV=left ventricle RV=right ventricle RLV=biventricular* A ARVC *M=major m=minor c=category LV= left ventricle RV=right ventricle RLV=biventricular* NC LVNC E Early, with type in parentheses NS Nonspecific phenotype NA Information non available 0 Unaffected*	H Heart *LV=left ventricle RV=right ventricle RLV=biventricular* M Muscle (skeletal) N Nervous C Cutaneous E Eye, Ocular A Auditory K Kidney G Gastrointestinal Li Liver Lu Lung S Skeletal 0 Absence of organ/system involvement*, e.g. in family members who are healthy mutation carriers; the mutation is specified in E and inheritance in G	N Family history negative U Family history unknown AD Autosomal dominant AR Autosomal recessive XLD X-linked dominant XLR X-linked recessive XL X-linked M Matrilineal 0 Family history not investigated* Undet Inheritance still undetermined S Phenotypically Sporadic (apparent or real)	G Genetic cause OC Obligate carrier ONC Obligate non-carrier DN *De novo* Neg Genetic test negative for the known familial mutation N Genetic defect not identified 0 No genetic test, any reason* G-A-TTR Genetic amyloidosis G-HFE Hemochromatosis *Non-genetic etiologies:* M Myocarditis V Viral infection (add the virus identified in affected heart) AI Autoimmune/immune-mediate; suspected (AI-S), proven (AI-P) A Amyloidosis (add type: A-K, A-L, A-SAA) I Infectious, non viral (add the infectious agent) T Toxicity (add cause/drug) Eo Hypereosinophilic heart disease O Other	ACC-AHA stage represented as letter A, B, C, D NA not applicable NU not used *followed by* NYHA class represented as Roman numeral I, II, III, IV

MOGE(S) classification of cardiomyopathies. MOGE(S) classification is inspired by the tumor-node-metastasis (TNM) staging system; it is a descriptive nosology algorithm that includes five descriptors of cardiomyopathies, inherited and noninherited. These five attributes are morphofunctional phenotype (M), organ involvement (O), genetic or familial inheritance pattern (G), etiologic (E) description of genetic defect or nongenetic cause, and the functional status (S) using the American College of Cardiology (ACC)/American Heart Association (AHA) stage (stage A-D) and New York Heart Association (NYHA) class (class I-IV). ARVC, arrhythmogenic right ventricular cardiomyopathy; LVNC, left ventricluar noncompaction. Reproduced with permission from Arbustini E, Narula N, Tavazzi L, et al. The MOGE(S) classification of cardiomyopathy for clinicians. J Am Coll Cardiol. 2014 Jul 22;64(3):304-301.[9]

Table 12-11 Cardiomyopathy and Indirect Myocardial Dysfunction: Functional Patterns and Causes

Functional Pattern	Left Ventricular Ejection Fraction*	Mechanisms of Heart Failure	Causes of Phenotype	Indirect Myocardial Dysfunction (Mimicking Cardiomyopathy)
Dilated	<40%	Impairment of contractility (systolic dysfunction)	Genetic; alcohol; peripartum; myocarditis; hemochromatosis; chronic anemia; doxorubicin (Adriamycin) toxicity; sarcoidosis; idiopathic	Ischemic heart disease; valvular heart disease; hypertensive heart disease; congenital heart disease
Hypertrophic	50% to 80%	Impairment of compliance (diastolic dysfunction)	Genetic; Friedreich ataxia; storage diseases; infants of diabetic mother	Hypertensive heart disease; aortic stenosis
Restrictive	45% to 90%	Impairment of compliance (diastolic dysfunction)	Amyloidosis; radiation-induced fibrosis; idiopathic	Pericardial constriction

*Normal, approximately 50% to 65%.

DILATED CARDIOMYOPATHY

Dilated cardiomyopathy

- 90% of cardiomyopathies
- 60% have associated genetic abnormalities
- 90% autosomal dominant
- May present in infancy with failure to thrive, tachypnea, and diaphoresis
- Else, ages 20-50
- Presents with fatigue, shortness of breath, palpitations, and fluid retention.

Dilated cardiomyopathy

- As myocardial function fails and the heart dilates, cardiac output falls
- Develop decreased exercise tolerance, diaphoresis, and tachypnea.
- As the heart continues to deteriorate, congestive signs such as hepatomegaly and rales develop, and a prominent gallop can be appreciated on examination.
- Systolic dysfunction

Dilated cardiomyopathy

- DCM is characterized by the presence of dilatation and systolic impairment of the left or both ventricles
- Unexplained by abnormal loading conditions
- Unexplained by coronary artery disease sufficient to cause the observed myocardial dilation and dysfunction
- There is ventricular chamber enlargement and systolic dysfunction with normal left ventricular (LV) wall thickness
- Is the end phenotype of heart muscle damage

Clinical diagnosis

- The PMI is laterally displaced and is diffuse.
- S3, S4 and regurgitation murmurs can be present
- Clinical diagnosis requires evidence of systolic dysfunction as demonstrated by a depressed left ventricular ejection fraction (EF) and evidence of left ventricle dilatation
- Generalized cardiomegaly without increased pulmonary vascular markings on chest x-ray

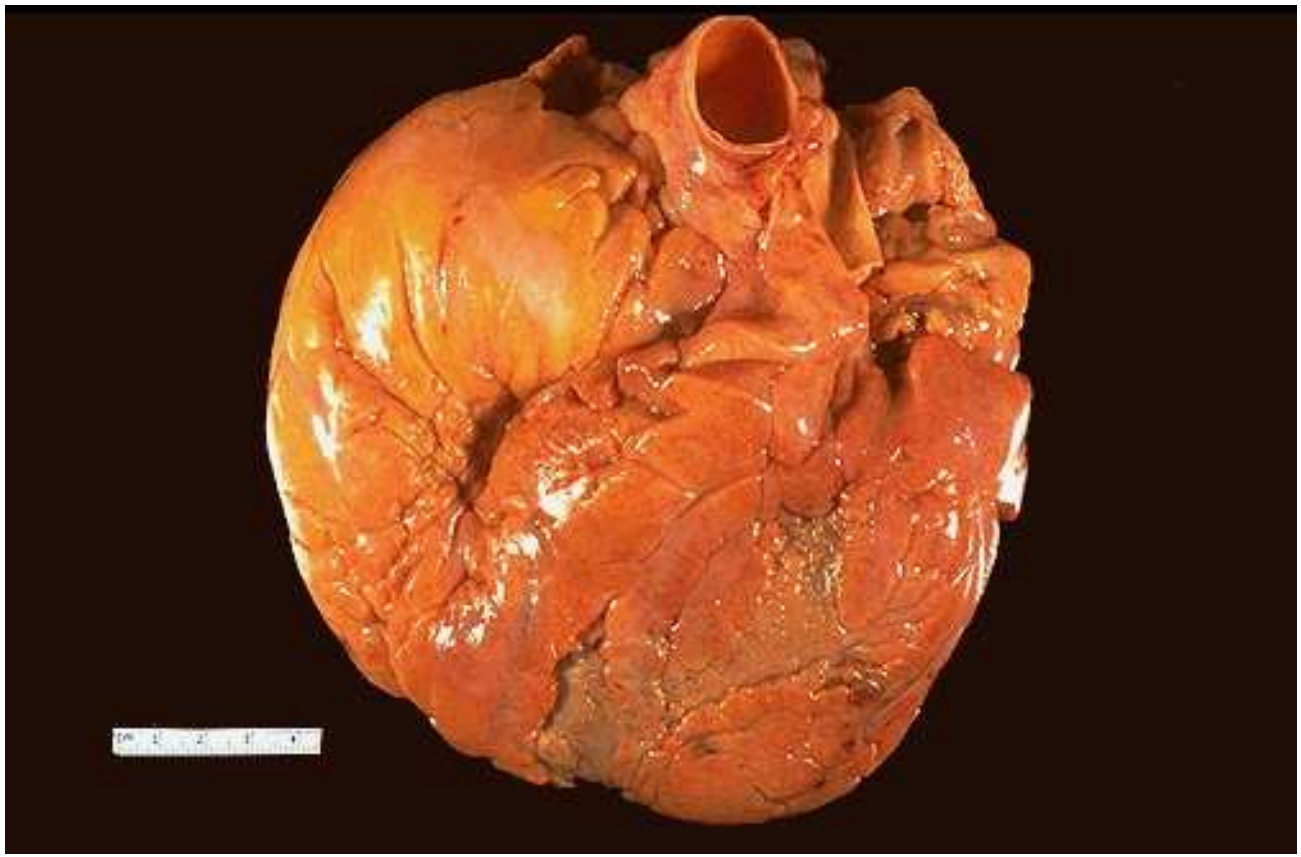
Testing

- Coronary angiography is routinely performed to exclude coronary atherosclerosis
- Both DCM and coronary artery disease may co-exist in the same patient
- Cardiac magnetic resonance may reveal evidence of hyper-trabeculation or left ventricular non-compaction
- Cardiac catheterization is useful to evaluate hemodynamic status and coronary artery anatomy.
- Endomyocardial biopsies can aid in diagnosis
- Etiologic diagnosis not apparent in 30%

Treatment

- Treat with afterload reducing agents and diuretics
- β-blockers not helpful in children
- May require cardiac transplant

Dilated cardiomyopathy



Globular appearance as all chambers are dilated.

https://webpath.med.utah.edu/CVHTML/CV117.html
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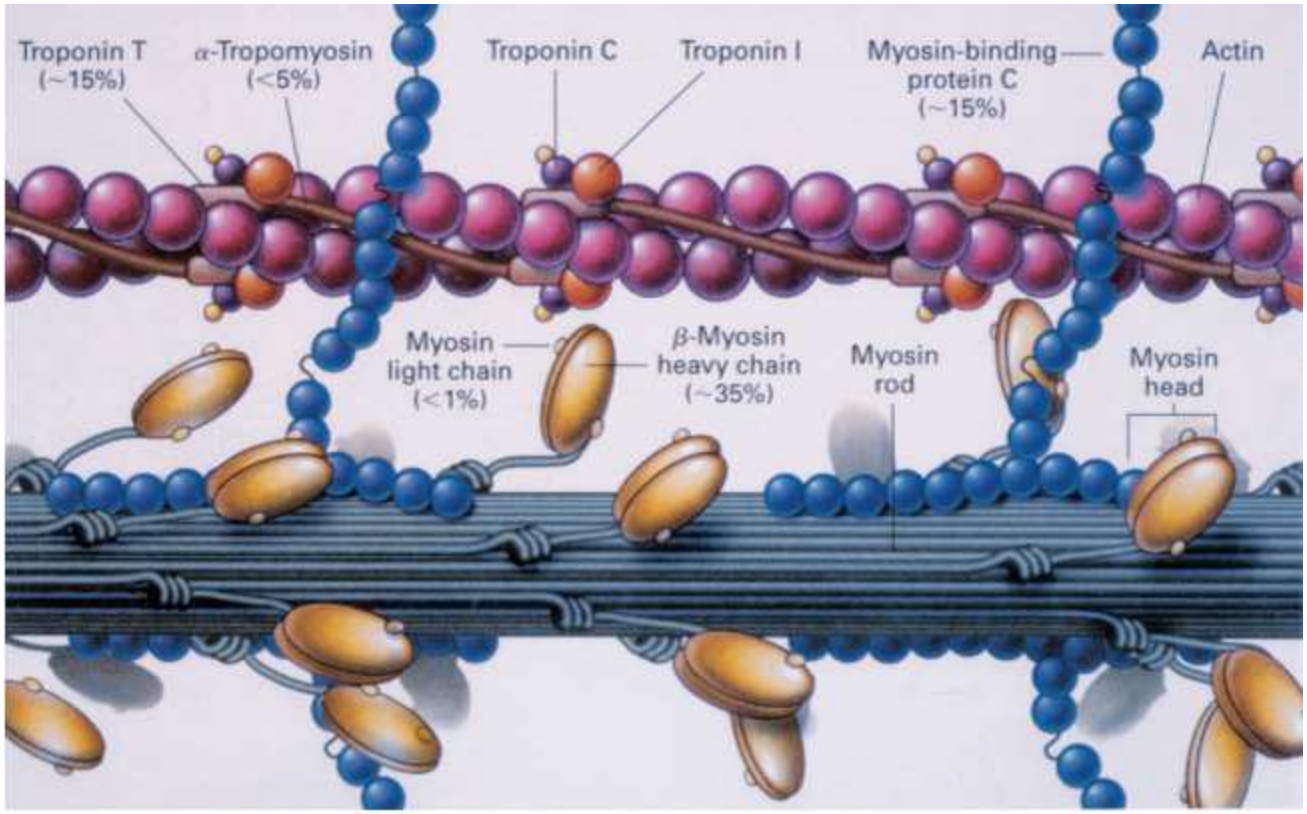
Sarcomeric proteins involved in cardiomyopathies



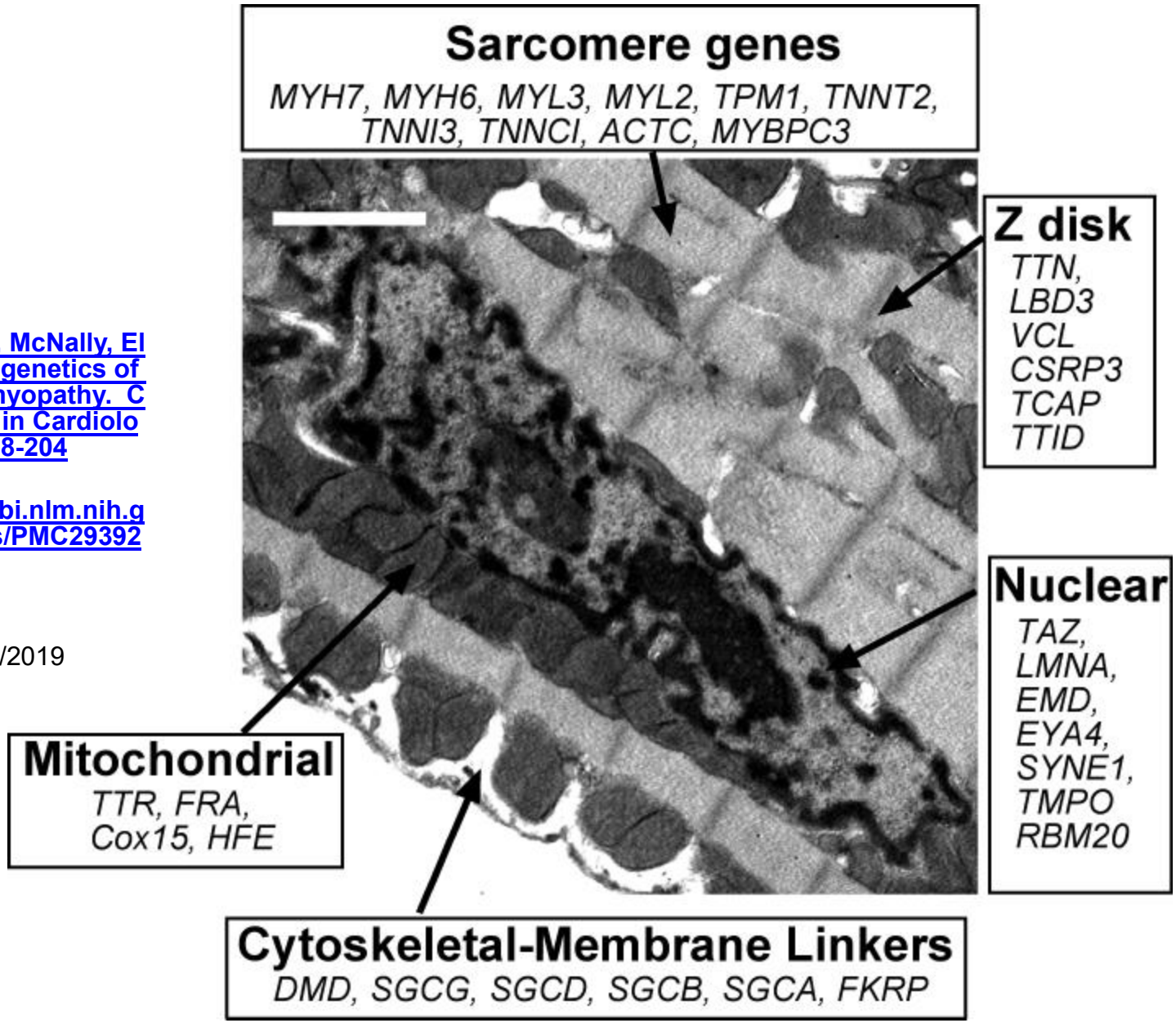
Source: Fuster V, O'Rourke RA, Walsh RA, Poole-Wilson P: *Hurst's The Heart*, 12th Edition: http://www.accessmedicine.com

Fig 81-4 Accessed 04/01/2010

Dellefave, Lisa, McNally, Elizabeth M, The genetics of dilated cardiomyopathy. Current Opinion in Cardiology (2010) 25:198-204

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2939233/

Accessed 12/07/2019



Major molecular abnormalities

- 20% involve TTN gene at 2q31.2
- Titin provides structure, flexibility, and stability to sarcomeres. Titin also plays a role in chemical signaling and in assembling new sarcomeres
- 3% TNNT2 mutation at 1q32.1
- Troponin T permits filament binding in sarcomeres

Major molecular abnormalities

- 10% MYH7 mutation at 14q11.2
- β-myosin heavy chain also found in Type I skeletal muscle fibers
- Necessary to form type II myosin needed for mechanical contraction
- 5-8% LMNA mutation at 1q22
- Lamina A and C are intermediate filament proteins that provide scaffolding in the nuclear envelope

Molecular abnormalities

- Two genes (LMNA and DMD) typically cause DCM, with or without arrhythmias
- They do not cause hypertrophic cardiomyopathy (HCM).
- Most DCM genes also cause other types of cardiomyopathy:
- HCM
- Restrictive cardiomyopathy
- Arrhythmogenic right ventricular cardiomyopathy

Dilated cardiolaminopathy

- 80% have conduction abnormalities
- Present with progressive prolongation of PR interval on EKG
- Slow development of LV dilatation or dysfunction
- 7% to 10% of cases
- Sudden death a risk
- Nuclear envelope genes
- LMNA, EMD, SYNE1, TMPO
- LMNA mutations account for the majority of DCM in this subgroup

Dilated cardiodystrophinopathy

- Typically manifest in male patients
- 80% of subgroup
- 6% of all cases in men
- Large DMD gene rearrangements at Xp21.2-22.1
- Both in-frame and out-of-frame deletions
- Protein expression lost at level of sarcolemma
- The dystrophin complex acts as an anchor, connecting each muscle cell's structural framework (cytoskeleton) with the lattice of proteins and other molecules outside the cell (extracellular matrix).

Dilated cardioemerinopathy

- Phenotypically resemble cardiolaminopathy
- Conduction abnormalities common
- Associated with muscular dystrophy
- Sudden death a risk
- X-linked recessive
- EMD gene at Xq28
- Emerin, the gene product, is a major component of the nuclear envelope
- Emery-Dreifuss muscular dystrophy

Dilated cardiozaspopathy

- 10% of cases
- Hyper-trabeculation and nuclear compaction are the clinical markers
- The presence of disproportionate, prominent LV trabeculae, a thin compacted layer, and deep intertrabecular recesses that are in continuity with the LV cavity and separated from the epicardial coronary arteries.

Dilated cardiozaspopathy

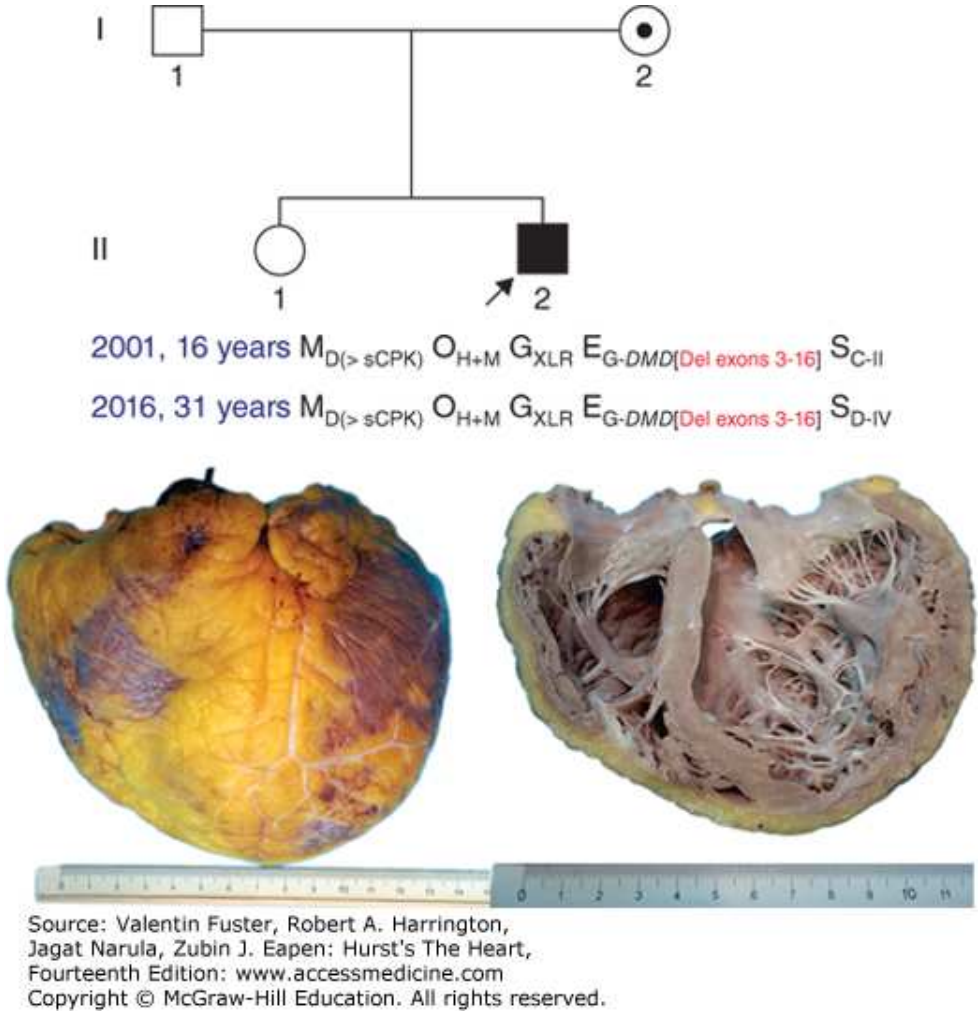
- Z-disc genes
- ACTN2, ANKRD1, BAG3, CRYAB, CSRP3, FHL2, LDB3, MYPN, MURC, NEXN, PGM1, VCL
- LDB3 at 10q23.2 most well studied
- Also associated with HCM and myofibrillar myopathy 4

Subtypes

- Dilated cardiodystrophinopathy
- Typically manifest in male patients
- 80% of subgroup
- 6% of all cases in men
- Large DMD gene rearrangements at Xp21.2-22.1
- Both in-frame and out-of-frame deletions
- Protein expression lost at level of sarcolemma
- The dystrophin complex acts as an anchor, connecting each muscle cell's structural framework (cytoskeleton) with the lattice of proteins and other molecules outside the cell (extracellular matrix).

Dilated cardiodystrophinopathy

- Associated with Duchenne and Becker muscular dystrophy
- X-linked muscular dystrophy
- May be heart specific, however
- Nuclear compaction noted in 30% of cases
- X-linked DCM has low arrhythmogenic risk



Dilated cardiodystrophinopathy. The figure shows the pedigree and the macroscopic view of a heart with dilated cardiomyopathy (DCM) from a young male patient who developed DCM at the age of 16 years; the disease showed slow progression to end-stage heart failure, and the patient underwent heart transplantation 15 years later. The dystrophin defect is not associated with severe muscle dystrophy.

Dilated cardiomyosinopathy

- 25% to 30% of DCM patients.
- Sarcomere gene abnormalities
- TTN, MYH7, MYBPC3, TNNT2, TNNI3, MYL2, MYL3
- MYH7 is paradigmatic (β-myosin heavy chain)
- Mutant myosins displaying decreased contractility lead to DCM.
- MYH7 and mitochondrial mutations together lead to DCM
- Mutant myosins with enhanced contractility lead to HCM

Dilated cardiotitinopathy

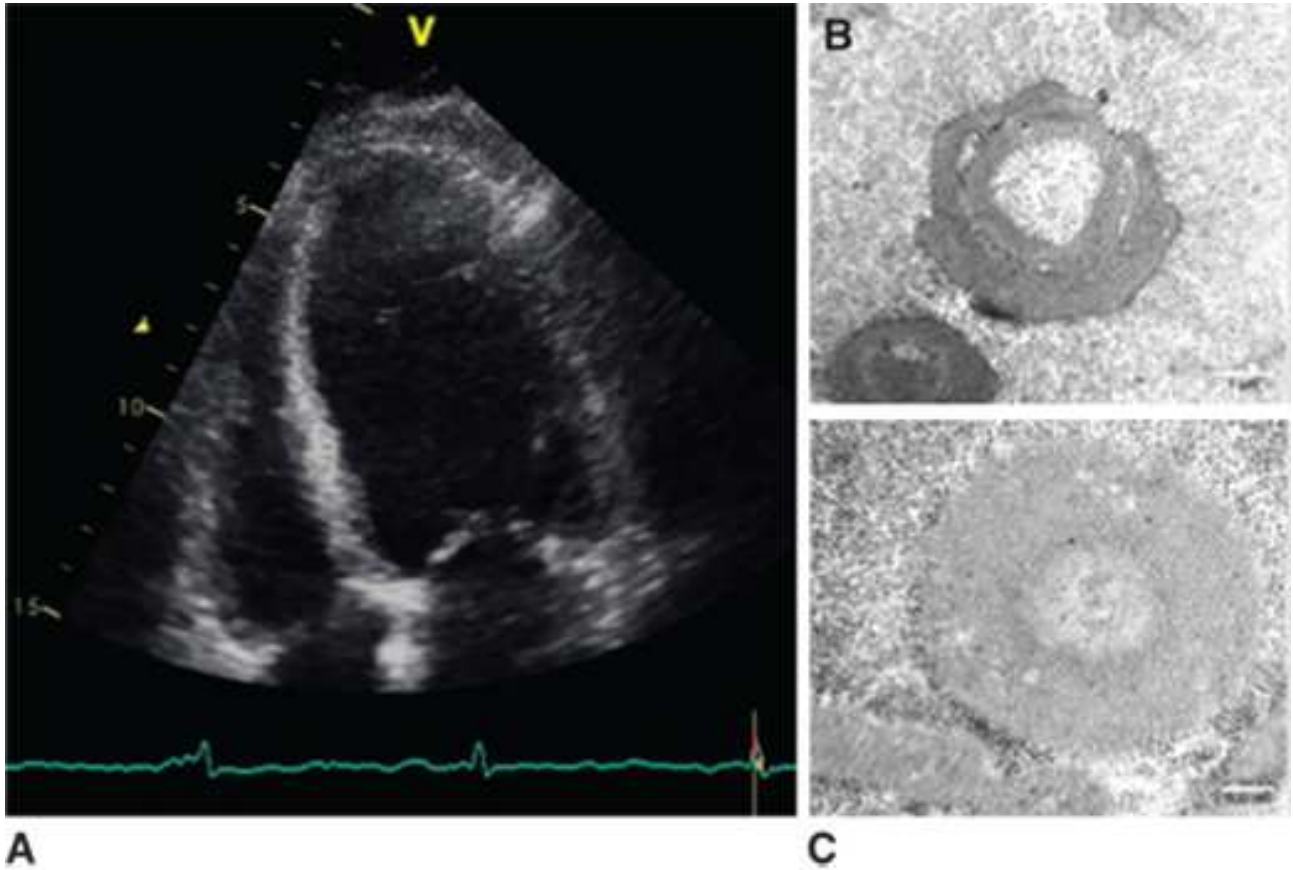
- Not accompanied by conduction defects or skeletal muscle disease
- The TTN gene encodes the largest human protein and the third most abundant striated muscle protein.
- N2B and N2BA isoforms are predominantly expressed at the cardiac level
- Truncation-predicting mutations have been identified in 25% of FDCMs and in 18% of sporadic DCMs
- Similar distribution noted in peripartum cardiomyopathy
- BUT 1 in 500 “normal” individuals carry truncation-predicting variants

Dilated cardiotitinopathy

- Cardiac troponin I mutation (TNNI3 T at 19q13.42)
- TTN mutations are also noted in:
- HCM
- Muscular dystrophy of the Limb-Girdle, type 2J
- Autosomal recessive early-onset myopathy with fatal cardiomyopathy
- Tardive tibial muscular dystrophy
- Proximal myopathy, with early respiratory muscle involvement

Dilated cardioMITOmyopathy

- 5% of cases
- Hearing loss, palpebral ptosis, myopathy, renal failure, cryptogenic stroke, diabetes, optic neuritis, and/or retinitis pigmentosa
- Nuclear mitochondrial genes
- G4.5, CTF1, SDHA, DNAJC19
- Cytochrome c affected
- Commonly observed in families in which mutation carriers also express non-cardiac traits
- Cardiomyopathy and encephalopathy



Mitochondrial cardiomyopathy. This figure shows the echocardiographic view (A) of the dilated cardiomyopathy (DCM) in a 53-year-old woman affected by mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke (MELAS) syndrome. Her endomyocardial biopsy (B and C) showed typically abnormal mitochondria. The DCM phenotype was associated with hearing loss and mild myopathy.

Dilated Phopsholambanopathy

- PLN at 6q22.31
- PLNR14del is noted in 10% of Dutch cases
- Phospholamban inhibits cardiac muscle sarcoplasmic reticulum Ca^{2+}-ATPase (SERCA2a) in the unphosphorylated state
- May also cause HCM
- Low voltage QRS complex and inverted T waves in V_{4-6}
- Sudden death a risk

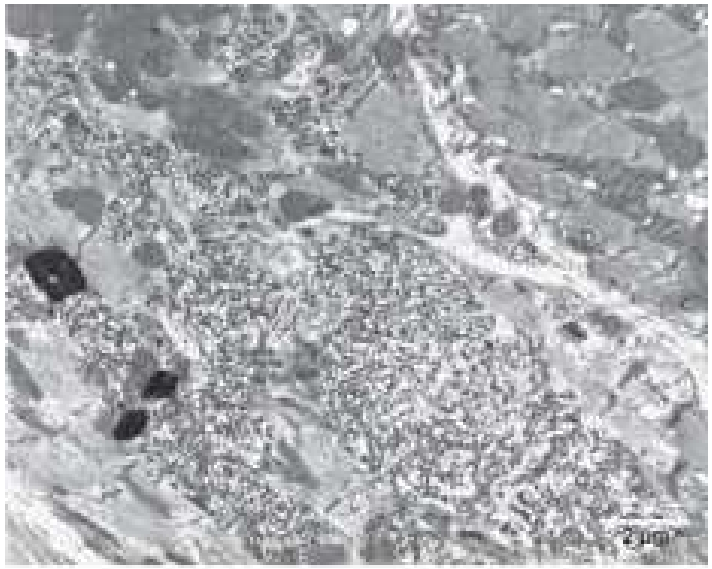
Molecular abnormalities in DCM

- In fewer than 1% of cases
- Dystrophin-associated glycoprotein complex
- SGCA, SGCB, SGCD at 17q21.33, 4q12, and 5q32-33 respectively (sarcoglycan)
- Associated with limb-girdle muscular dystrophy
- Genes coding intermediate filaments connecting sarcolemma with sarcomeres
- DES at 2q35 (desmin)
- Conduction defects common

Molecular abnormalities in DCM

- Genes whose products are active in Golgi apparatus machinery
- FKTN at 9q31.2 (fukutin)
- Glycosylates α-dystroglycan (anchoring protein)

A



B

A. Endomyocardial biopsy showing marked endocardial fibrosis
B. Electron micrograph showing granular collections of desmin

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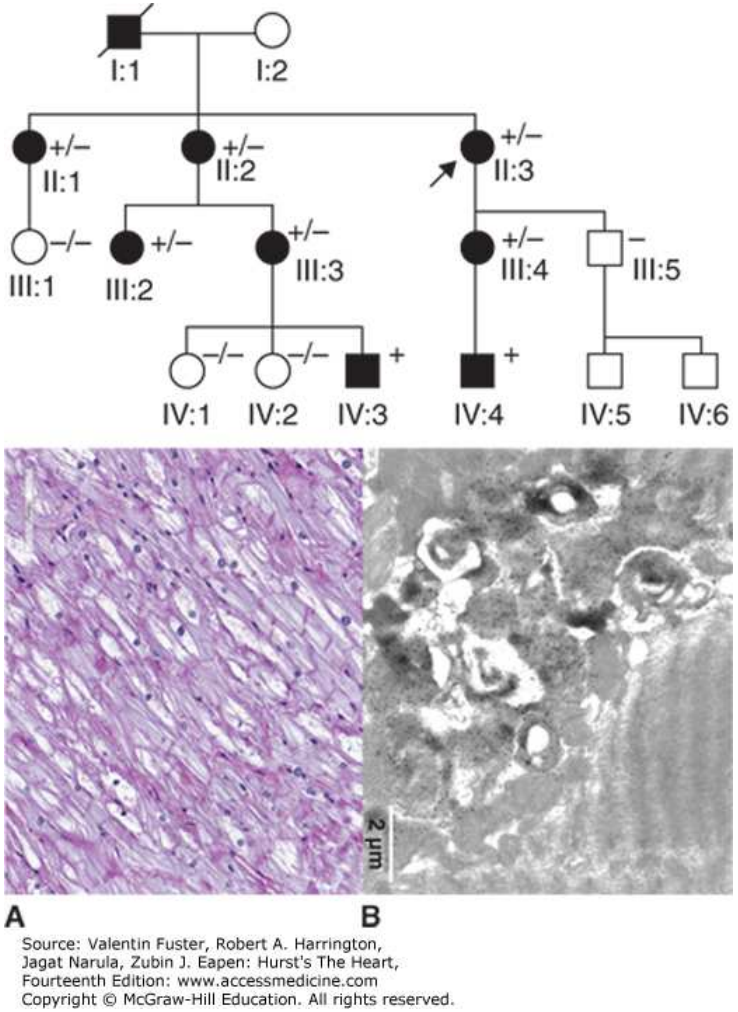


The pedigree shows a typical family with the X-linked Anderson-Fabry disease (AFD), cardiac variant, caused by p.(Asn215Ser) in α-galactosidase. In the bottom half of the figure, the pathologic features of AFD in endomyocardial biopsy are shown. A. The hematoxylin and eosin stain shows a large number of vacuolated myocytes (glycosphingolipids are extracted in formalin-fixed, paraffin-embedded tissues). B. Immunogold electron microscopy view shows typical lamellar and dense osmiophilic bodies specifically immune-labeled by anti-GB3 antibodies. Pedigree symbols are as follows: circles represent females, squares represent males, diagonal lines represent deceased, and solid-filled symbols denote the presence of the phenotype.

Molecular abnormalities in DCM

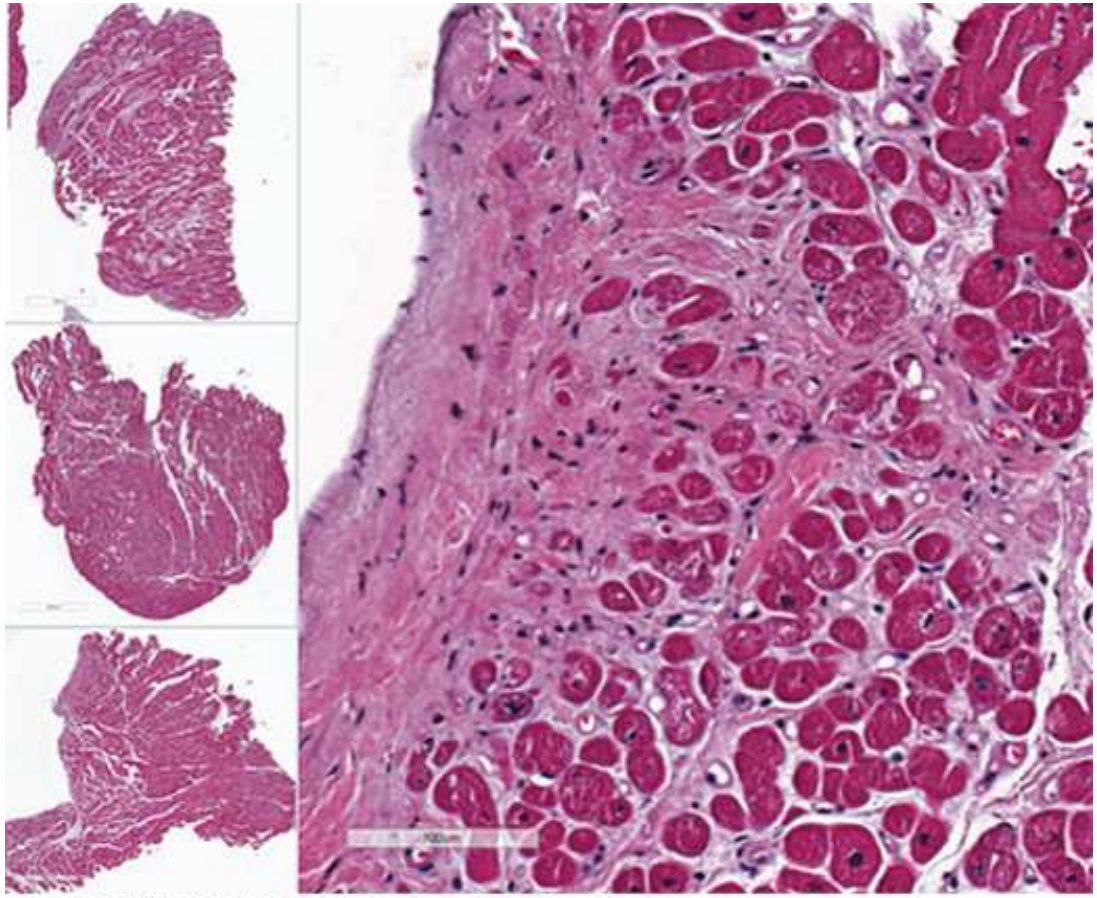
- Sodium channel defects
- SCN5A at 3p22.2 (Brugada syndrome)
- Long QT interval
- Potassium channel defects
- ABCC9 at 12p12
- CHRM2 at 7q33 (muscarinic receptor)
- Autosomal recessive
- DOLK at 9q31 (defective o-mannosylation of sarcomere)

Prevention of sudden death

- Criteria for ICD implantation in patients with DCM
- Confirmed disease-causing LMNA mutation
- NYHA Class IIa, Level B functional status
- Non-sustained ventricular tachycardia during ambulatory EKG monitoring
- LV ejection fraction (LVEF) < 45% on initial evaluation
- Male
- Non-missense mutations (insertion, deletion, truncation, or mutations affecting splicing)

Autoimmune/immune-mediated DCM

- Systemic sclerosis
- HLA susceptibility
- Fetal micro-chimerism inducing graft versus host disease
- Interstitial fibrosis in up to 40% of cases
- May have mild inflammation of myocardium or pericardium
-



Endomyocardial biopsy in systemic sclerosis. The figure shows the endomyocardial biopsy of a 59-year-old woman diagnosed with dilated cardiomyopathy and systemic sclerosis in the same clinical occasion. The endomyocardial biopsy shows interstitial fibrosis and sparse inflammatory cells in the context of the fibrosis. There is no evidence of vasculitis or active myocarditis.

Autoimmune/immune-mediated DCM

- Rheumatoid arthritis
- DCM accounts for about 20% of mortality
- 50% of patients have pericarditis
- Thickening and calcification of heart valves
- Pericardial thickening
- Coronary atherosclerosis (accelerated)
- Steroids, hydroxychloroquine use, as well as extra-articular involvement as risk factors
- AA amyloid deposition in up to 28% of patients
- Associated with restrictive cardiomyopathy

Autoimmune/immune-mediated DCM

- Systemic lupus erythematosus
- Diastolic dysfunction is detected in 45% of patients without evidence of cardiac disease
- Is the principal cause of death
- Hypomethylation of CpG sites seem to be associated with increased production of autoantibodies
- anti-dsDNA, anti-SSA, anti-Sm, and anti-RNP
- Also influence endothelial-inflammatory cell interactions and inflammatory responses.

Autoimmune/immune-mediated DCM

- NCF2, encoding a core component of the multiprotein NADPH oxidase, confers susceptibility to SLE in individuals of European heritage
- Steroids and immunosuppressant therapy as risk factors
- Anti-phospholipid, anti-cardiolipin antibodies, and lupus anticoagulant are produced in 30% of patients but only account for 10% of thrombotic events
- Accelerated atherosclerosis common
- 45% of patients will have a myocardial infarction

Toxic causes of DCM

- Drug toxicity leading to structural and persistent myocardial damage and dysfunction
- Anthracyclines (lipid peroxidation)
- Anti-HER2 antibodies
- Tyrosine kinase inhibitors
- Catecholamine toxicity (Cocaine)
- Clozapine
- Lithium
- Alcohol (acetaldehyde)
- Cobalt
- Thiamine deficiency ("wet Beriberi")

Peripartum DCM

- Occurs during the final month of gestation or as late as 5 months post partum
- 45% present in first week after delivery
- 75% present by the end of the first month
- Systolic dysfunction
- LVEF <45%
- Diagnosis of exclusion
- Age >30 years, multiparity, hypertension, and obesity as risk factors
- More common in those of sub-Saharan African heritage

Peripartum DCM

- TTN gene abnormality present in 17%
- DCM unmasked by pregnancy
- Other mechanisms proposed:
- Selenium deficiency
- Fetal-mother micro-chimerism
- Increased levels of prolactin
- Increased blood volume, erythropoietin, angiotensin responsiveness
- High output cardiac failure
- Prolonged use (>4 weeks) sympathomimetic agents

Table 12-13 Major Causes of Myocarditis

Infections
Viruses (e.g., coxsackievirus, ECHO, influenza, HIV, cytomegalovirus)
Chlamydiae (e.g., *Chlamydophyla psittaci*)
Rickettsiae (e.g., *Rickettsia typhi*, typhus fever)
Bacteria (e.g., *Corynebacterium diphtheriae, Neisseria meningococcus, Borrelia* (Lyme disease)
Fungi (e.g., *Candida*)
Protozoa (e.g., *Trypanosoma cruzi* [Chagas disease], toxoplasmosis)
Helminths (e.g., trichinosis)
Immune-Mediated Reactions
Postviral
Poststreptococcal (rheumatic fever)
Systemic lupus erythematosus
Drug hypersensitivity (e.g., methyldopa, sulfonamides)
Transplant rejection
Unknown
Sarcoidosis
Giant cell myocarditis

HIV, Human immunodeficiency virus.

Spike
protein

Viral causes of DCM

- Sudden-onset heart failure occurs in one who was relatively healthy in the hours to days previously.
- Usually secondary to overwhelming viremia with tissue invasion in multiple organ systems including the heart.
- Active myocarditis characterized by myocyte necrosis and a mononuclear cell infiltrate
- Coxsackie B3 (an RNA virus) is the most common cause
- Infection initiated by transmembrane coxsackie-adenovirus receptor
- Directly cytotoxic

Viral causes of DCM

- Adenoviruses, coxsackie A virus, echoviruses, parvovirus B19, cytomegalovirus, influenza A virus and HIV as other causes
- Gradual onset disease may follow upper respiratory tract infection or gastroenteritis in the previous month.
- Most cases of will clear spontaneously
- 5% develop chronic changes
- May have a late post-infectious or autoimmune component.

Viral causes of DCM

- Parvovirus B19 (a DNA virus) is a common finding in chronic disease
- Parvovirus enters by endocytosis with antibody-bound C1q
- Does not replicate in myocyte
- Triggers innate immunity response

Testing

- Echocardiogram will demonstrate a poorly functioning ventricle with varying degrees of ventricular dilation.
- May see diffusely low voltages on ECG.
- Elevated inflammatory markers may be present (e.g., ESR, CRP).
- Endomyocardial biopsy will demonstrate lymphocytic infiltrate and viral PCR positivity

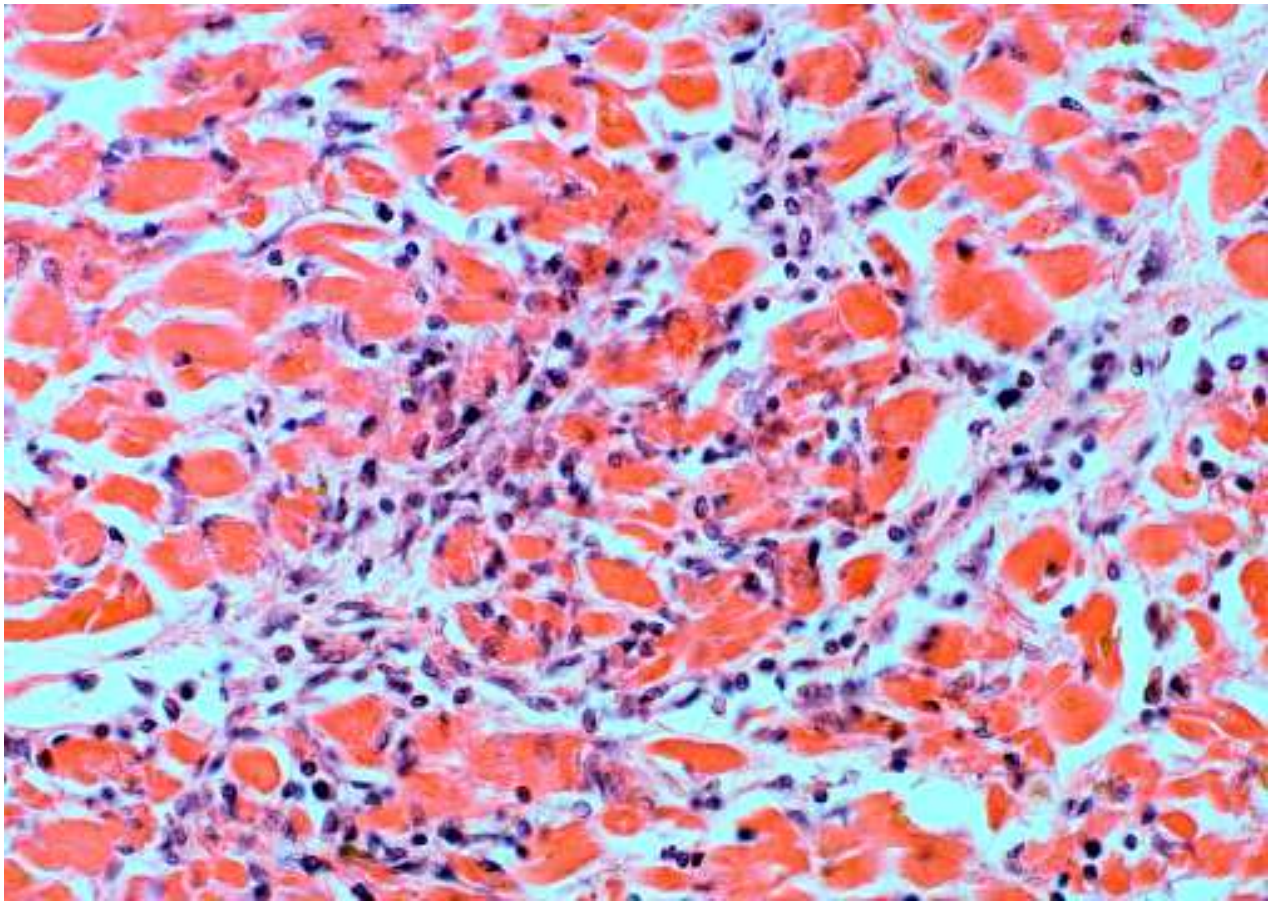
Bacterial causes of DCM

- Staphylococcus and Streptococcus in co-infections with influenza virus
- Corynebacterium diphtheria
- Increasing incidence worldwide
- Gram positive rod with clubbed ends
- Toxin released by organism (associated with pseudomembrane in oropharynx as well)
- Borrelia burgdorferi
- Myocarditis is present in 5% of those with Lyme disease.

Inflammatory causes of DCM

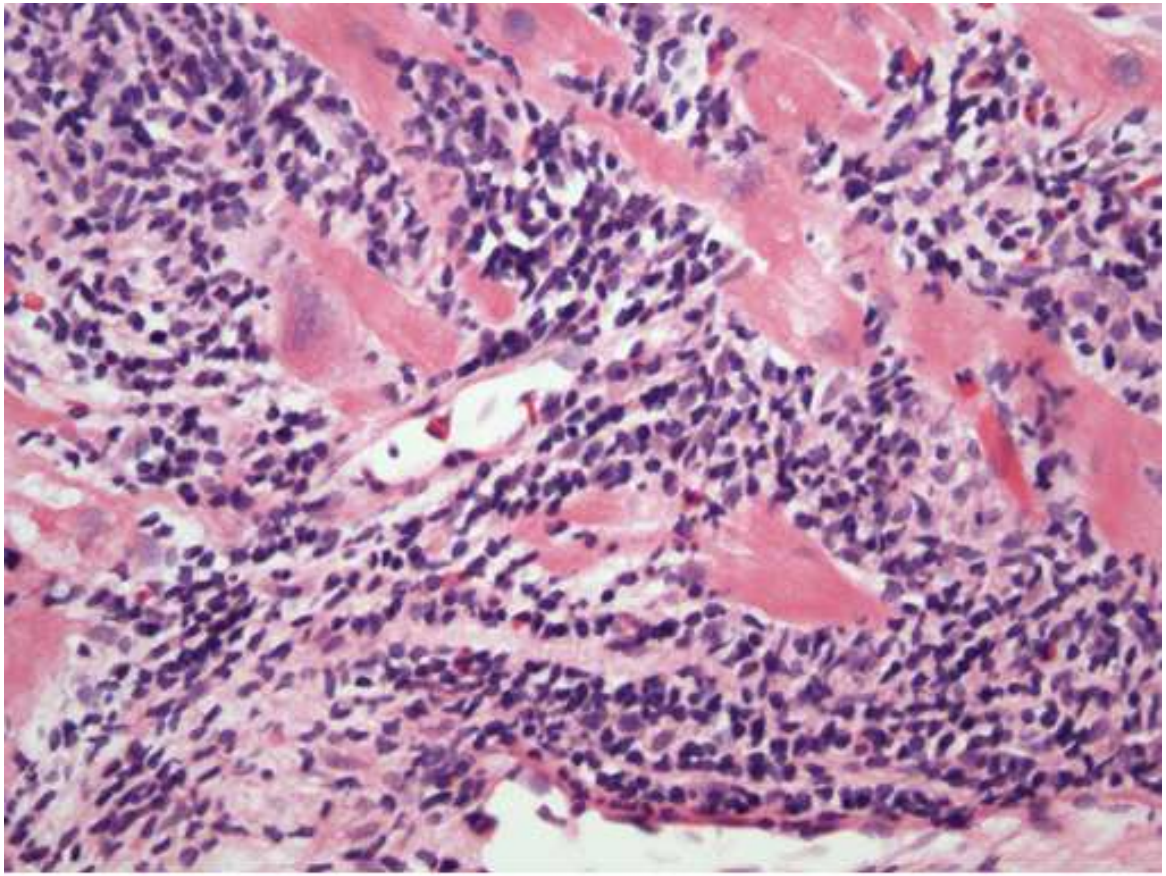
- Trypansoma cruzi
- 85% have myocarditis (Chagas disease).
- Parasitization of myofibers (leishmanial form)
- Toxoplasma gondii
- Trichina spirella is the most common helminthic cause.
- Patchy myocarditis
- Eosinophils prominent in inflammatory infiltrate
- Larvae do not encyst as they do in skeletal muscle

Viral myocarditis

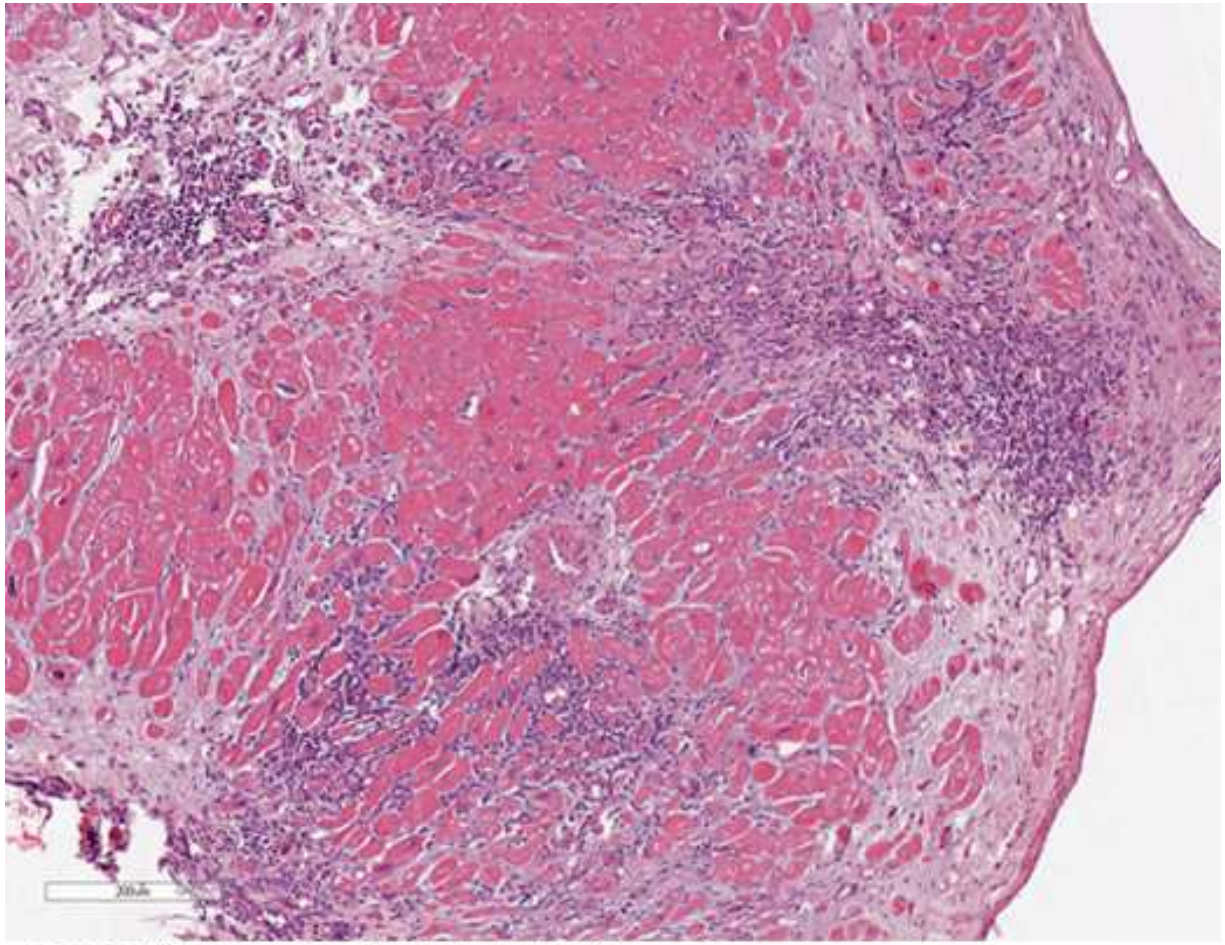


Interstitial lymphocytic infiltrate

https://webpath.med.utah.edu/CVHTML/CV067.html
Accessed 12/10/2019



Acute myocarditis. Microscopic image of an endomyocardial biopsy showing massive infiltration with mononuclear cells and occasional eosinophils associated with clear myocyte damage. The myocyte nuclei are enlarged and reactive. Such extensive involvement of the myocardium would lead to extensive replacement fibrosis even if the inflammatory response could be suppressed. Hematoxylin and eosin–stained section, 200× original magnification. (Image courtesy of Robert Padera, MD, PhD, Department of Pathology, Brigham and Women's Hospital, Boston.)



Coxsackie B3 myocarditis with areas of inflammation, necrosis, and granulation tissue formation

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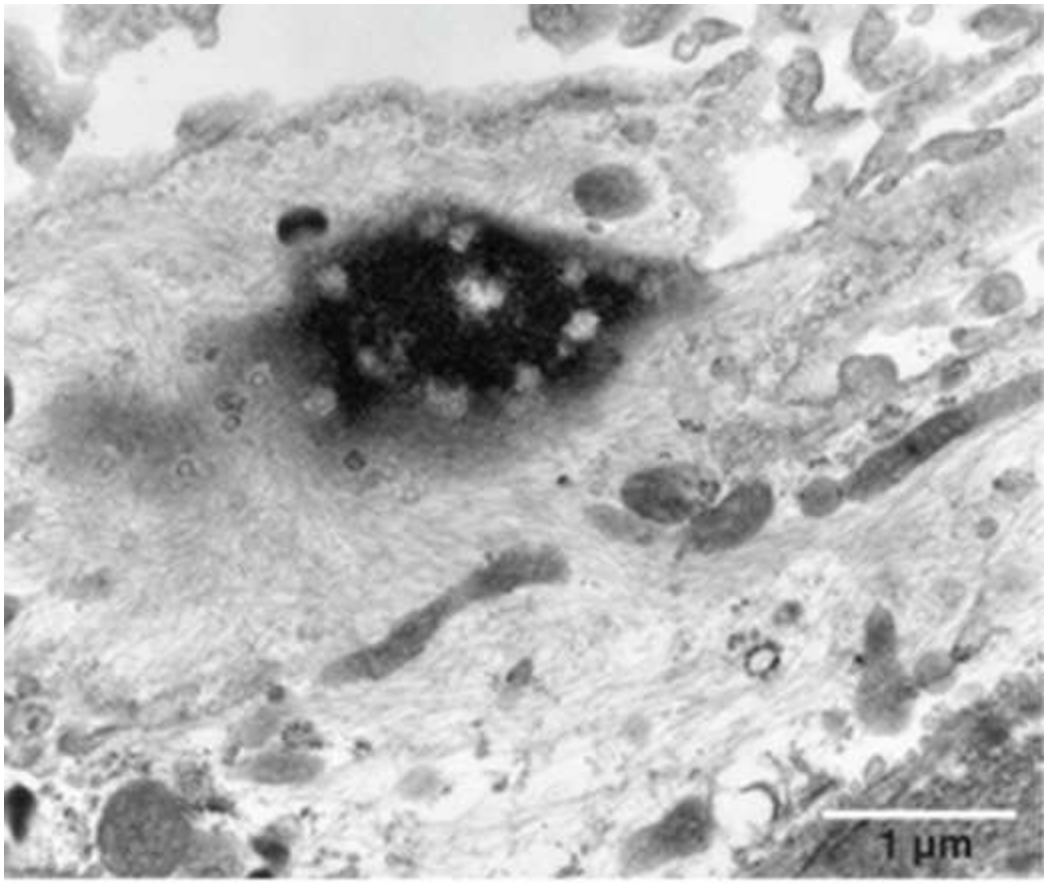


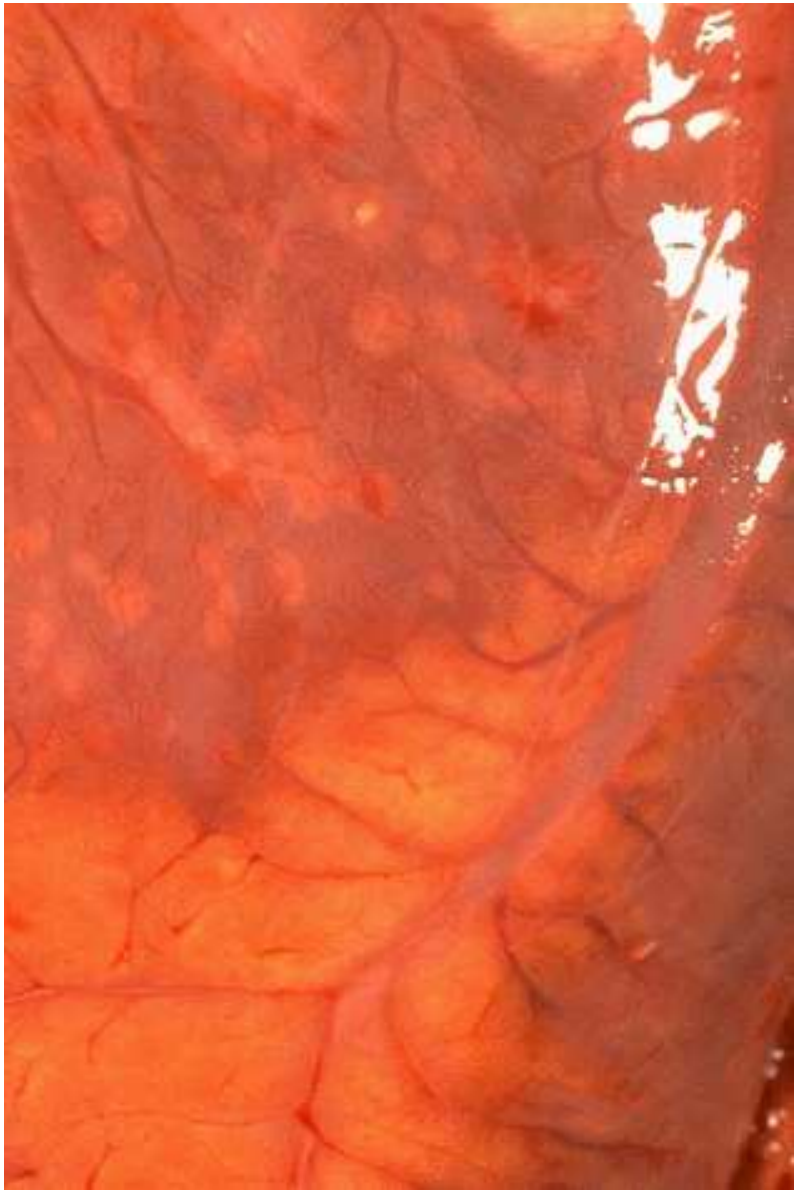
B

Source: Valentin Fuster, Robert A. Harrington, Jagat Narula, Zubin J. Eapen: Hurst's The Heart, Fourteenth Edition: www.accessmedicine.com

Parvovirus in endothelial cell

Accessed 04/20/2020

Myocardial abscesses



Septic emboli to myocardium

https://webpath.med.utah.edu/CVHTML/CV052A.html
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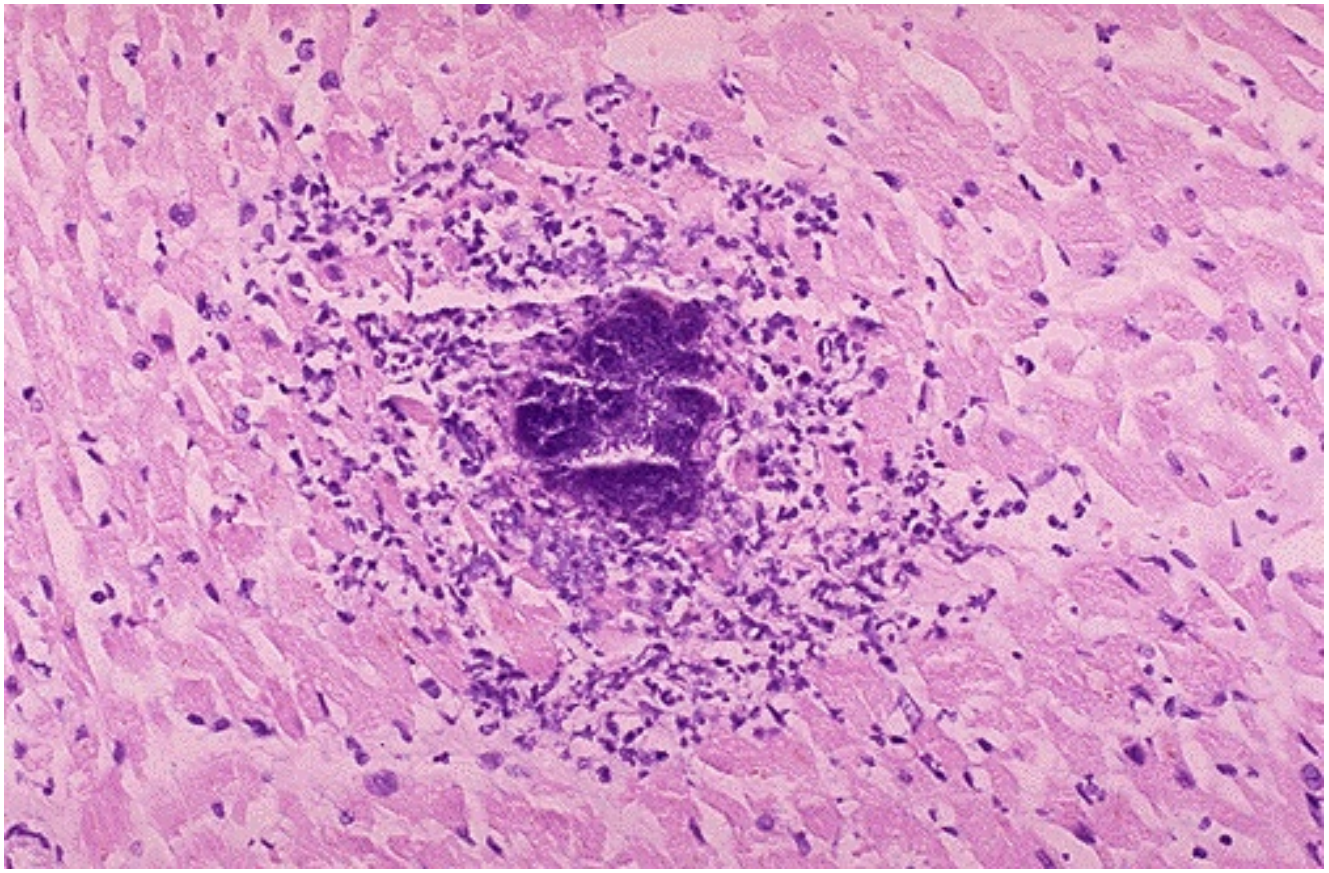
Myocardial abscess



Bacterial colonies with acute inflammatory infiltrate and myocardial necrosis

https://webpath.med.utah.edu/CVHTML/CV053.html
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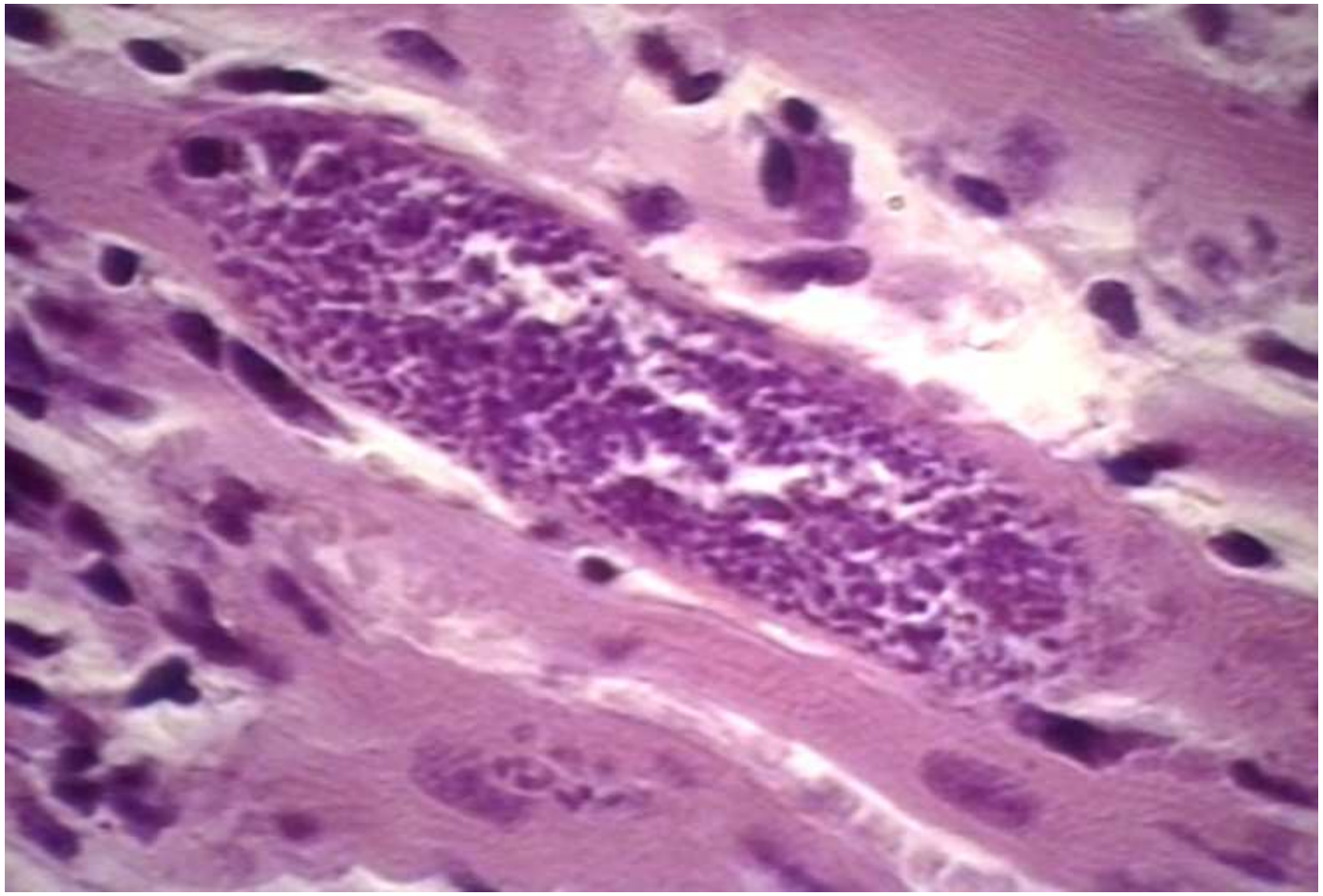
Chaga’s disease



Leishmanial form

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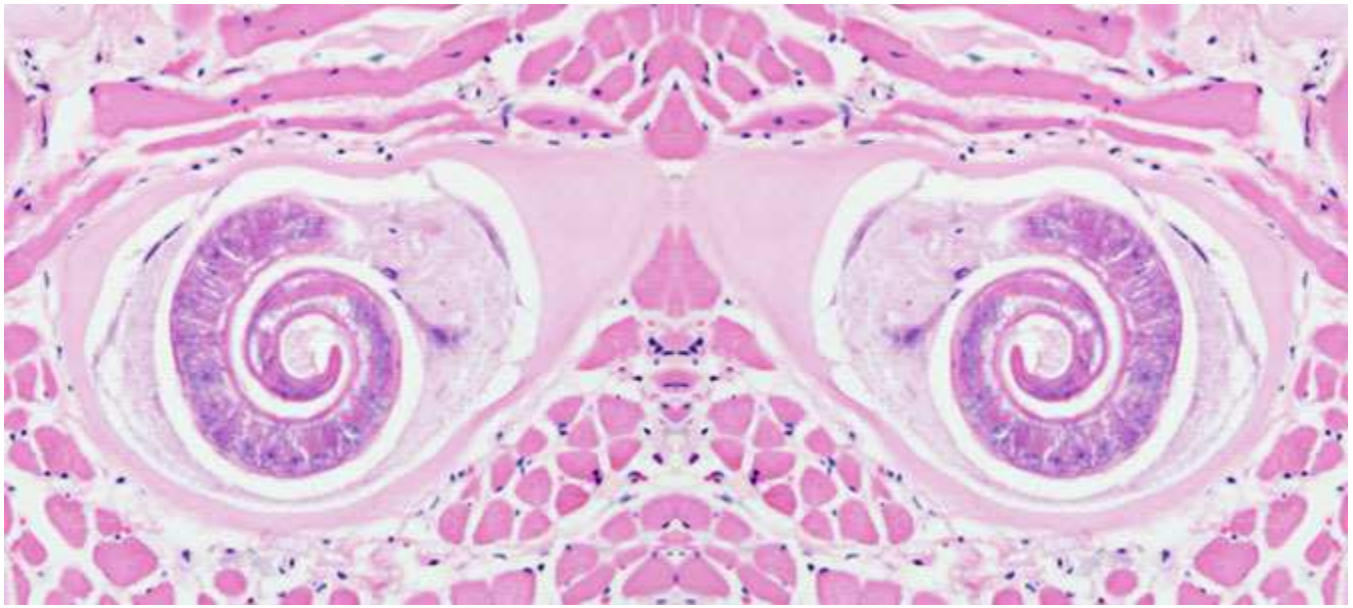
Trichinella



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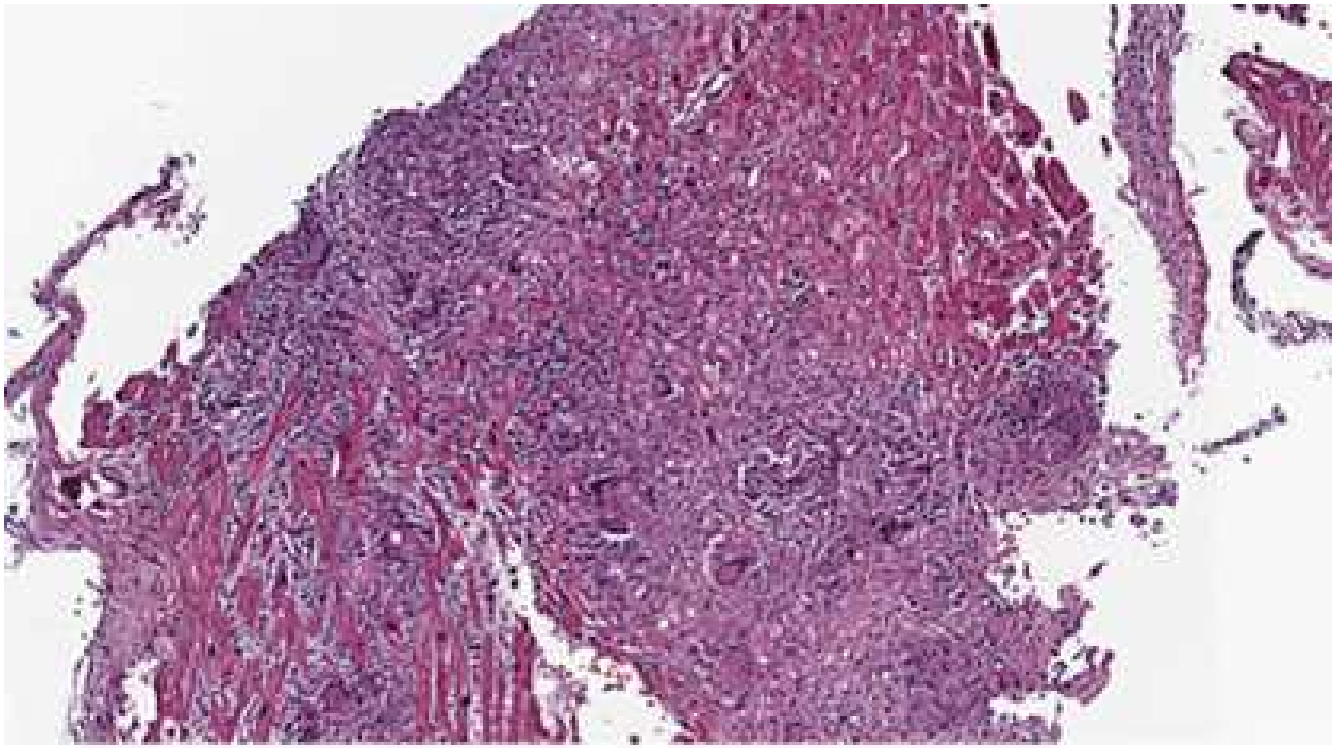
Non-infectious myocarditis

- Giant cells are the morphologic marker of giant cell myocarditis and sarcoidosis
- Giant cell myocarditis is characterized by a chemokine profile related to toll-like receptors and dendritic cells
- Usually presents with cardiogenic shock
- Rare disease
- Multifactorial

Non-infectious myocarditis

- Sarcoid
- Predilection for septum (conduction disturbance)
- 25% involve heart
- Noncaseating granuloma with giant cells and epithelioid histiocytes
- Hypereosinophilic syndromes
- Eosinophilic Granuloma with Polyangiitis (Churg-Strauss)
- Asthma, mononeuritis complex as well
- MPO- ANCA antibodies



B

Active Sarcoid

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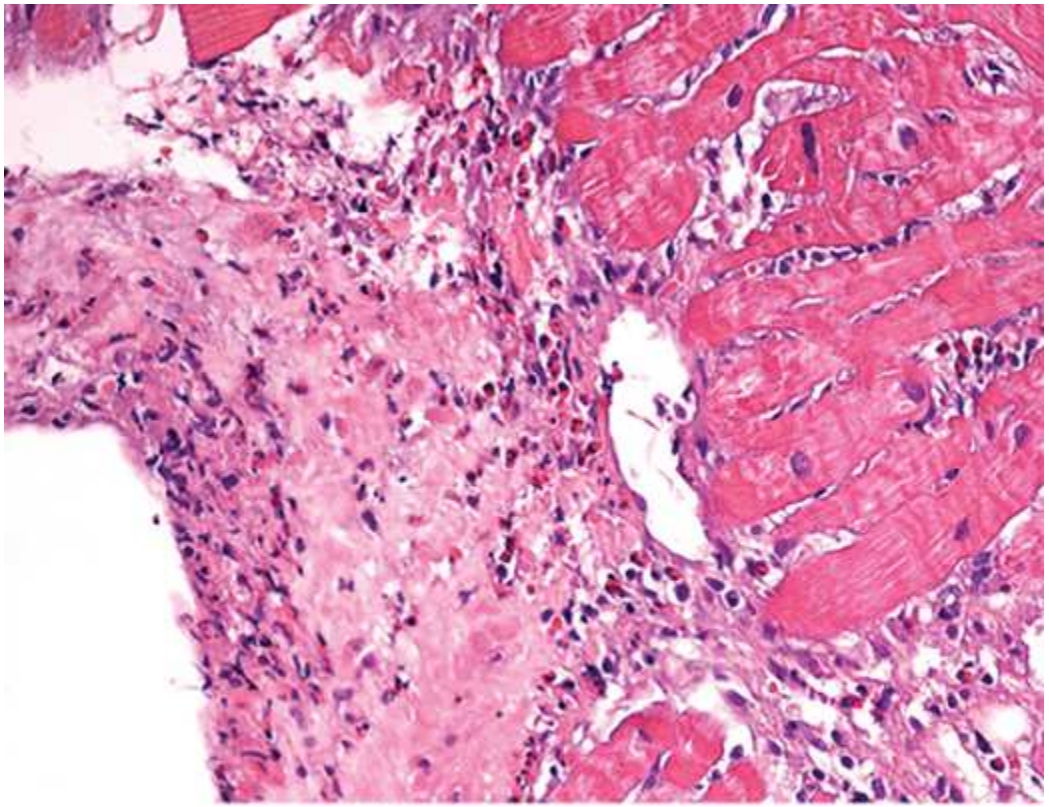
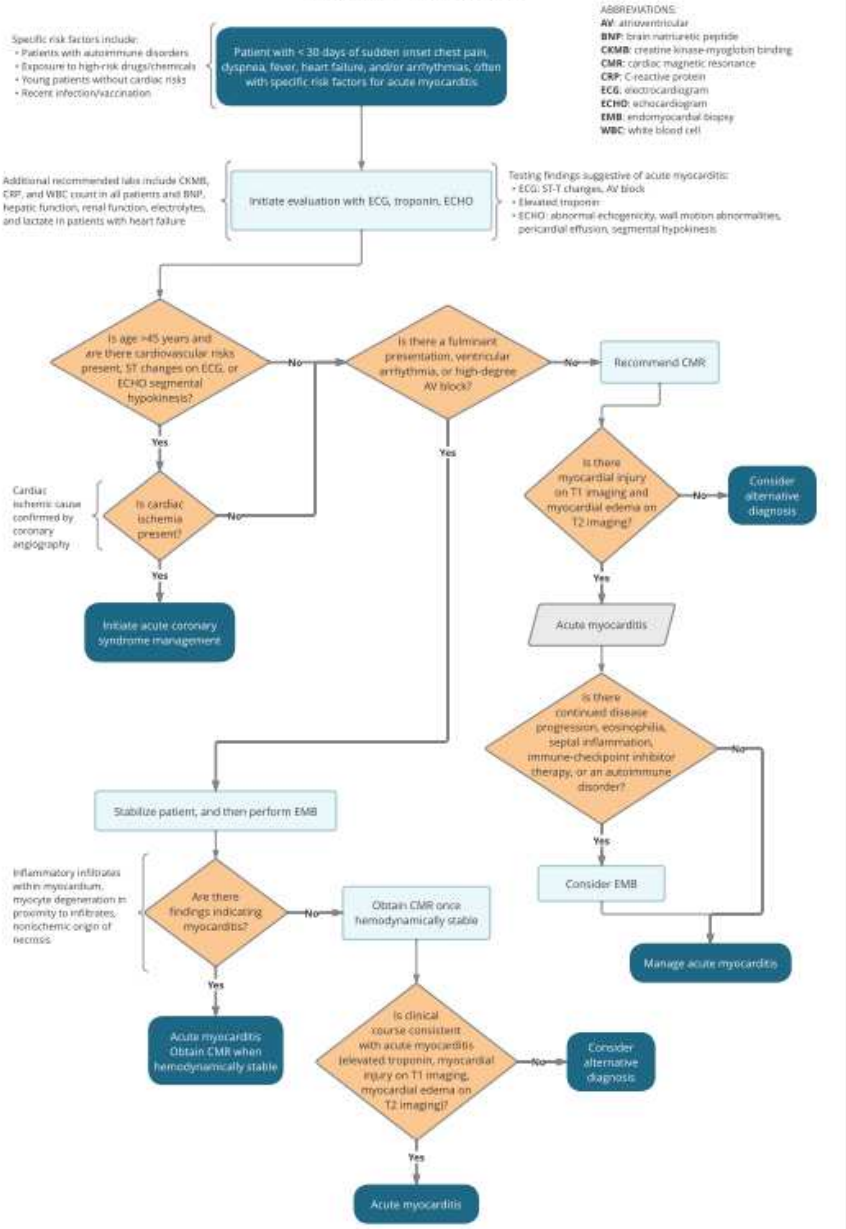


A

Hypereosinophilic syndrome

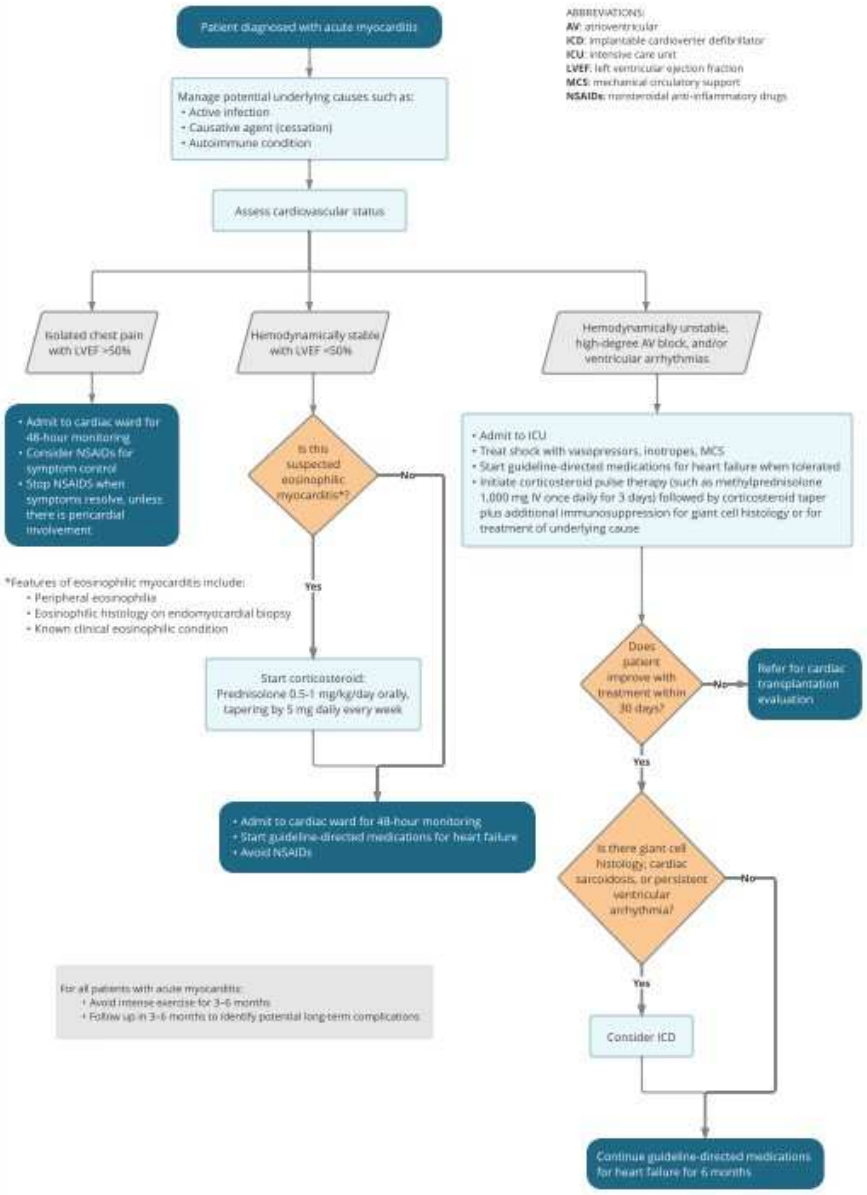
Accessed 04/20/2020

Acute Myocarditis Diagnosis



REFERENCES: JAMA 2023 Apr 4;329(13):1098–1113 · Circ J 2023 Apr 25;87(5):674–754 · Circ Heart Fail 2020 Nov;13(11):e007405

Acute Myocarditis Management



REFERENCES: JAMA 2023 Apr 4;329(13):1098–1113 · Circ J 2023 Apr 25;87(5):674–754 · Circ Heart Fail 2020 Nov;13(11):e007405

HYPERTROPHIC CARDIOMYOPATHY

HCM

- Left ventricular hypertrophy (LVH) in the absence of abnormal loading conditions, such as severe hypertension or valve disease
- 30-40% of cardiomyopathies in children
- Adolescents and young adults
- 50-60%, autosomal dominant
- Defective energy transfer from mitochondrion to sarcomere
- β-myosin heavy chain, cardiac troponin T or I, α-tropomyosin, and myosin-binding protein C are abnormal

HCM

- 5% of patients have metabolic or storage disorders (e.g., Pompe), neuromuscular disease (e.g., Freidrich Ataxia), and genetic syndromes such as cardio-facial-cutaneous disorders (Noonan syndrome) or phakomatoses.

HCM

- Apical hypertrophy reduces ventricular volume
- 10% have concentric hypertrophy (restricted filling)
- Left ventricular septum three times thicker than free wall (asymmetric hypertrophy)
- Prominent in sub aortic region (25%)
- Dynamic dysfunction

HCM

- Flow against the abnormally positioned mitral valve apparatus in systole causes a drag force on a portion of the mitral valve leaflets that pushes the leaflets into the LV outflow tract.
- Obstruction to the LV outflow typically varies with loading conditions and contractility of the ventricle
- Usual cause of dyspnea
- Mid-cavity obstruction can also be present as a result of hypertrophied papillary muscles abutting against the septum.

Clinical diagnosis

- May be asymptomatic despite having significant hypertrophy
- May present with symptoms of inadequate coronary perfusion or heart failure
- Peripheral vasodilatation
- Angina, syncope, palpitations, or exercise intolerance.
- 20% of patients will have transient loss of consciousness
- Atrial fibrillation in 25-30% of older patients
- May present with sudden cardiac death with exercise.

Clinical diagnosis

- Some patients develop a left precordial bulge with a diffuse point of maximal impulse.
- An LV heave or an S_4 gallop usually present.
- If outflow tract obstruction exists
- Paradoxical split of S_2
- Crescendo-decrescendo murmur systolic murmur that is best heard at the left sternal border and radiates to the apex
- Does not radiate to carotids
-

Clinical diagnosis

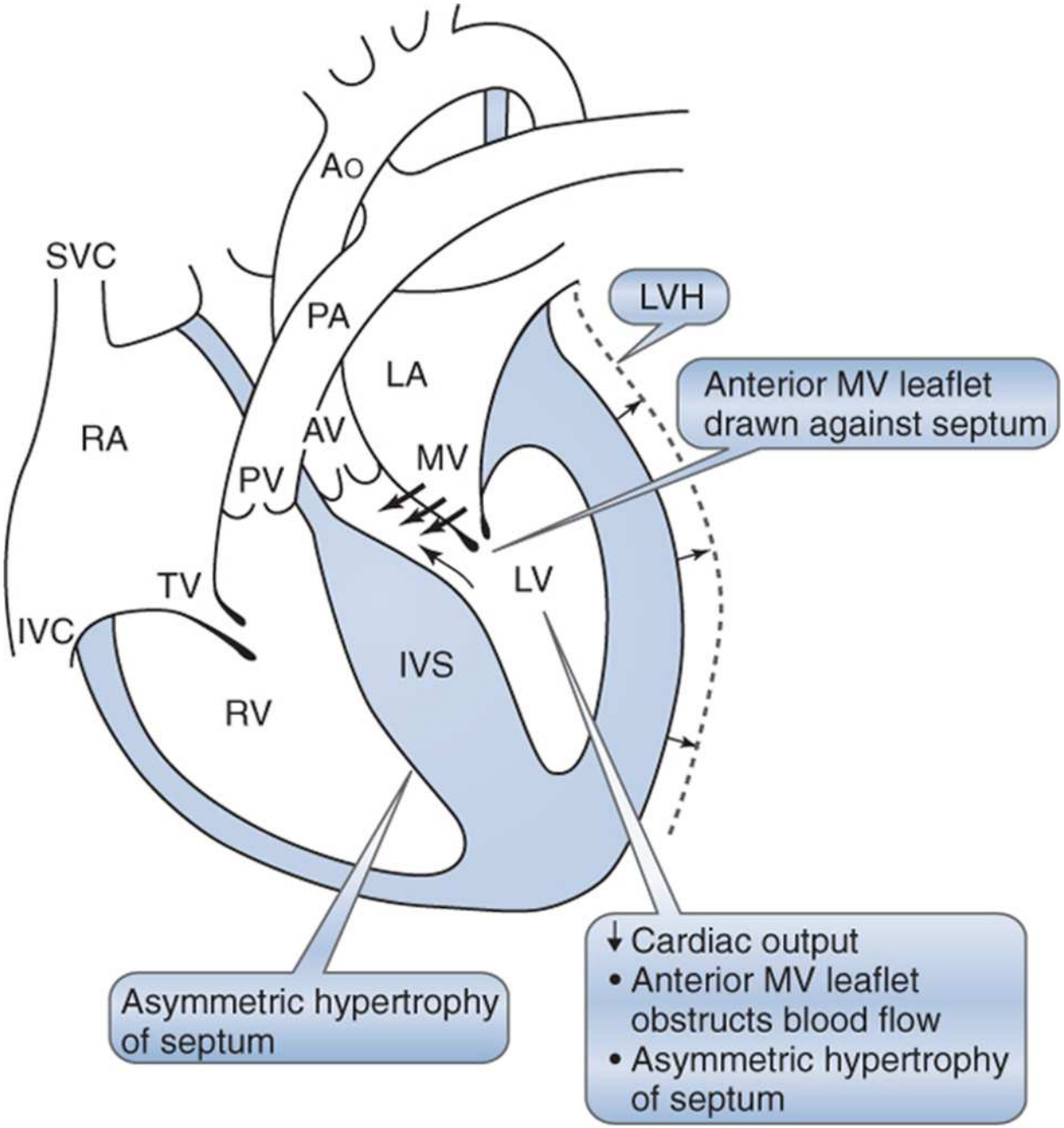
- Passive leg elevation decreases the intensity of the murmur (LR+ 8.0; LR- 0.2).
- Valsalva increases the intensity of the murmur
- From the standing position to a prompt squat, the murmur will markedly decrease in intensity, as a result of increases in afterload and preload.
- From the squatting to standing position, there will be an increase in intensity of the murmur immediately as afterload is reduced.
- A progressive increase in intensity of the murmur will continue for the next four to five beats as preload to the left side of the heart is reduced. (LR+ 4.5; LR- 0.1).

Clinical diagnosis

- With mitral regurgitation
- Holosystolic murmur
- Diastolic flow rumble.

Testing

- Boot shaped heart on chest x-ray.
- Repolarization abnormalities common
- Giant negative T-wave inversion in the precordial and/or inferolateral leads suggests involvement of the LV apex
- Echocardiography demonstrates septal thickening and dynamic outflow obstruction.

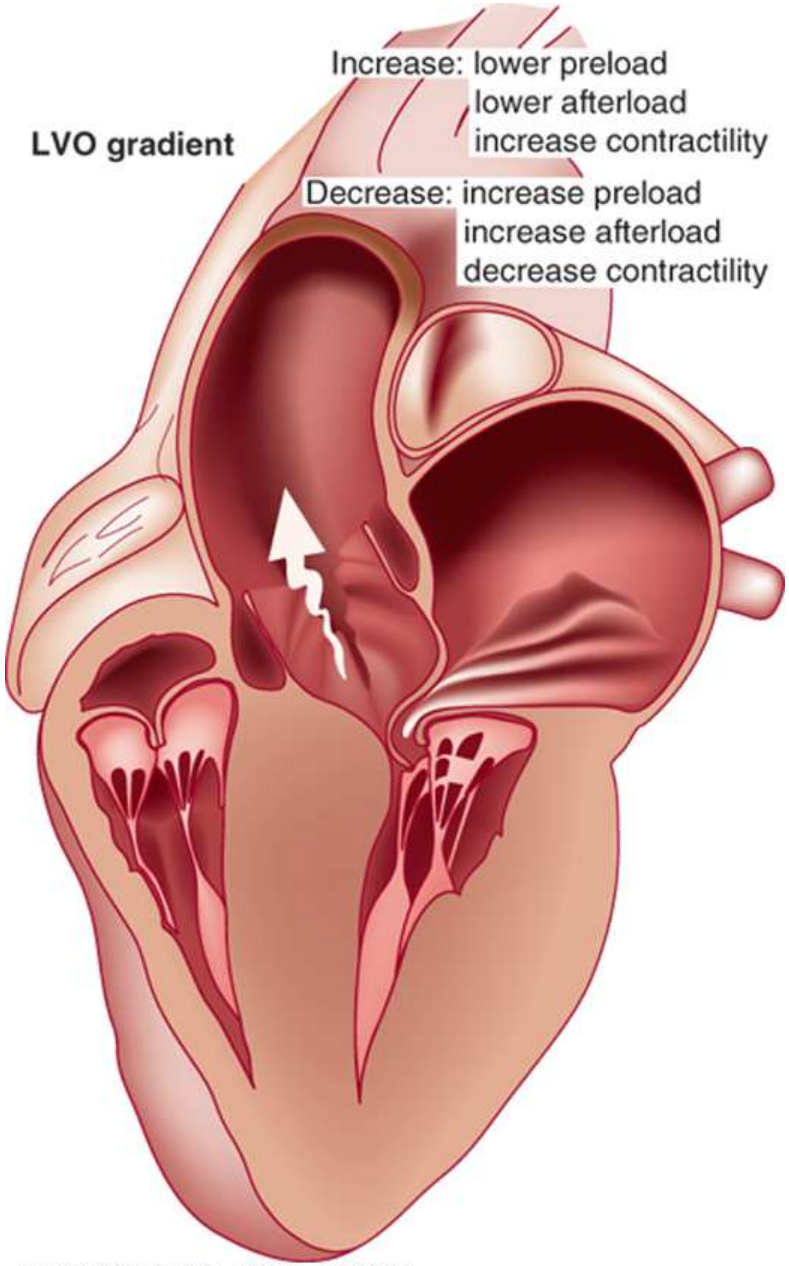


Treatment

- Affected patients are restricted from competitive athletics and isometric exercise due to associated risk of sudden cardiac death.
- Patients with resting or latent LV outflow tract obstruction:
- β-blockers
- Reduce heart rate (increase preload)
- Decrease myocardial contractility
- Verapamil
- Decrease myocardial contractility
- Disopyramide

Treatment

- Implantable cardioverter defibrillator
  - Patients with severe symptoms despite medical therapy and an LV outflow tract gradient may require additional intervention.
  - Surgical myectomy and mitral valve repair.
  - 10% terminate as dilated cardiomyopathy



Pathology

- Gross examination of the heart demonstrates asymmetric septal hypertrophy with a small LV cavity
- The mural endocardium may be thickened
- if LV outflow tract obstruction is present:
- Often a plaque located on the upper septal area where the mitral valve repeatedly has come in contact with the septum.
- The left atrium is usually dilated
- A result of mitral regurgitation and diastolic dysfunction.

Pathology

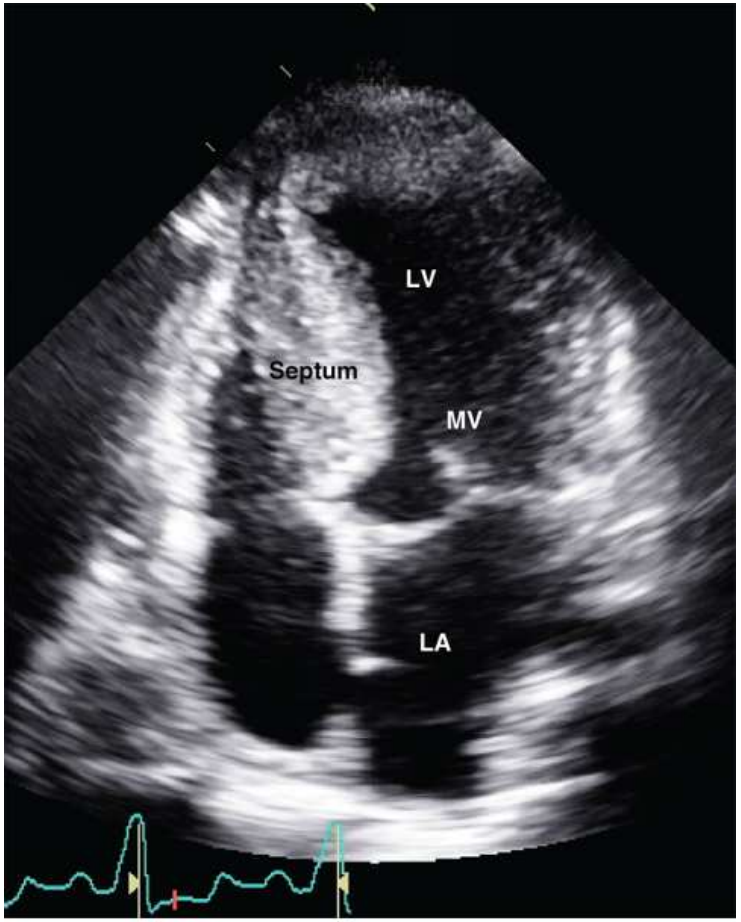
- The mitral valve itself may be abnormal
- Elongation of the mitral chordae and anterior displacement of hypertrophied papillary muscles.
- Abnormal attachments of the mitral valve chordae into the septum
- Insertion of the papillary muscle head directly into the mitral leaflets
- Epicardial coronary arteries are usually normal
- If they follow an intramural course they may be compressed during ventricular systole.

Pathology

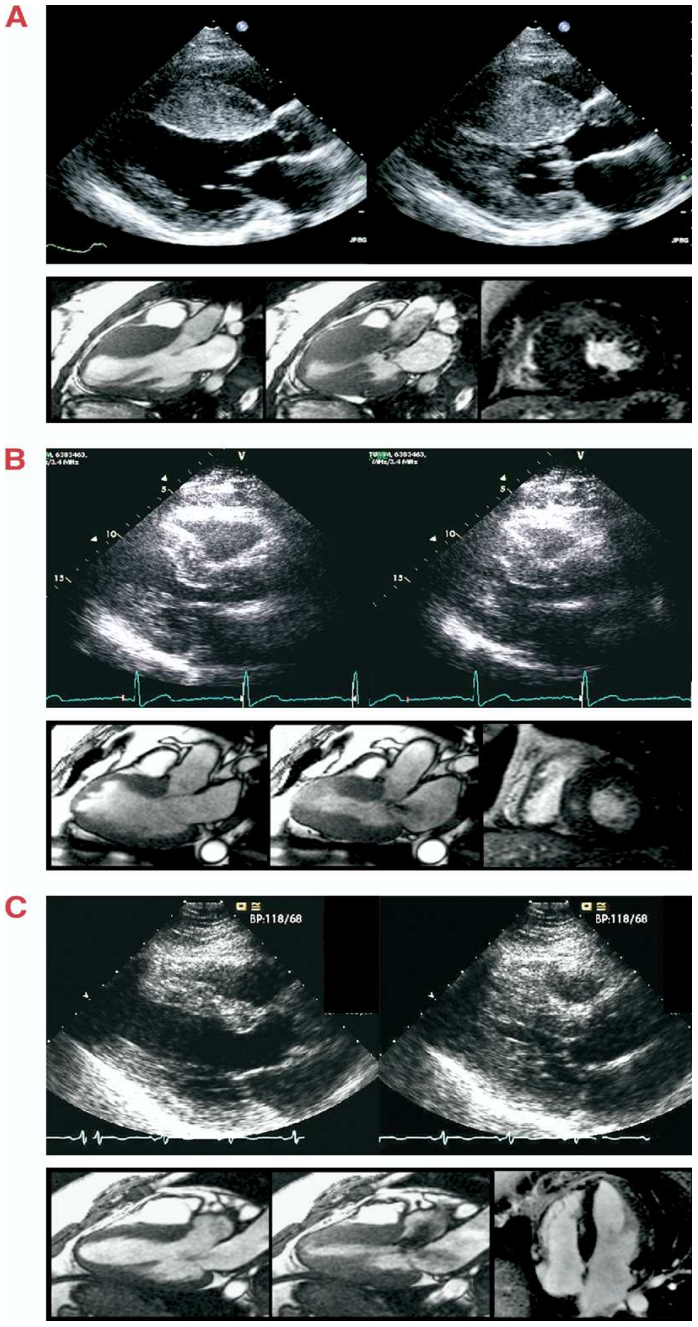
- Left ventricular apical rotation and twist are dependent on the pattern of left ventricular hypertrophy.
- In patients with a sigmoidal septal curvature, left ventricular apical rotation and twist are increased as compared to patients with a reverse septal curvature.
- Increased ventricular trabeculation is common.
- The extravascular compressive forces caused by gradients due to the outflow obstruction may lead to more extensive microvascular dysfunction and subendocardial ischemia.

Pathology

- Left ventricular twist is increased as left ventricular basal rotation is augmented. The increased basal rotation is explained by:
- (1) by loss of counteraction of the subendocardial fiber helix, caused by endocardial ischemia due to microvascular dysfunction; and,
- (2) the larger radius differences between the subepicardium and subendocardium in hypertrophic muscle may increase the dominant action of the subepicardial fibers and increase basal rotation.



Hypertrophic cardiomyopathy. This echocardiogram of hypertrophic cardiomyopathy shows asymmetric hypertrophy of the septum compared to the lateral wall of the left ventricle (LV). The mitral valve (MV) is moving anteriorly toward the hypertrophied septum in systole. The left atrium (LA) is enlarged. Note that the echocardiographic and pathologic images are vertically opposite, such that the LV is by convention on the top right in the echocardiographic image and bottom right in the pathologic images. (Image courtesy of Justina Wu, MD, Brigham and Women's Hospital, Boston.)

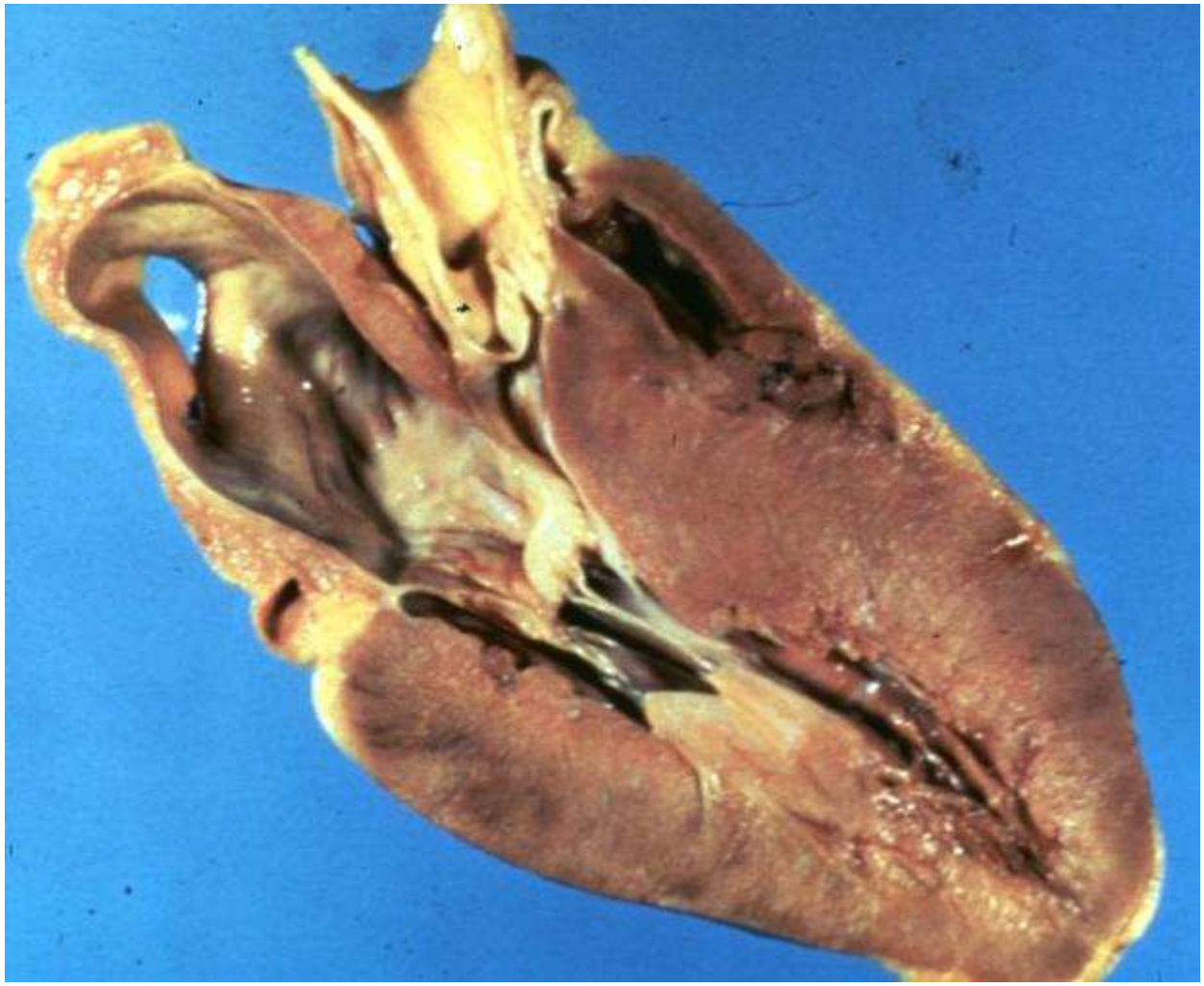


(A) Reverse curvature septum HCM shows a predominant mid-septal convexity toward the left ventricular cavity with the cavity itself often having an overall crescent shape.
Dynamic subaortic obstruction is present in this example with systolic anterior motion of the mitral
leaflets and turbulent flow in the outflow tract. Prominent foci of myocardial fibrosis are present in the anteroseptum and inferoseptum.

(B) Sigmoid septum HCM shows a generally ovoid left ventricular cavity with the septum being concave to the cavity and a prominent basal septal bulge. Subaortic obstruction is present in this example with systolic anterior motion of the mitral leaflets and a posteriorly directed jet of mitral regurgitation. A small amount of myocardial fibrosis is seen in the septum.

(C) Neutral septum HCM shows an overall straight septum that is neither predominantly convex nor concave toward the left ventricle cavity. Subaortic

Hypertrophic cardiomyopathy



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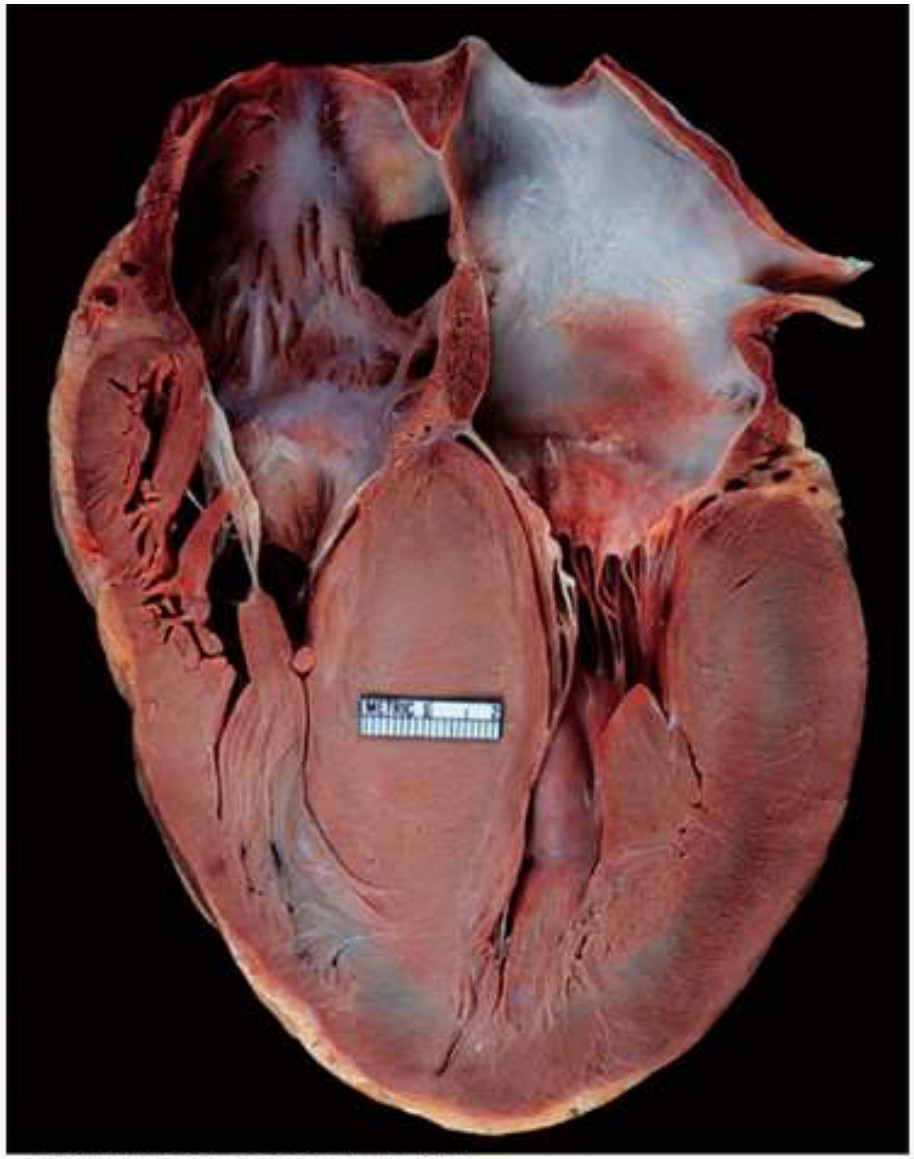
Accessed 12/09/2019



Source: Valentin Fuster, Robert A. Harrington, Jagat Narula, Zubin J. Eapen: Hurst's The Heart, Fourteenth Edition: www.accessmedicine.com

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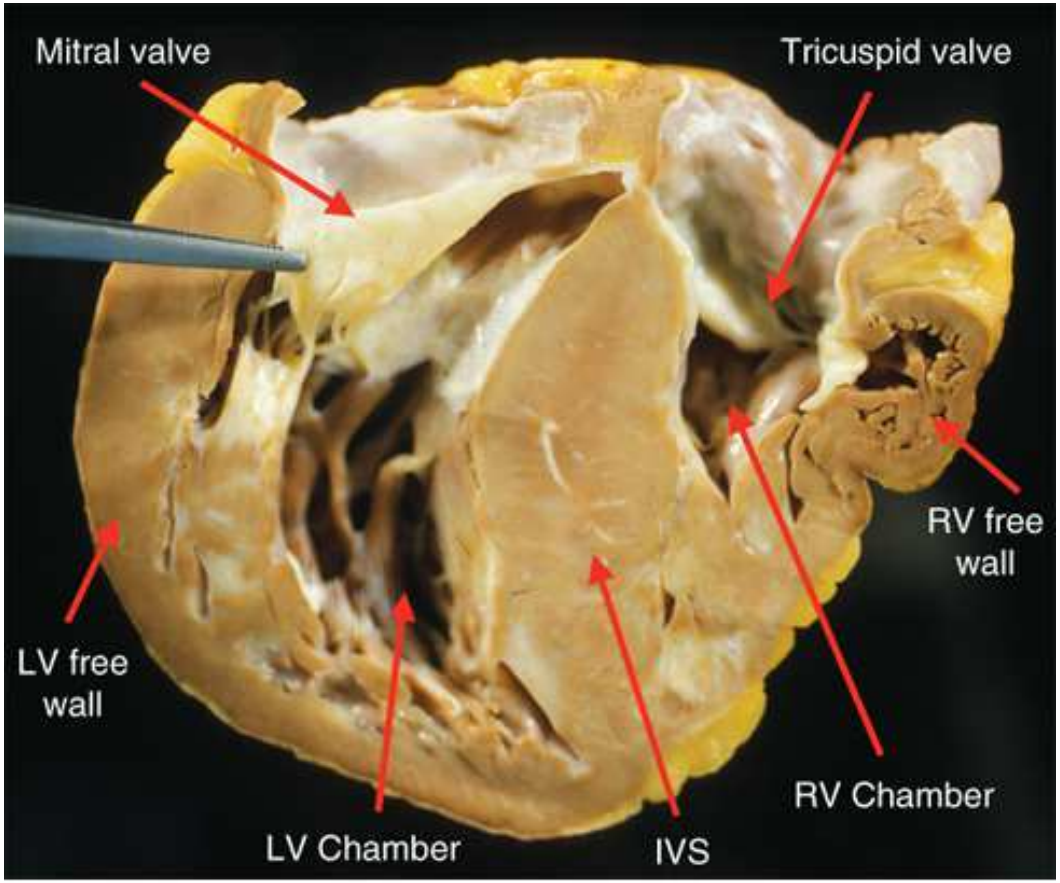
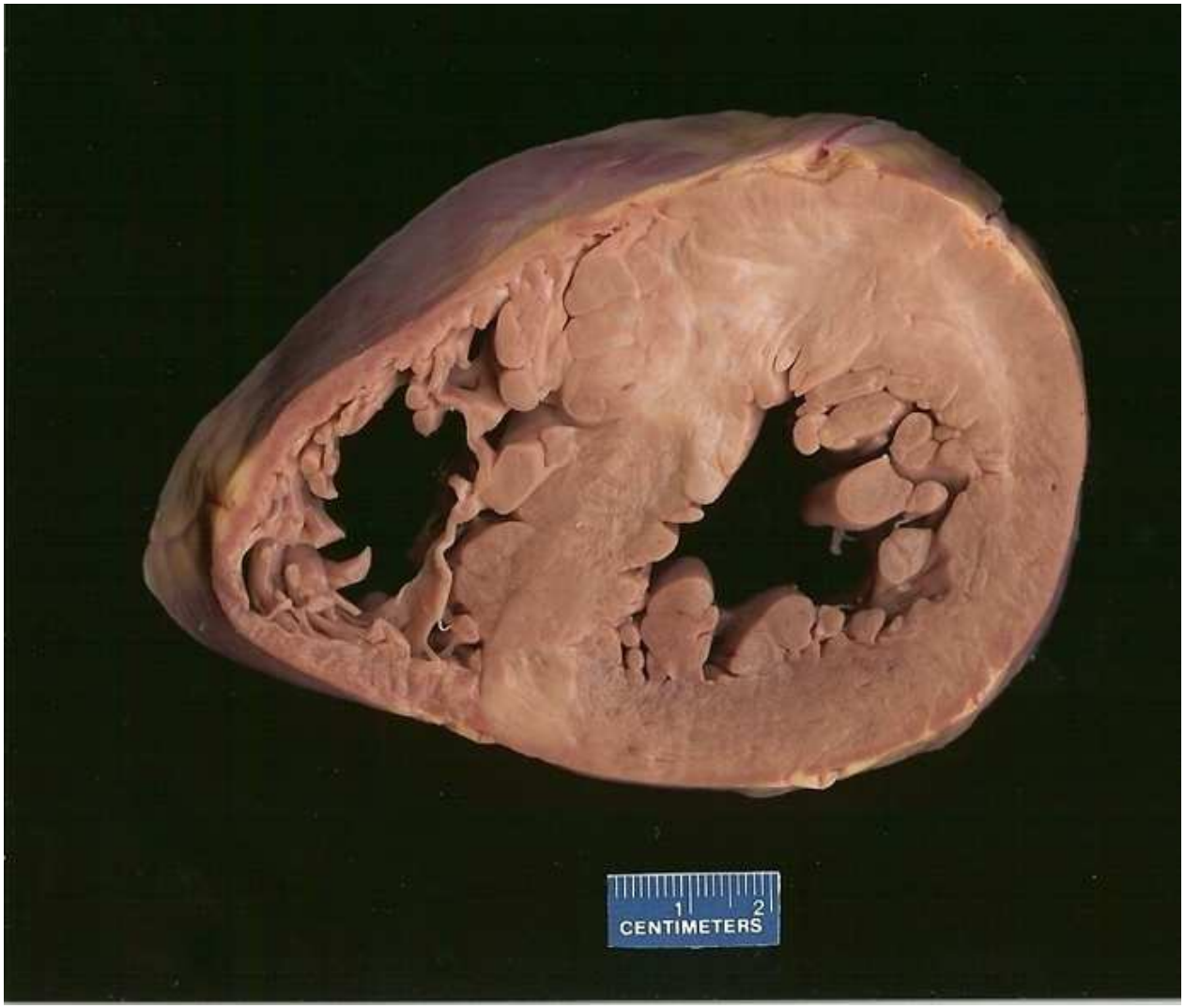
04/20/2020



Hypertrophic cardiomyopathy. Gross specimen of a heart with hypertrophic cardiomyopathy removed at the time of transplantation, showing asymmetric septal hypertrophy (septum much thicker than left ventricular free wall) with the septum bulging into the left ventricular outflow tract causing obstruction. The forceps are retracting the anterior leaflet of the mitral valve, demonstrating the characteristic plaque of systolic anterior motion, manifest as endocardial fibrosis on the interventricular septum in a mirror-image pattern to the valve leaflet. There is patchy replacement fibrosis, and small thick-walled arterioles can be appreciated grossly, especially in the interventricular septum. IVS, interventricular septum; LV, left ventricle; RV, right ventricle. (Image courtesy of Robert Padera, MD, PhD, Department of Pathology, Brigham and Women's Hospital, Boston.)

Hypertrophic obstructive cardiomyopathy



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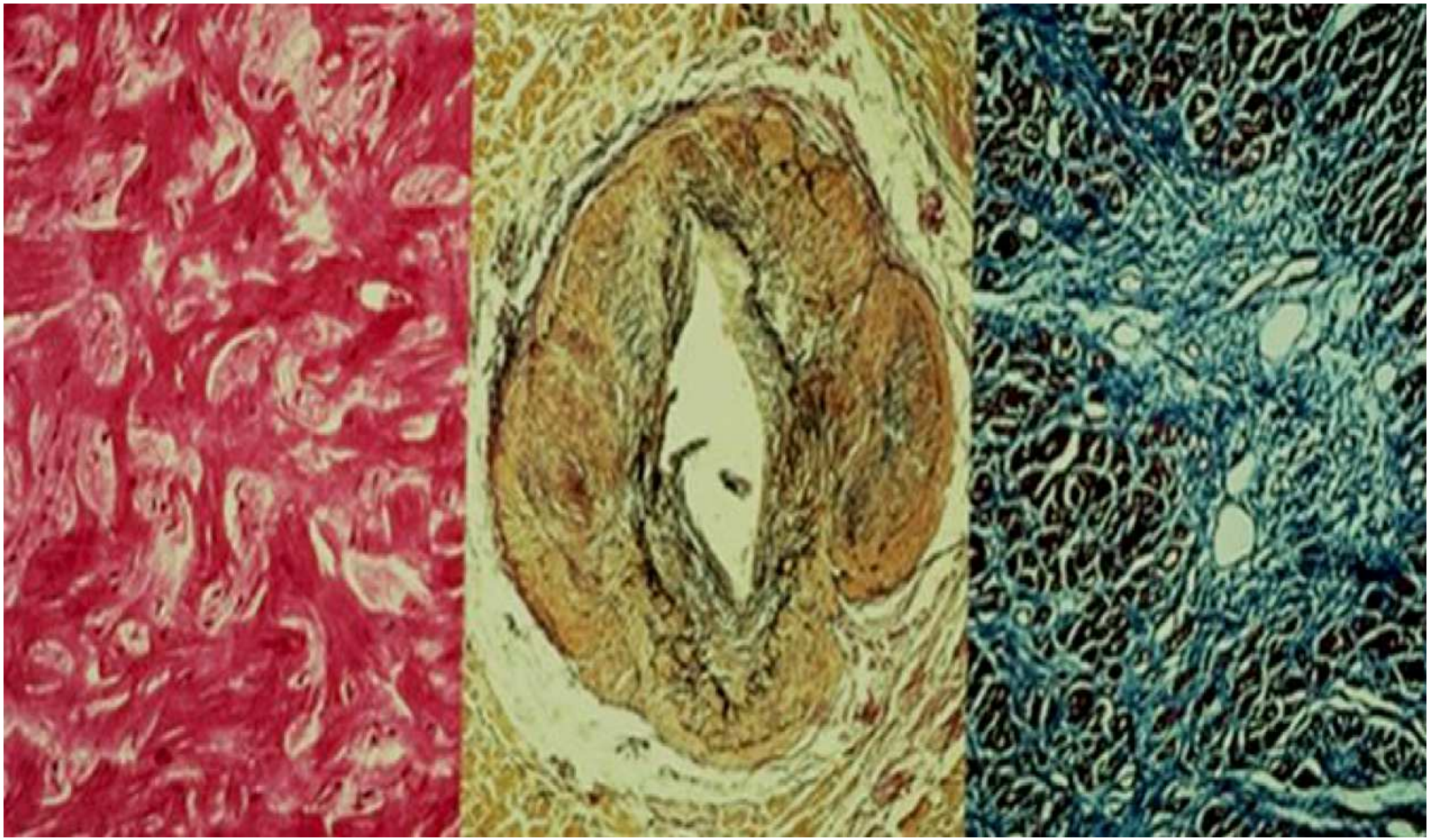
Accessed 12/09/2019

Hypertrophic cardiomyopathy



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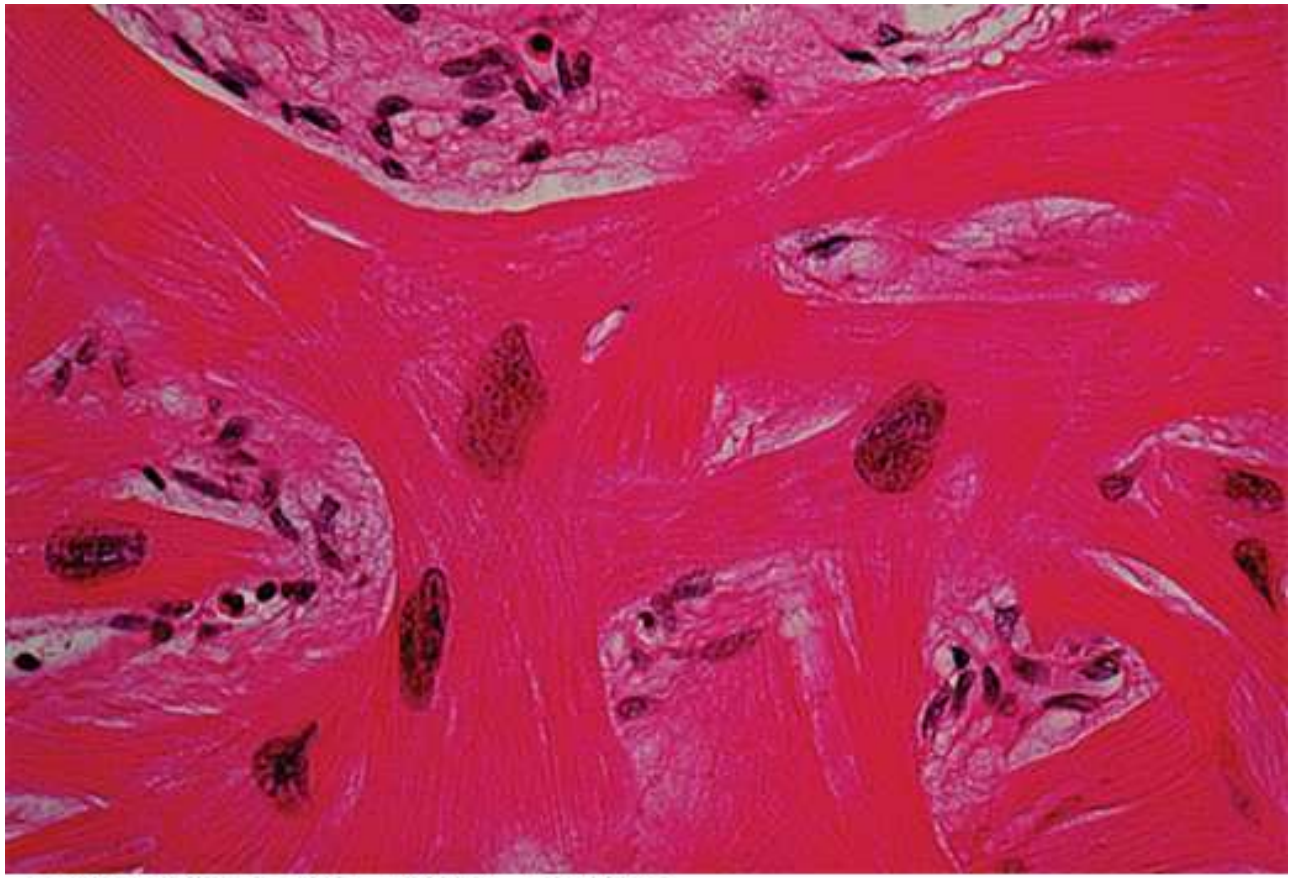
Accessed 12/09/2019



Histopathology

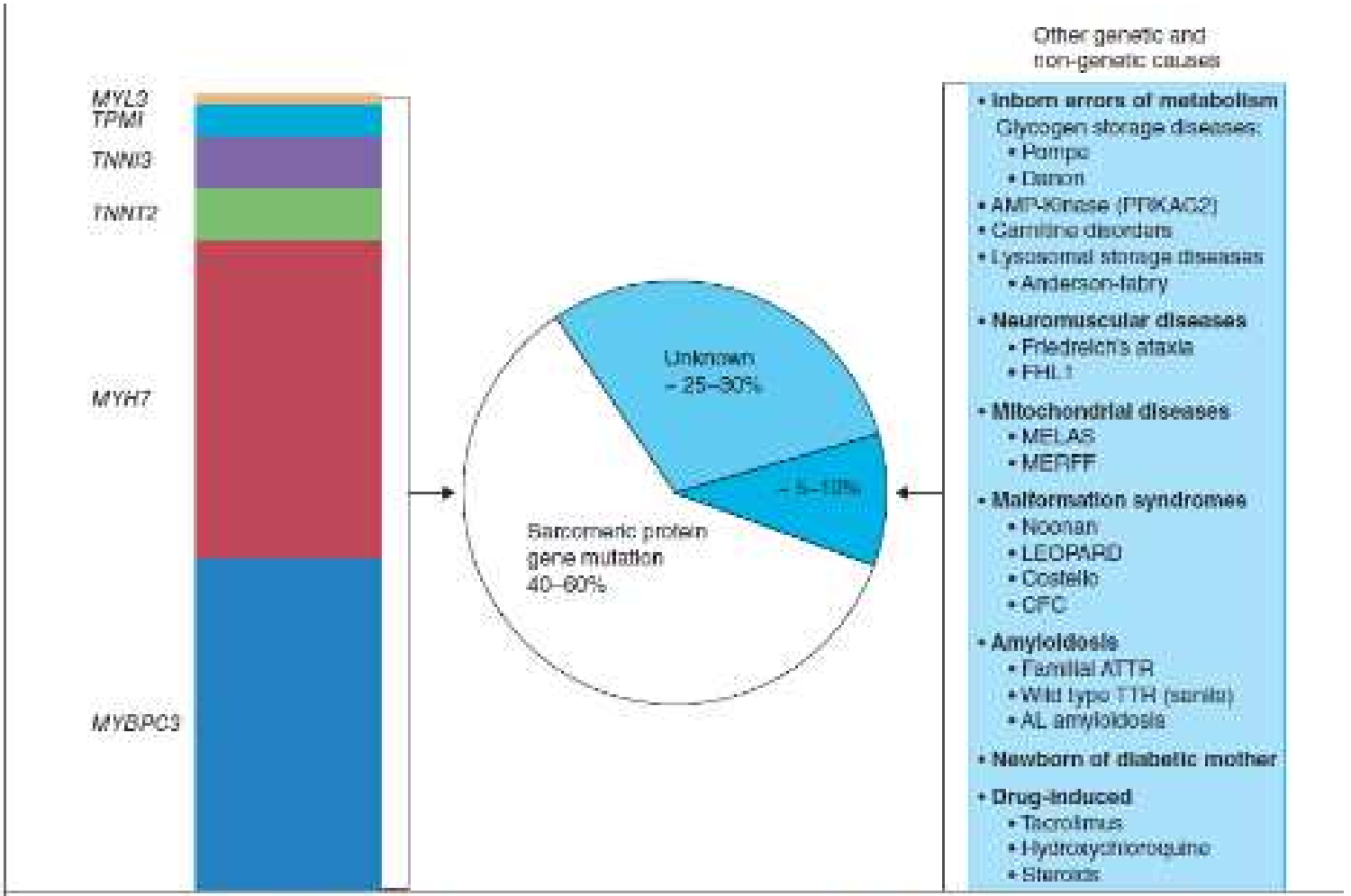
Giant myocytes

Myofiber disarray

Fibrosis

Molecular changes in HCM

- 75%-80% involve cardiac myosin heavy chain (MYH7) and cardiac myosin binding protein C (MYBPC3)
- A mis-sense mutation in which the abnormal protein is incorporated into the sarcomere (MYH7)
- Nonsense mutation or SNP frame shift leading to haploinsufficiency (MYBPC3)



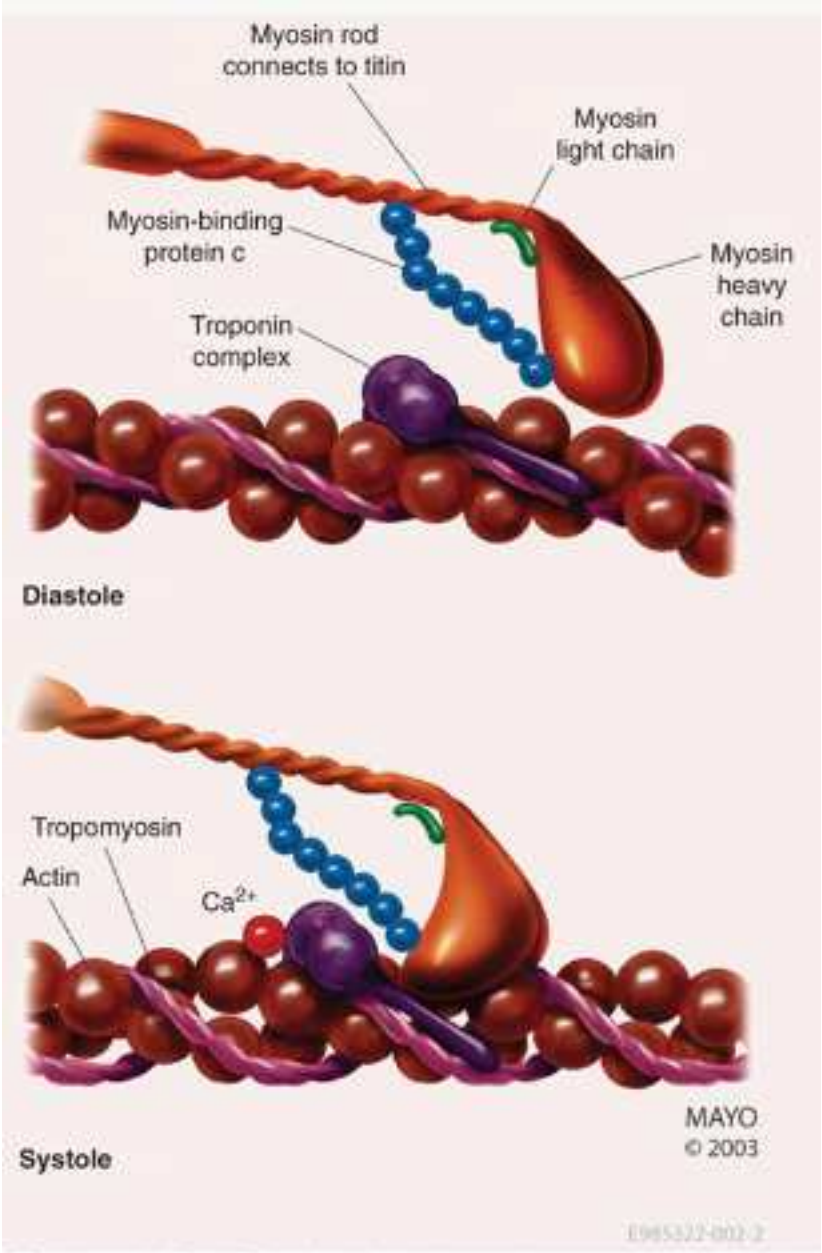
The majority of cases in adolescents and adults are caused by mutations in sarcomere protein genes. AL = amyloid light chain; ATTR = amyloidosis, transthyretin type; CFC = cardiofaciocutaneous; FHL-1 = Four and a half LIM domains protein 1; LEOPARD = lentigenes, ECG abnormalities, ocular hypertelorism, pulmonary stenosis, abnormal genitalia, Retardation of growth, and sensorineural deafness; MELAS = mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes; MERRF = myoclonic epilepsy with ragged red fibres; MYL3 = myosin light chain 3; MYBPC3 = myosin-binding protein C, cardiac-type; MYH7 = myosin, heavy chain 7; TNNI3 = troponin I, cardiac; TNNT2 = troponin T, cardiac; TTR, transthyretin.

Table 1. Frequency of Genetic Mutations in HCM by Septal Contour

Characteristics	Reverse	Sigmoid	Neutral	Apical
Genotype positive (%)	79	8	41	30
Family history of HCM (%)	45	21	34	22
Family history of SCD (%)	19	10	16	11
Type of mutation				
None (%)	21	92	59	68
MYBPC3 (%)	34	5	19	14
MYH7 (%)	29	2	13	14
MYL2 (%)	4	0	3	3
TNNT2 (%)	3	1	0	3
TNNI3 (%)	2	1	3	0
TPM1 (%)	2	0	0	0
ACTC (%)	1	0	0	0
Multiple mutations (%)	5	0	3	0

ACTC = actin; HCM = hypertrophic cardiomyopathy; MYBPC3 = myosin binding protein C; MYH7 = myosin heavy chain; MYL2 = myosin light chain; SCD = sudden cardiac death; TNNI3 = troponin I; TNNT2 = troponin T; TPM1 = α-tropomyosin.

Syed, Imran S, Ommen, Steve R, Breen, Jerome F, Tajik, A Tamil, "Hypertrophic Cardiomyopathy: Identification of Morphological Subtypes by Echocardiography and Cardiac Magnetic Resonance Imaging," Journal of the American College of Cardiology: Cardiovascular Imaging (2008) 1:376-378. D O I : 1 0 . 1 0 1 6 / j . j c m g . 2 0 0 8 . 0 2 . 0 0 8



Source: Valentin Fuster, Robert A. Harrington, Jagat Narula, Zubin J. Eapen: Hurst's The Heart, Fourteenth Edition: www.accessmedicine.com

Molecular changes in HCM

- Mutations in cardiac troponin T (TNNT2), troponin I (TNNI3), α- tropomyosin (TPM1), myosin light chains (MYL2, MYL3), and cardiac actin (ACTC1) account for 15% to 20% of mutation-positive individuals.

- Mutations in other sarcomere or related genes, including Z-disc protein genes like muscle LIM protein (CSRP3) or calcium-handling genes such as phospholamban (PLN), account for fewer than 1% of cases each.

Molecular changes in HCM

- 5% to 10% of cases are caused by metabolic or storage disorders
- The three most common metabolic causes of HCM
- All with a prevalence of approximately 1%
- Anderson-Fabry disease
- Glycogen storage disease caused by PRKAG2 mutations
- Danon disease.

RESTRICTIVE CARDIOMYOPATHY

Restrictive cardiomyopathy

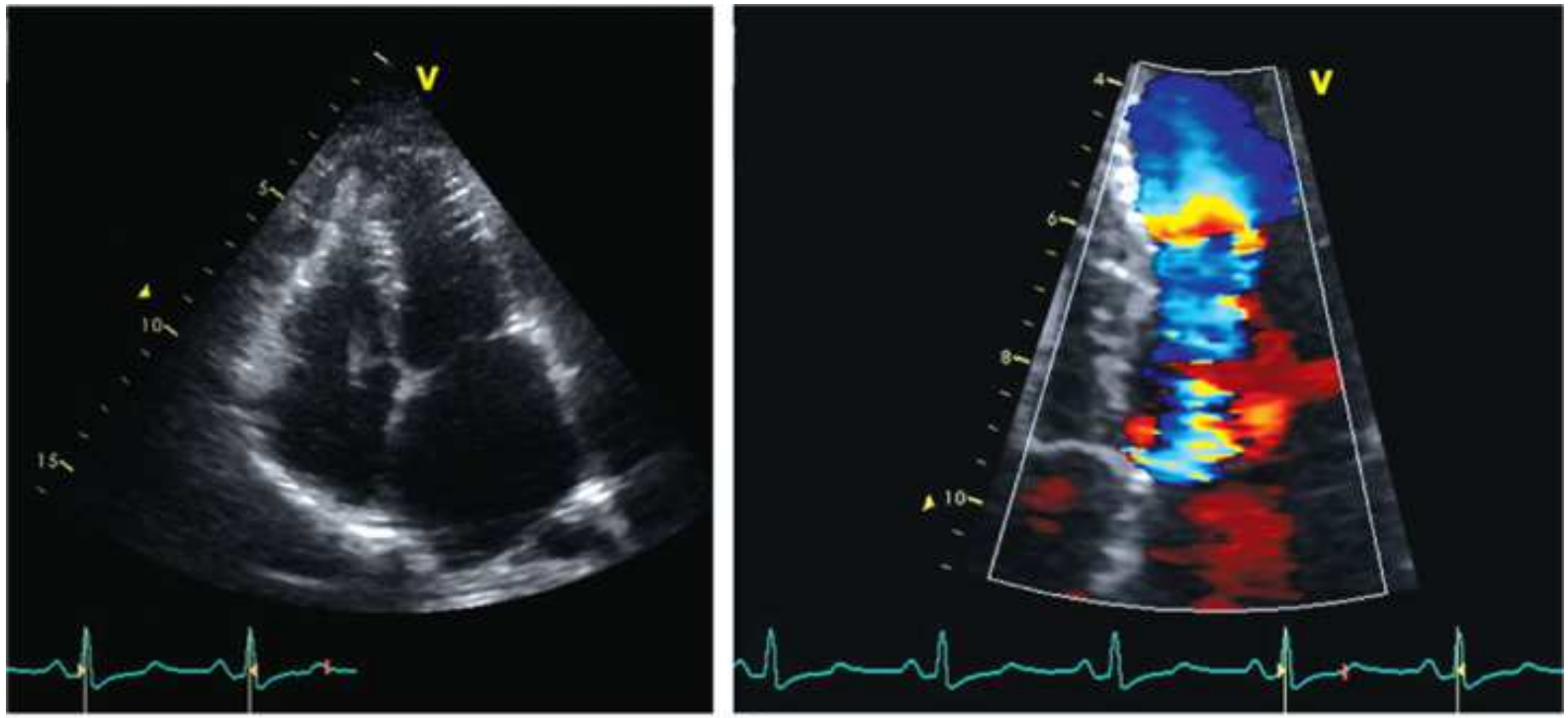
- Diastolic dysfunction
- Systolic function preserved
- Restrictive physiology can be observed in diseases affecting endocardium, myocardium, and epipericardial layers/structures
- There is increased myocardial stiffness that causes a precipitous elevation of ventricular pressure matched by a limited increase in volume
- There is normal or reduced volume of one or both ventricles
- There is normal wall thickness

Restrictive cardiomyopathy

- Usually presents before age 5
- Infants may present with failure to thrive, fatigue, syncope
- Atrial enlargement on EKG
- LV compliance diminished
- Brain natriuretic protein (BNP) elevated.
- TNNI3 mis-sense mutation common
- TNNT2 mutations are less common
- Differentiate from constrictive pericarditis with echocardiogram
- Endomyocardial biopsy to exclude treatable causes

Restrictive cardiomyopathy

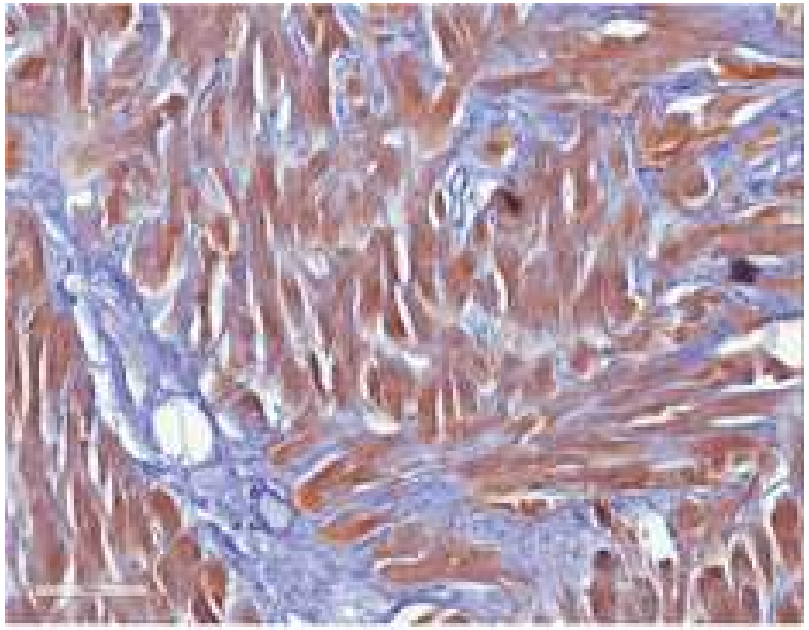
- Kussmmaul sign (classic) is a rise in jugular venous pressure with inspiration
- Thrombotic events may be seen.
- Arrhythmias also may be present.
- ACE inhibitors
- Reduce afterload
- Reduce contractile force:
- Calcium channel blockers
- β-blockers



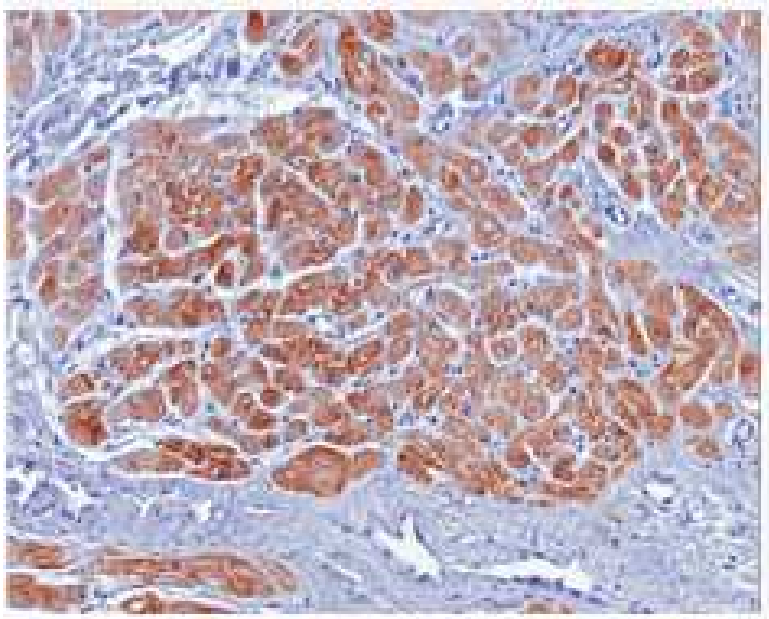
A B

Male, First diagnosis: 10 years → Follow-up: 7 years

$M_{H(Obs)}$ O_H G_{AD} $E_{G\text{-}TNNI3[p.Leu144Gln]}$ $S_{C\text{-}I}$



A



B

Anti-troponin immunostain demonstrating myocyte disarray and fibrosis in restrictive cardiomyopathy.

Accessed 04/15/2020

Restrictive cardiomyopathy

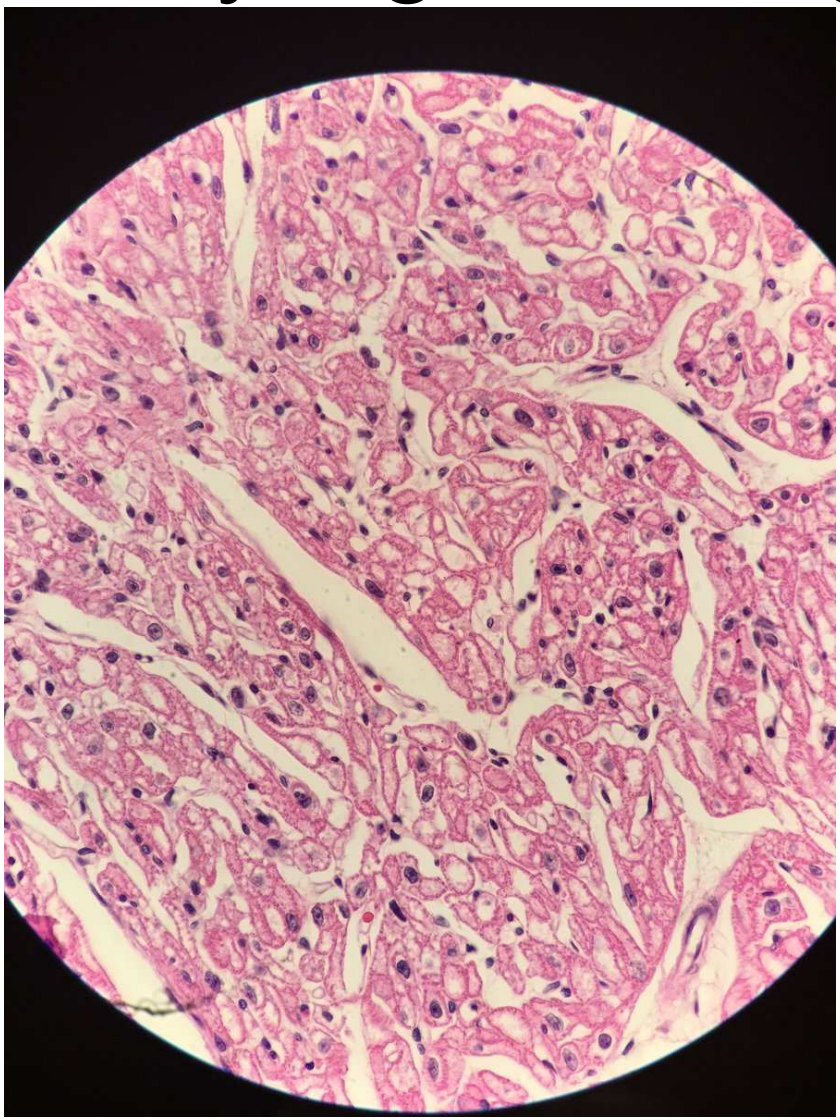
- Multiorgan diseases
- The myocardium is partially infiltrated by non-contractile tissue or extracellular material.
- This infiltration of the myocardium impairs the ability of the heart to dilate and fill properly.
- Pompei's glycogenosis
- Amyloidosis (TTR gene as well as light chain disease)
- Pan-cardiac involvement
- Hemochromatosis
- Sarcoidosis

Restrictive cardiomyopathy

- Pseudoxanthoma elasticum
- Endocardial fibrosis
- Etiology unknown
- Right atrial dilatation.
- Right ventricle fibrosis at the apical level.

  Fibrosis embeds the right ventricular trabeculae, obliterates the apex of the right ventricle, and fixes the tricuspid valve apparatus.
- Other valves are spared

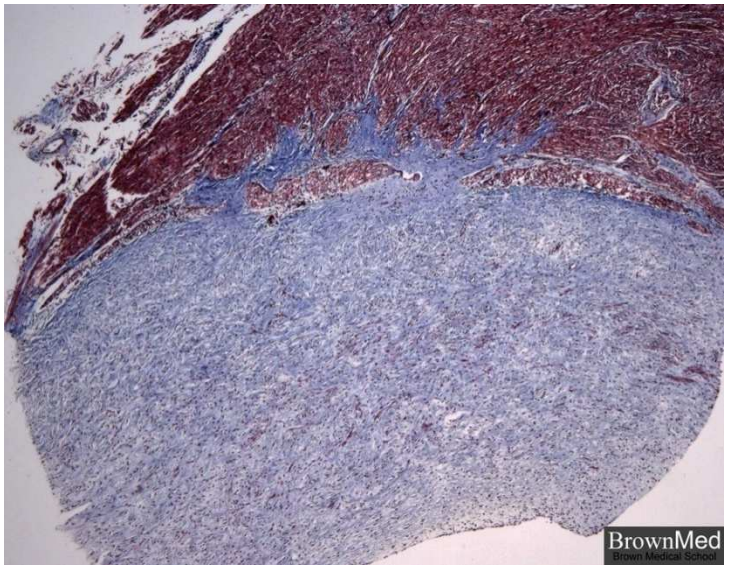
Glycogen storage disease

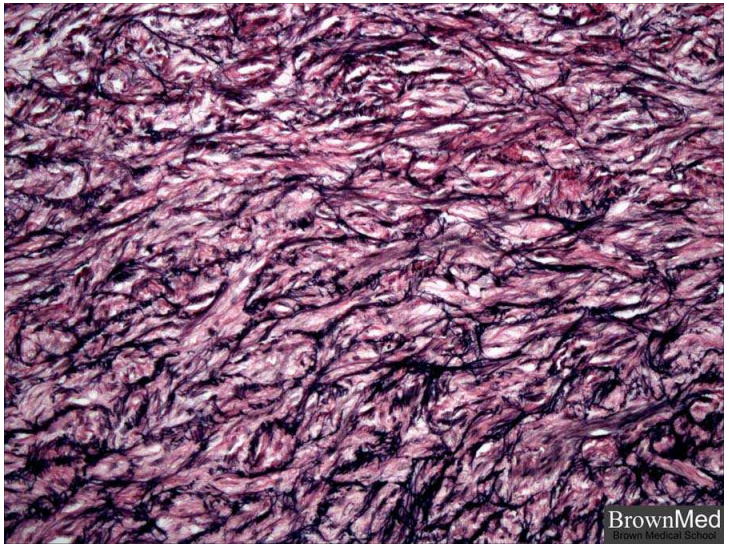


Glycogen containing vacuoles (excessive).
Glycogen is normally found in a newborn heart.
The heart biopsy is of a 5 month-old.

https://twitter.com/seattlequinns/status/960693080889241602
Accessed 12/10/2019

Endomyocardial fibrosis



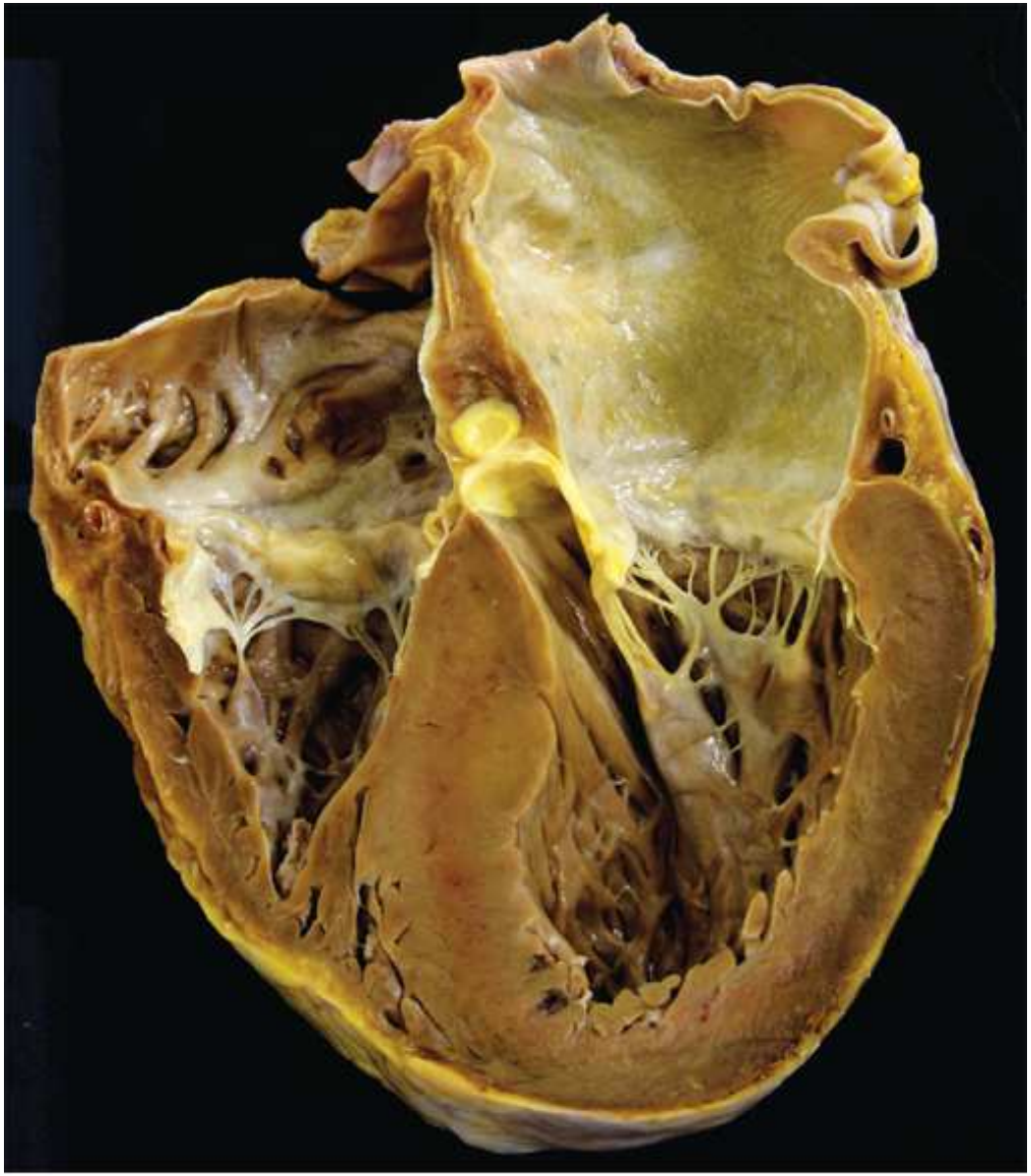


Upper:
Trichrome stain demonstrating fibrosis and proliferation of elastic fibers with infiltration of myocardium.
A reactive process

Lower:
Von Giesen stain
demonstrating elastic fibers

https://www.brown.edu/Courses/Digital_Path/systemic_path/cardio/endofibro-micro2.html

Accessed 12/10/2019



Amyloidosis

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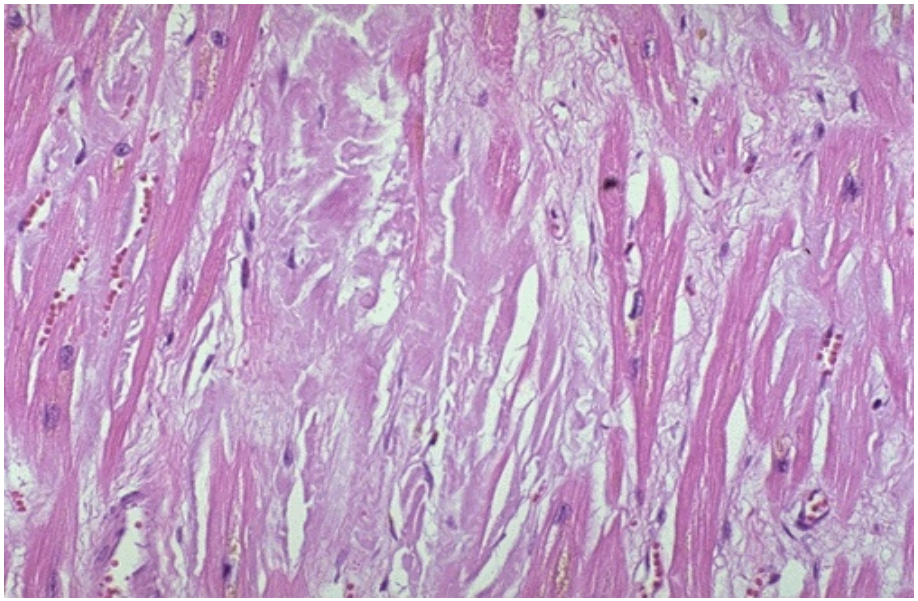
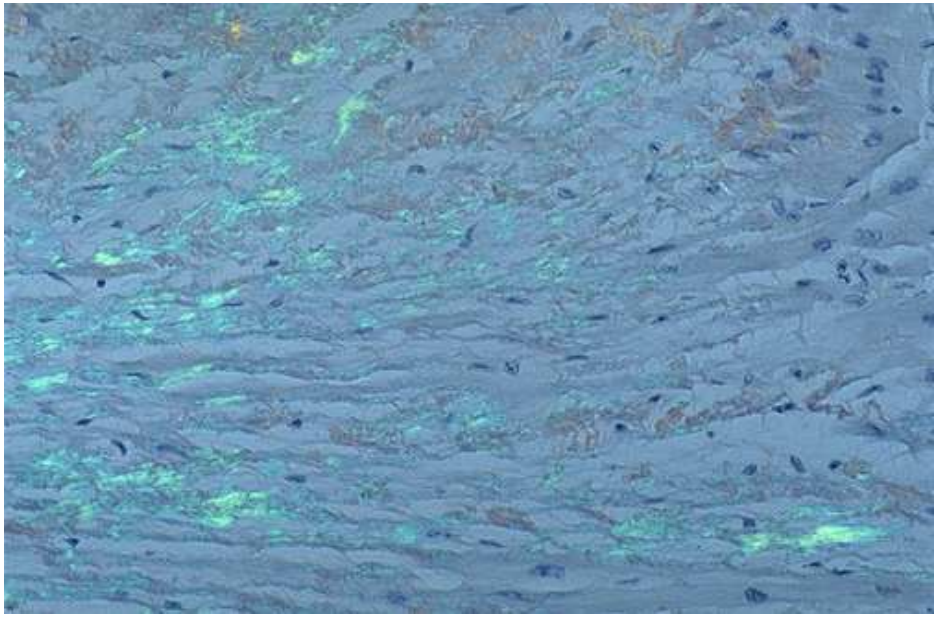
Amyloidosis





Amorphous pink material demonstrated between myocardial fibers (Upper) that stains orange-red on Congo Red stain but here is apple-green as polarized light is used to visualize the infiltrate (Lower)

Upper: https://webpath.med.utah.edu/CVHTML/CV072.html
Lower: https://webpath.med.utah.edu/CVHTML/CV073.html

Accessed 12/10/2019

Hemochromatosis

- Hemochromatosis reflects life-long iron accumulation.
- Symptoms usually appear after the liver has accumulated 20 gm storage iron.
- Normally, the liver stores 0.5gm Iron.
- Principally noted in northern Europeans (1 in 8 is a carrier).
- Presents around age 40
- Males predominate (5-7:1).
- When diagnosed in women, it is generally 10-20 years after menopause. (Menses cause loss of iron).

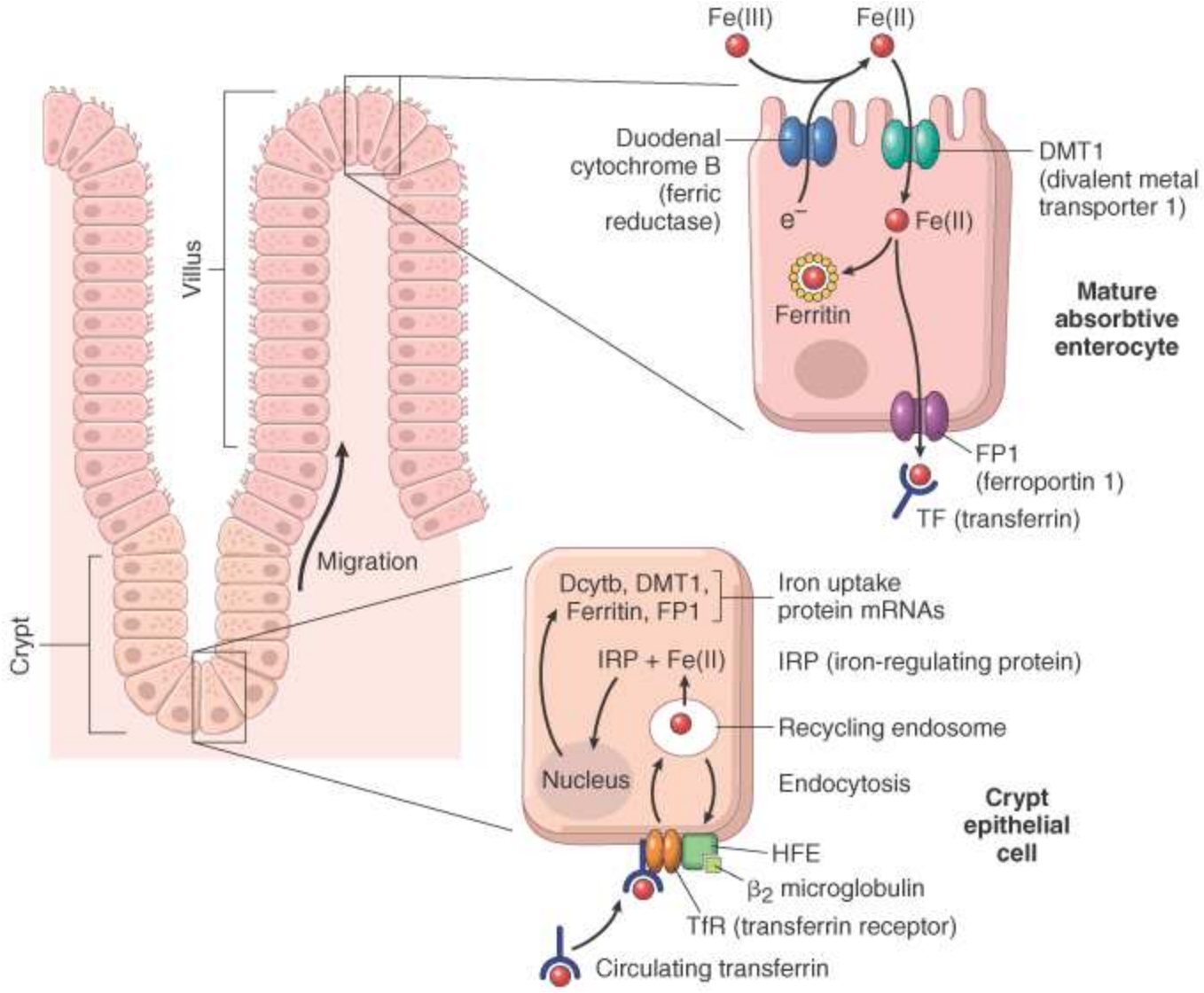
Hemochromatosis

- Cirrhosis develops in 60% of patients
- Degenerative joint disease (chondrocalcinosis) in 40%
- Acute synovitis
- Hypogonadism in 25-50% (deranged hypothalamic pituitary axis)
- Restrictive cardiomyopathy (interstitial fibrosis)
- Hemosiderin as ferritin is deposited principally in hepatocytes, but also in
- Islet cells of the pancreas, producing type 1 diabetes mellitus, and in
- Skin, increasing melanin production.
- This complex is called “bronze diabetes” (75-80%)

Hemochromatosis

- Total body content of iron is tightly regulated by intestinal absorption.
- Excessive iron is toxic as iron catalyzes lipid peroxidation.
- The free radicals produced also react with iron.
- Stimulates fibrosis.

Iron absorption and transport



Hemochromatosis

- HFE and TfR2 gene mutations cause the classic form of hemochromatosis.
- Transferring receptor 2 is highly expressed in hepatocytes; mediates the uptake of transferrin bound iron.
- H63D (Histidine to aspartate at postion 63 is a second common mutation and is noted world-wide.)
- Decrease hepcidin synthesis.

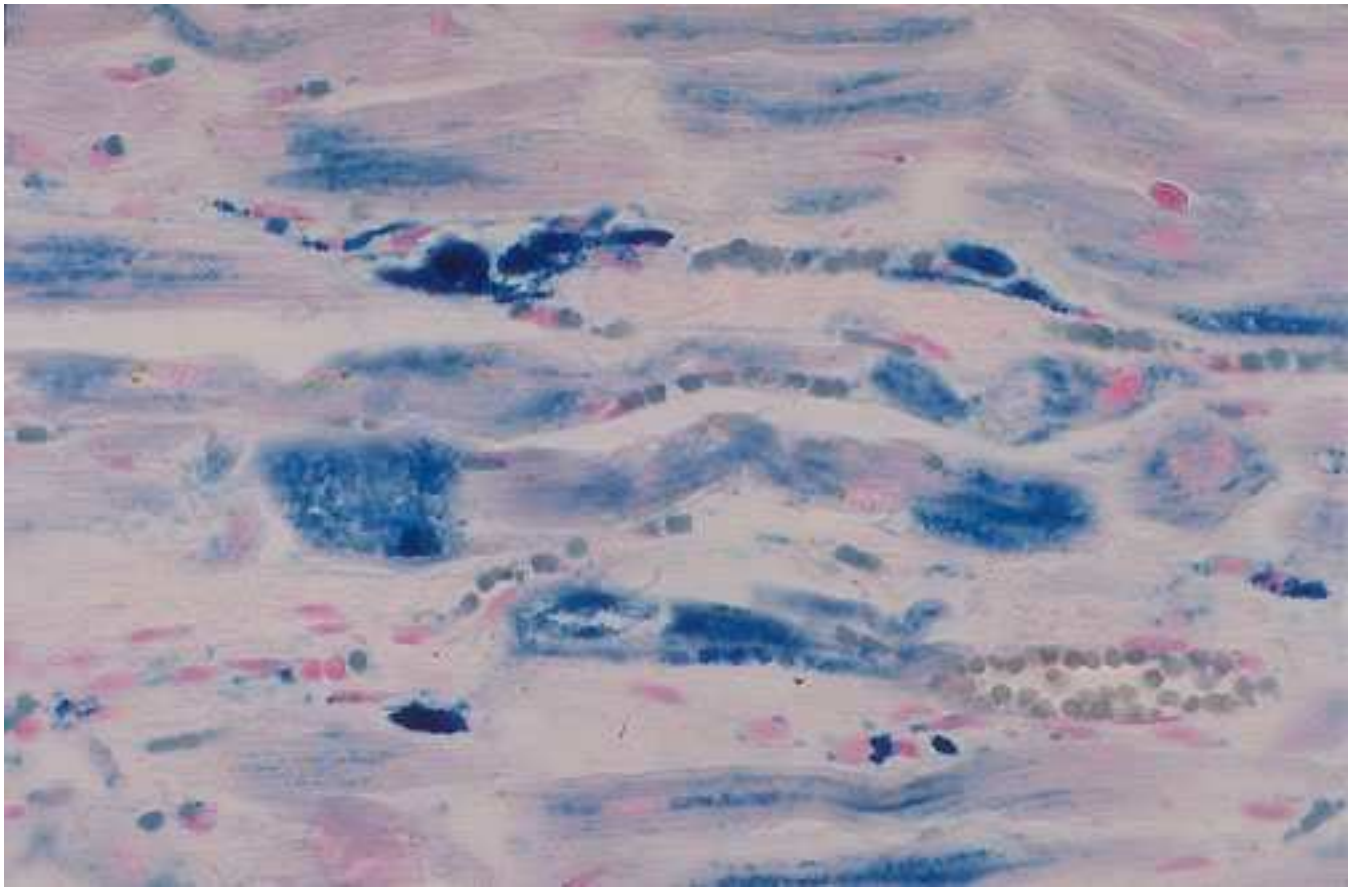
Hemochromatosis

- The HFE gene produces an HLA class I-like molecule that regulates intestinal absorption of iron by enabling the binding of iron to transferrin at the transferrin receptor.
- The gene is found at 6p21.3, close to HLA-A3 locus.
- Mutation permits net transfer at maximum, resulting in iron overload. Net iron accumulation of 0.5-1.0 gm/yr.
- The C28Y mutation of HFE gene (affects β-2 microglobulin domain) is of limited penetrance.
- Heterozygous frequency 11%
- Found in >70% of cases of hereditary hemochromatosis.

Hemochromatosis

- Lack of hepcidin expression causes hemochromatosis.
- Hepcidin is a liver expressed antimicrobial peptide, encoded by the HAMP gene
- Binds to the cellular iron efflux channel ferroportin, causing internalization and proteolysis of the channel, preventing the release of Fe^{2+} from intestinal cells and macrophages.
- A serine protease (TMPRSS6) acts as an iron sensor and suppresses HAMP expression.
- Hepcidin lowers plasma iron levels.

Hemochromatosis



Iron deposition in cardiac myocytes demonstrated on Prussian Blue stain.

https://webpath.med.utah.edu/CVHTML/CV164.html

Accessed 12/10/2019

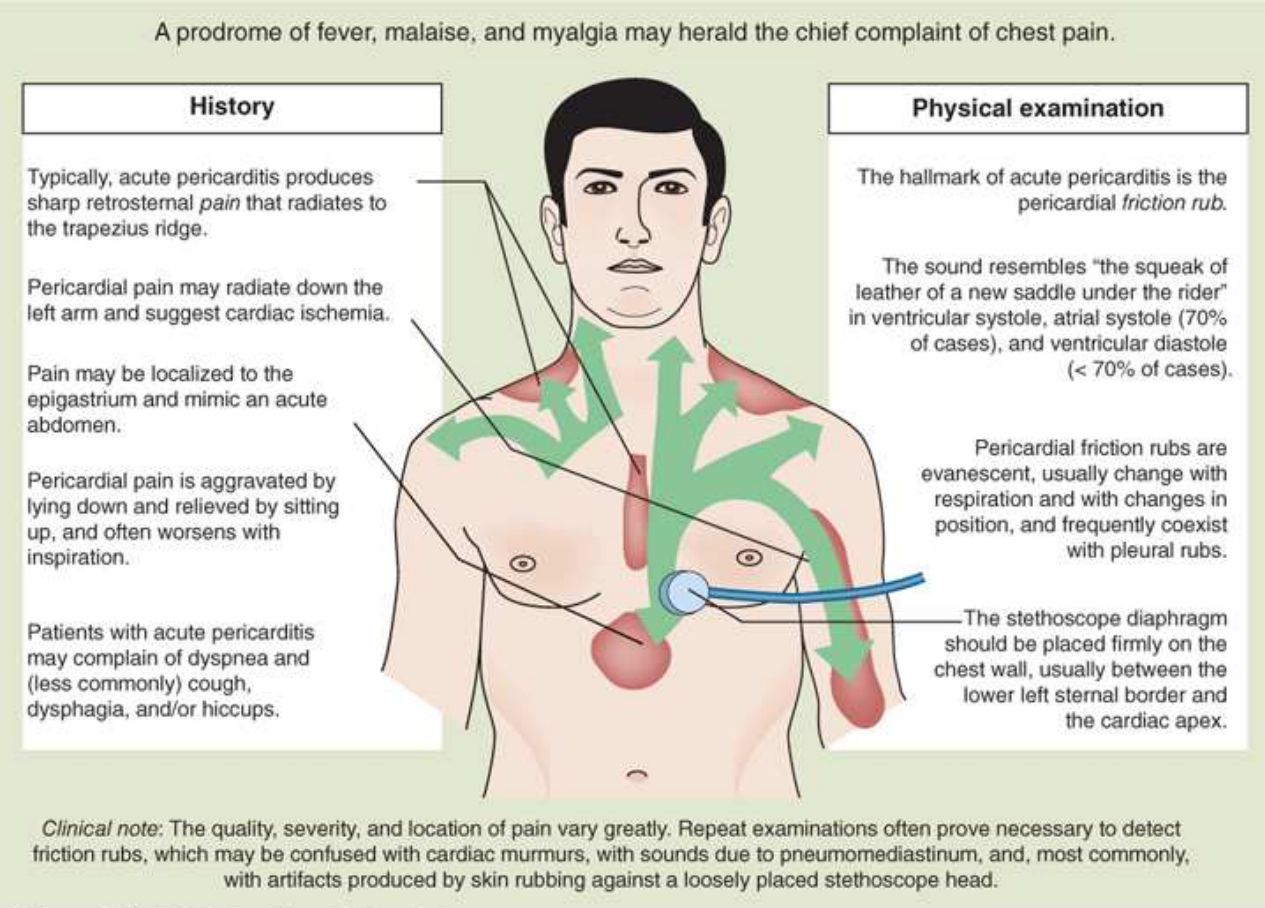
Diabetic cardiomyopathy

- Ventricular dysfunction in the absence of coronary atherosclerosis and hypertension
- Concentric LVH
- Diastolic dysfunction
- Microvascular deposition of advanced glycation end-products in small myocardial vessels
- If heart failure with reduced ejection fraction, respond to ACE inhibitors, Angiotensin II receptor blockers, β-blockers, mineralocorticoid receptor antagonists
- If ejection fraction preserved, respond to diuretics and life-style modifications

Takotsubo cardiomyopathy

- Presents as angina
- Most common in women over 50 years of age
- Precipitated by significant emotional stress
- Bereavement (“broken heart”)
- Physical illness
- Extreme pain
- Acute brain injury
- 30% have no known cause
- Catecholamine release
- Left ventricular apex weakened and enlarges while narrowing noted at mid-level of ventricle
- Spontaneous recovery

PERICARDIAL DISEASE



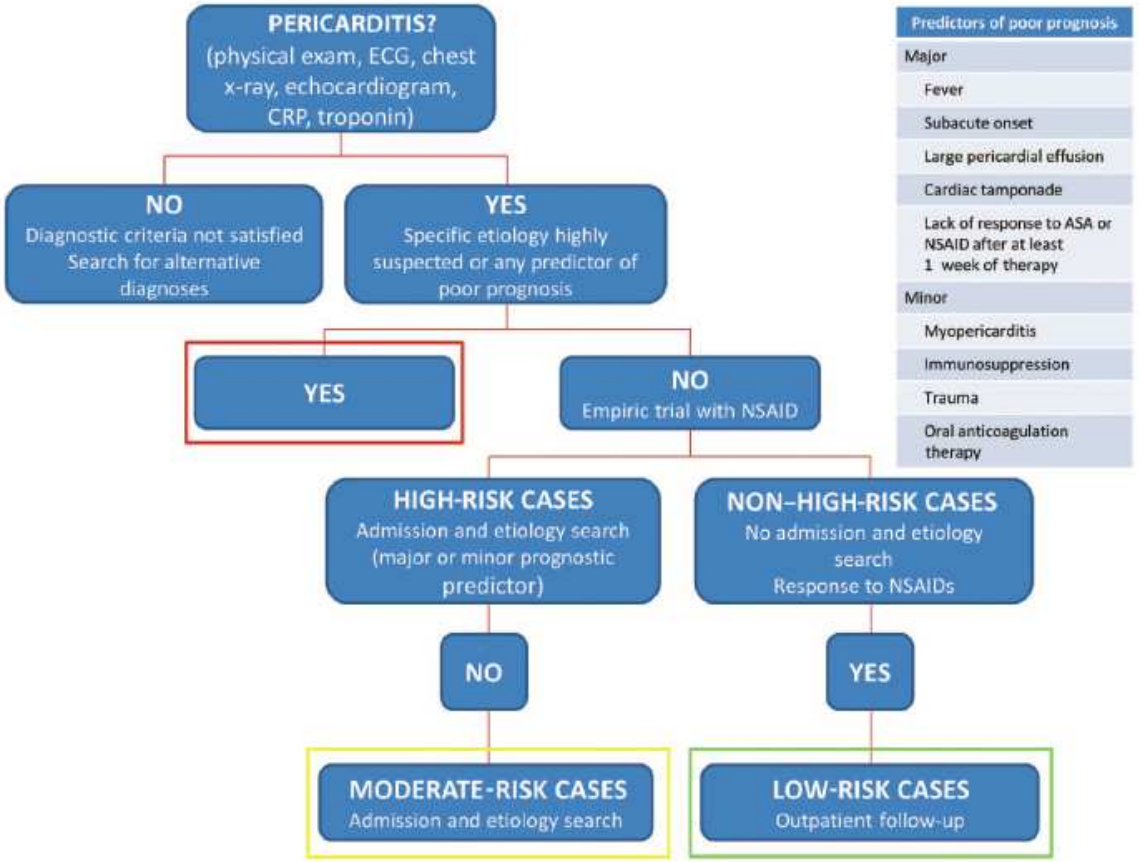
Clinical features of acute pericarditis: history and physical examination. Reproduced with permission from Hoit BD. Acute pericarditis: diagnosis and differential diagnosis. Hosp Pract. 1991;27:23-43.

Pericarditis

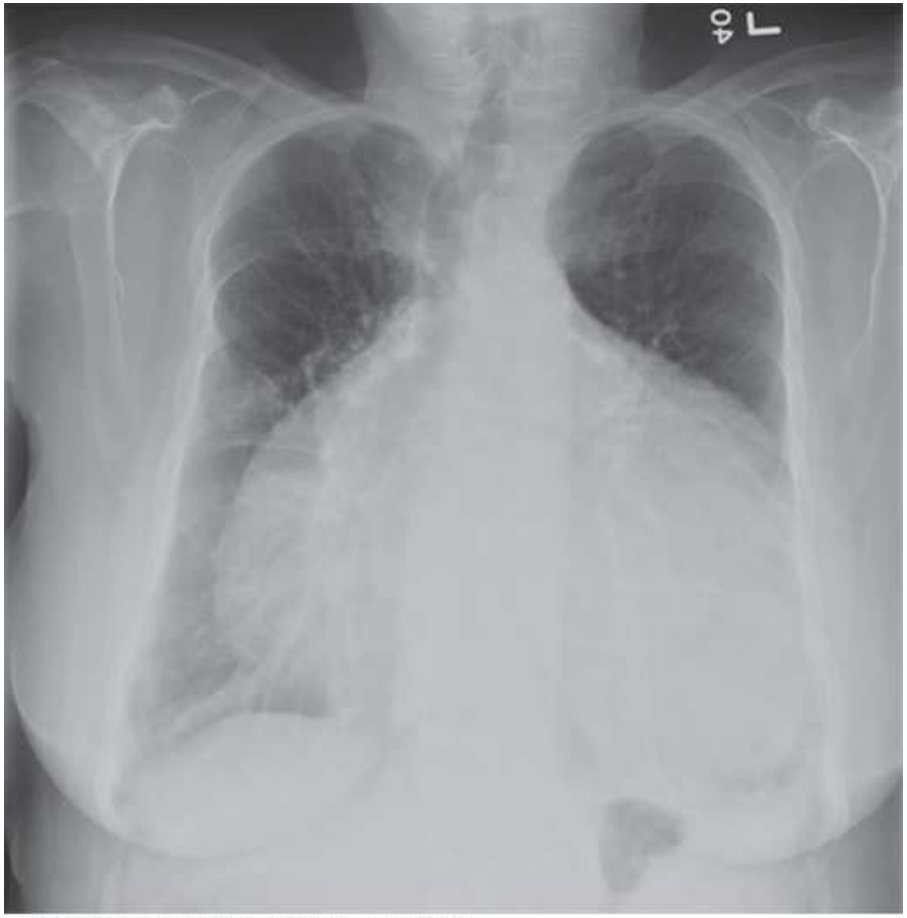
- Chest pain made worse by deep inspiration and decreased by leaning forward.
- Fever and tachycardia.
- Shortness of breath.
- 30%, Pericardial friction rub (scratchy).
- Independent of respiration
- Usually viral origin in children
- Coxsackievirus, mumps, Epstein-Barr, adenovirus, influenza, and HIV
- Pneumococci, streptococci, staphylococci, and Haemophilus influenza less common
- Purulent pericarditis

Pericarditis

- Pericardial sac may hold up to 500ml fluid without causing significant cardiac dysfunction
- EKG changes seen in 60% of patients
- PR depression in limb leads earliest sign of injury
- AVR shows PR elevation ("knuckle sign")
- Subepicardial involvement
- Widespread ST elevation
- Diagnosis requires two of three:
- Pericardial chest pain, rub, EKG changes
- 25% recur after 4-6 weeks symptom free



Algorithm for evaluation and triage of patients with acute pericarditis. ASA, acetylsalicylic acid; CRP, C-reactive protein; ECG, electrocardiogram; NSAID, nonsteroidal anti-inflammatory drug.



Chest radiography in a patient with a large pericardial effusion. Note the marked enlargement of the cardiac silhouette with a “water bottle–shaped” configuration in this patient with a large pericardial effusion. Used with permission from Dr. Nandan S. Anavekar, Mayo Clinic, Rochester, MN USA.

Table 12-14 Causes of Pericarditis

Infectious Agents
Viruses
Pyogenic bacteria
Tuberculosis
Fungi
Other parasites
Presumably Immunologically Mediated
Rheumatic fever
Systemic lupus erythematosus
Scleroderma
Postcardiotomy
Postmyocardial infarction (Dressler) syndrome
Drug hypersensitivity reaction
Miscellaneous
Myocardial infarction
Uremia
Following cardiac surgery
Neoplasia
Trauma
Radiation

TABLE 265-1

Classification of Pericarditis

Clinical Classification
I. Acute pericarditis (<6 weeks)
A. Fibrinous
B. Effusive (serous or sanguineous)
II. Subacute pericarditis (6 weeks to 6 months)
A. Effusive-constrictive
B. Constrictive
III. Chronic pericarditis (>6 months)
A. Constrictive
B. Adhesive (nonconstrictive)

Pericarditis

- Acute serous
- Non-infectious inflammatory disease
- Acute rheumatic fever and systemic lupus erythematosus as examples
- 2-5% proceed to constrictive pericarditis
- Lymphatic tumor spread
- Primary viral pericarditis may have associated myocarditis
- <1% proceed to constrictive pericarditis

Pericarditis

- Fibrinous and serofibrinous
- Presents with position dependent sharp pleuritic pain and fever
- Pericaridal friction rub prominent
- BUT may be absent If fluid separates both layers of the pericardium
- Acute myocardial infarction
- Post-myocardial infarction (Dressler's syndrome)
- Auto-immune phenomenon
- Cardiac surgery
- Uremia
- Trauma

Pericarditis

- Purulent or suppurative
- Inflammatory
- Direct extension from adjacent organs (usually, lung)
- Hematogenous seeding
- Lymphatic extension
- Reddened, granular serosal surface of the heart
- Scarring as organization of the fluid occurs
- Adhesions as a result of organization may not cause significant cardiac dysfunction
- But may lead to constrictive pericarditis in 20-30%
- Mimics restrictive cardiomyopathy

Pericarditis

- In non-developed societies, Mycobacterium tuberculosis is principal bacterial cause
- Heals by scarring
- In developed societies:
- Streptococcus, Staphylococcus, Neisseria, Legionella, and Chlamydia are common bacterial causes
- Legionella (10% of community acquired pneumonia)
- H. influenzae in children
- Viral causes are:
- Coxsackie A or B, Echovirus, Herpes viruses, Measles virus, Adenovirus, hepatitis viruses, HIV

Pericarditis

- Hemorrhagic
- Usually malignant neoplasm spread

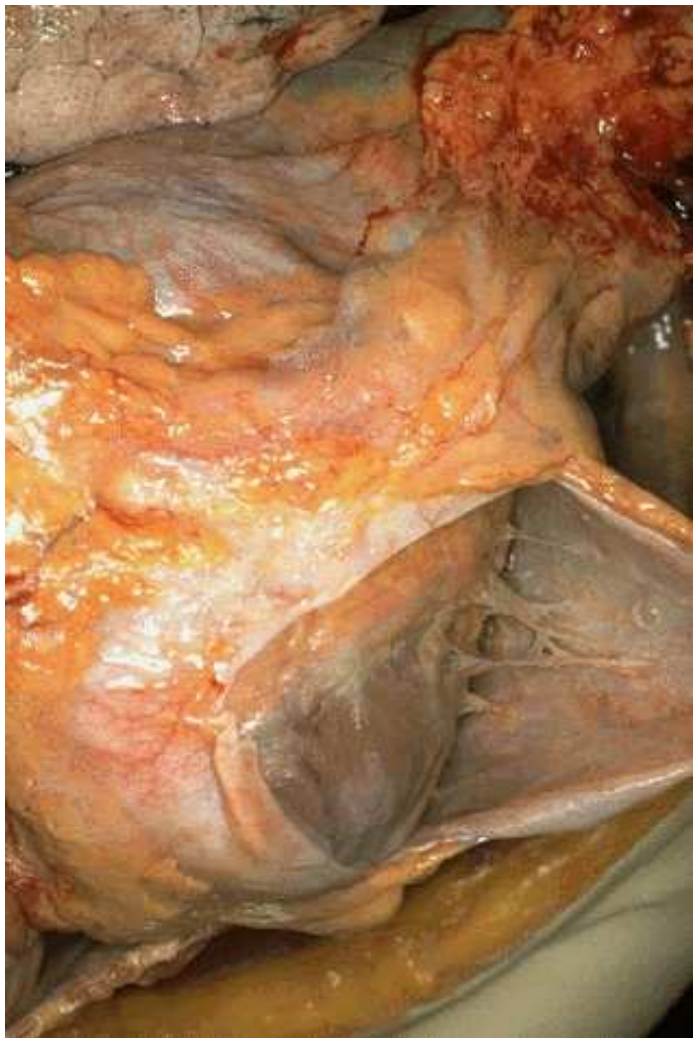
Testing

- ST elevation in chest leads for the first few days.
- Then, T wave inversion.
- PR depression is a specific finding in acute pericarditis.
- If organized
- Chamber movement restricted.
- Paradoxical pulse.
- Diminished QRS voltage (may see alteration in complex height with respiration).

Treatment

- Pericardiocentesis necessary to establish etiology.
- Drainage needed for effusions of infection.
- Treat with anti-inflammatory agents, colchicine, steroids.
- Infections treated with antibiotics.
- Avoid anticoagulants.

Fibrinous pericarditis

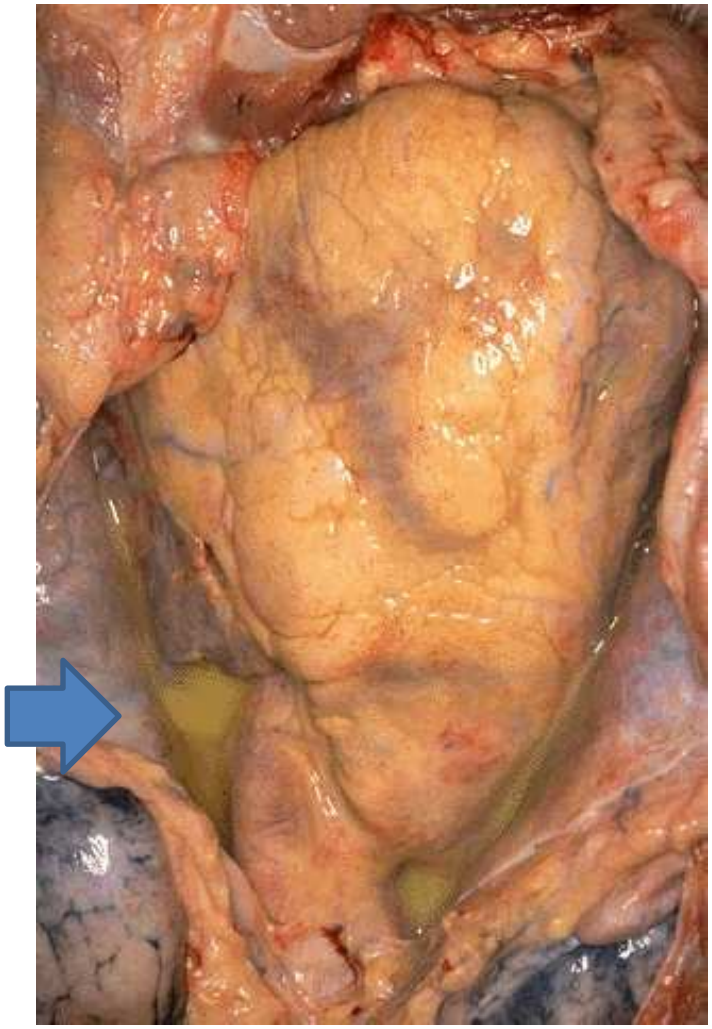


Thin strands of fibrinous material between epicardium and pericardium.

Pericardial window.

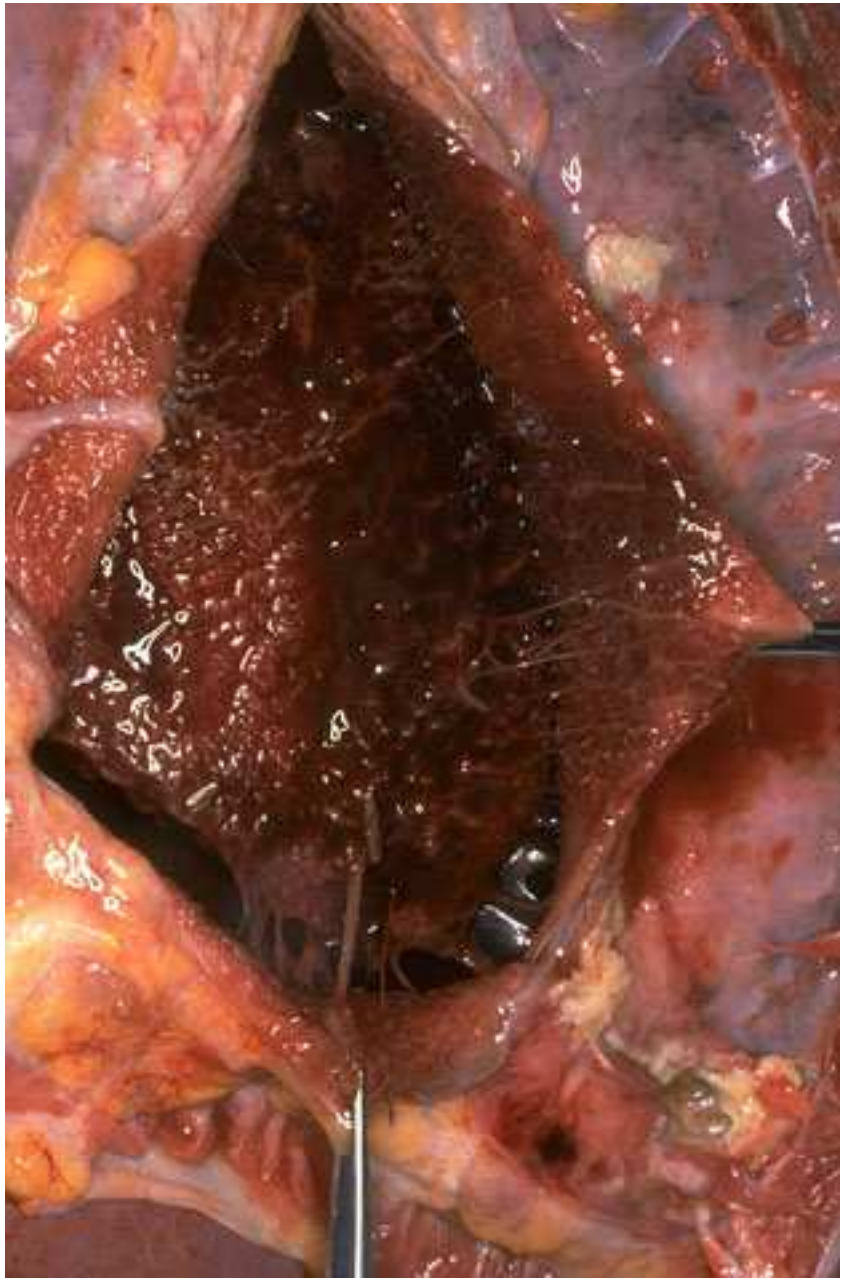
https://webpath.med.utah.edu/CVHTML/CV045.html
Accessed 12/10/2019

Purulent pericarditis



Yellow exudate in pericardial sac inferiorly (arrow)

https://webpath.med.utah.edu/CVHTML/CV051.html
Accessed 12/10/2019



Hemopericardium

Fibrinous pericarditis with hemorrhage.

Pericardial window.

https://webpath.med.utah.edu/CVHTML/CV049.html
Accessed 12/10/2019

Cardiac tamponade

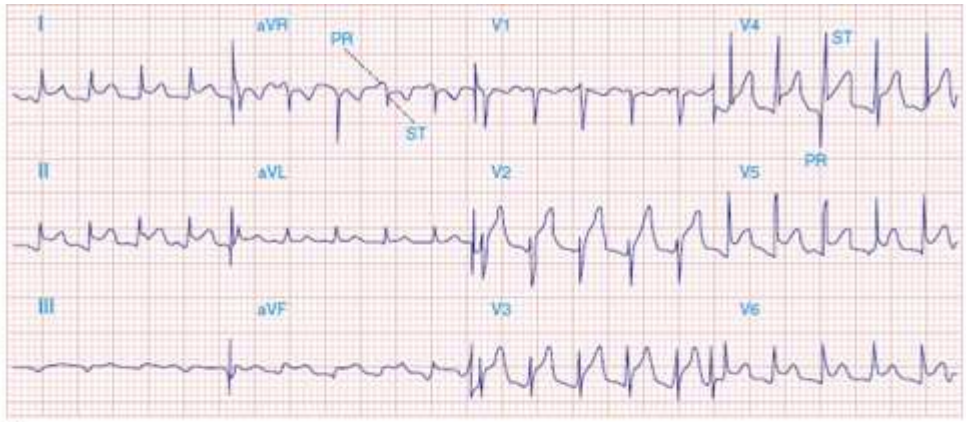
- Compression of heart due to increase in fluid within pericardial sac
- Rapidly accumulating pericardial effusion (acute)
- Pericardial sac has time to dilate if the effusion slowly accumulates
- Muffled heart sounds
- Pulsus paradoxus is characteristic
- Drop in arterial blood pressure by >10 mmHg during inspiration

Physiology of tamponade

- Inspiration increases preload
- Right ventricle enlarges
- Right ventricle enlargement displaces intraventricular septum
- Diminished effective left ventricular volume (and volume ejected)
- Cardiac output falls
- Left atrial pressure increases

Cardiac tamponade

- Beck's triad
- Dyspnea
- Pulsus Paradoxus
- (May terminate) in pulseless electrical activity
- Echocardiography or CT for evaluation
- and to distinguish from restrictive cardiomyopathy
- Direct needle drainage as emergency procedure
- Pericardial window
- Surgery to remove portion of the pericardium
- No fluid accumulation



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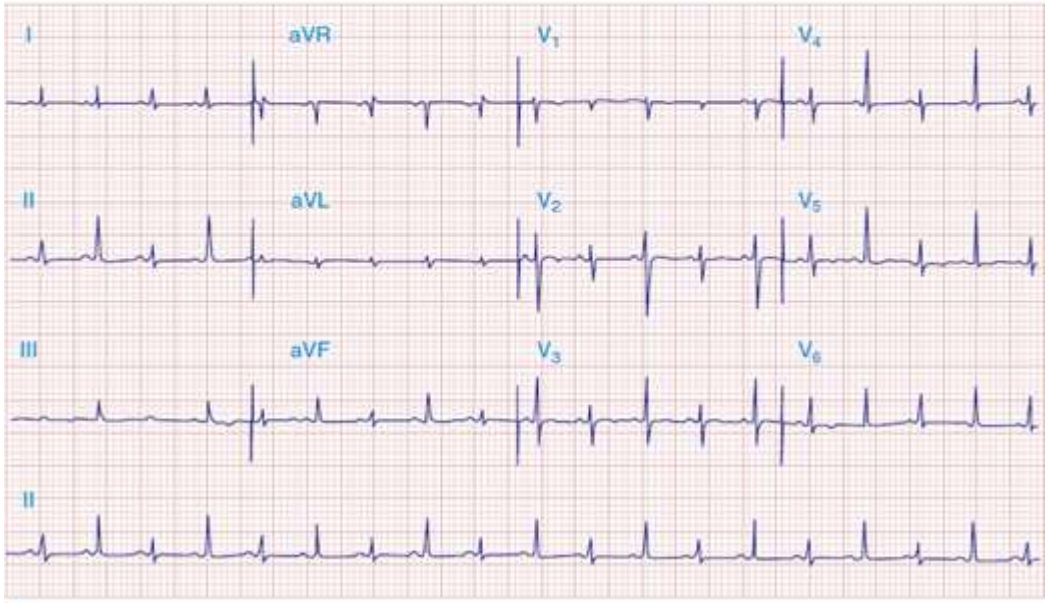

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