CARDIOMYOPATHY

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DEFINITION

- *Cardiomyopathies are a heterogeneous group of diseases of the myocardium associated with mechanical and/or electric dysfunction that usually (but not invariably) exhibit inappropriate ventricular hypertrophy or dilatation and are due to a variety of causes that frequently are genetic. Cardiomyopathies either are confined to the heart or are part of generalized systemic disorders."*

MOGES CLASSIFICATION

to identify different classes of cardiomyopathy

morphology

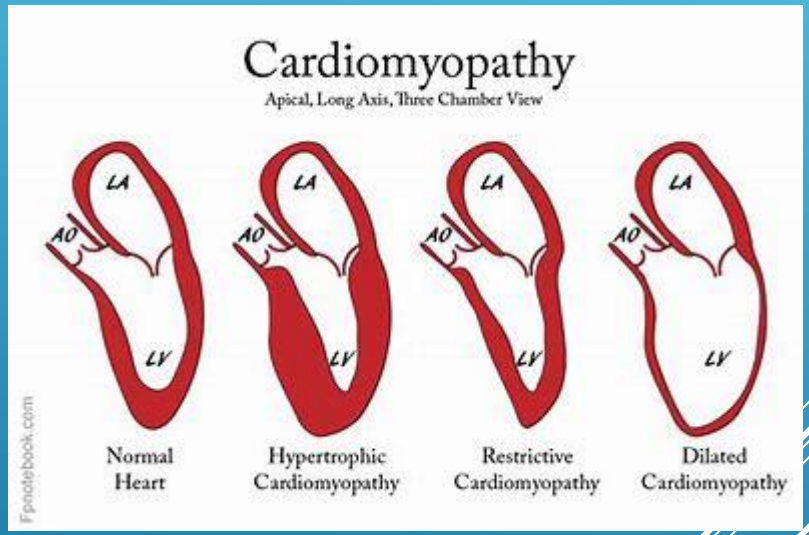
- M refers to the phenotype (eg, DCM and HCM)
- O refers to organ involvement (eg, with/without extracardiac involvement)
- G refers to genetic transmission (eg, autosomal dominant or recessive)
- E refers to etiology (eg, genetic with diseased gene and mutation, if known),
- S refers to disease stage.

CARDIOMYOPATHY

<u>WHO Classification</u>

anatomy & physiology of the LV

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



DCM

Dilatation of the Left or both ventricles that is not explained by abnormal loading conditions or coronary artery disease. DCM is characterized by cardiac enlargement with ventricular walls of approximately normal thickness and varying extents of fibrosis. The patients develop progressive HF with reduced ejection fraction, tachyarrhythmias, and an increased risk of sudden death. .Mitral and tricuspid regurgitation because of annular dilatation are frequent and intensify the hemodynamic burden.

DCM: ETIOLOGY

Ischemic → most common 70%
Valvular
Hypertensive
Familial
Idiopathic
Inflammatory
- **Infectious**
  - **Viral – Cox B, CMV, HIV**
  - **Ricketsial - Lyme Disease**
  - **Parasitic - Chagas' Disease, Toxoplasmosis**
- **Non-infectious**
  - **Collagen Vascular Disease (SLE, RA)**
  - **Peripartum**

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

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

Nutritional
- **Thiamine, selenium, carnitine**

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

DILATED CARDIOMYOPATHY

↓ EF

- Dilation *and* impaired contraction of ventricles:
  - Reduced *systolic* function with or without heart failure
  - Characterized by myocyte damage
  - Multiple etiologies with similar resultant pathophysiology

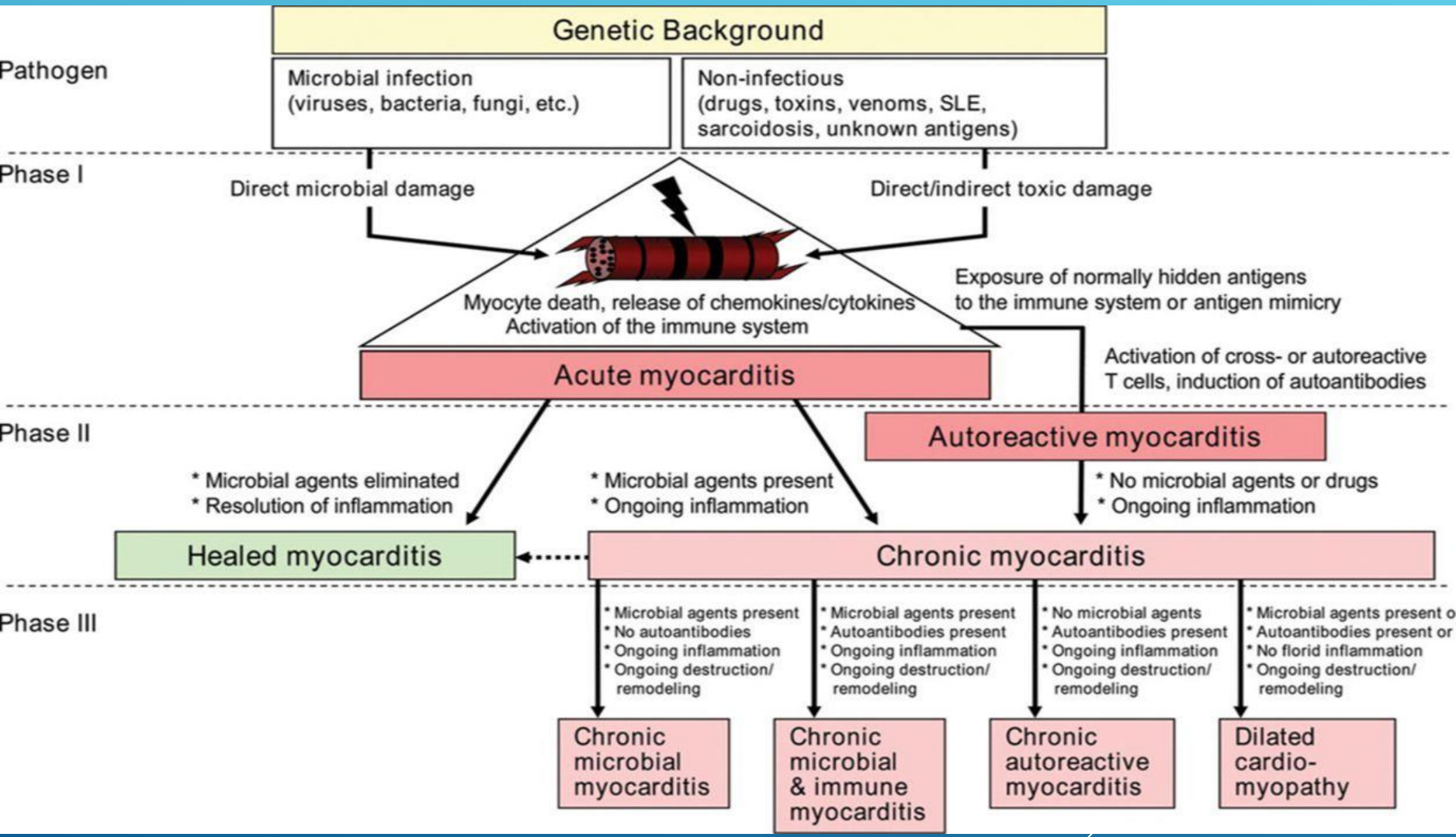
- **idiopathic**
  - incidence of idiopathic dilated CM 5-8/100,000
  - incidence likely higher due to mild, asymptomatic cases
  - 3X more prevalent among males and African-Americans

DCM: INHERITED

Familial cardiomyopathy

- 30% of idiopathic
- Inheritance patterns
  - Autosommal dom (most common)/rec, x-linked, mitochondrial
- Associated phenotypes:
  - Skeletal muscle abn., neurologic, auditory
- Mechanism:
  - Abnormalities in:
    - Energy production
    - Contractile force generation
  - Specific genes coding for:
    - **The gene that encodes titin—the giant protein that controls the stiffness of the sarcomere—is the most common and is responsible for ≈20% of cases of familial DCM.**

DCM-MYOCARDITIS



DCM: INFECTIOUS

- Acute viral myocarditis
- Coxasackie B or echovirus
- Self-limited infection in young people
- Mechanism:
- Myocyte cell death and fibrosis
- Immune mediated injury
- BUT no change with immunosuppressive drugs

NON-INFECTIOUS MYOCARDITIS

- inflammation, and immune reactions are involved in the pathobiology of many cardiomyopathies
- Noninfectious, immune-driven causes of myocarditis include allergic reactions to drugs, Kawasaki disease, systemic lupus erythematosus, and Löffler endocarditis

cardiac MRI

- CMR provides a powerful tool in the recognition and assessment
- Gold standard is Biopsy

DCM: TOXIC

Alcoholic cardiomyopathy

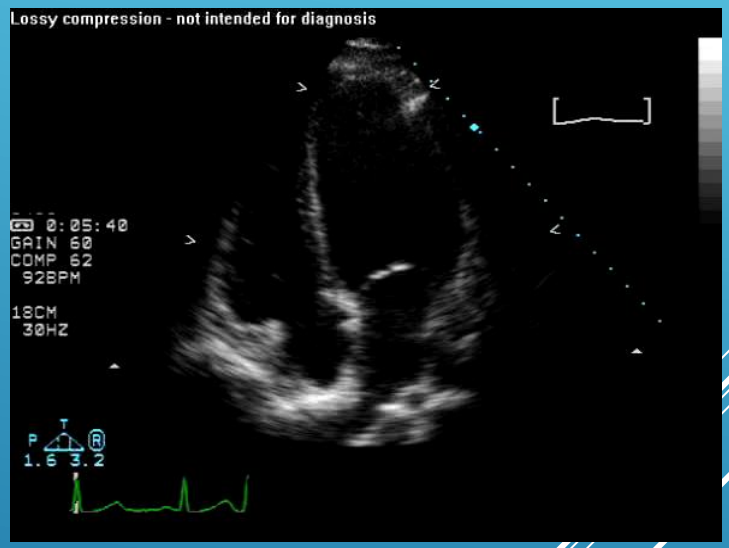
- Chronic use
- Reversible with abstinence if early on
- Mechanism:
  - Myocyte cell death and fibrosis
  - Directly inhibits:
    - mitochondrial oxidative phosphorylation
    - Fatty acid oxidation

*irreversible if 4 years alcoholic

DCM: PERIPARTUM

Diagnostic Criteria

- 1 mo pre, 6 mos post
- Echo: LV dysfunction
- Epidemiology/Etiology
- 1:4000 women
- Risk factors: AA, Multiple pregnancies, Alcohol, Tobacco
- Proposed mechanisms:
  - Inflammation

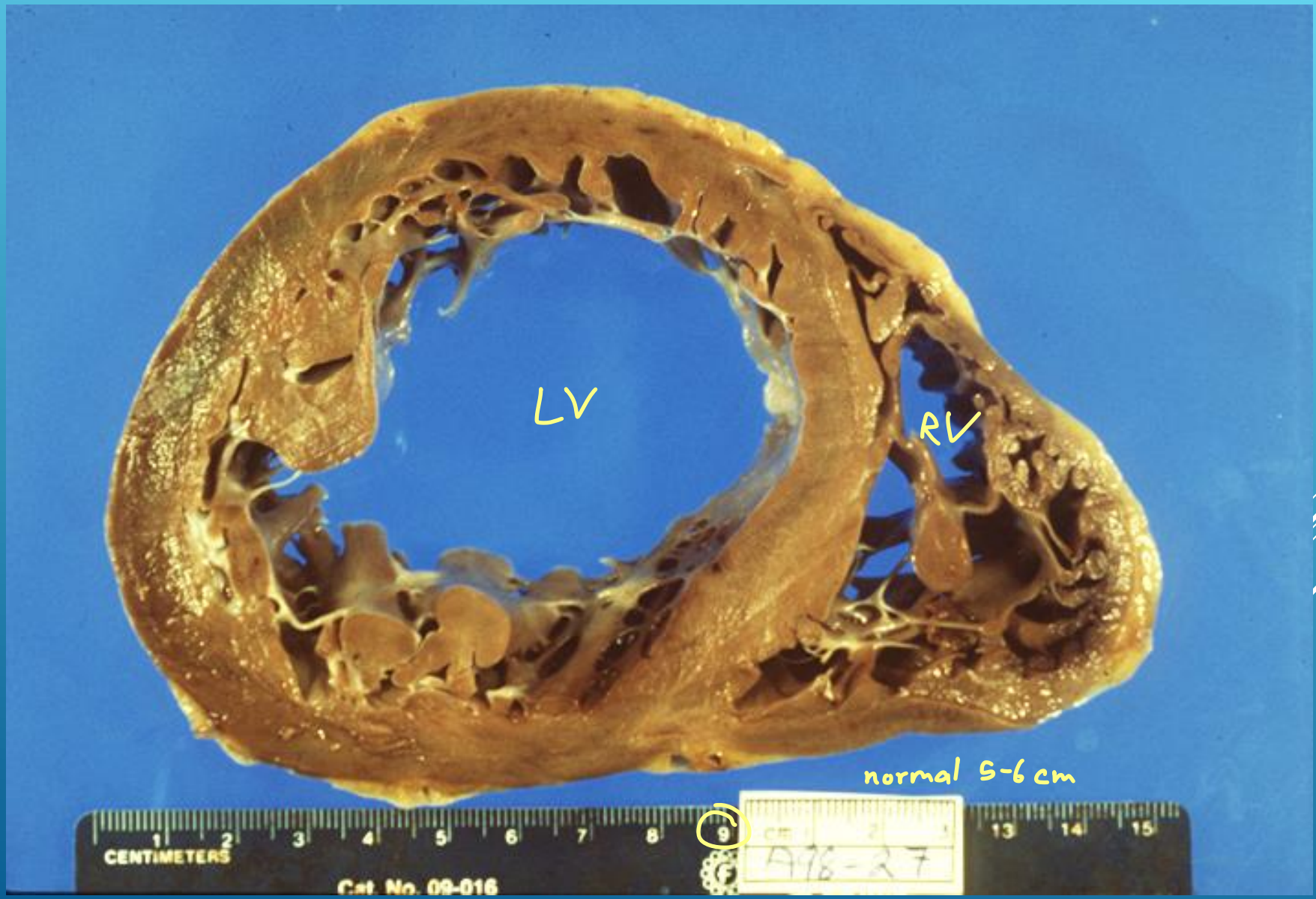


advanced age

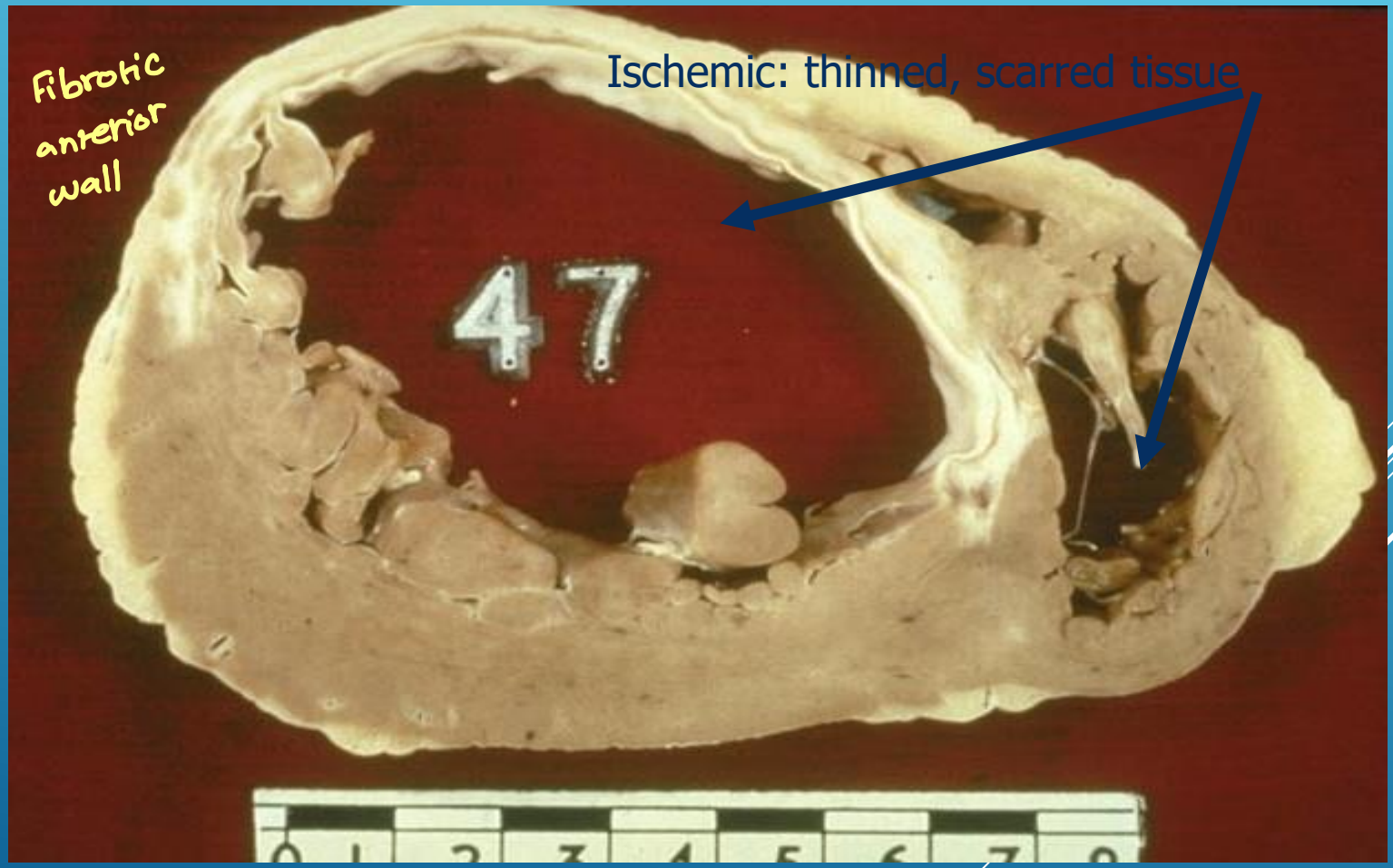
pre-eclampsia, smoking

prolactin release

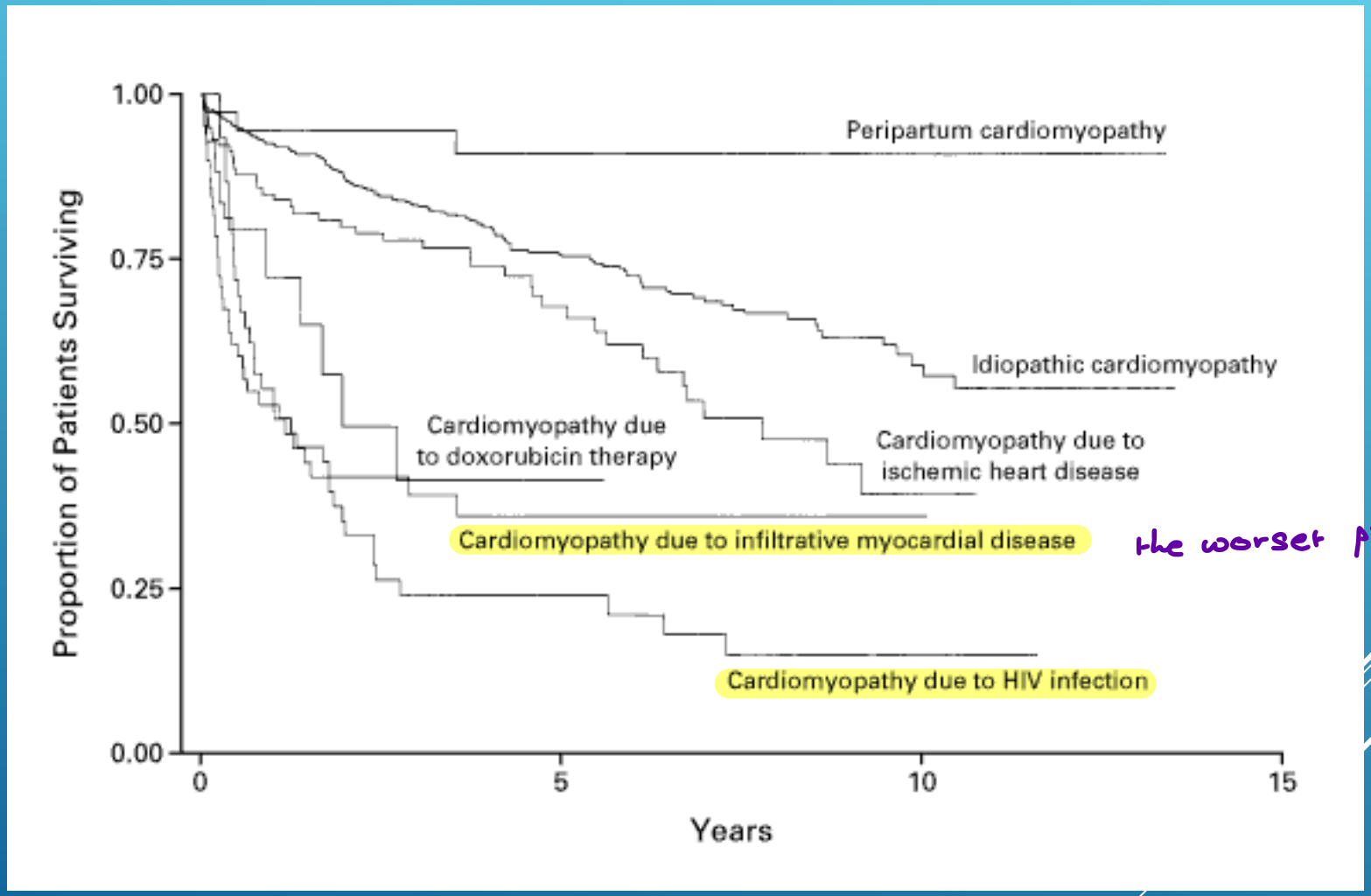
IDIOPATHIC CARDIOMYOPATHY



ISCHEMIC CM


Fibrotic anterior wall
Ischemic: thinned, scarred tissue
47

PROGNOSIS DEPENDS ON ETIOLOGY



1230 pts. referred for unexplained CM. Felker GM. NEJM 2000;342:1077

HYPERTROPHIC CARDIOMYOPATHY

Left ventricular hypertrophy not due to pressure overload
Hypertrpohy is variable in both severity and location:
- -asymmetric septal hypertrophy
- -symmetric (non-obstructive)
- -apical hypertrophy Japanese hyp

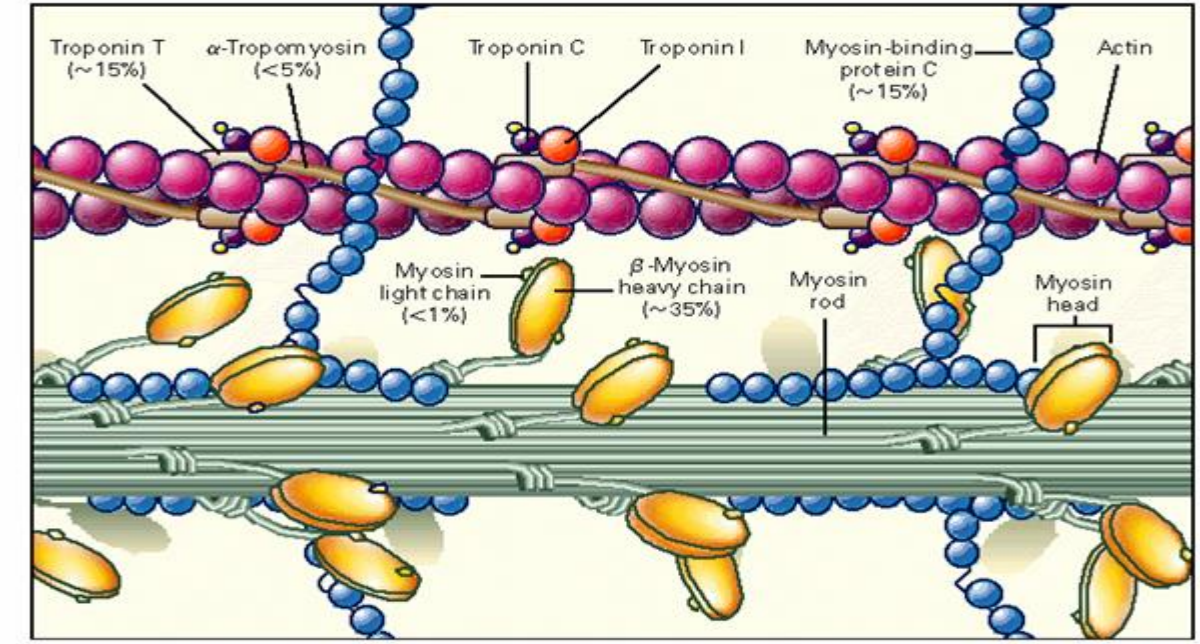
Vigorous systolic function, but impaired diastolic function
- impaired relaxation of ventricles
- elevated diastolic pressures

prevalence as high as 1/500 in general population
- mortality 1% /y

ETIOLOGY

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

1. β-MHC (Beta Myocin Heavy Chain)
2. cardiac troponin T
3. myosin binding protein C
4. α-tropomyosin



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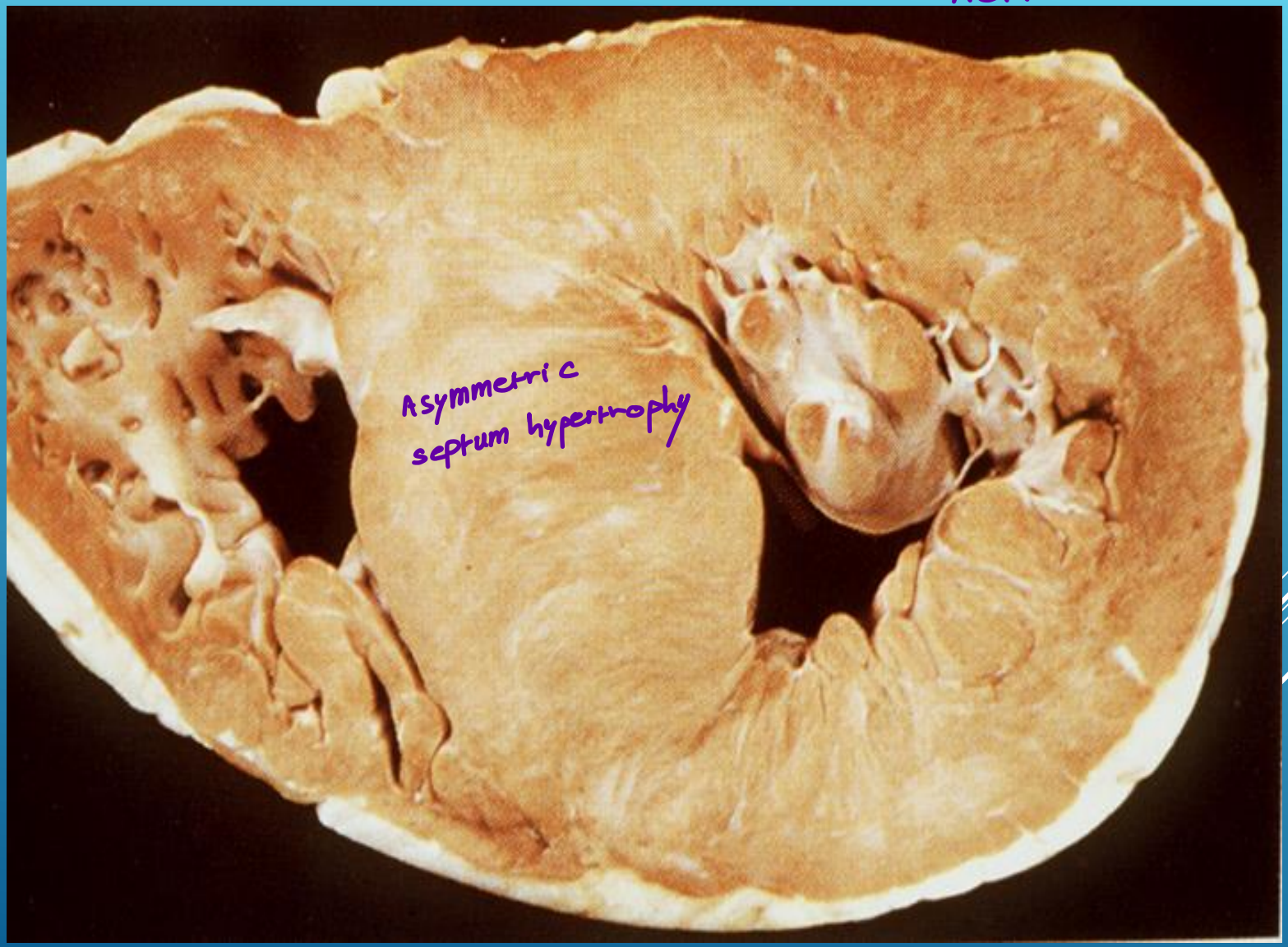

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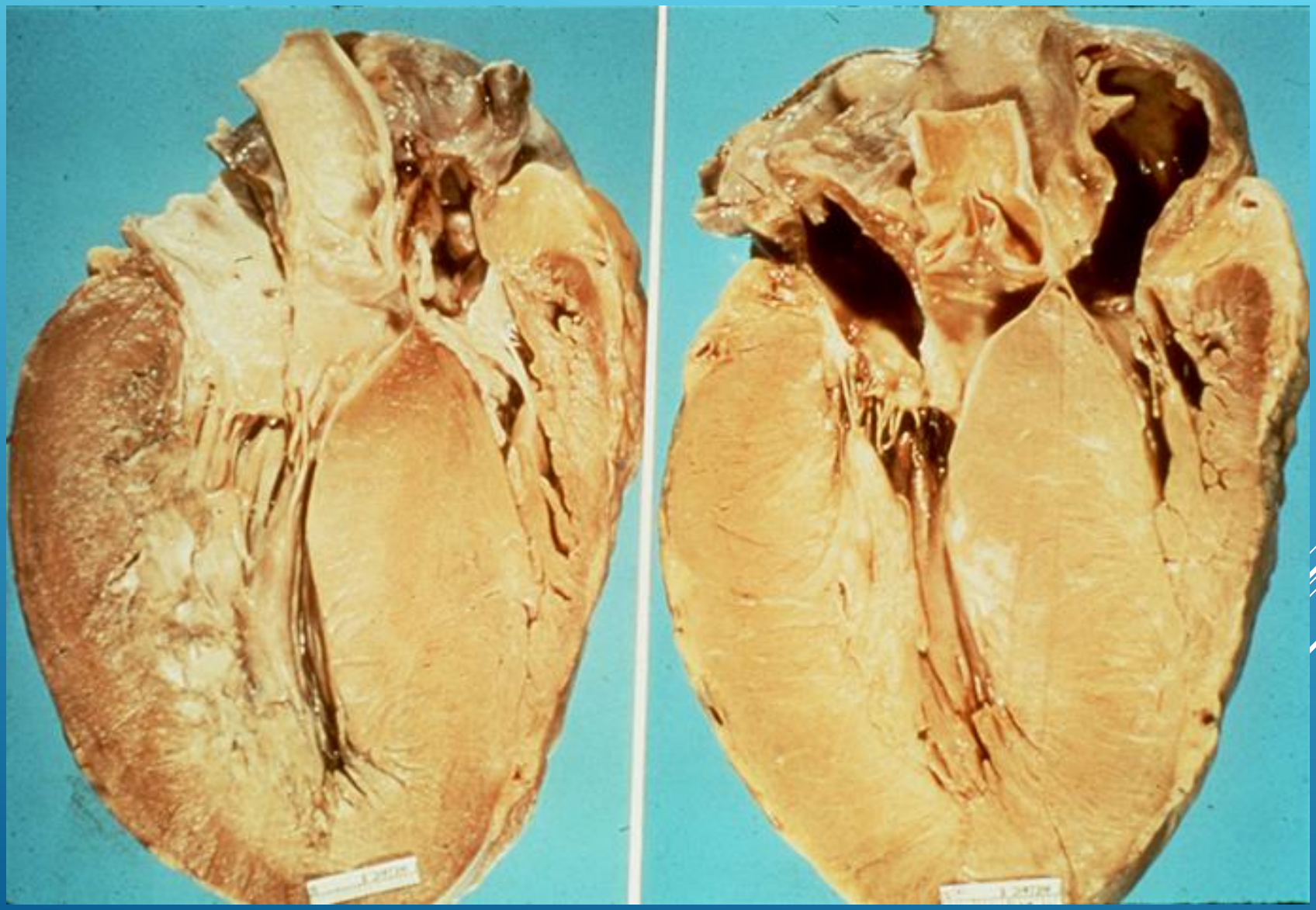
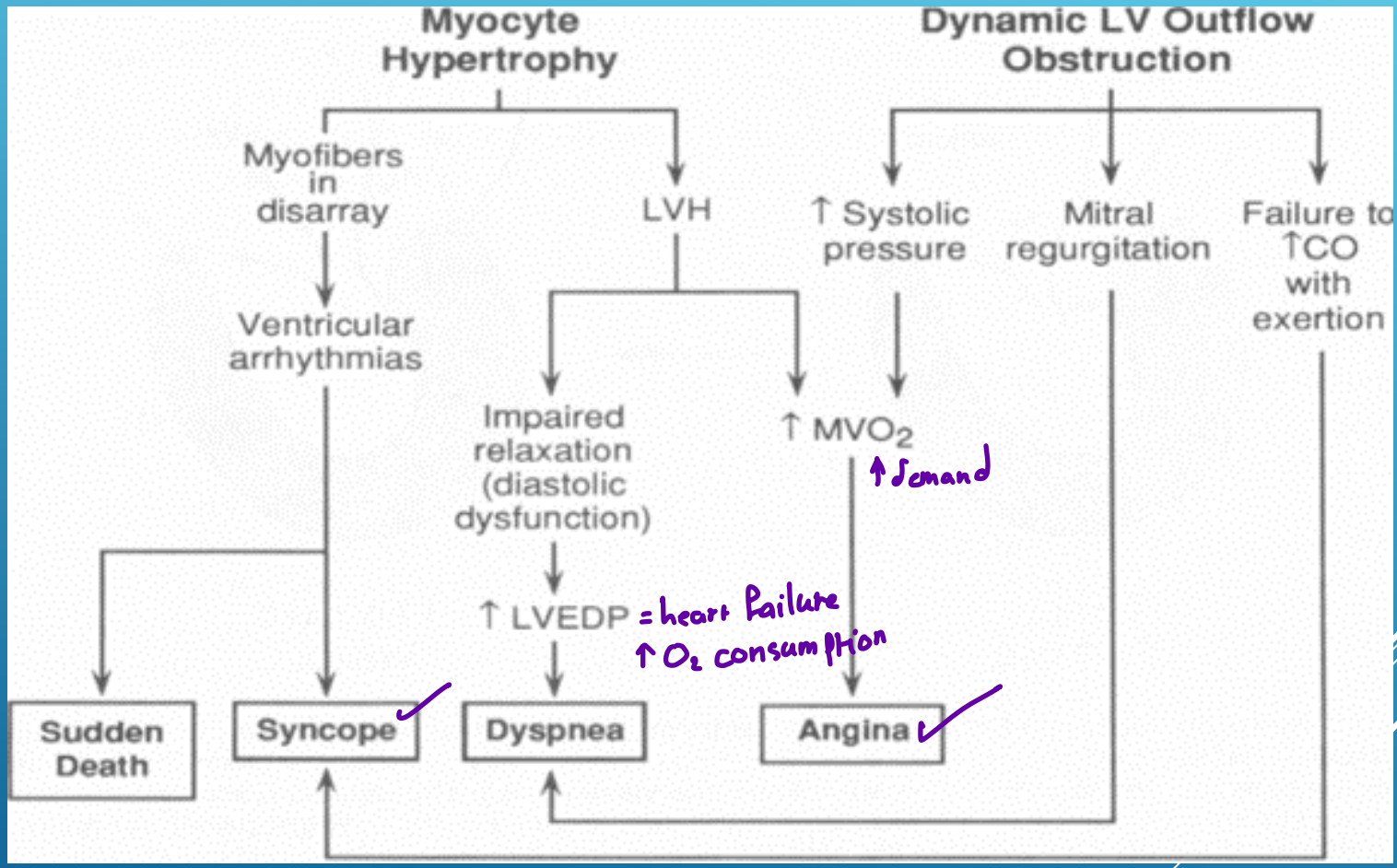


PATHOPHYSIOLOGY



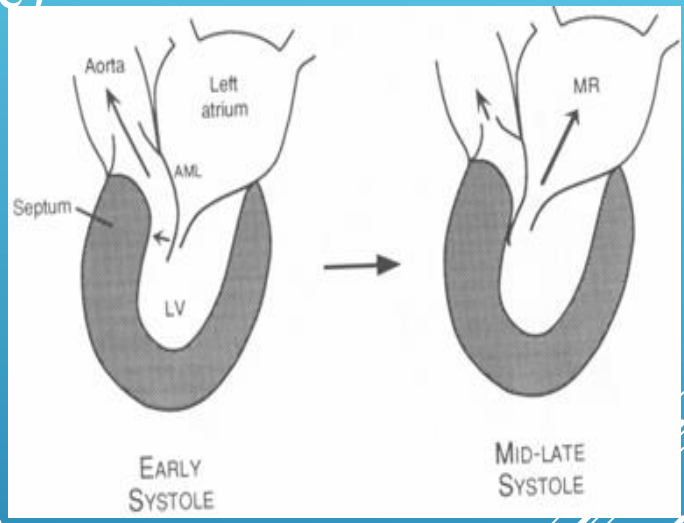
cardiac arrest can be the first presentation

HCM WITH OUTFLOW OBSTRUCTION

Dynamic LVOT obstruction (may not be present at rest)

SAM (systolic anterior motion of mitral valve)

LVOT Obstruction ⇒ LVOT gradient
⇒ ↑wall stress ⇒ ↑MVO2 ⇒ ischemia



negative suction

Dyspnea and angina more related to diastolic dysfunction than to outflow tract obstruction

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

PHYSICAL EXAM

Bisferiens pulse ("spike and dome")
S4 gallop
Crescendo/Descrescendo systolic ejection murmur

↑ obstruction

HOCM vs. Valvular AS

straining

	Intensity of murmur	
	HOCM	AS
Valsalva (↓preload, ↓ afterload)	↑	↓
Squatting (↑ preload, ↑ afterload)	↓	↑
Standing (↓preload, ↓ afterload)	↑	↓

Holosystolic apical blowing murmur of mitral regurgitation

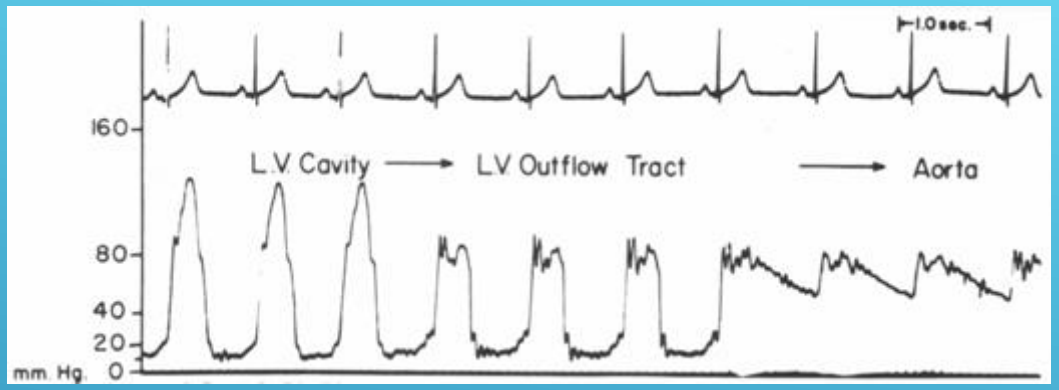
DIAGNOSTIC STUDIES

- EKG
  - NSR → normal sinus rhythm
  - LVH extreme → left ventricular hypertrophy
  - septal Q waves
- 2D-Echocardiography
  - LVH; septum >1.4x free wall
  - LVOT gradient by Doppler
  - Systolic anterior motion of the mitral valve
- Cardiac Catheterization
  - LVOT gradient and pullback
  - provocative maneuvers → medications & Valsulva
  - Brockenbrough phen

HCM-ASH using contrast

CARDIAC CATHETERIZATION

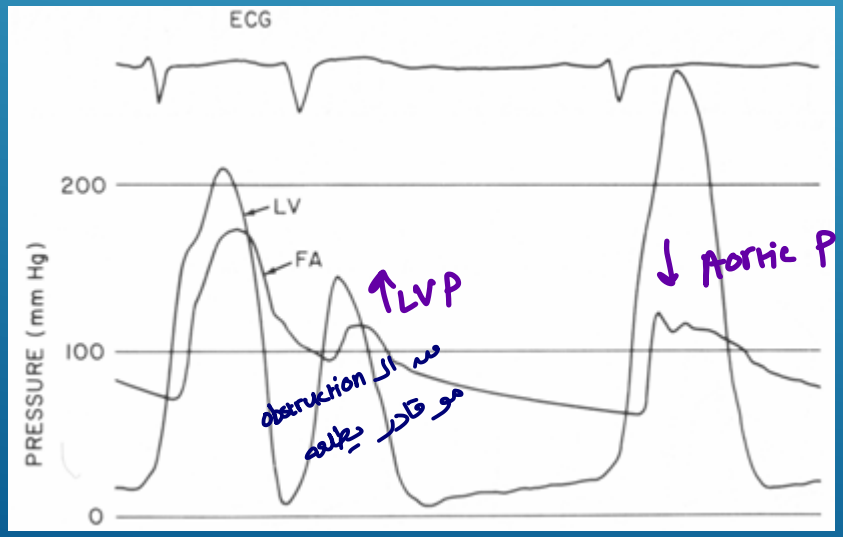
LV pullback



Brockenbrough-Braunwald Sign

failure of aortic pulse pressure to rise post PVC

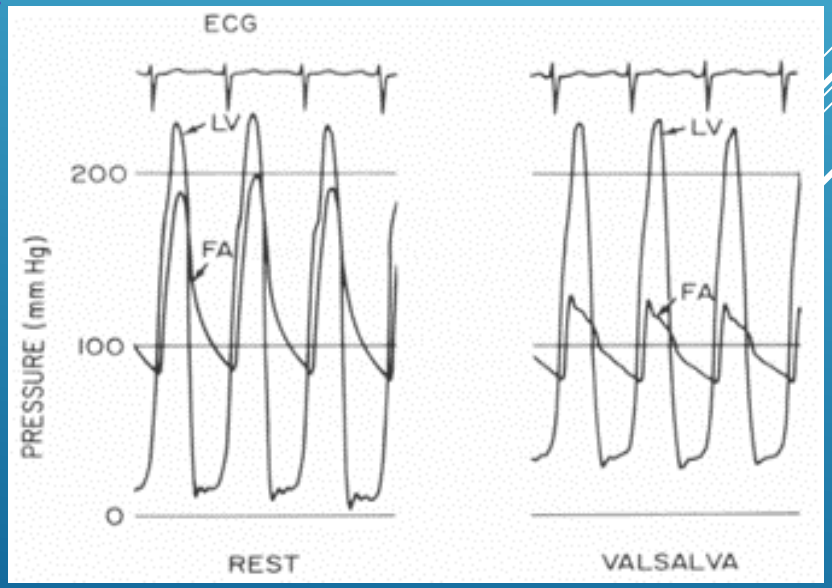
premature ventricular



Provocative maneuvers:

Valsalva

amyl nitrate inhalation



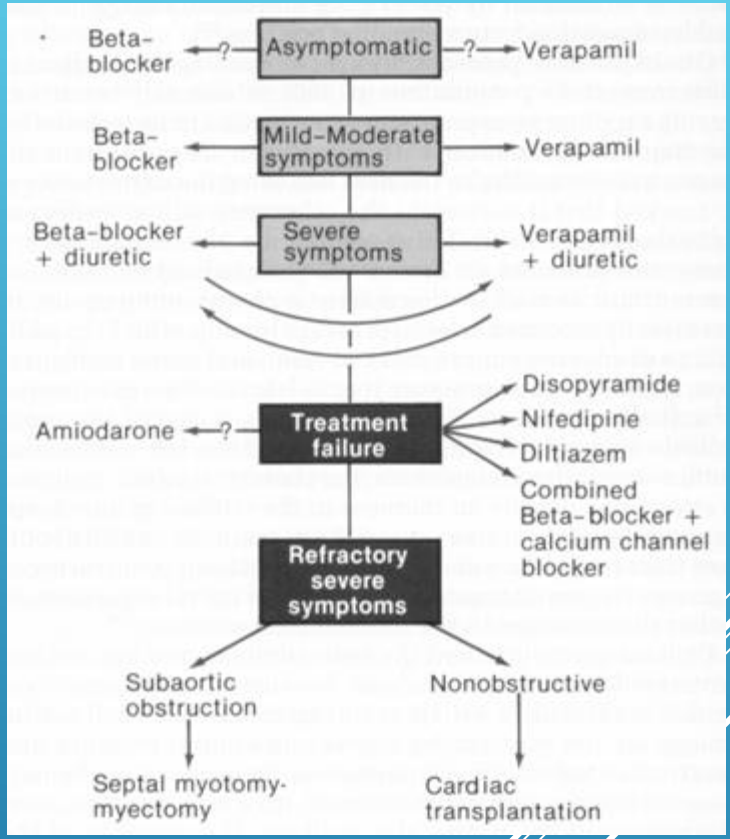
TREATMENT

For symptomatic benefit

1. β-blockers
   - ↓ mvO2
   - ↓ gradient (exercise)
   - ↓ arrythmias
2. Calcium Channel blockers

3. AICD for sudden death
   automatic implantable cardioverter defibrillator

4. Antibiotic prophylaxis for endocarditis



HCM: SURGICAL TREATMENT

For severe symptoms with high outflow gradient

Myomyectomy

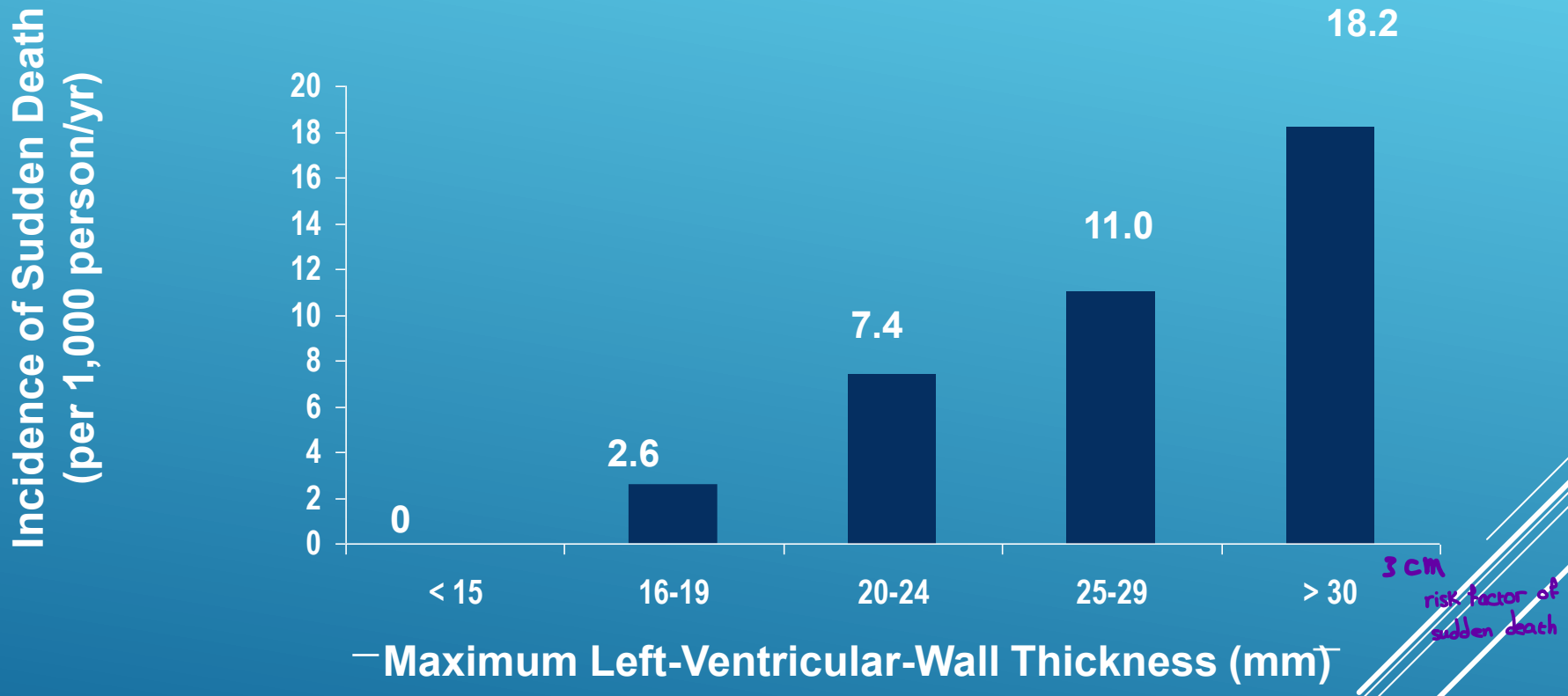
- removal of small portion of upper IV septum
- +/- mitral valve replacement
- 5 year symptomatic benefit in ~ 70% of patients

ETOH septal ablation → non-surgical procedure

ethanol

AICD to prevent sudden death

WALL THICKNESS AND SUDDEN DEATH IN HCM



Spirito P. *N Engl J Med*. 2000;342:1778-1785.

AICD INDICATIONS

Implantable cardioverter defibrillator

- Survivors of SCD sudden cardiac death
- Non-Sustained VT
- Family hx of SCD in young family members
- Septal thickness ≥30 mm 3 cm
- Uexplained syncope

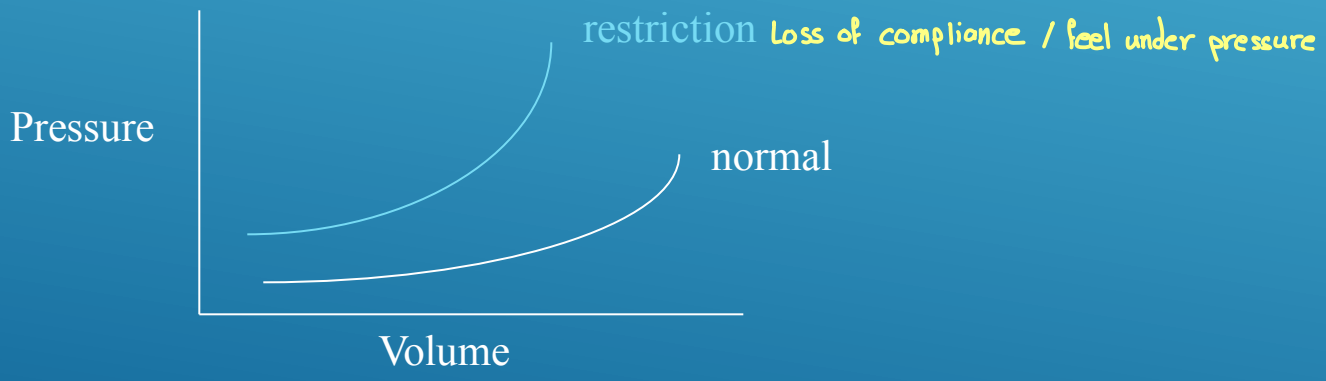
HCM VS ATHLETES HEART

- Athlete's heart
  - DEFINITION: Symmetric <14mm
  - No obstruction
  - LA size <4cm
  - Reversible if exercise was stopped for 3 months
  - Maintaining LV cavity

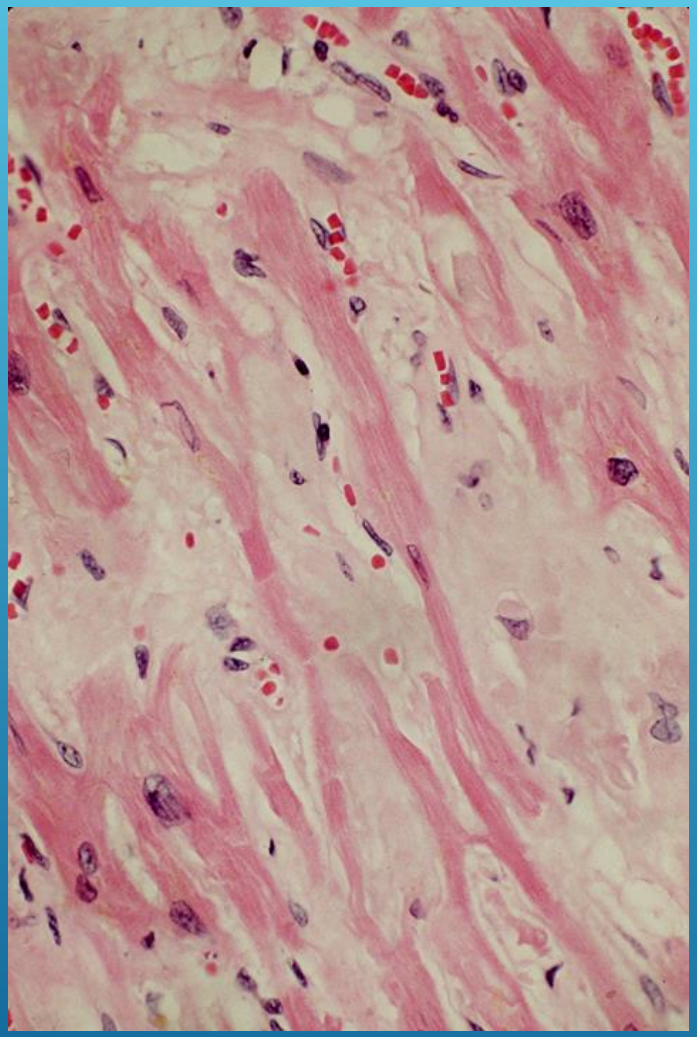
RESTRICTIVE CARDIOMYOPATHY

Characterized by:

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



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



Amyloid infiltrative CM

TABLE 4. CAUSES OF RESTRICTIVE CARDIOMYOPATHY.

Myocardial

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

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

Storage disorders
- * Hemochromatosis
- Fabry's disease
- Glycogen storage disease

Endomyocardial

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

AMYLOIDOSIS

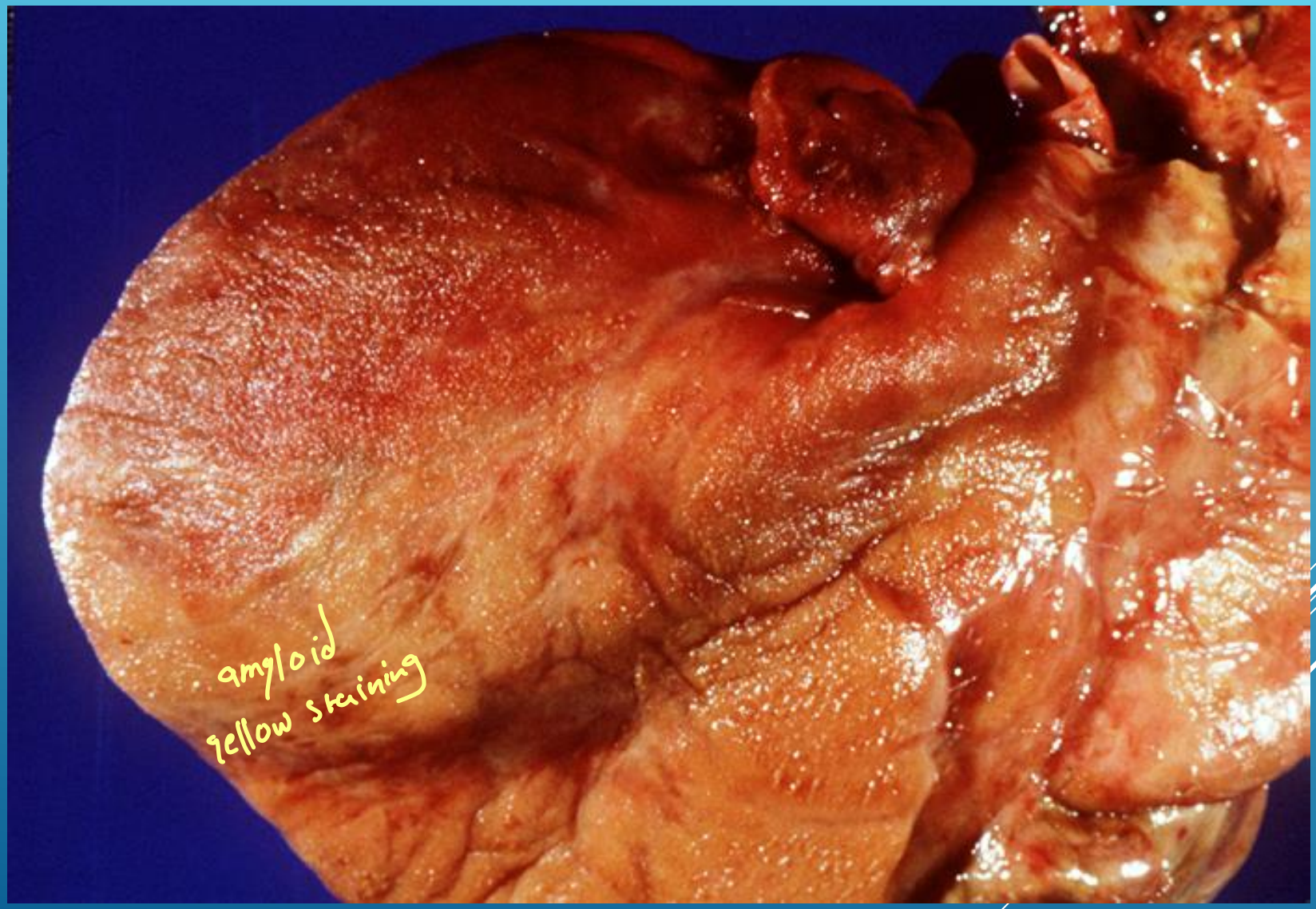
Amyloidosis is caused by protein misfolding in which extracellular aggregates of the misfolded proteins form fibrils

Primary Amyloidosis
- immunoglobulin light chains -- multiple myeloma

Secondary Amyloidosis
- deposition of protein other than immunoglobulin
  - senile
  - familial
  - chronic inflammatory process

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

AMYLOID CARDIOMYOPATHY



AMYLOID

- CMR is a sensitive diagnostic technique for amyloid cardiomyopathy. Late gadolinium enhancement (LGE) has been shown in >80% of patients, including patients without evidence of this disorder by echocardiography
- positron emission tomography (PET).
- A definitive diagnosis of this condition still requires histological verification. biopsy

AMYLOID TREATMENT

- Therapy of light-chain amyloidosis includes autologous bone marrow stem cell transplantation and drugs that include dexamethasone, melphalan, immunomodulatory agents, and the proteasome inhibitor bortezomib.

SARCOIDOSIS

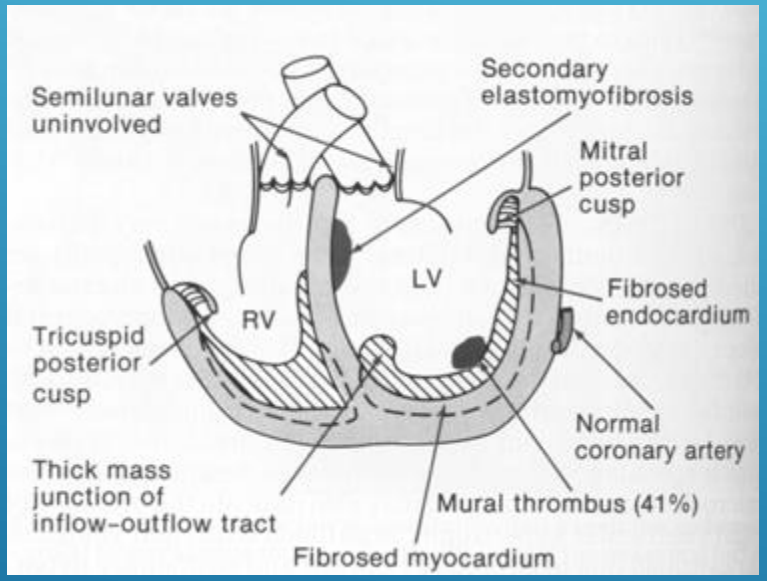
- Sarcoidosis is an inflammatory condition in which non-caseating granulomas involve multiple organs
- Restriction
- Conduction System Disease
- Ventricular Arrhythmias (Sudden Cardiac Death)

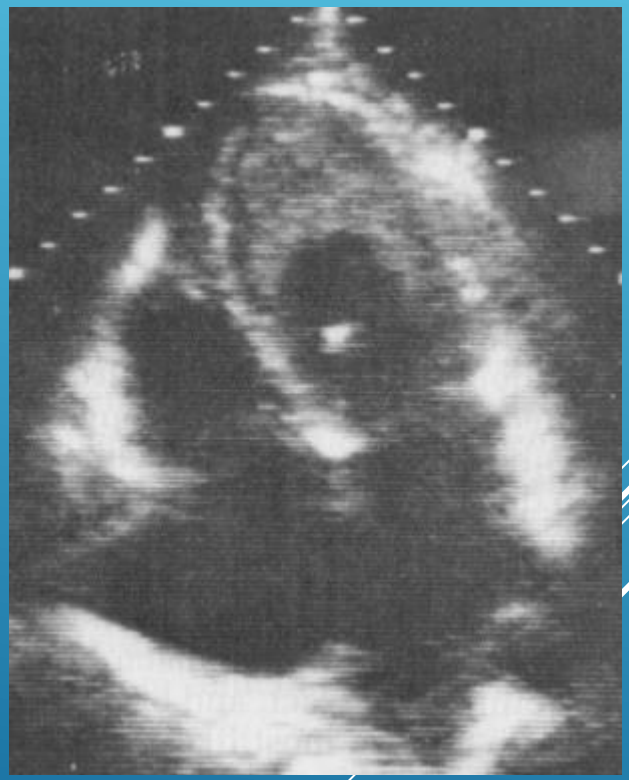
steroids

Current therapy involves glucocorticoids, supplemented by other immunosuppressive agents if necessary.

ENDOMYOCARDIAL FIBROSIS

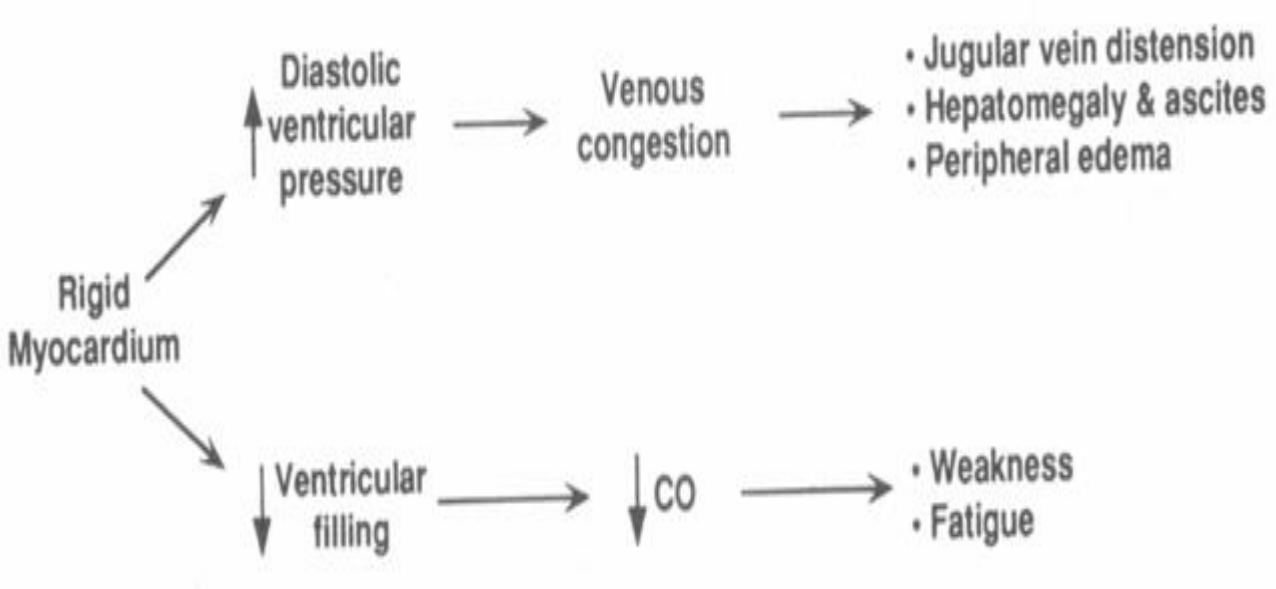
Endemic in parts of Africa, 15-25% of cardiac deaths in equatorial Africa
hypereosinophilic syndrome (Loffler's endocarditis)





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

PATHOPHYSIOLOGY OF RESTRICTION



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

CLINICAL FINDINGS

how the patient presents?

Dyspnea
Orthopnea/PND Paroxysmal nocturnal dyspnea
Peripheral edema
Ascites/Hepatomegaly

Fatigue/ ↓exercise tolerance

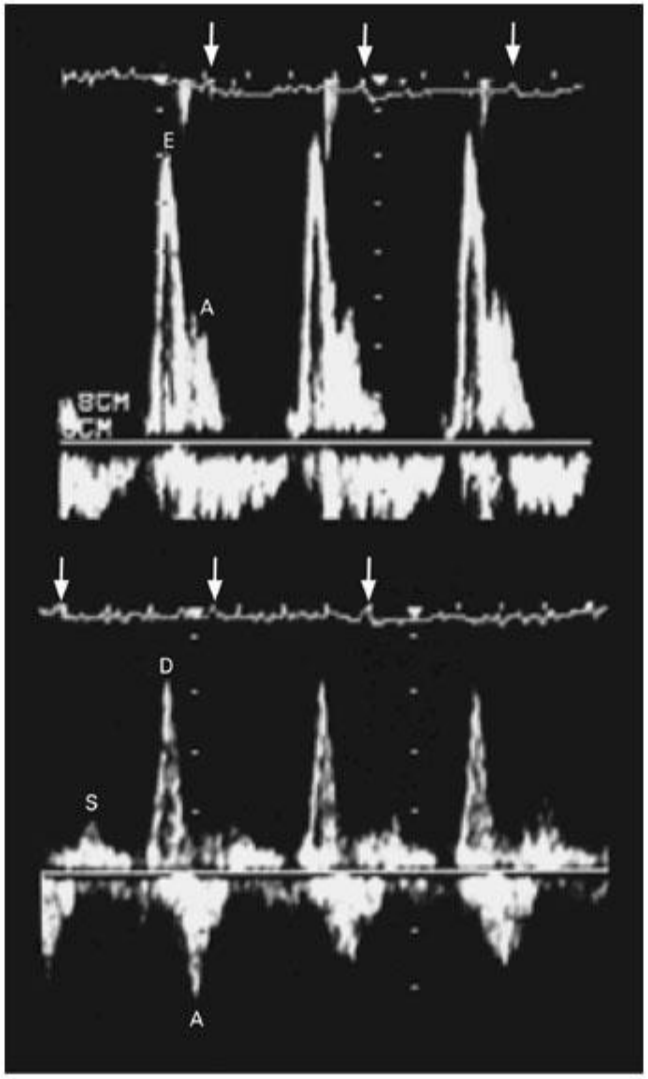
Clinically mimics constrictive Pericarditis

DIAGNOSTIC STUDIES

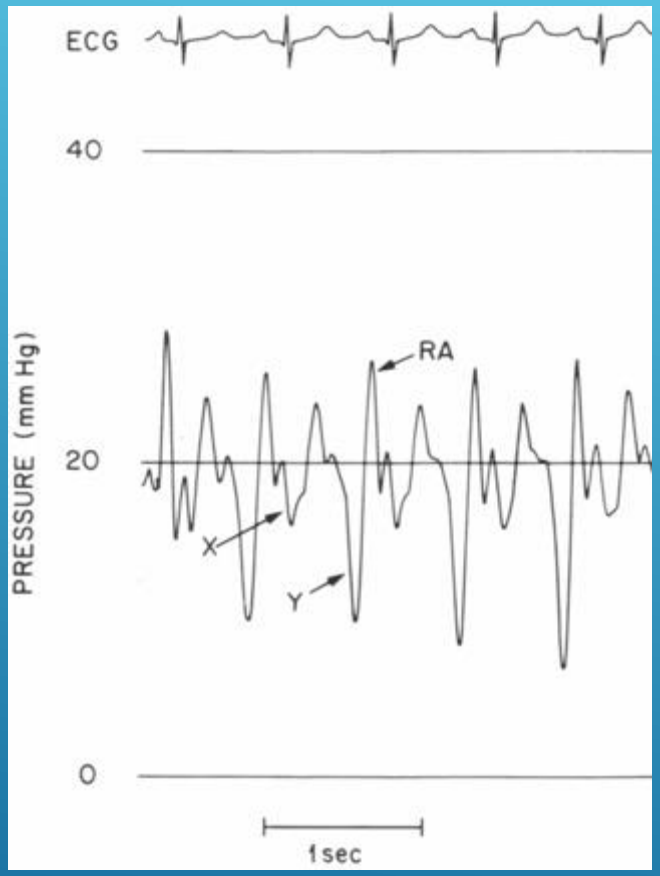
2D-Echo/Doppler-
mitral in-flow velocity
rapid early diastolic filling

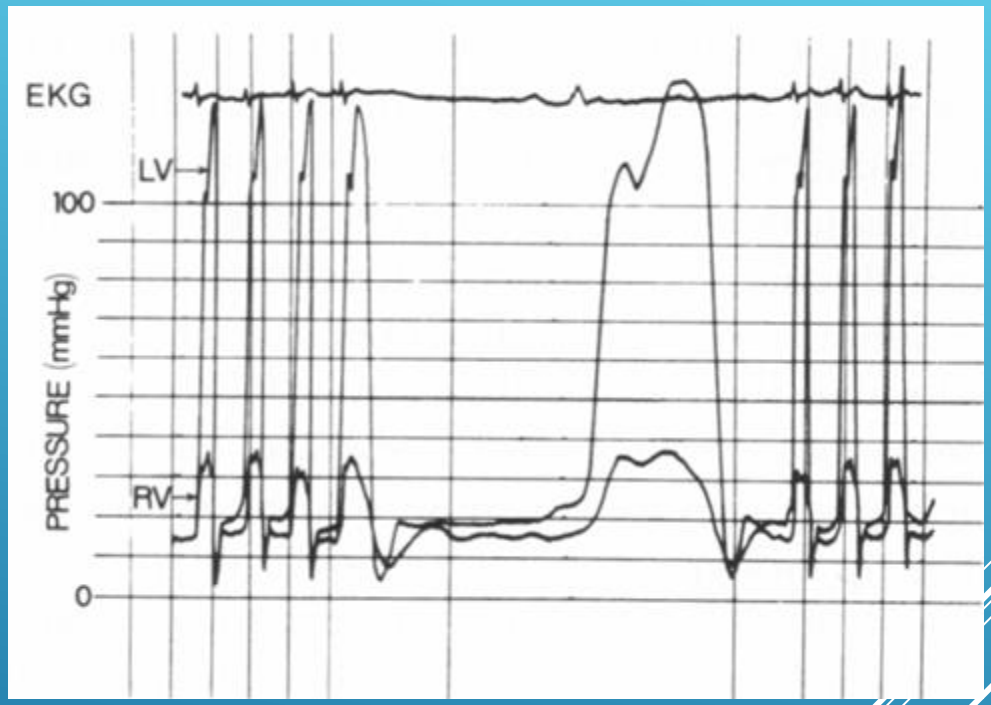
Catheterization –
diastolic pressure equilibration
restrictive vs constrictive
hemodynamics

Endomyocardial biopsy-
definite Dx of restrictive pathology



CARDIAC CATHETERIZATION





Prominent y descent
rapid atrial emptying

Restrictive

"dip and plateau"
rapid ventricular filling

then abrupt cessation of blood flow due to non-compliant myocardium

TREATMENT

Treat underlying cause

- Amyloid (melphalan/prednisone/colchicine)
- Endomyocardial Fibrosis (steroids, cytotoxic drugs, MVR)
- Hemochromatosis (chelation, phlebotomy)
- Sarcoidosis (steroids)

Diuretics, and other treatment options for HF

Pacemaker for conduction system disease

Anticoagulation for thrombus

Transplant is the best treatment

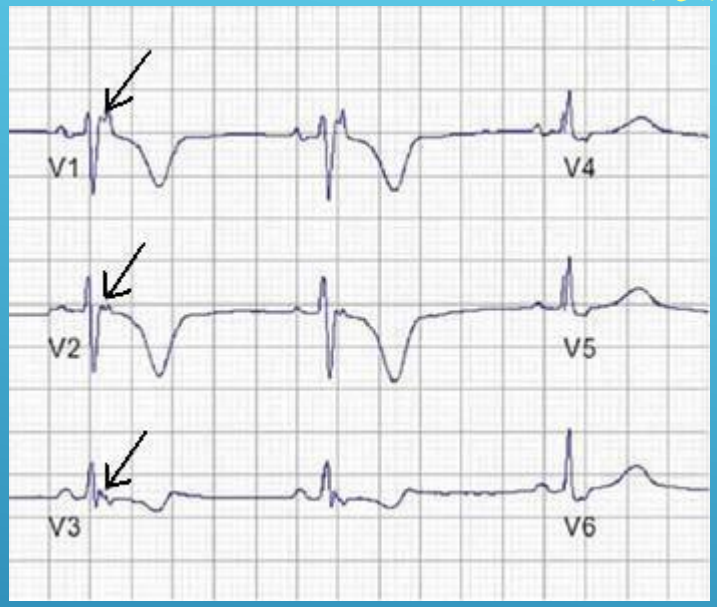
ARRHYTHMOGENIC RV DYSPLASIA(ARVD)

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

ARVD

- Abnormalities in intercellular adhesion molecules, desmosomes, cause cell death and fibrofatty replacement.
- These abnormalities are caused by mutations in genes, such as *PKP2* and *DSP*, encoding plakophilin 2 and desmoplaking, respectively. Inheritance in most cases is by Mendelian dominant transmission.
- The epsilon wave of delayed repolarization following the QRS complex is helpful in diagnosis.
- Contrast-enhanced cardiac magnetic resonance (CMR) best

notch behind the QRS complexes

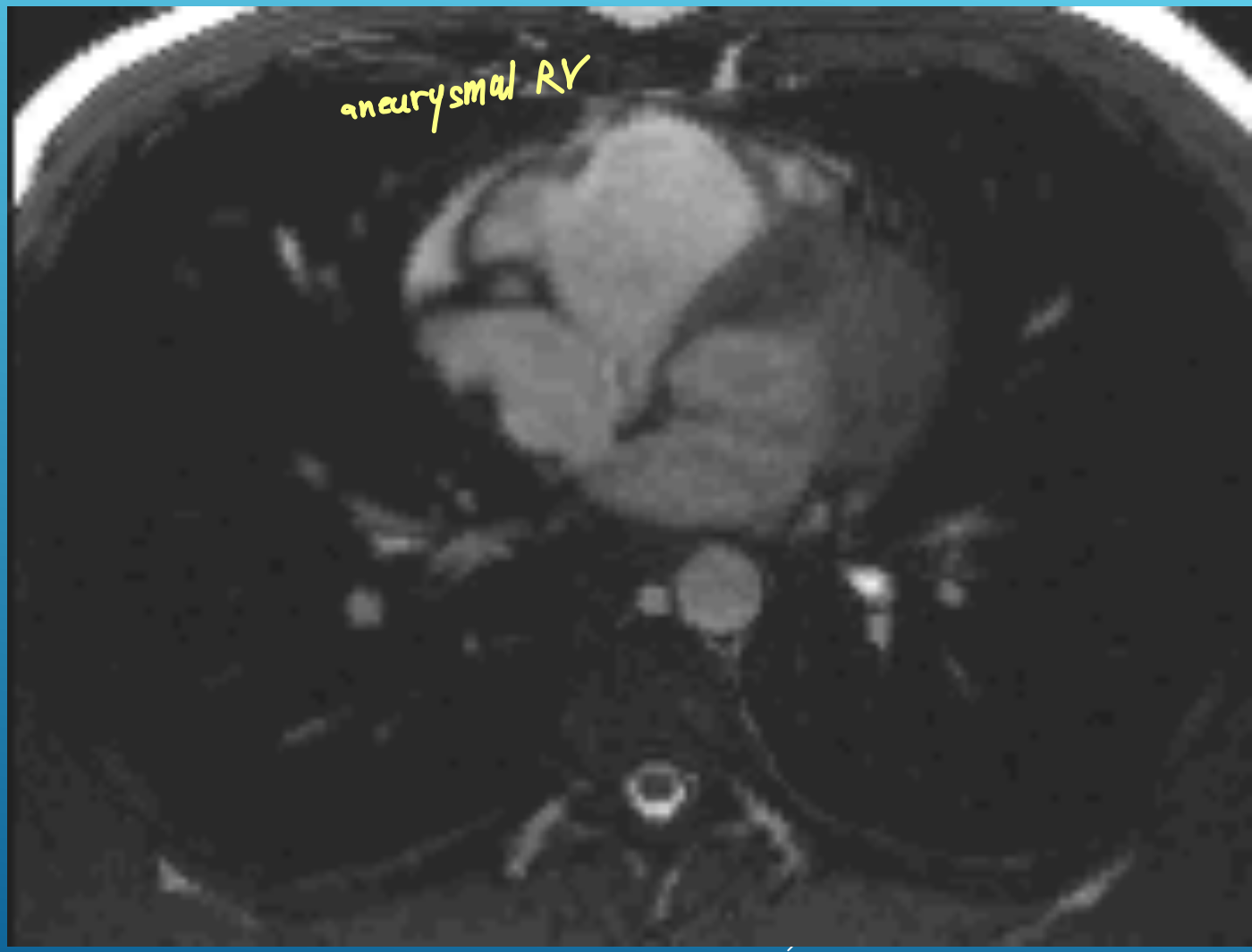


ARVD ECG-EPSILON WAVE

ARVD TREATMENT

- Treatment consists of the cessation of heavy physical exertion and competitive athletics.
- recurrent ventricular tachycardia, epicardial catheter ablation may be effective. Implantation of a cardioverter/defibrillator is indicated in patients who have experienced ventricular fibrillation or refractory ventricular tachycardia.
- Patients with intractable HF may require cardiac transplantation.
- Genetic screening should be performed in family members

MRI: RV DYSPLASIA



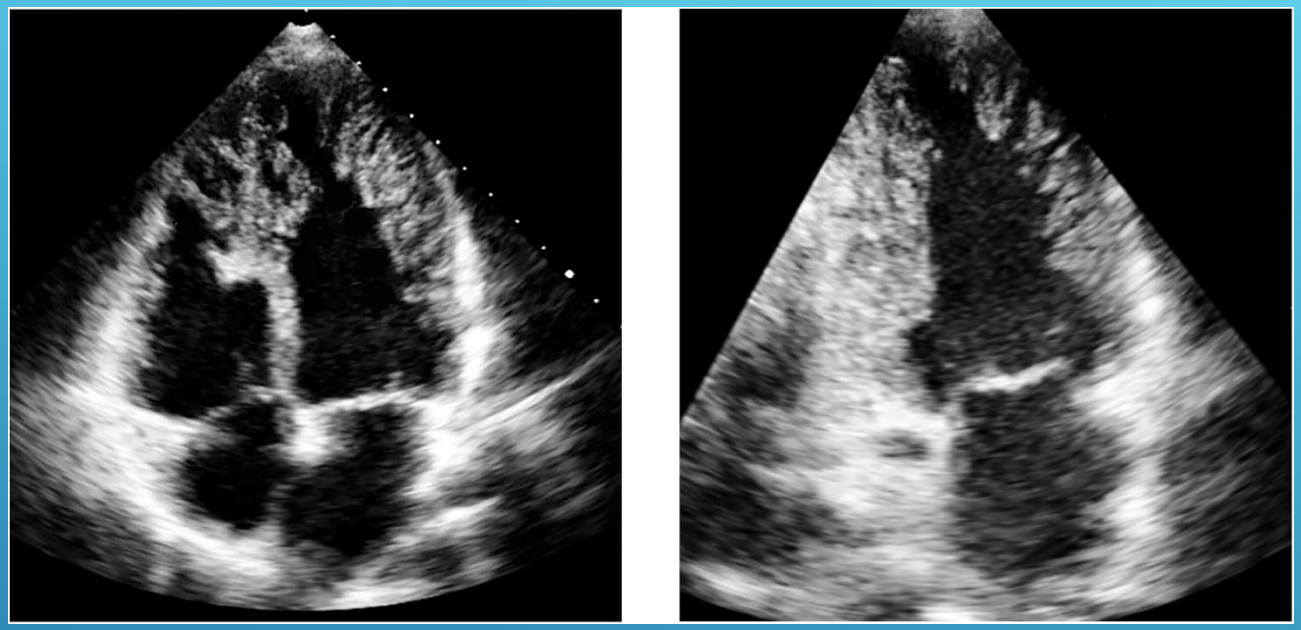
LV NONCOMPACTION

Diagnostic Criteria

- Prominent trabeculations, deep recesses in LV apex

Prognosis and Treatment

- Increased risk of CHF, VT/SCD, LV thrombosis
- Hereditary risk
  - Screening of offspring



Myocardium is interrepted (non compaction)

LV NONCOMPACTION

THANK YOU