Echocardiography in Systemic Diseases

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DISCLOSURE

Relevant Financial Relationship(s)

None

Off Label Usage

None

Echo in Systemic Diseases

- Systemic diseases with secondary cardiac involvement are uncommon

But

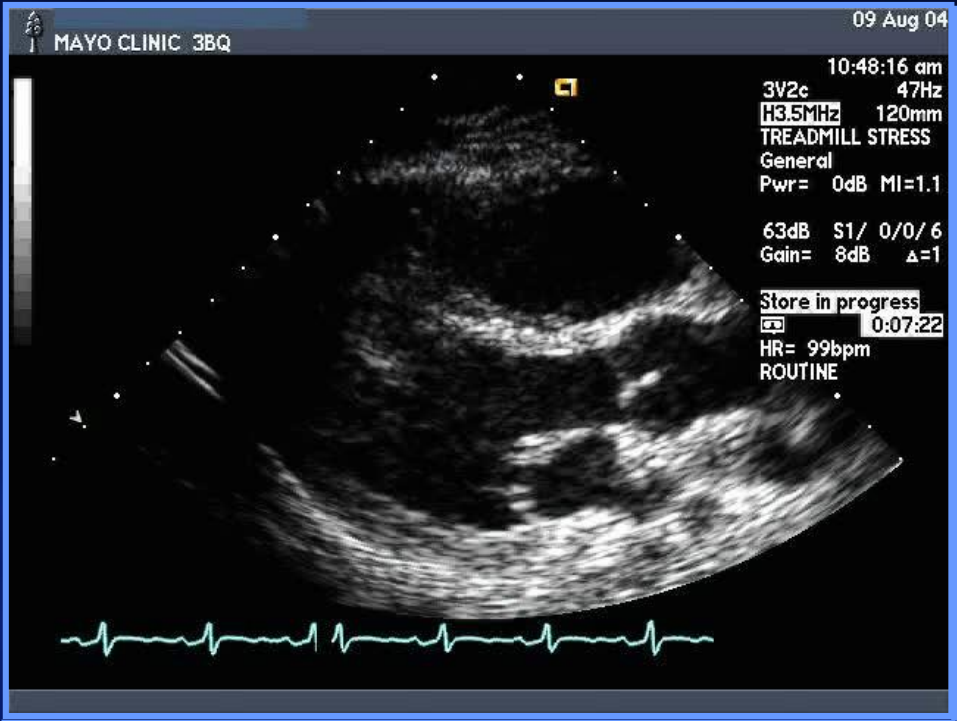
- Echo can identify unique, characteristic features and echo may be the first clue to the underlying systemic illness

Cardiac Involvement in Systemic Diseases

- Autoimmune
- Endocrine
- Collagen Vascular Diseases
- Malignancy
- Amyloid/Infiltrative Diseases
- Radiation Induced Heart Disease
- Drug Induced Valvulopathy

Case

- 27 y/o female who presents with dyspnea, chest pain, and fatigue
  - NYHA class III
- Abnormal nuclear perfusion stress test led to coronary arteriography
  - Normal coronaries but LV gram suggestive of “Hypertrophic CM” (EF 75%)
- Elevated Sedimentation Rate
- Referred to Mayo Clinic → Echo performed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TREADMILL STRESS
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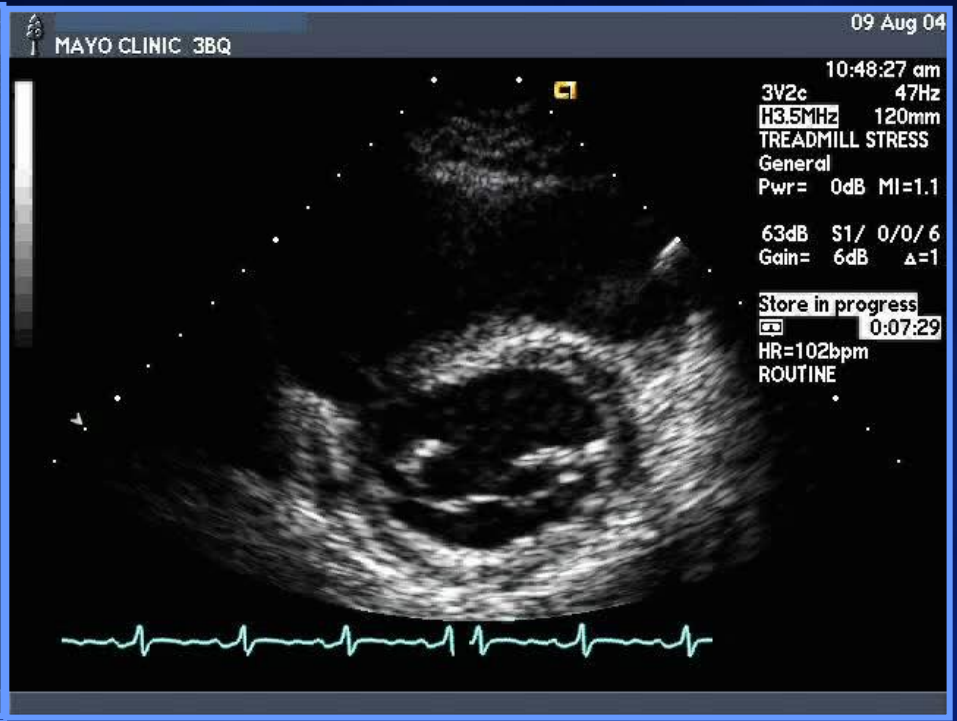
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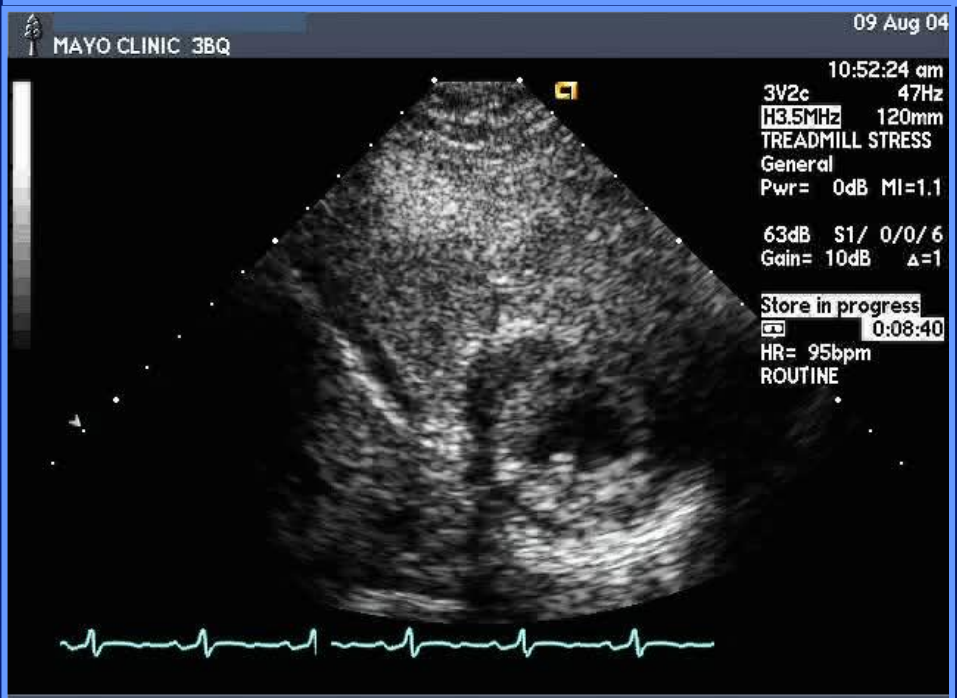
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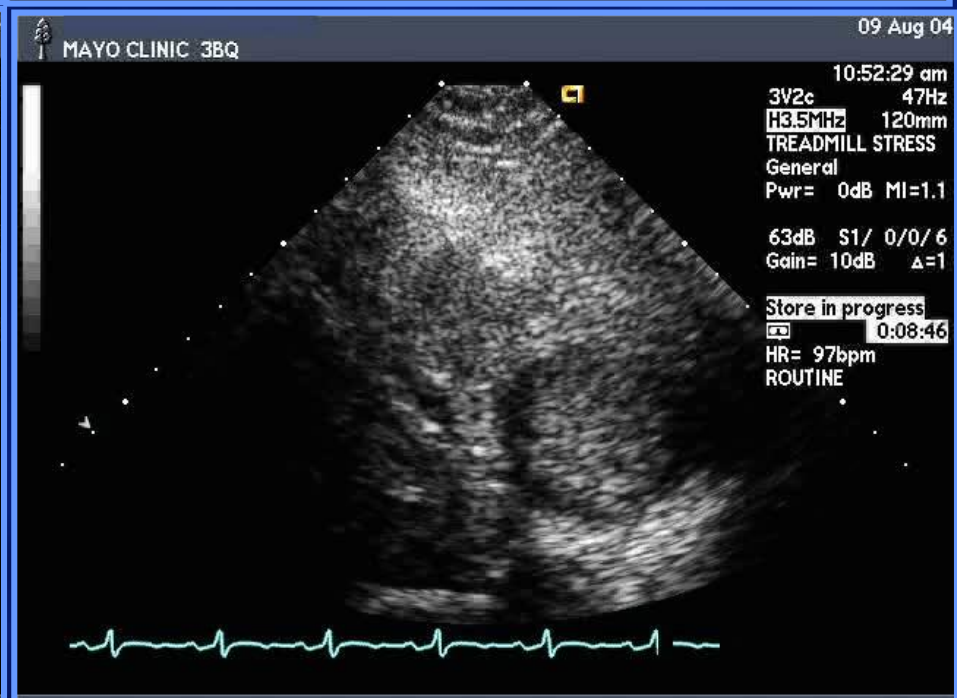
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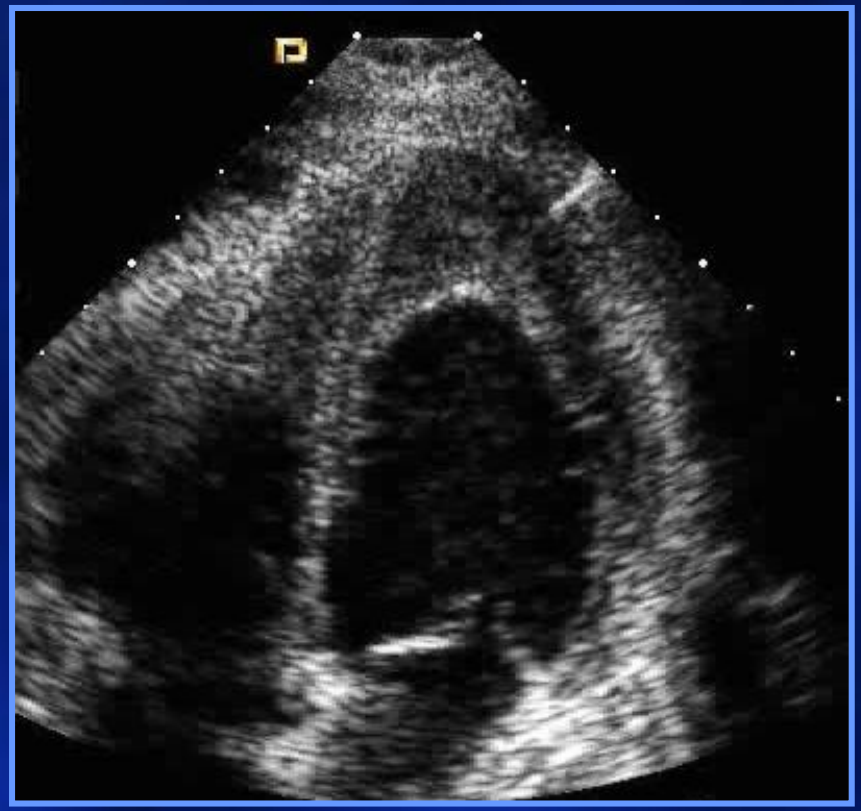
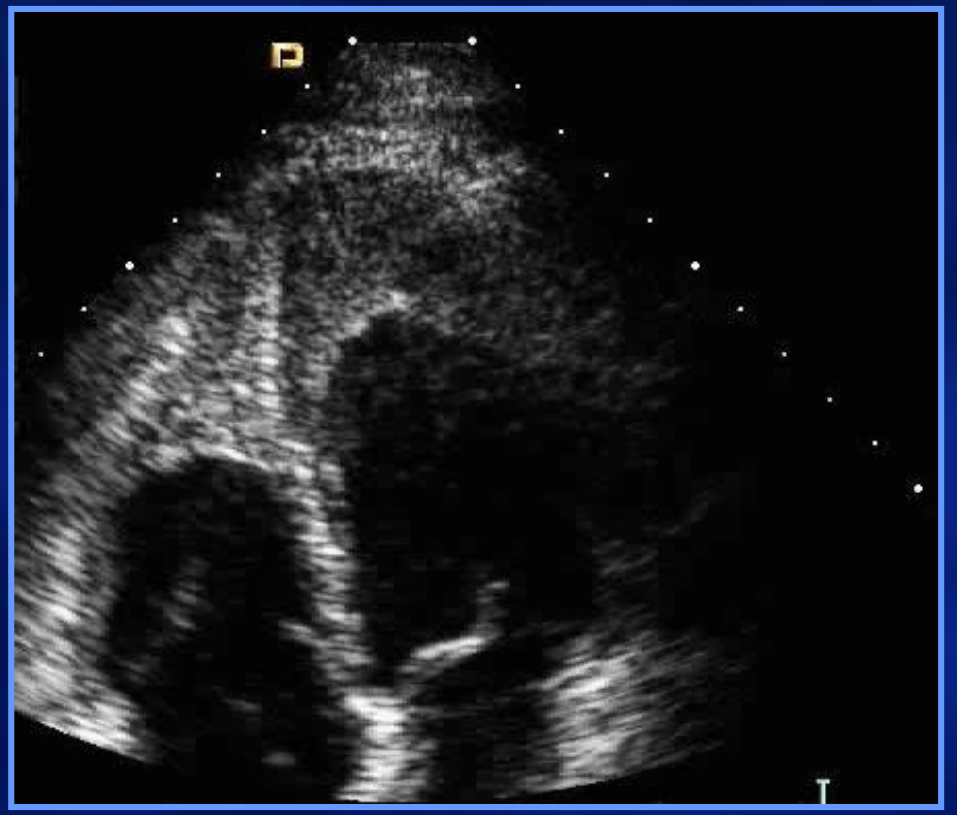
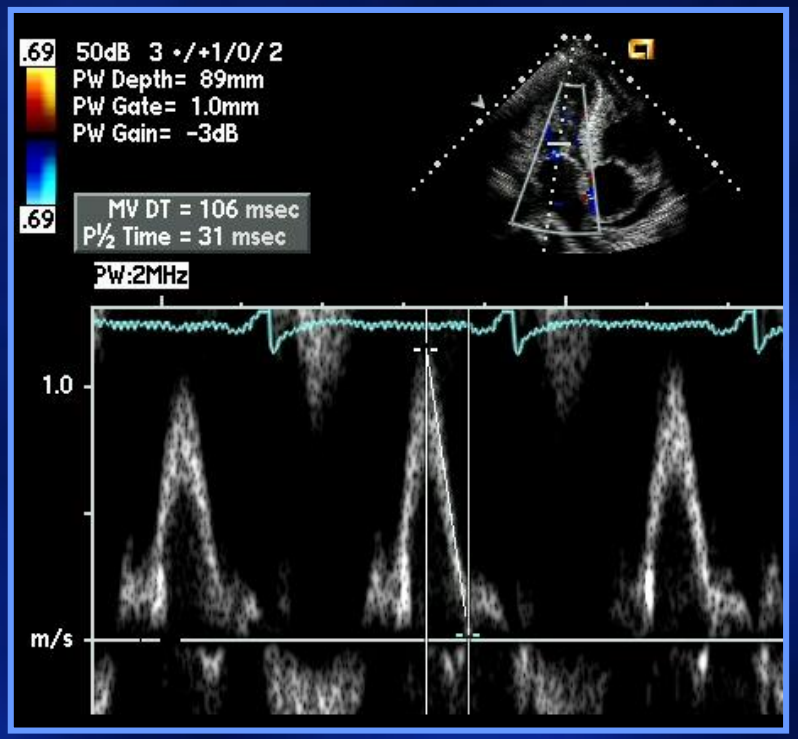
ROUTINE

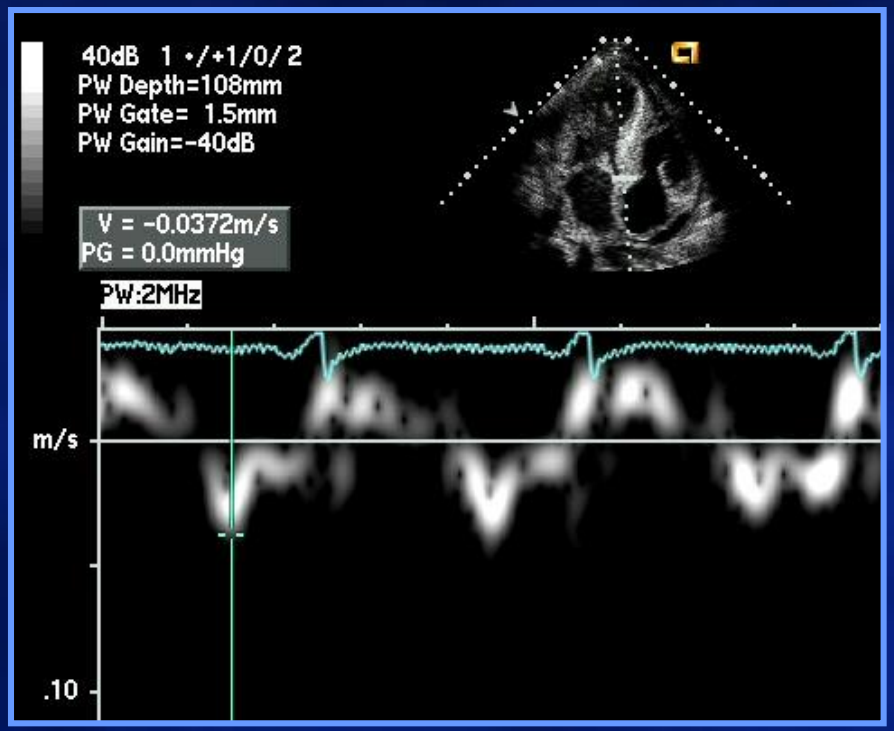
Apical 4 Chamber View





Diastolic Function



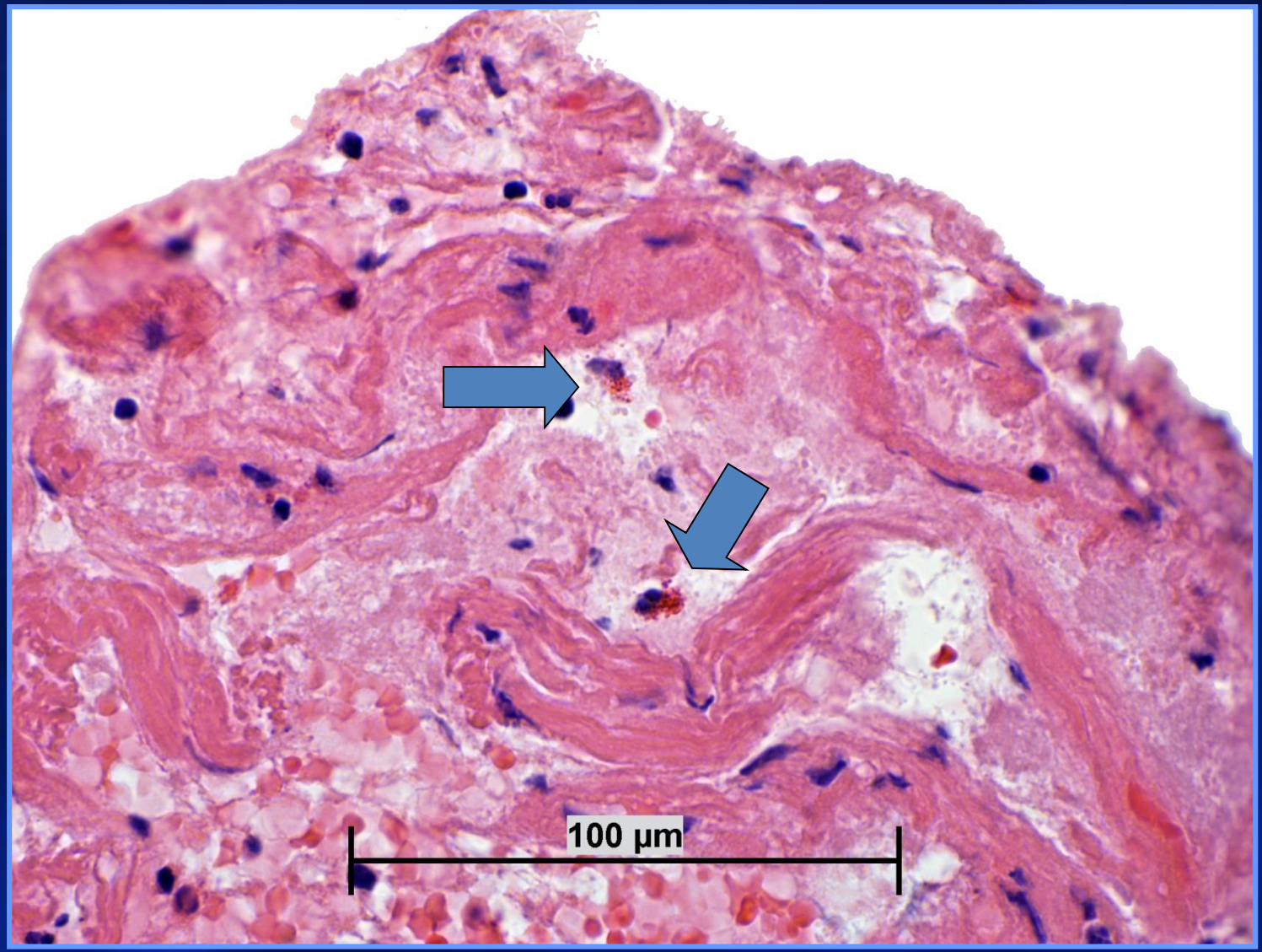


- MV Dec. Time = 105 msec
- MV Emax = 1.1 m/sec
- e' = 0.04 m/sec
- E/e' 28

What is the Diagnosis?

1. Hypertrophic Cardiomyopathy (Apical Variant)
2. Amyloidosis
3. Eosinophilic Endomyocardial Disease
4. LV Noncompaction
5. LV Myxoma

RV Biopsy (H&E Stain)



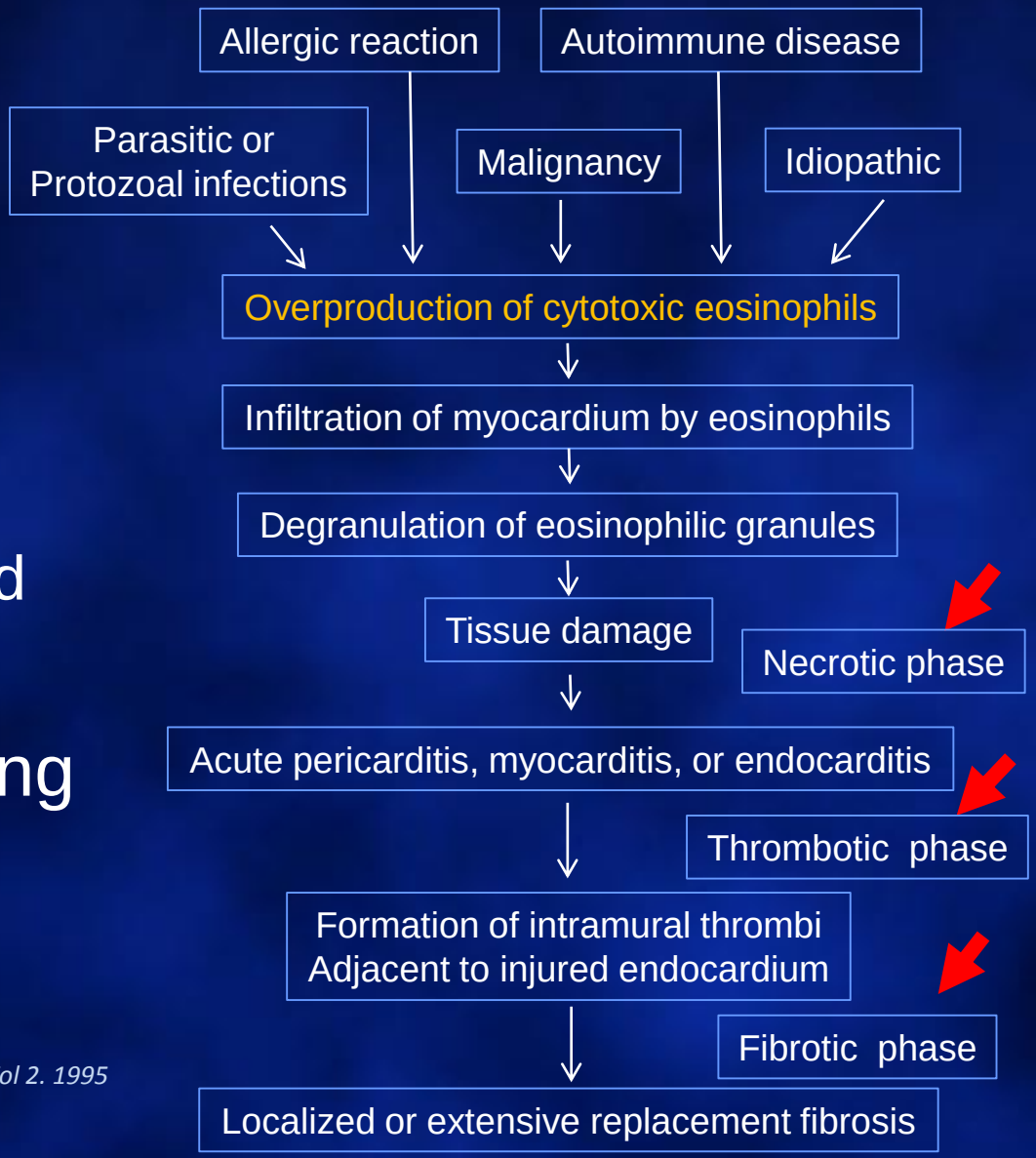
Hypereosinophilic Syndrome Cardiac Manifestations

- Persistent increase in eosinophil count eosinophil count > 1500 cells/mm3
- CHF (dyspnea)
  - Restrictive Cardiomyopathy
  - Mitral regurgitation
- Systemic embolization

Eosinophilic Heart Disease

4 Stages:

1) Acute inflammatory myocarditis
2) Eosinophil rich thrombus deposition
   - Mediated by injured endothelium
3) Endocardial thickening
   - Valve involvement
4) Fibrosis



Hirota Y: In Abelmann WH, Braunwald E [eds]: Atlas of Heart Diseases. Vol 2. 1995

Hypereosinophilic Syndrome (HES)

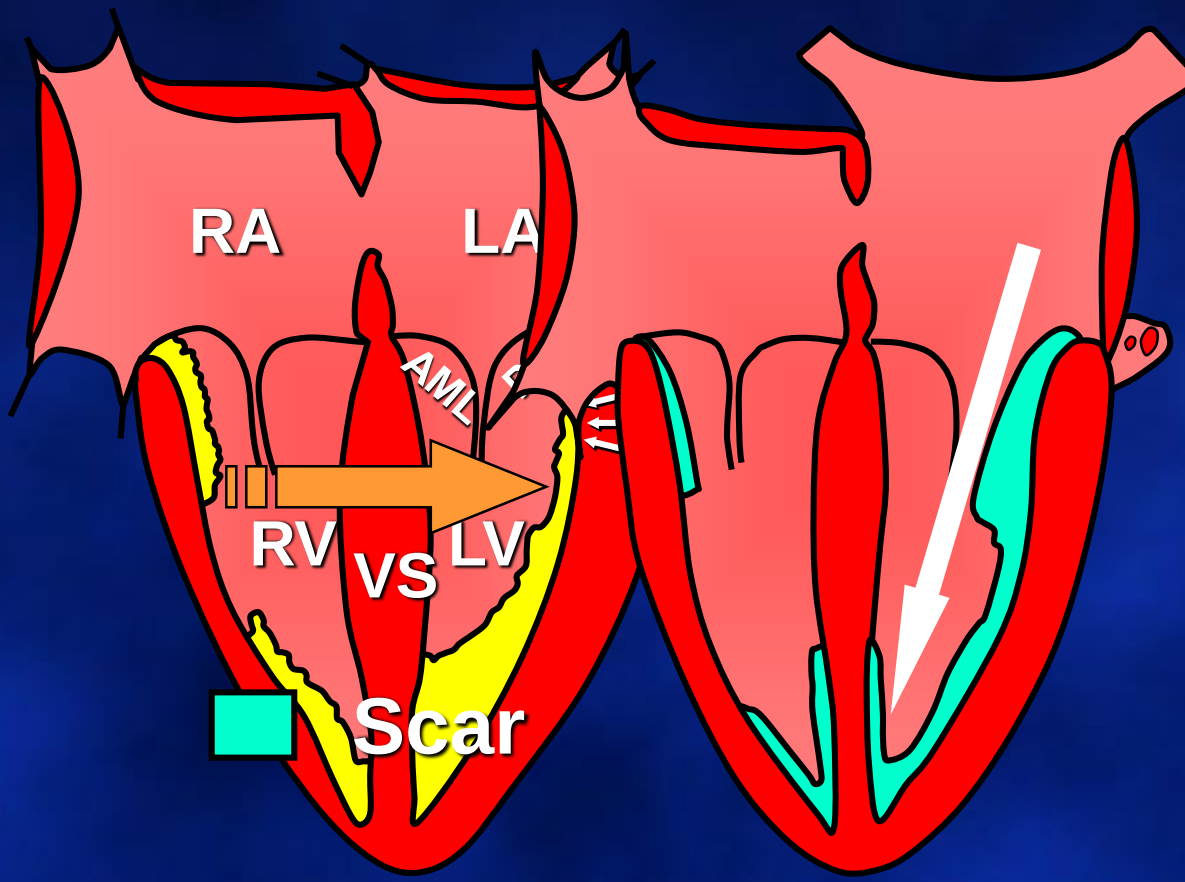
Cardiac Involvement: 40-60% of patients

2-D Echo & Doppler Findings

- **LV > RV inflow apical thrombo-obliteration, endocardial thickening**
- **Restrictive diastolic dysfunction**
- **Subvalvular thrombosis, leaflet entrapment MV > TV Leaflets; MR&TR**

Ommen, Am J Cardiol 2000

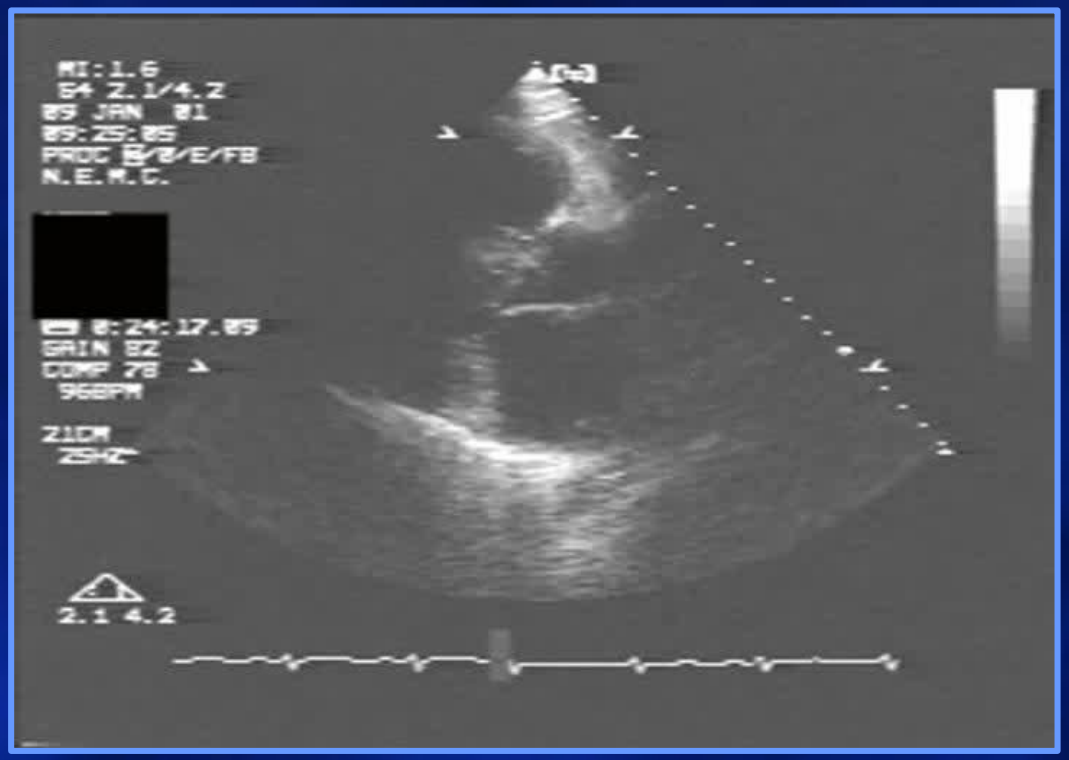
Natural History
Hypereosinophilic Syndrome



Myocarditis → Thrombus → Fibrosis

Image courtesy of Leslie Elvert RDCS

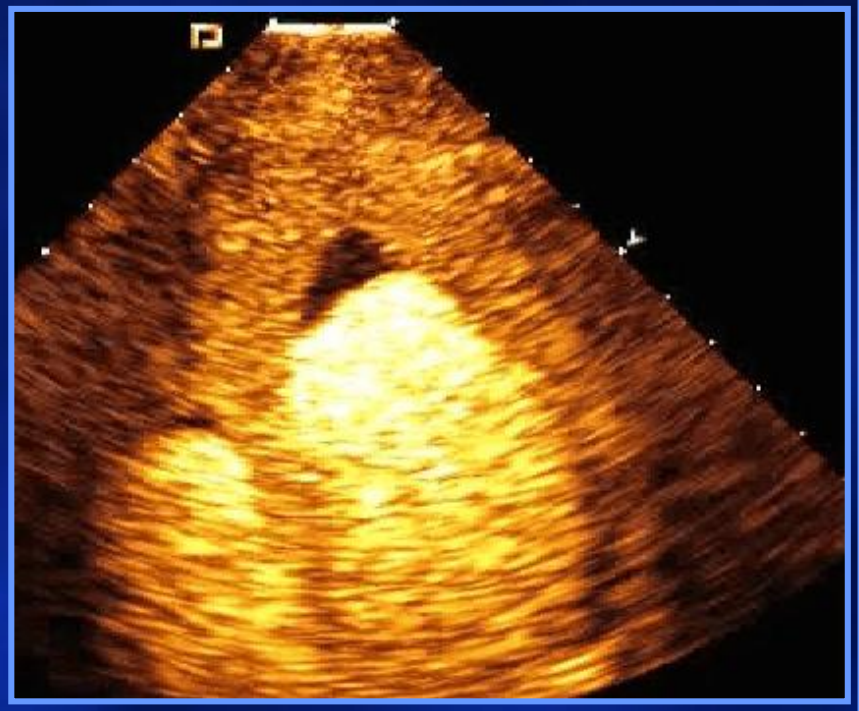
Basal LV Fibrosis with Mitral Posterior Leaflet Tethering

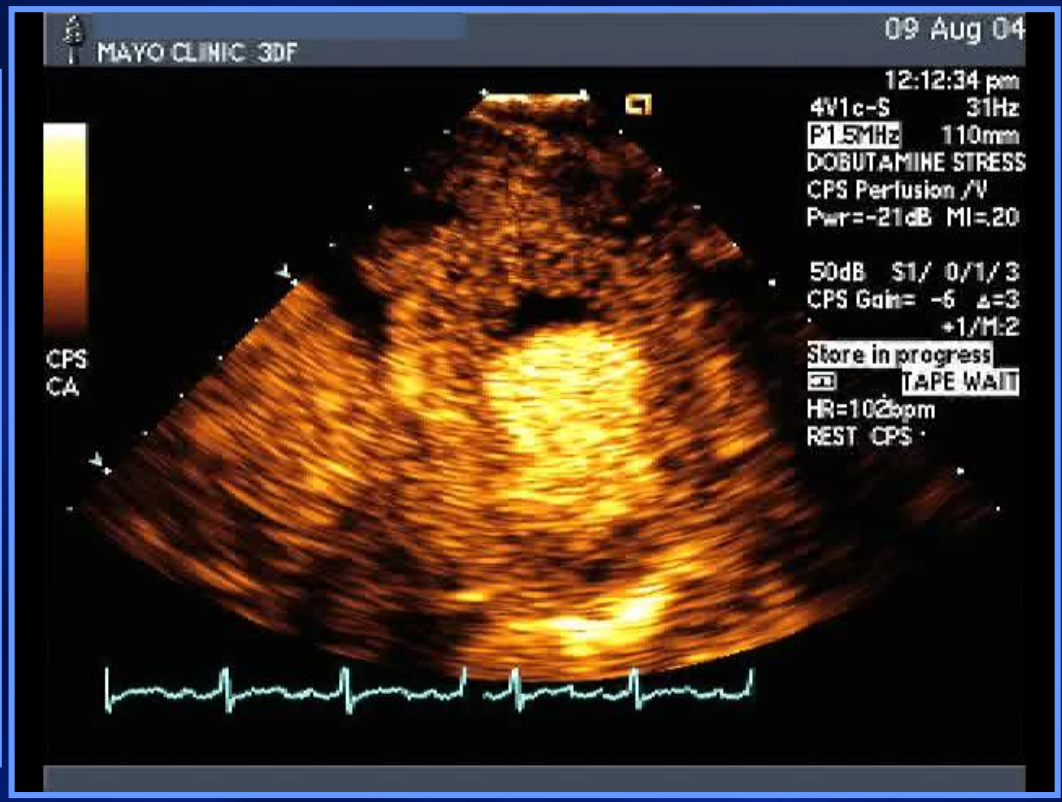


- Courtesy of Dr. Natesa Pandian

Eosinophilic Heart Disease

Contrast Helpful





Hypereosinophilic Syndrome

Treatment

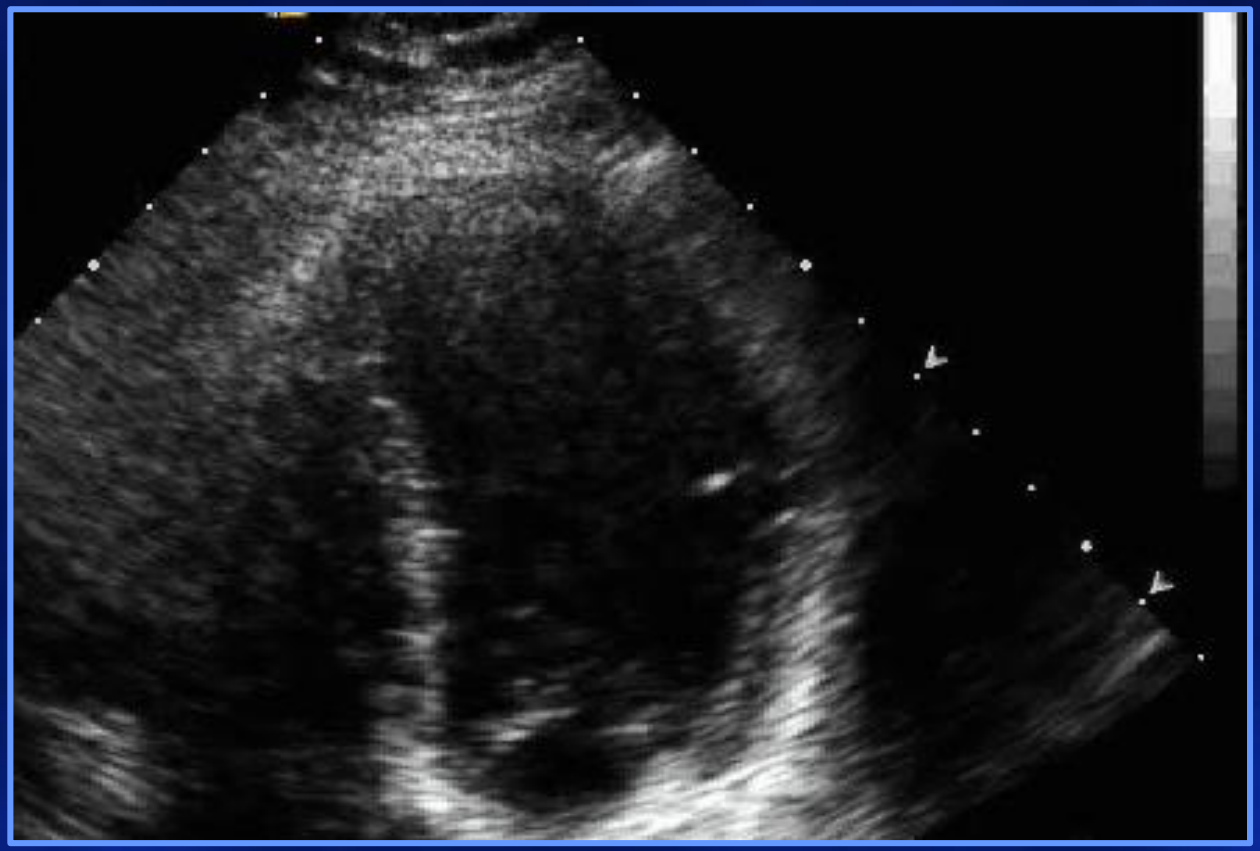
- Medical therapy
  - Corticosteroids
  - Hydroxyurea
  - Interferon
  - CHF Meds
- Surgical Therapy
  - Palliative

Echo Differential Diagnosis

- Apical hypertrophic CM
- LV Noncompaction
- LV tumor
  - Myxoma
  - Papillary fibroelastoma
- Ischemic LV dysfunction with apical thrombus

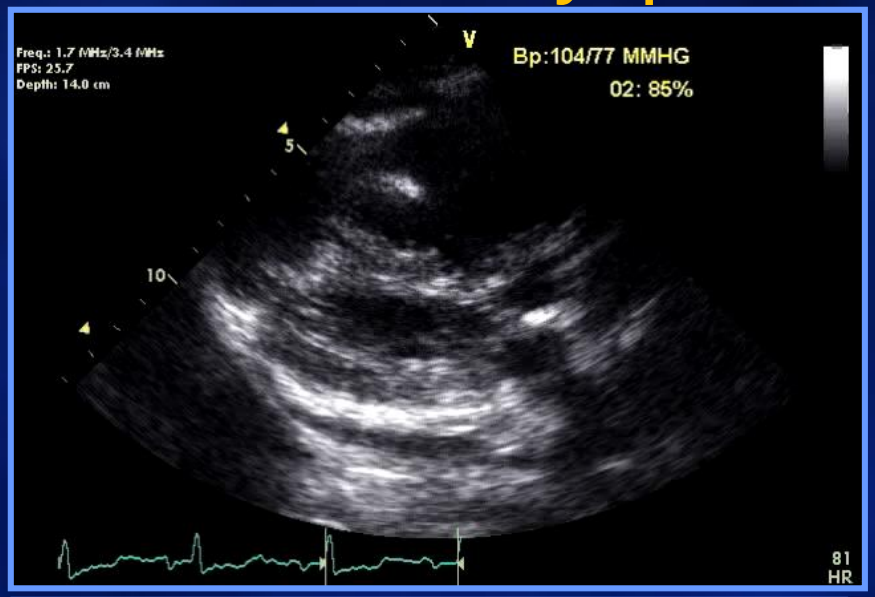
Our Case:

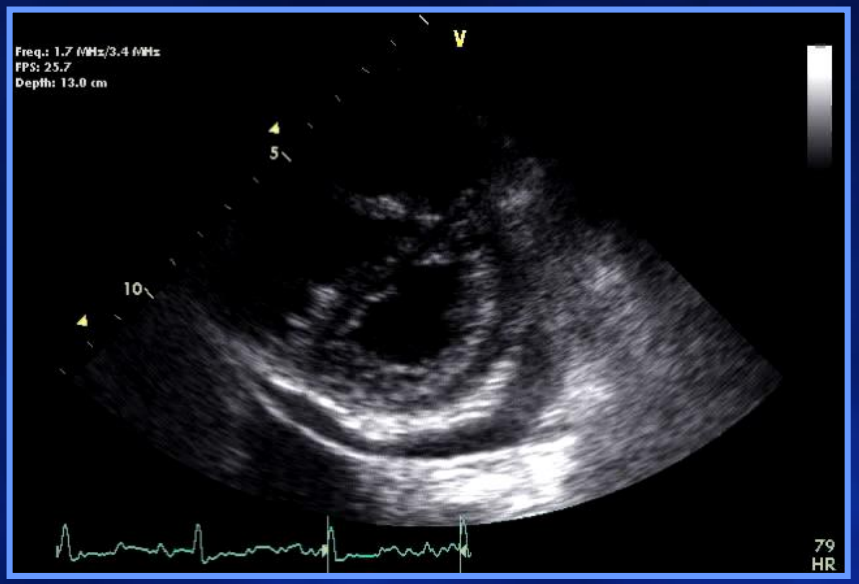
TTE after 2 months of anticoagulation and 1 month of prednisone therapy

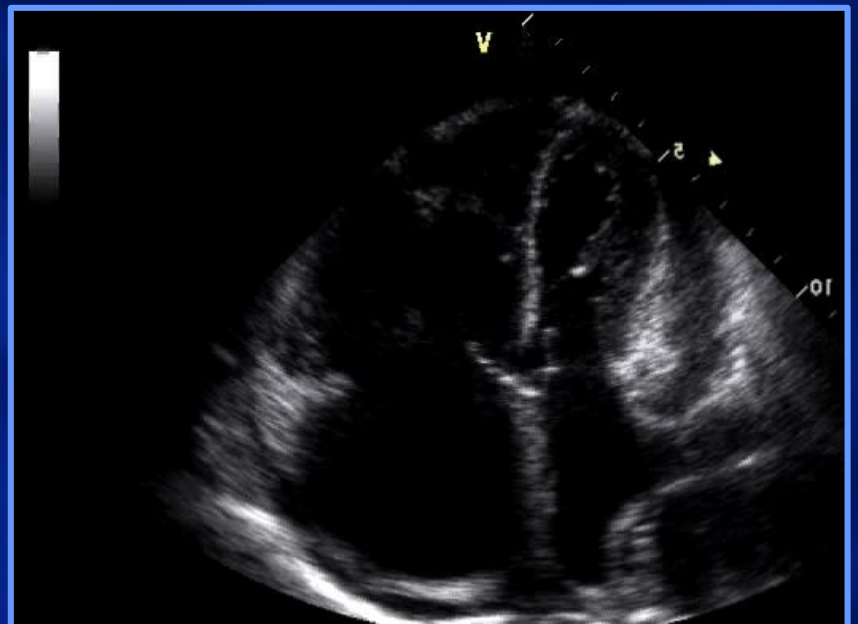


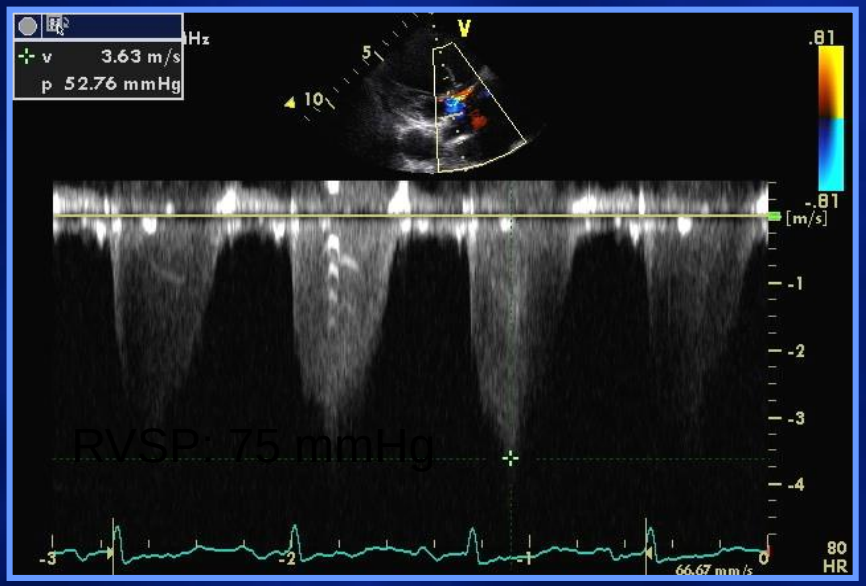
Patient with CREST Syndrome:

Dyspnea and Edema







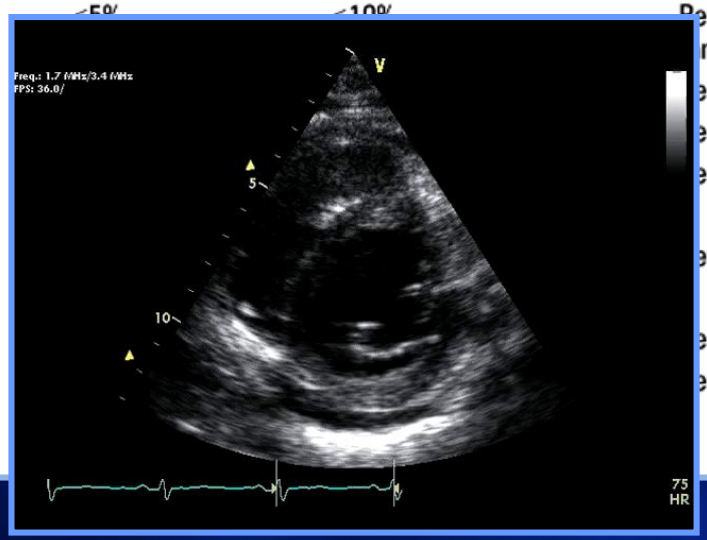


Scleroderma and Pulmonary HTN

- PH present in 8-12% of scleroderma patients
  - Higher risk in CREST patients
- Accounts for 30% of deaths
- Screening for PH recommended
- RV dysfunction, cardiac index and pericardial effusion are markers of poor prognosis in PH

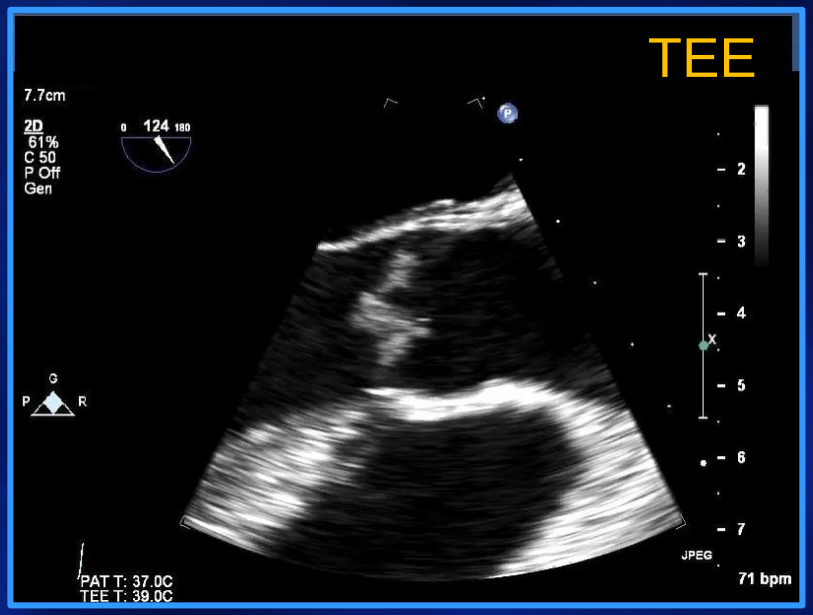
Pericardial Involvement in Systemic Disease

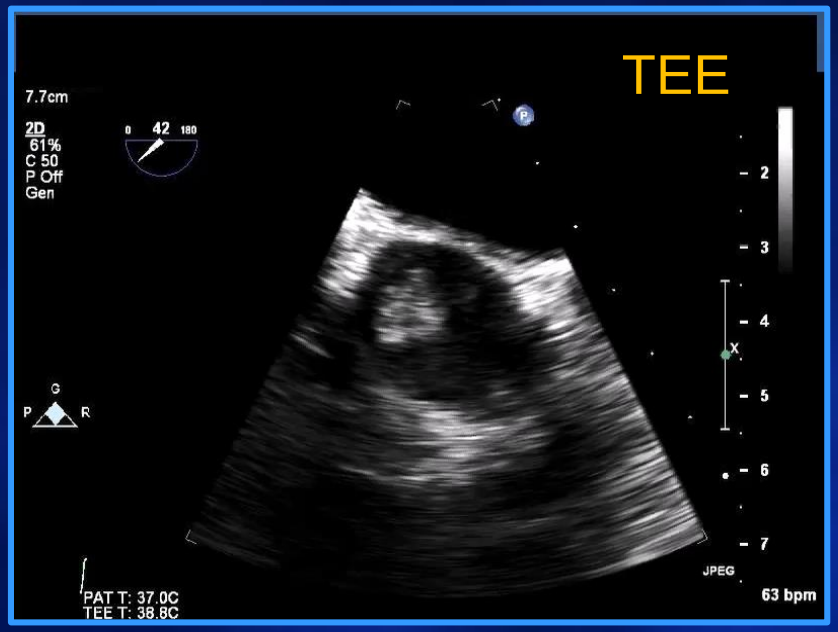
SID	Estimated overall prevalence* (%)	Estimated frequency of pericardial involvement (%)	Type of pericardial involvement
Vasculitis	<10%		
Takayasu arteritis	Rare	Rare (case reports)	Pericardial effusion, pericarditis
Giant cell arteritis	Rare	Rare (case reports)	Pericardial effusion, pericarditis
Polyarteritis nodosa	Rare	Rare (case reports, series)	Pericarditis
Kawasaki disease	<5%	30%	Pericardial effusion, pericarditis
Churg–Strauss syndrome	<5%	20–25%	Pericardial effusion, pericarditis
Wegener granulomatosis	<5%	<10%	Pericardial effusion, pericarditis
Connective tissue diseases	80–90%		
Systemic lupus erythematosus	50–60%	>50%	Pericardial effusion, pericarditis
Rheumatoid arthritis	20–30%	10–30%	Pericardial effusion (30%), pericarditis (10%)
Systemic sclerosis	5–10%	Symptomatic <20%, overall >60%	Pericardial effusion, pericarditis
Polymyositis and dermatomyositis			ericarditis, pericardial effusion, cardiac mponade (case reports)
Mixed connective tissue disease			ericarditis, pericardial effusion
Sjögren syndrome			ericarditis
Behçet's disease			ericarditis
Granulomatous diseases			
Sarcoidosis			ericardial effusion, pericarditis
Autoinflammatory diseases			
Familial Mediterranean fever			ericarditis
TNF receptor-1 associated periodic syndrome (TRAPS)			ericarditis



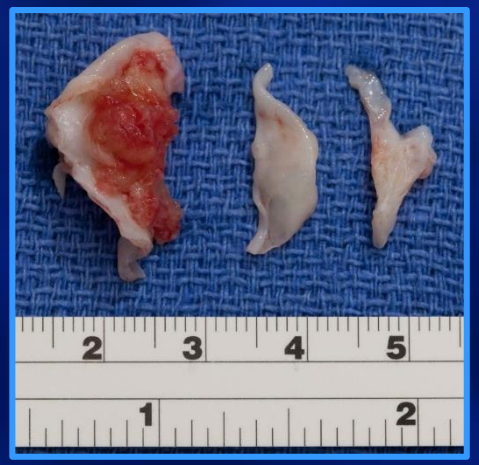
Imazio M: Heart, 2011

33 Year Old Female → Multiple Strokes



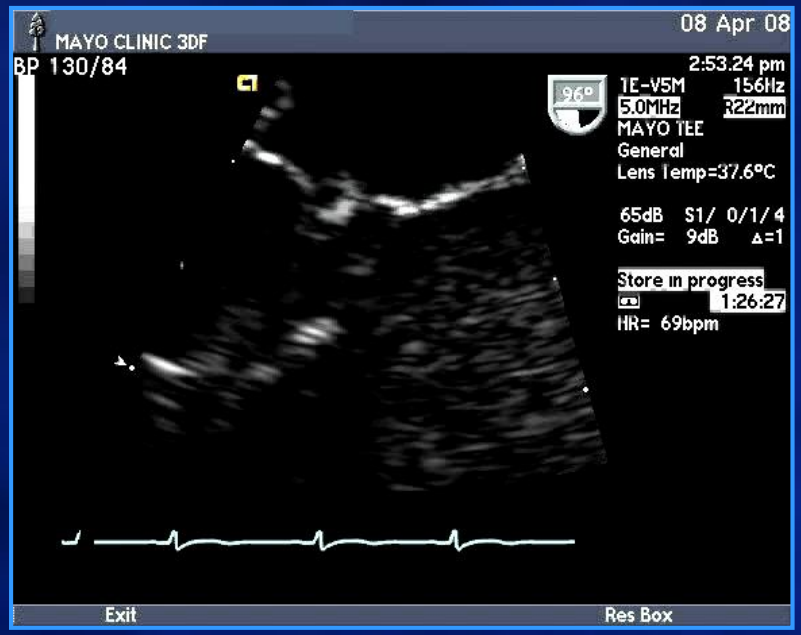


- ANA positive and Antiphospholipid antibodies present
- Libman-Sacks endocarditis



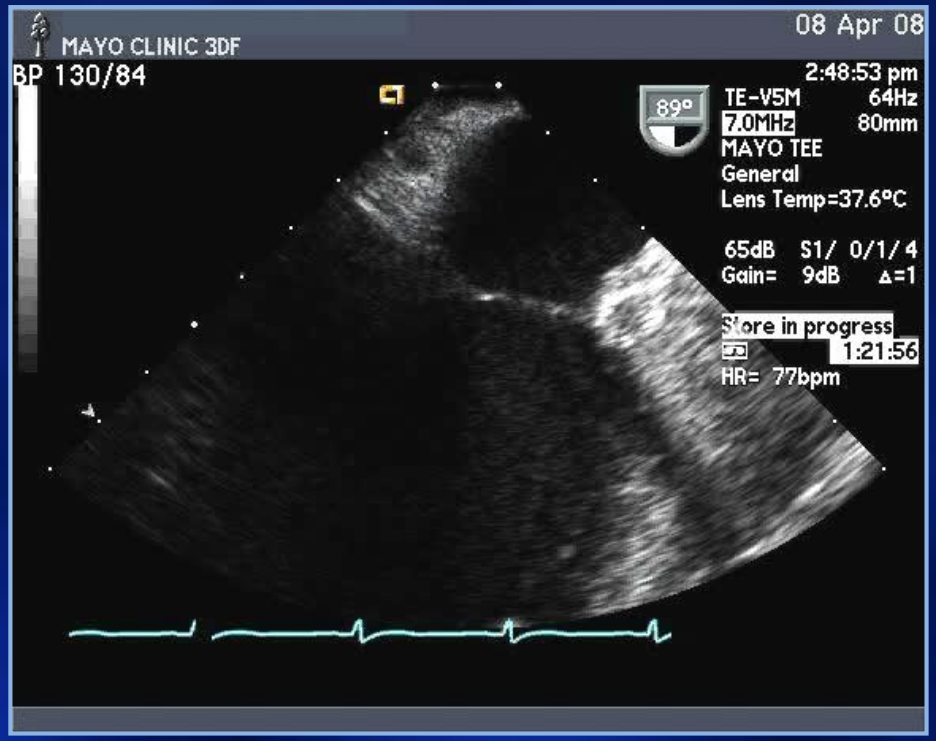
Systemic Lupus Erythematosus Cardiac Involvement

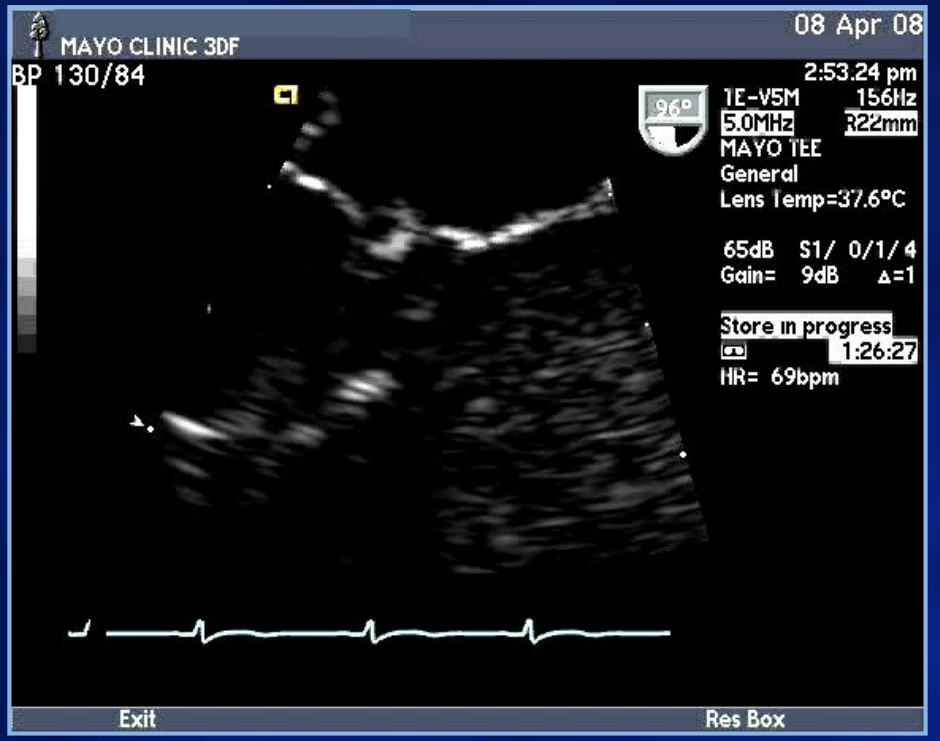
- Pericarditis (fluid ANA+)
  - 50-60% of cases
- Lupus anticoagulant
- Anticardiolipin or Antiphospholipid Abs
- Myocarditis
- Coronary arteritis
- Libman-Sacks (Marantic) vegetations



18 y.o. female with occipital stroke

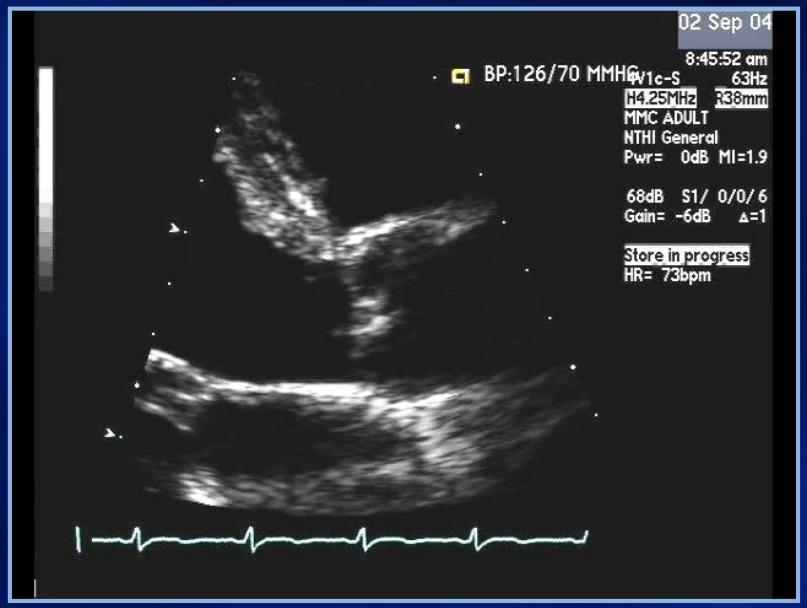
TEE

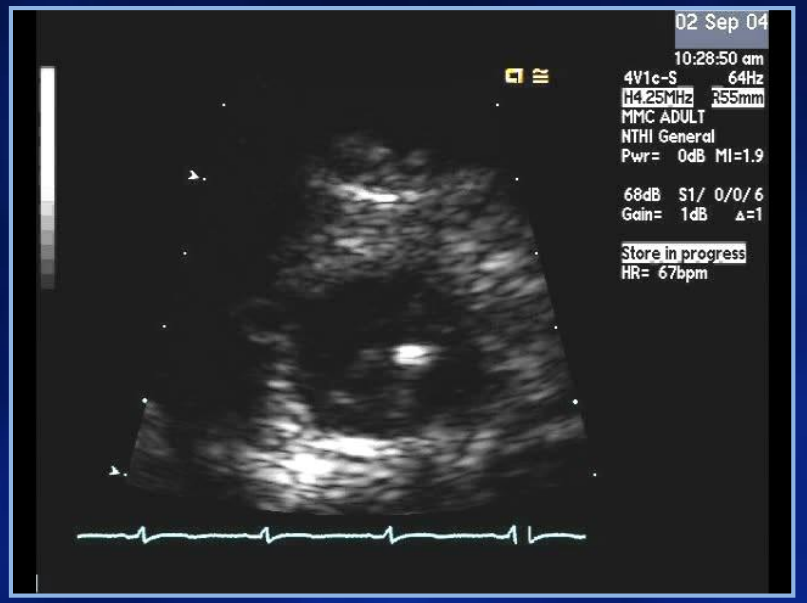


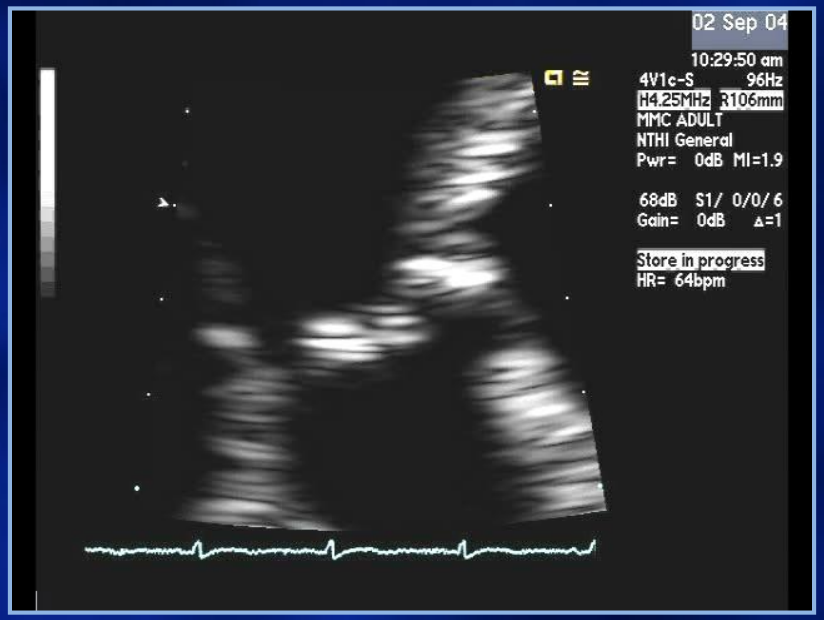


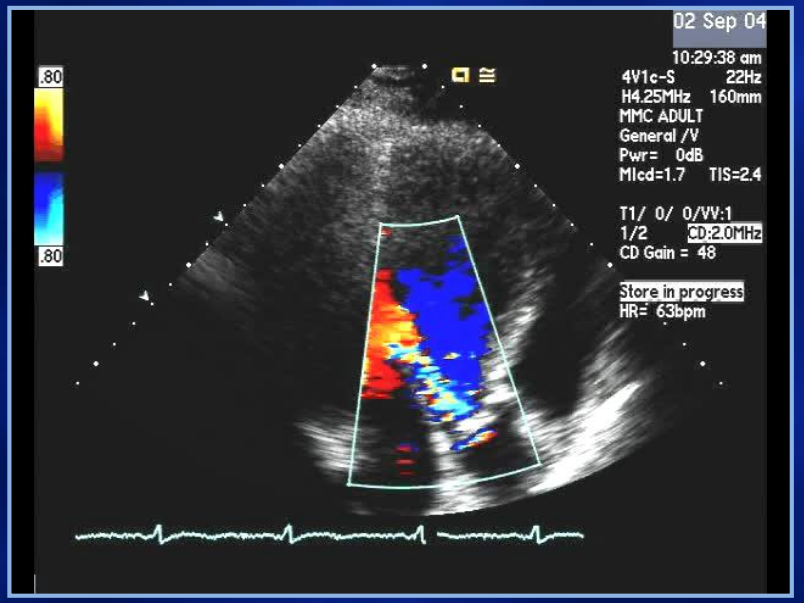
- Lupus anticoagulant + antiphospholipid antibodies present
- Libman-Sacks endocarditis

Not only the mitral valve!

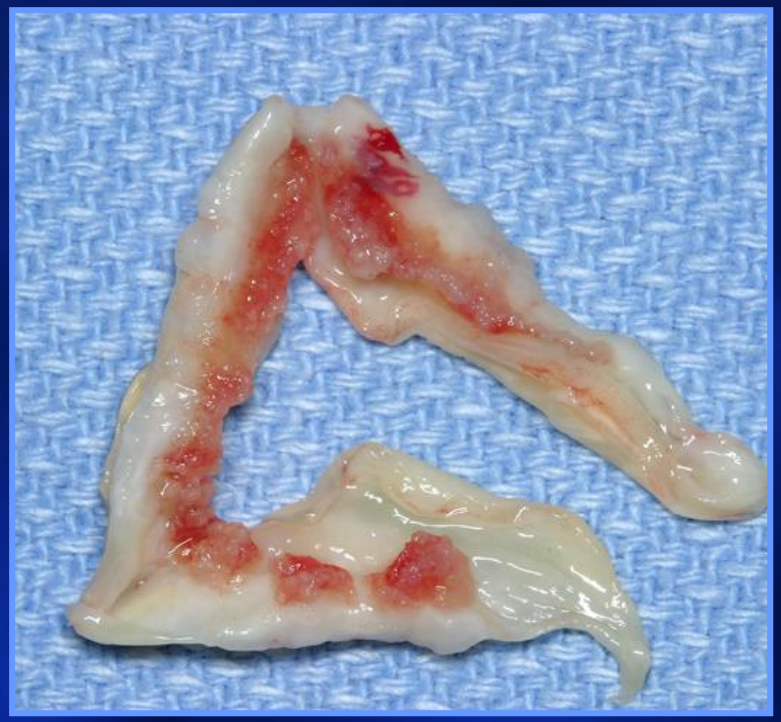








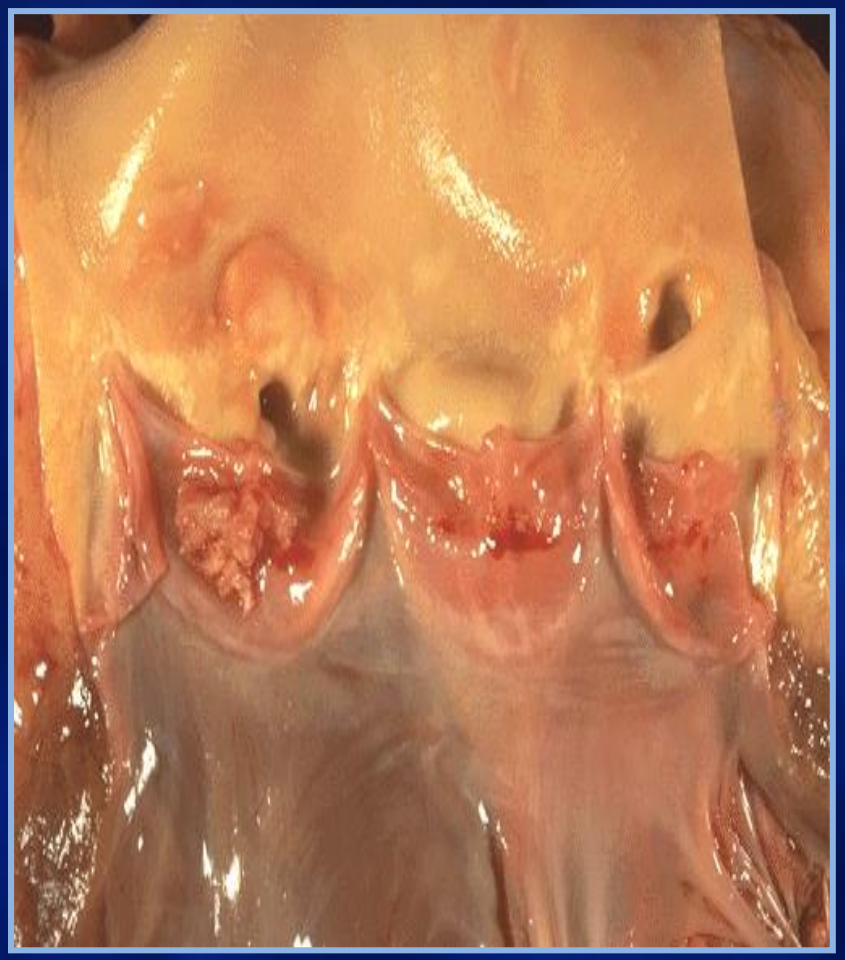
Antiphospholipid Syndrome
Diagnosis confirmed at surgery



- IgG and IgM Antiphsopholipid antibody
- Importance of recognition
  - Unlikely repair
  - Choice of prosthesis
    - Avoid bioprosthesis if possible
  - Anticoagulation

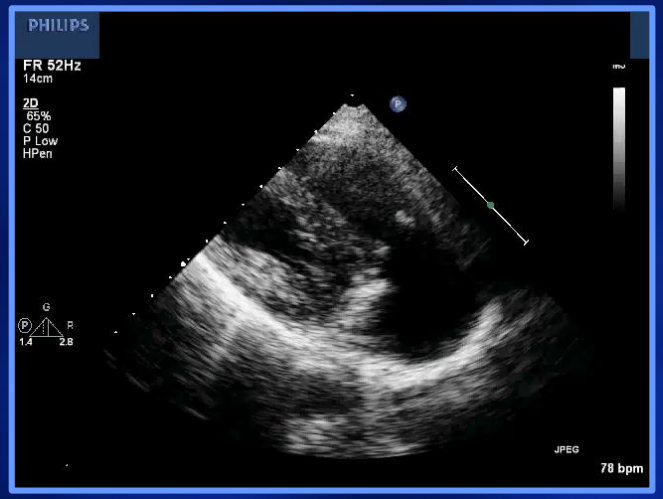
Systemic Lupus Erythematosus Cardiac Involvement

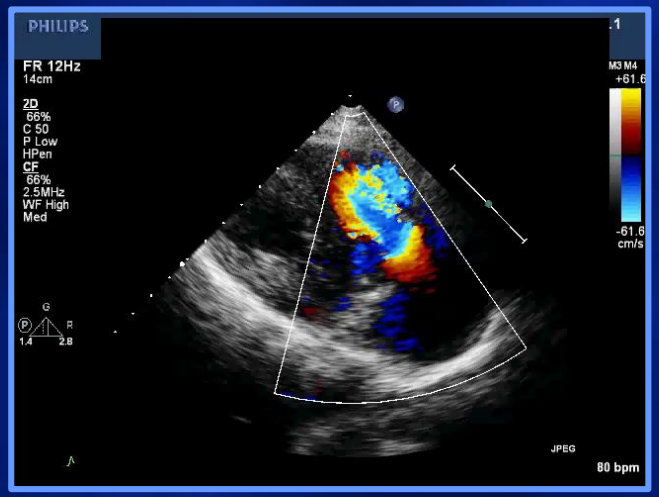
- Pericarditis (fluid ANA+)
- Lupus anticoagulant
- Anticardiolipin antibodies
- Myocarditis
- Coronary arteritis
- Libman-Sacks (Marantic) vegetations



Courtesy of W Edwards MD

A 68-year-old man presents with fatigue and abdominal bloating. On cardiac exam, the jugular venous pressure revealed “CV” waves to angle of the jaw. An RV lift is present. There is a grade 2/6 pansystolic murmur at the lower sternal border that gets louder with inspiration. There is a soft systolic ejection murmur and diastolic murmur at the second left interspace. In addition, there is an enlarged and pulsatile liver. Images obtained from his TTE are shown.

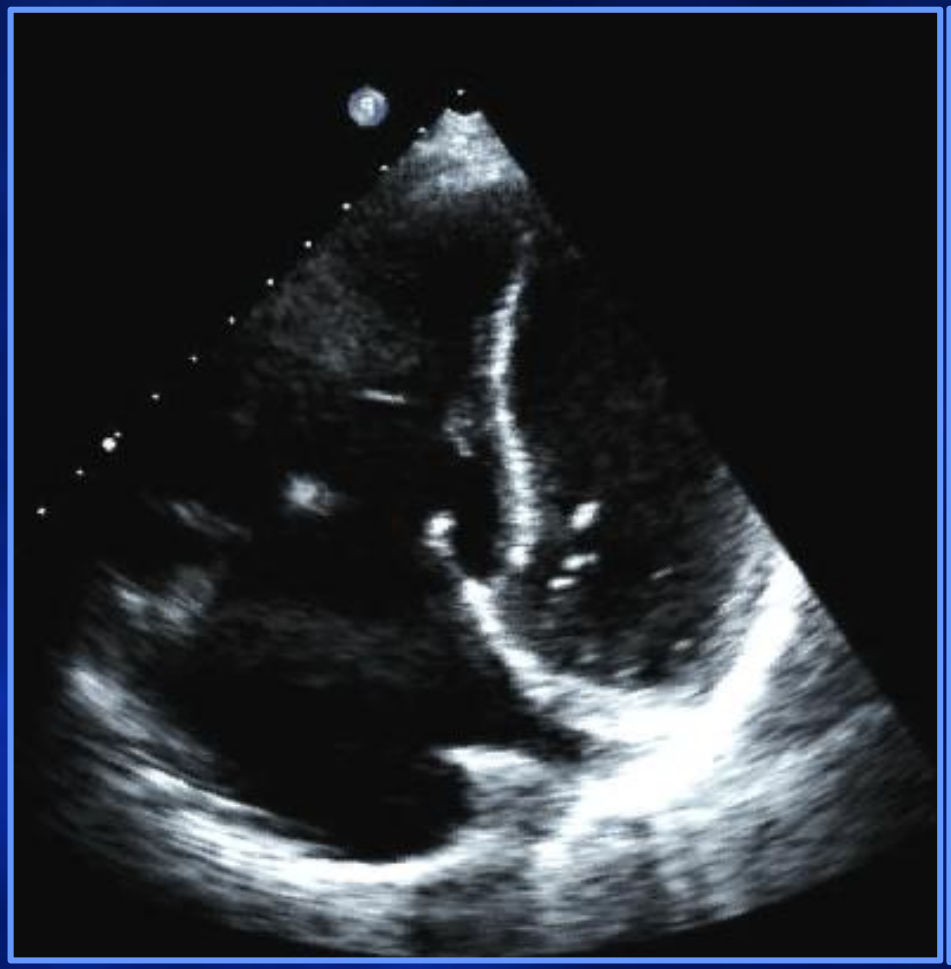


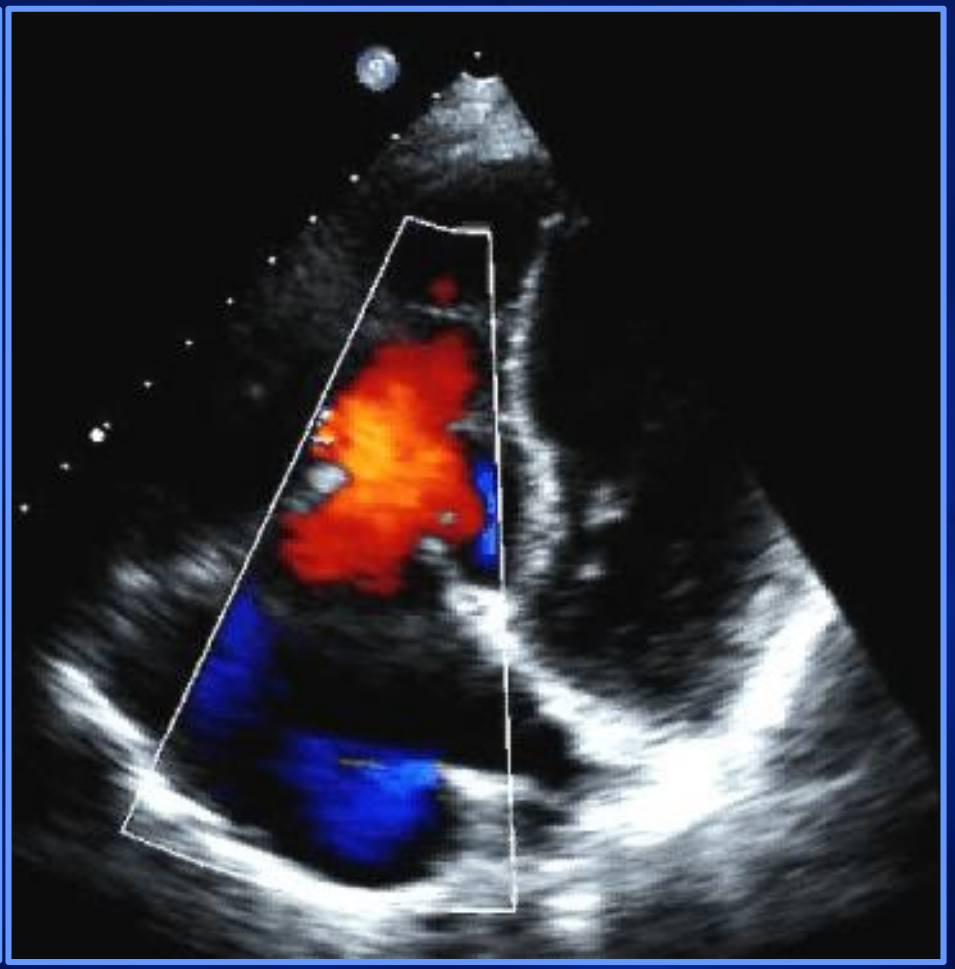


Which of the following is the most likely diagnosis?

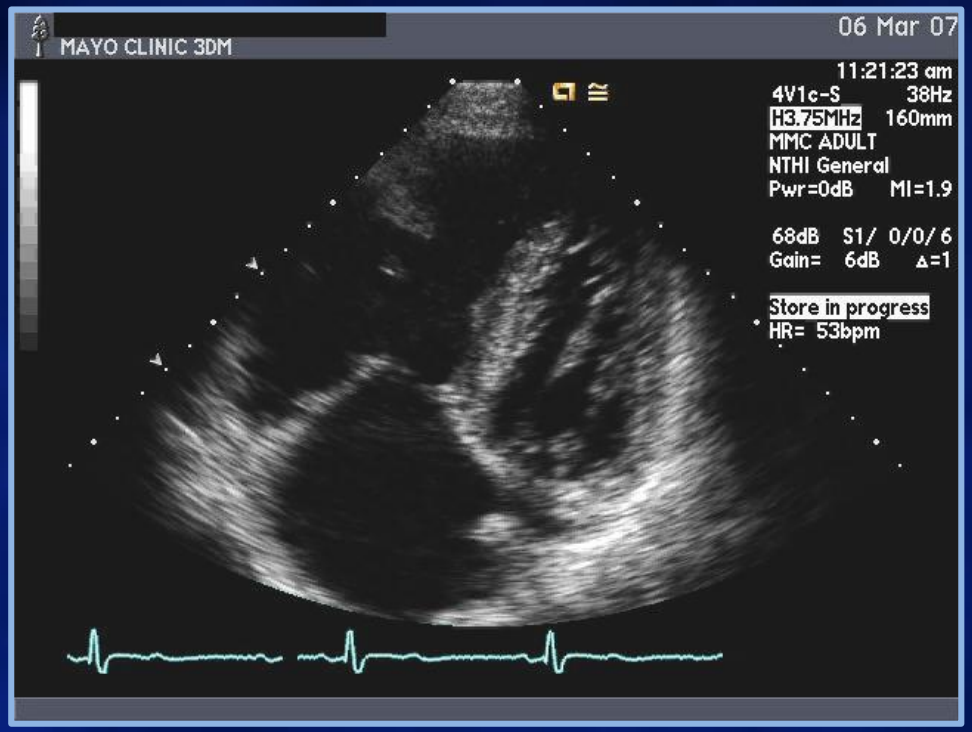
A. Rheumatic heart disease
B. Carcinoid heart disease
C. Ebstein’s anomaly
D. Endocarditis

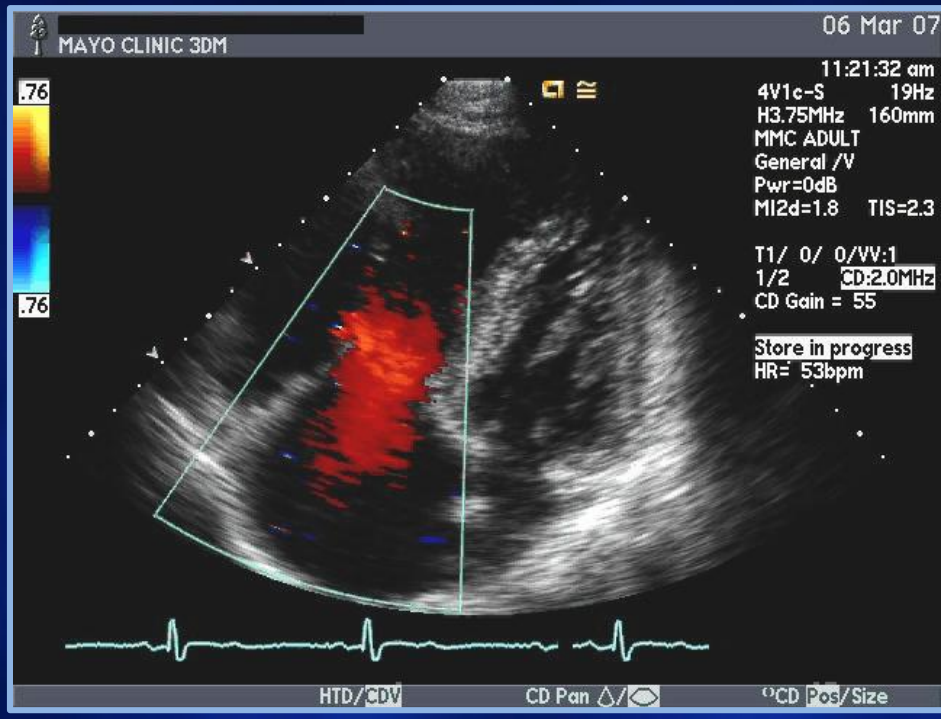
39 year old male with diarrhea, flushing and weight loss

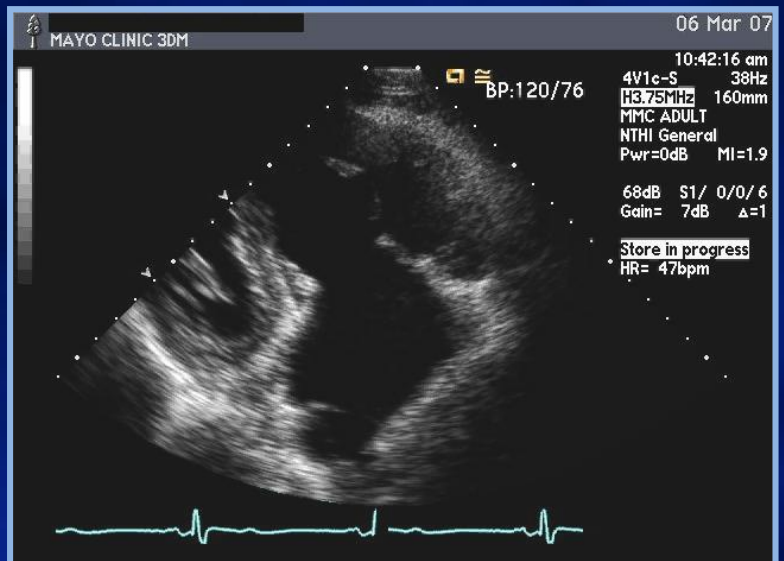


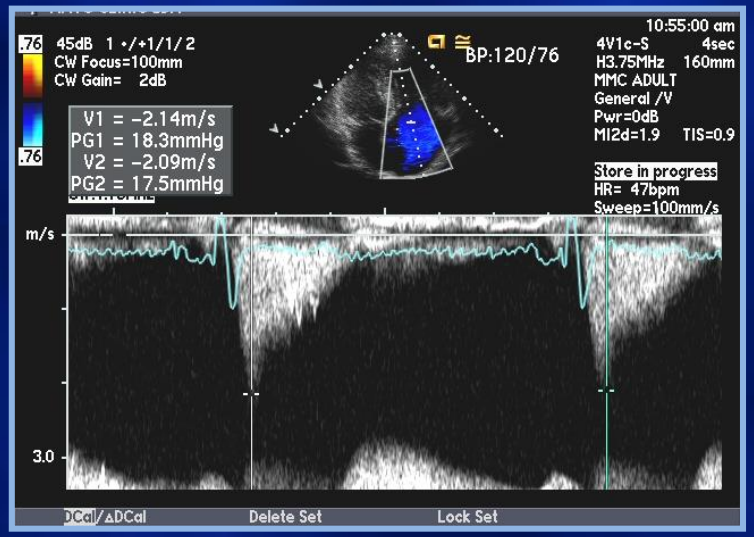


Carcinoid Syndrome

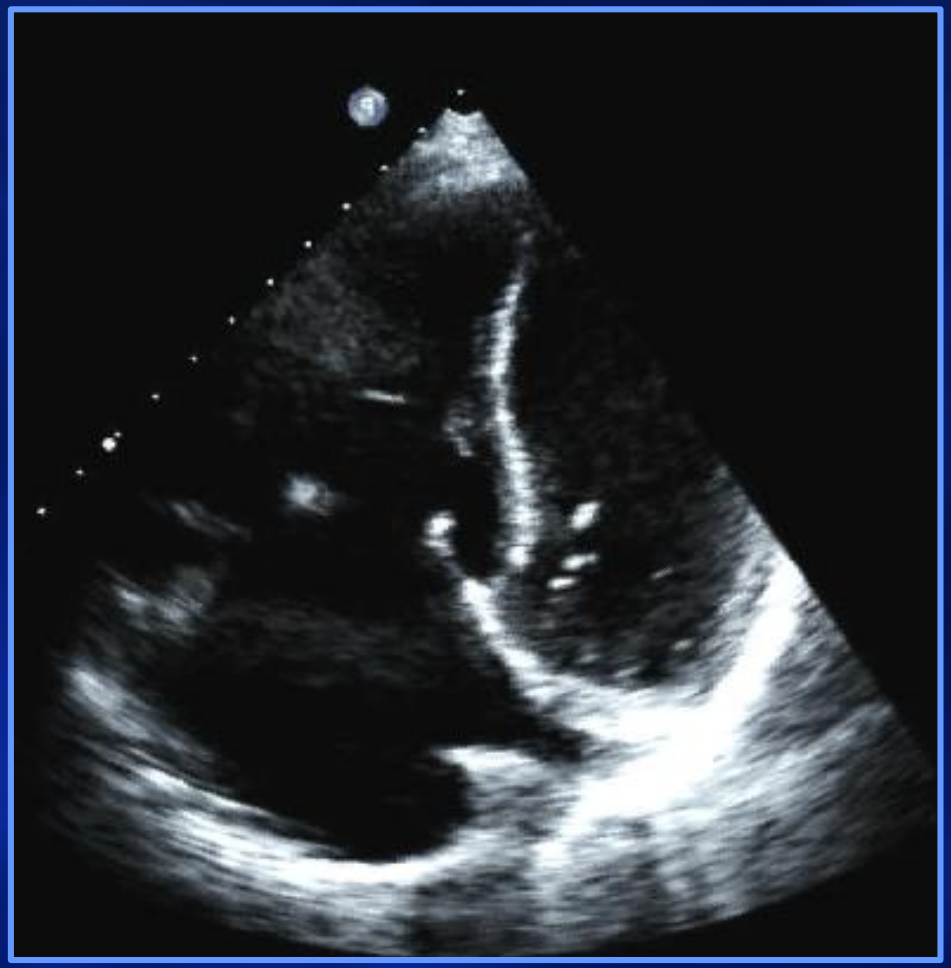








Carcinoid: Echo Features



Tricuspid valve

- Thickened leaflets
- Retracted leaflets
- Fixed semi-open position

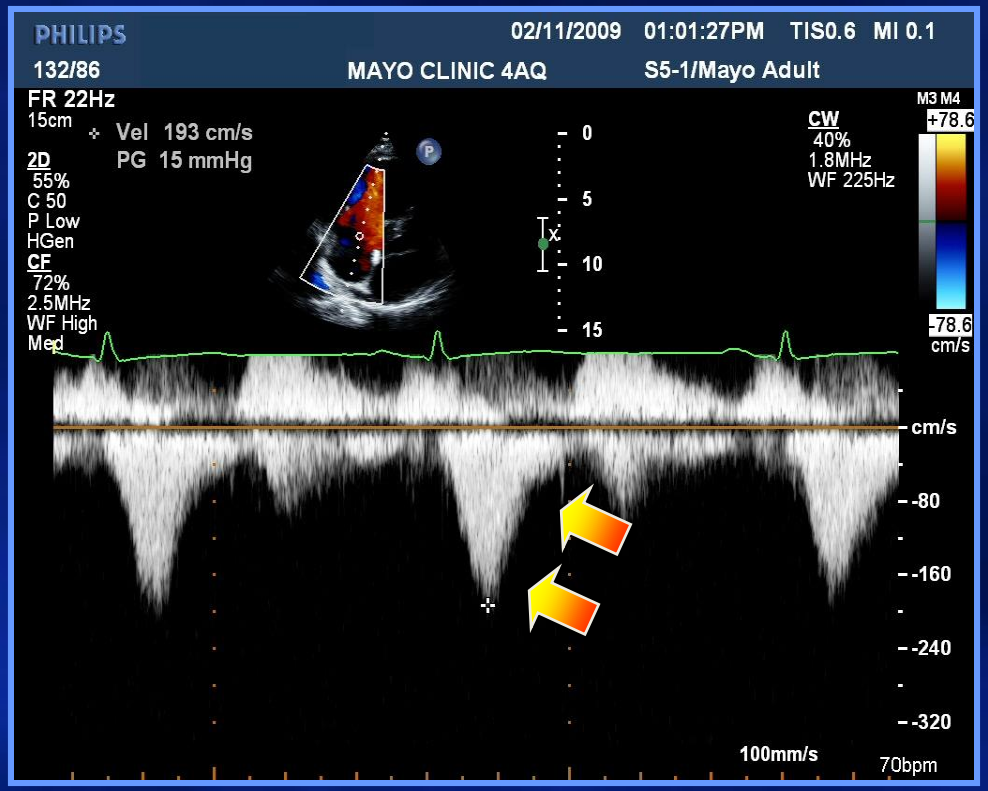
Pulmonary valve

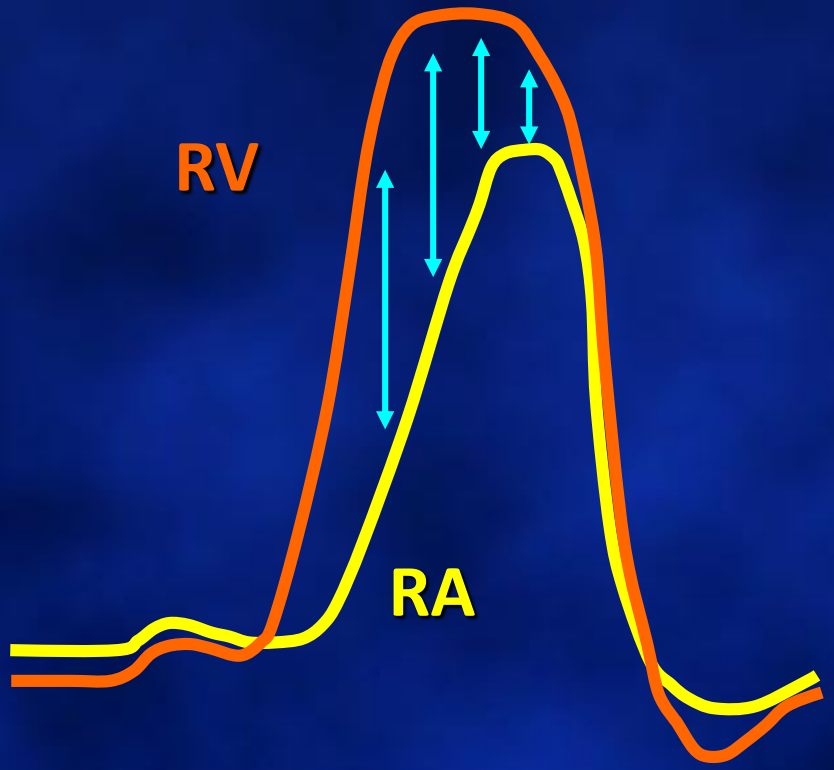
- Thickened cusps
- Retracted and rigid

Severe (Torrential) Tricuspid Regurgitation

Systolic RV → RA pressure equalization

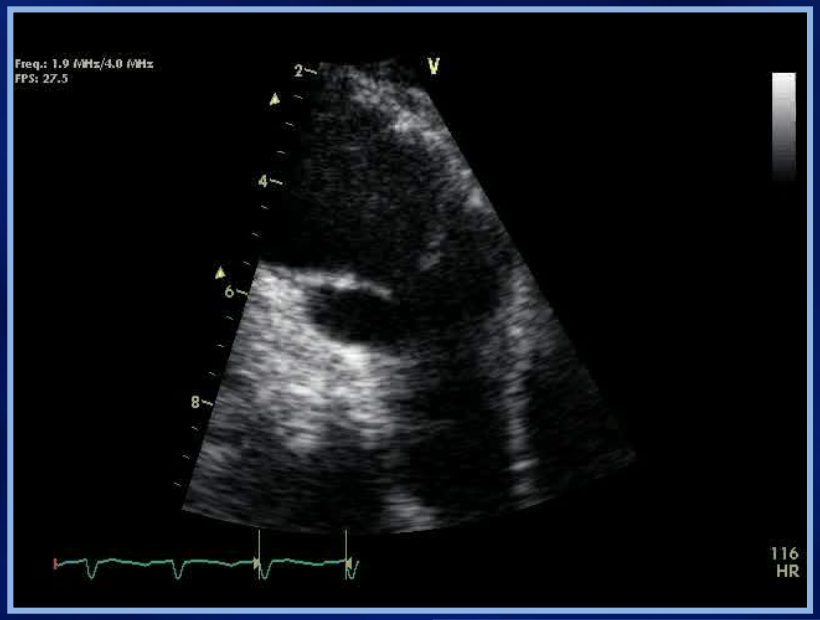
TR CW Doppler

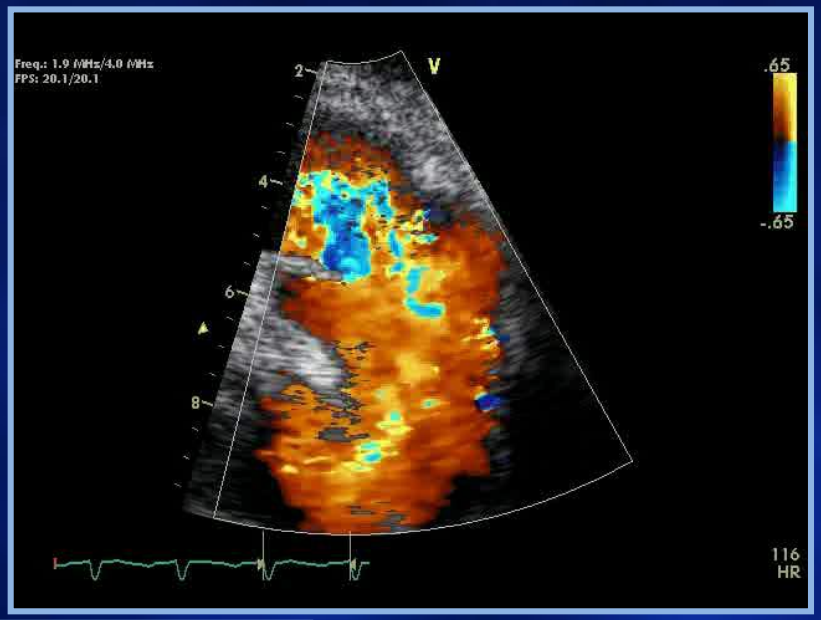


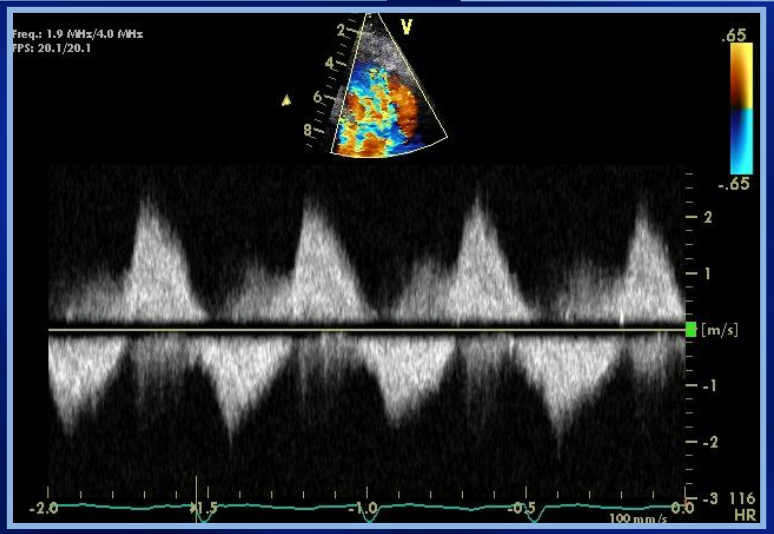


Courtesy of Dr. WK Freeman

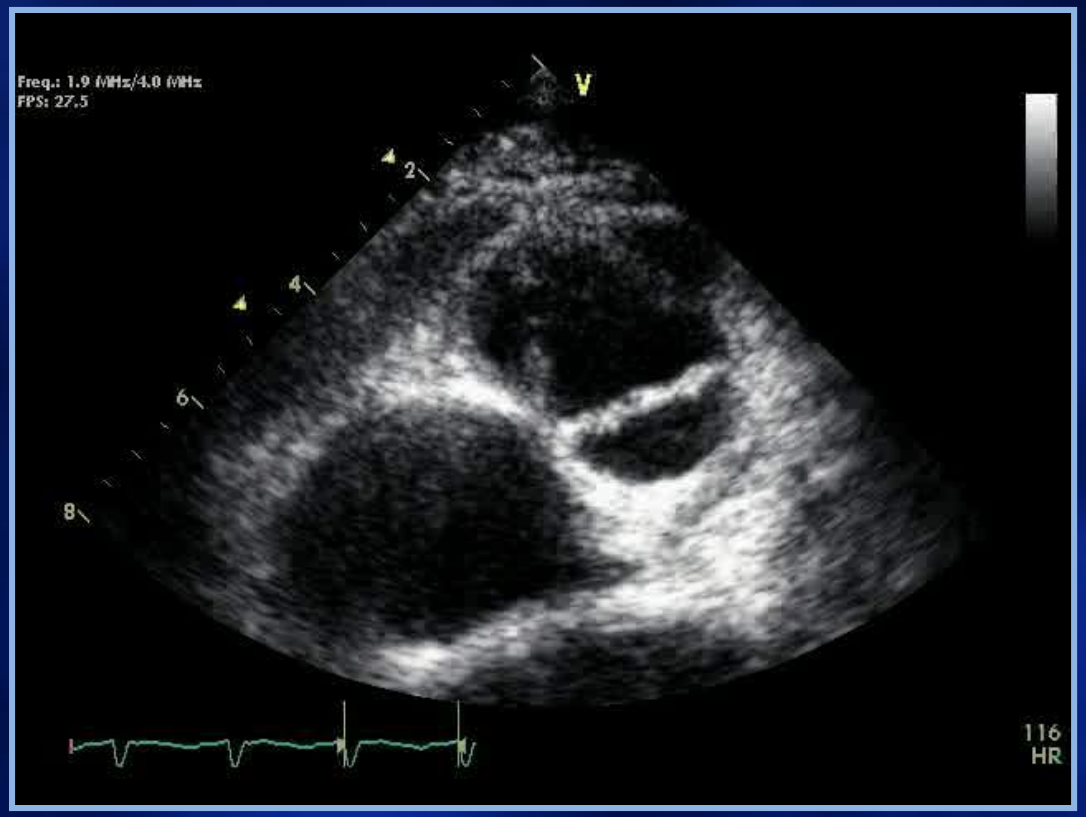
Pulmonary Valve Involvement

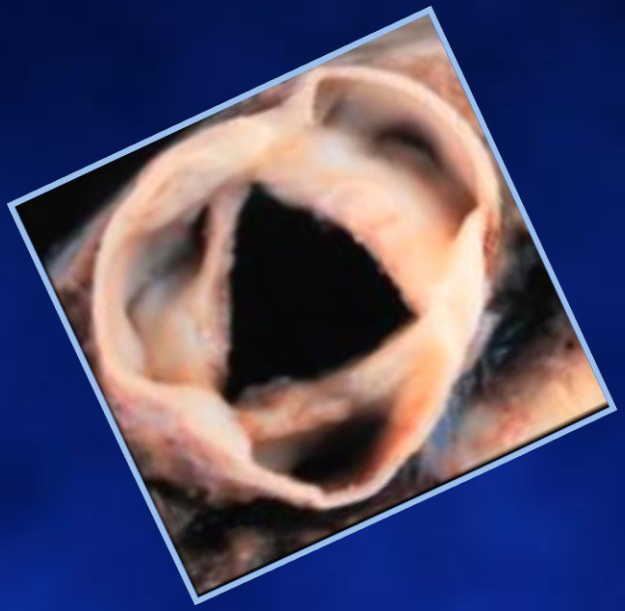






Pulmonary Valve Involvement





Adapted from Mayo Image Data Base, William Edwards, MD

Carcinoid Tumors

- Arise from the GI tract
- Slowly growing
- Produce vasoactive substances
  - bradykinin
  - histamine
  - serotonin
  - prostaglandins
  - catecholamines
  - 5-HIAA

Carcinoid Heart Disease

- Carcinoid tumors: 1-2/100,000
- Carcinoid syndrome in 20-30%
- Deposition of a matrix-like material on the valves and endocardium of the right side of the heart
- Treatment of tumor does not cause regression of valve disease

Connolly HM. Curr Cardiol Rep. 2006

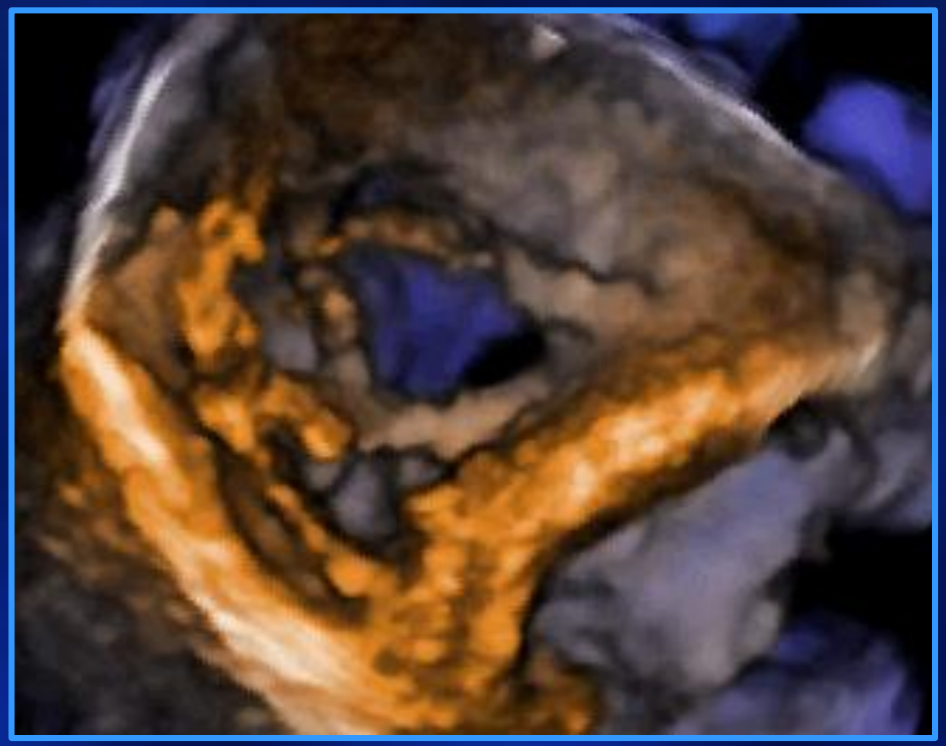
Carcinoid Heart Disease

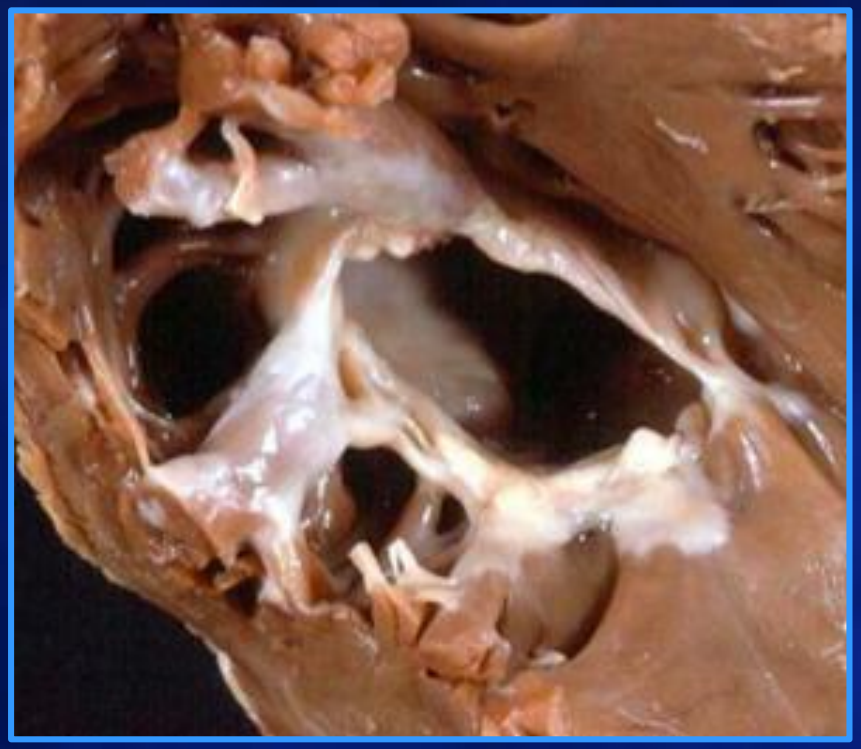
Echo findings:

- Thickening and retraction of immobile tricuspid valve leaflets
- Severe tricuspid valve regurgitation
- May have similar findings in pulmonic valve
- Only 10-15% of cases involve left-sided valves
  - intra-cardiac shunt, primary bronchial carcinoid, primary gonadal carcinoid

Connolly HM. Curr Cardiol Rep. 2006

Carcinoid Syndrome: 3D TTE





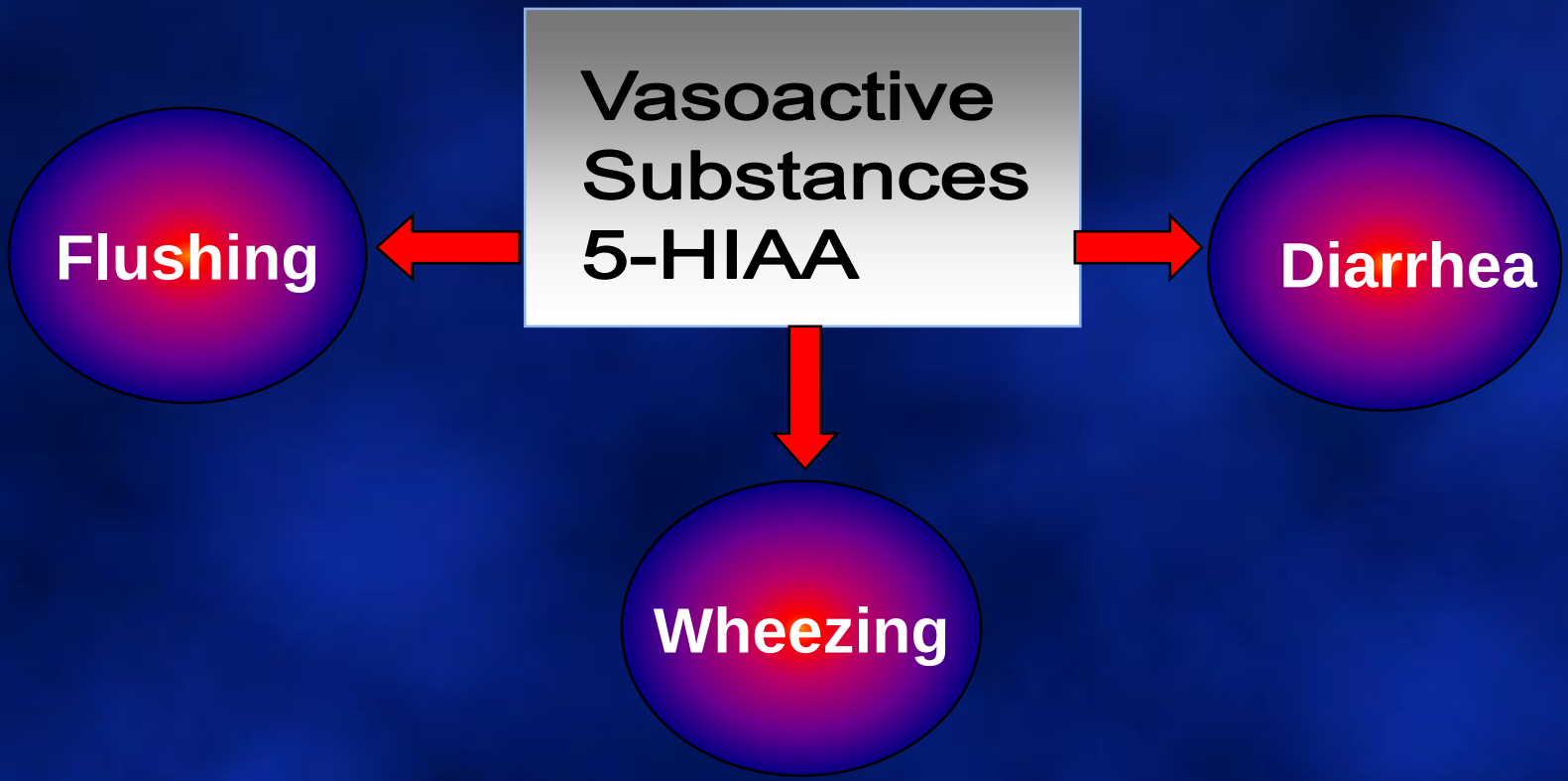
Courtesy of Denisa Muraru, MD, PhD
Padua, Italy

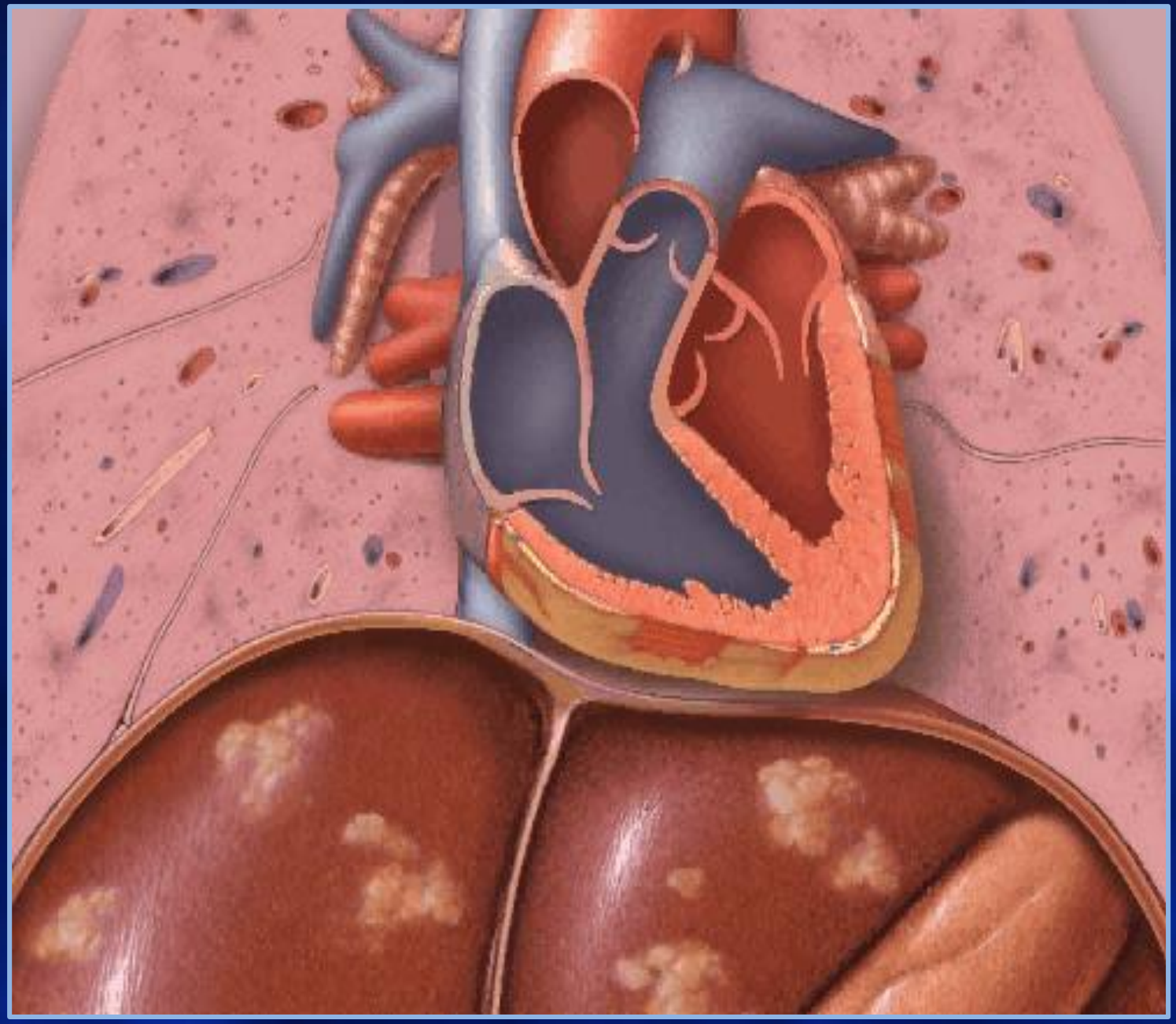
Eur Heart J Cardiovasc Imaging 2012

Carcinoid Heart Disease

Over 50% of patients with Carcinoid

Syndrome develop cardiac involvement





Courtesy of Dr. Heidi Connolly

JACC Vol. 25, No. 2
February 1995:410–6

Outcome of Cardiac Surgery for Carcinoid Heart Disease

HEIDI M. CONNOLLY, MD, FACC, RICK A. NISHIMURA, MD, FACC, HUGH C. SMITH, MD, FACC, PATRICIA A. PELLIKKA, MD, FACC, CHARLES J. MULLANY, MD, LARRY K. KVOLS, MD

Rochester, Minnesota

Objectives. The hypothesis was that cardiac surgery for symptomatic carcinoid heart disease in conjunction with adjunctive therapy could improve the long-term outlook of patients with carcinoid heart disease.

Background. Patients with carcinoid heart disease have a dismal prognosis; most die of progressive right heart failure within 1 year after onset of symptoms. Improved therapies for the systemic manifestations of the carcinoid syndrome have resulted in symptomatic improvement and prolonged survival in patients without heart disease.

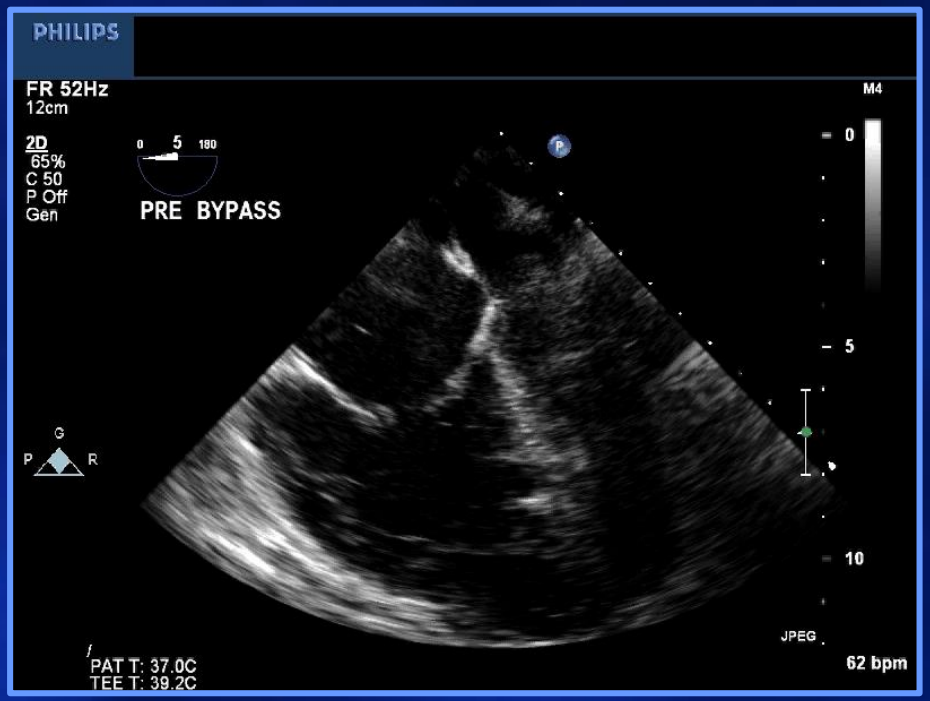
Methods. Twenty-six patients with symptomatic carcinoid heart disease underwent valvular surgery. Preoperative clinical, laboratory, Doppler echocardiographic and hemodynamic factors were evaluated. The survival of the surgical group was compared with that of a control group of 40 medically treated patients.

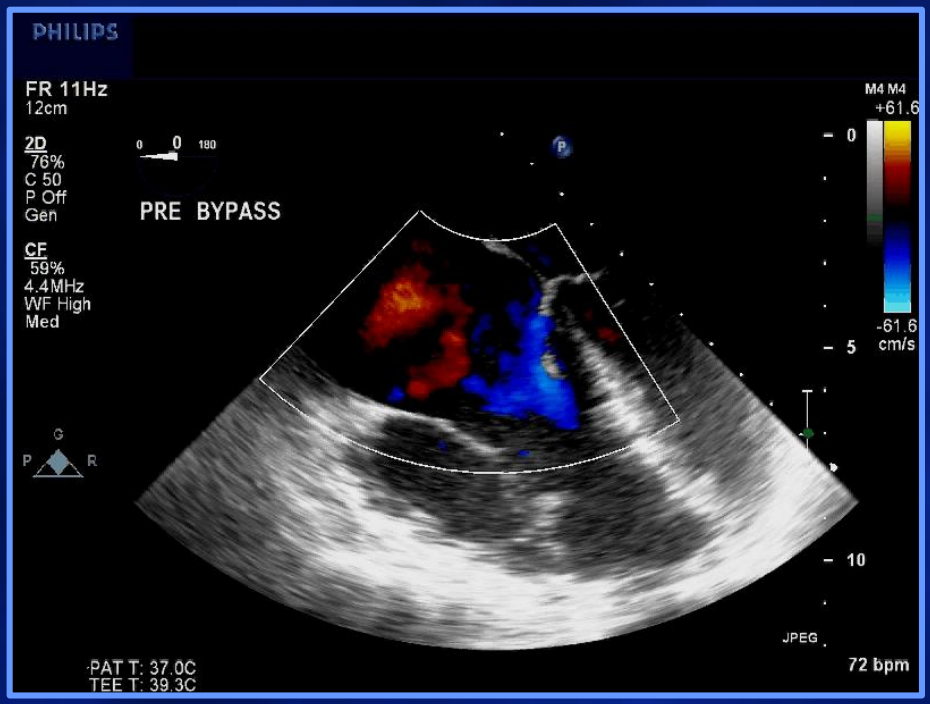
Results. There were nine perioperative deaths (35%), primarily from postoperative bleeding and right ventricular failure. Of the 17 surgical survivors, 8 were alive at a mean of 28 months of follow-up. The postoperative functional class of the eight surviving patients was substantially improved. Late deaths were primarily due to hepatic dysfunction caused by metastatic disease. The only predictor of operative mortality ($p = 0.03$) was low voltage on preoperative electrocardiography (limb lead voltage ≤5 mm). Predictors of late survival included a lower preoperative somatostatin requirement and a lower preoperative urinary 5-hydroxyindoleacetic acid level. There was a trend toward increased survival for the surgical group compared with the control group.

Conclusions. Because new therapies have improved survival in patients with the malignant carcinoid syndrome, cardiac involvement has become a major cause of morbidity and mortality. Valve surgery is the only definitive treatment. Although cardiac surgery carries a high perioperative mortality, marked symptomatic improvement occurs in survivors. Surgical intervention should therefore be considered when cardiac symptoms become severe.

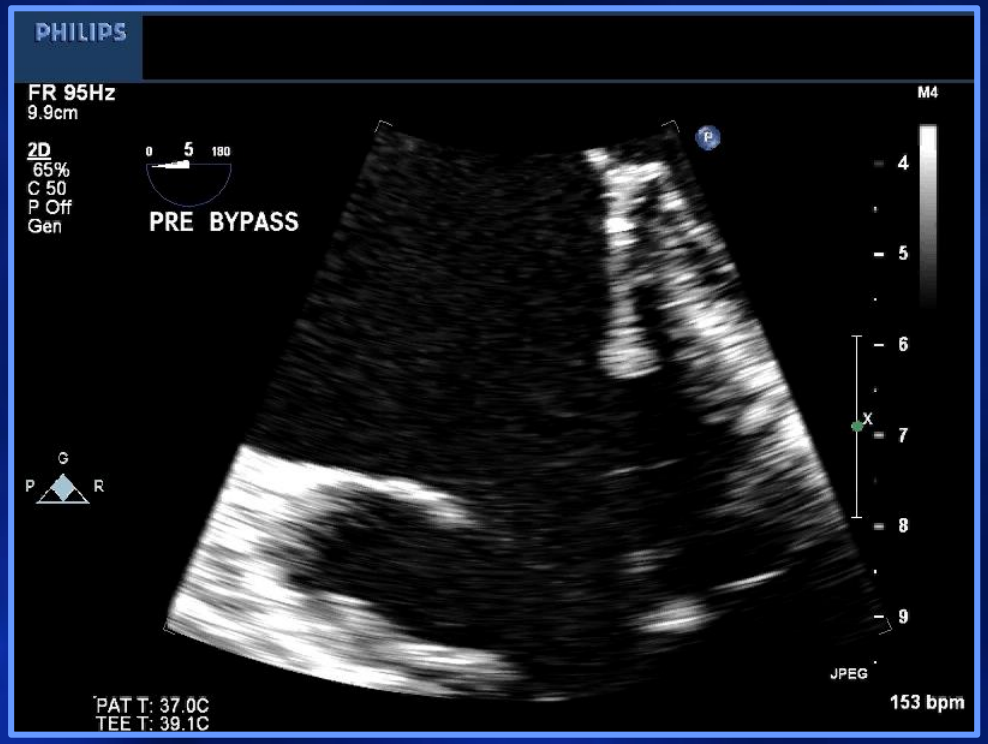
(J Am Coll Cardiol 1995;25:410–6)

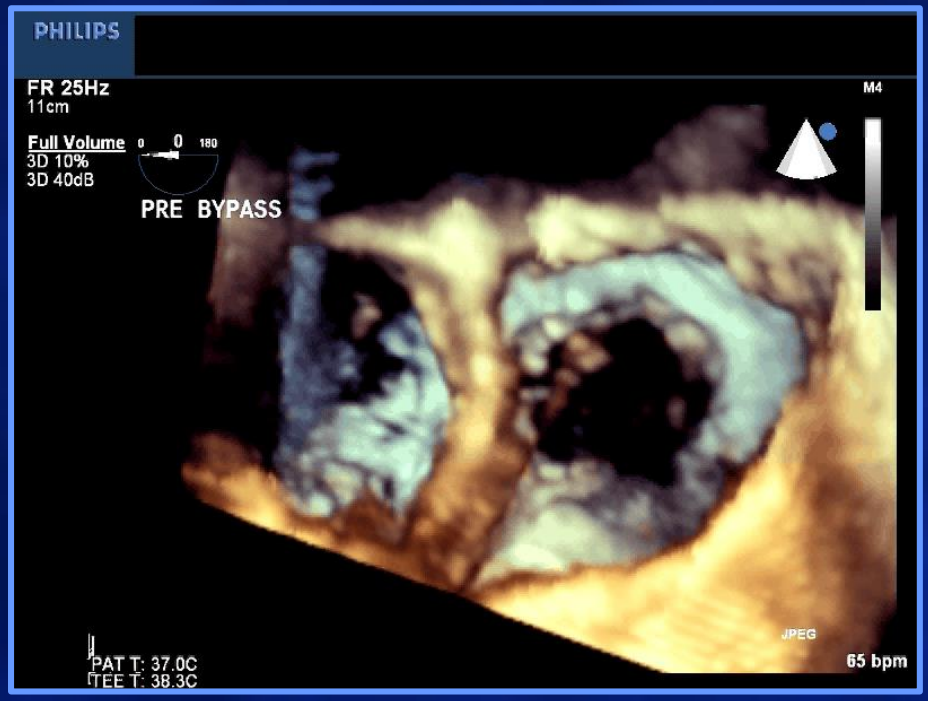
TEE
(4 chamber View)



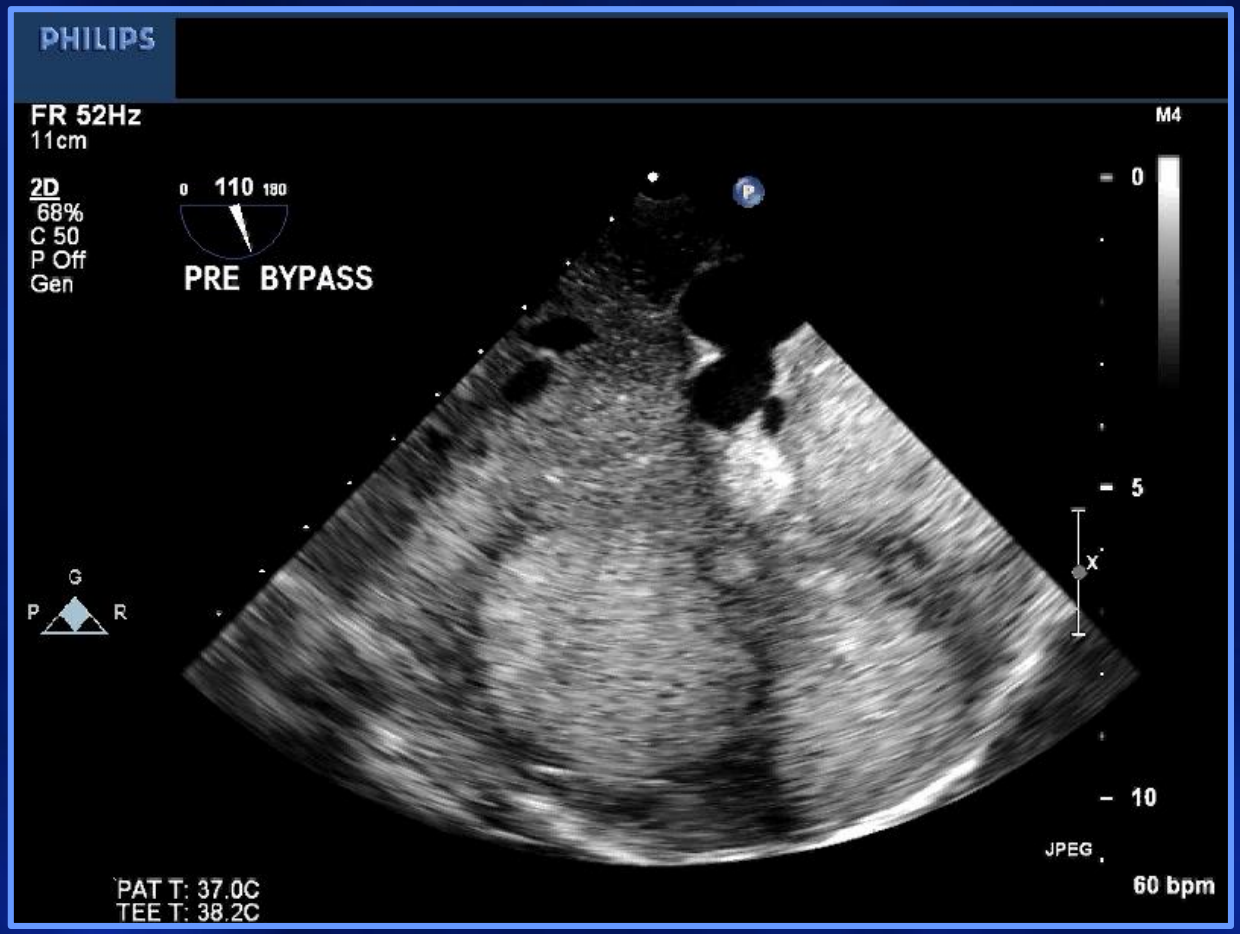


Carcinoid Heart Disease

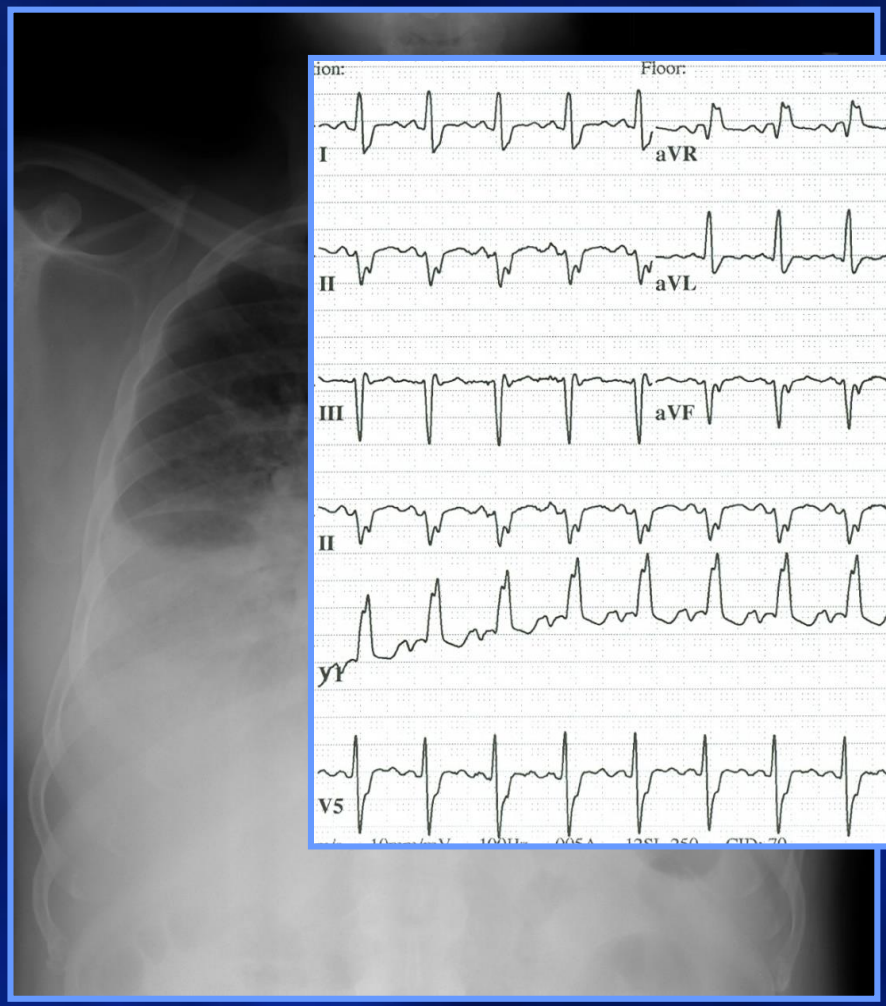


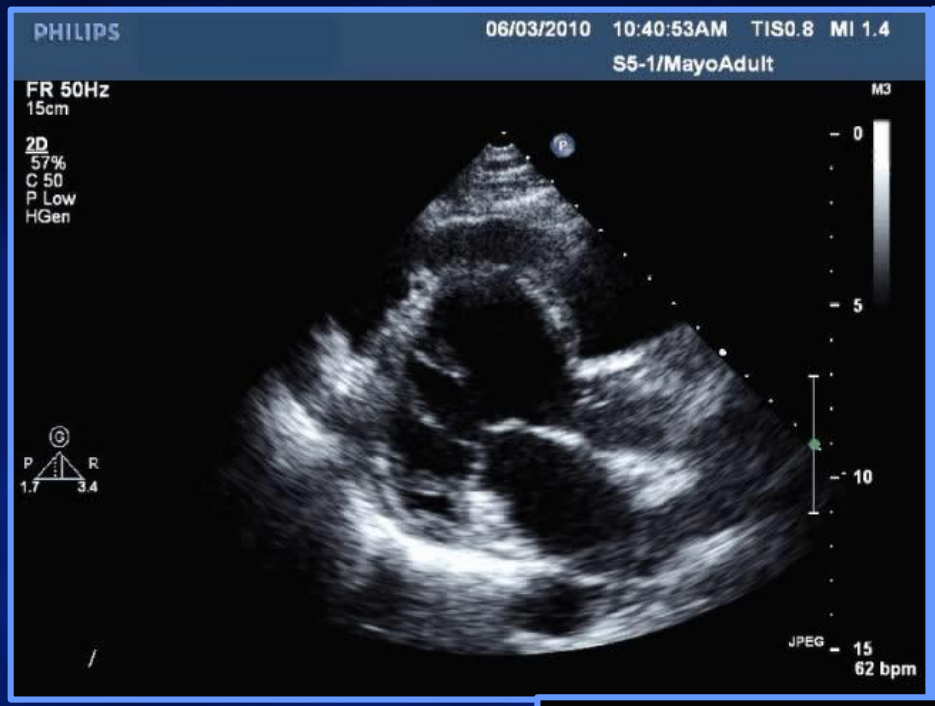


Carcinoid Tumor: : Liver Metastases



58 yo man with pulmonary infiltrates and syncope

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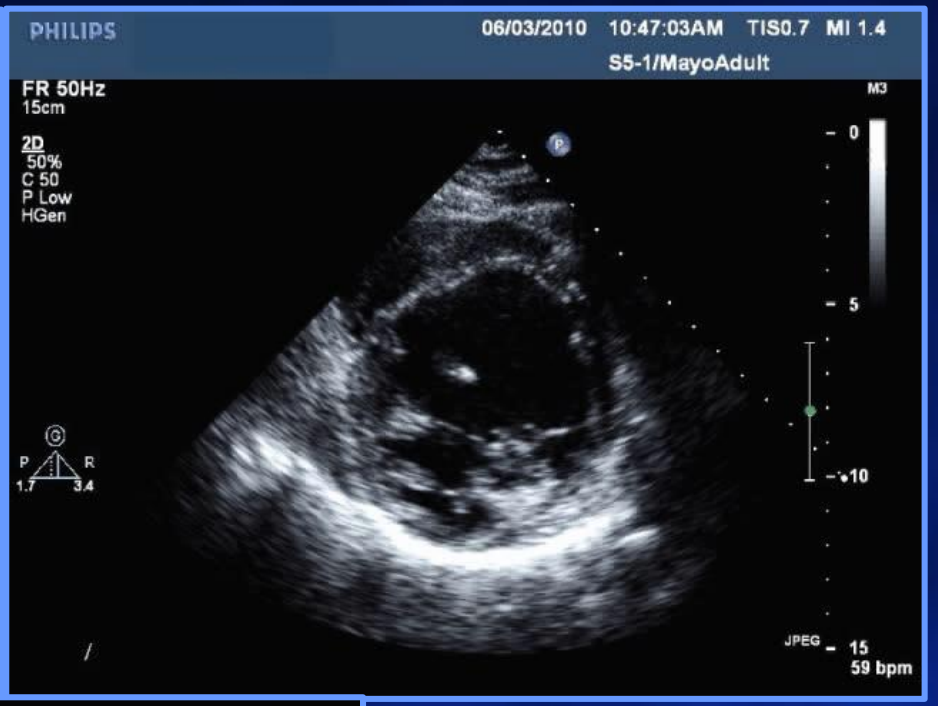
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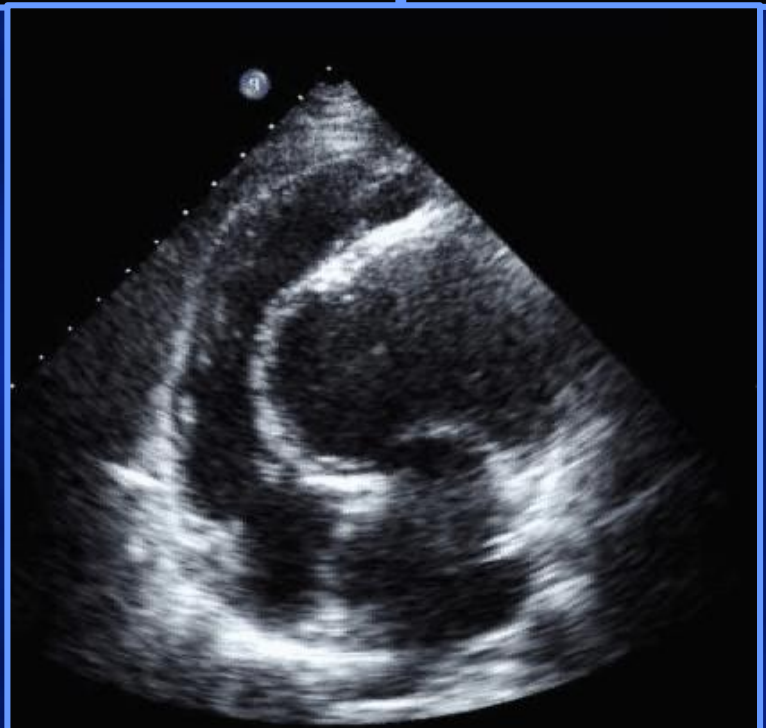
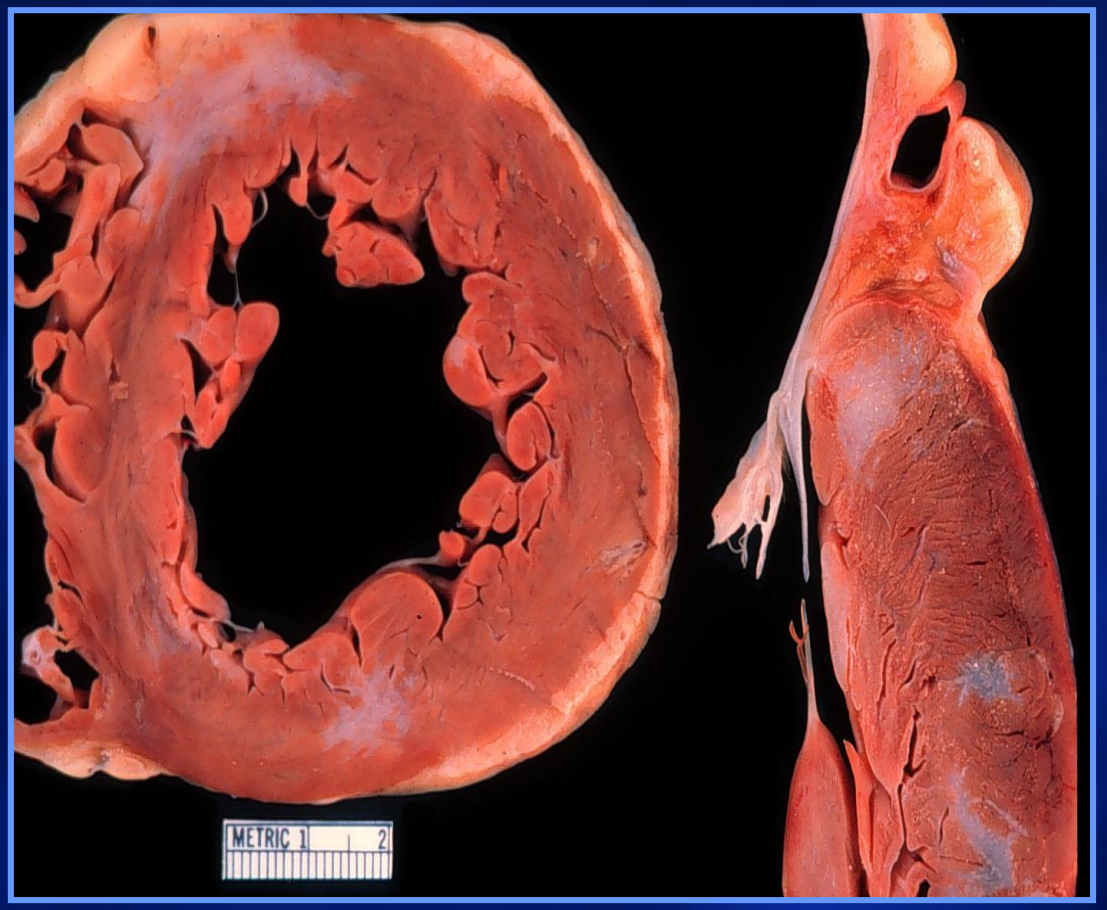


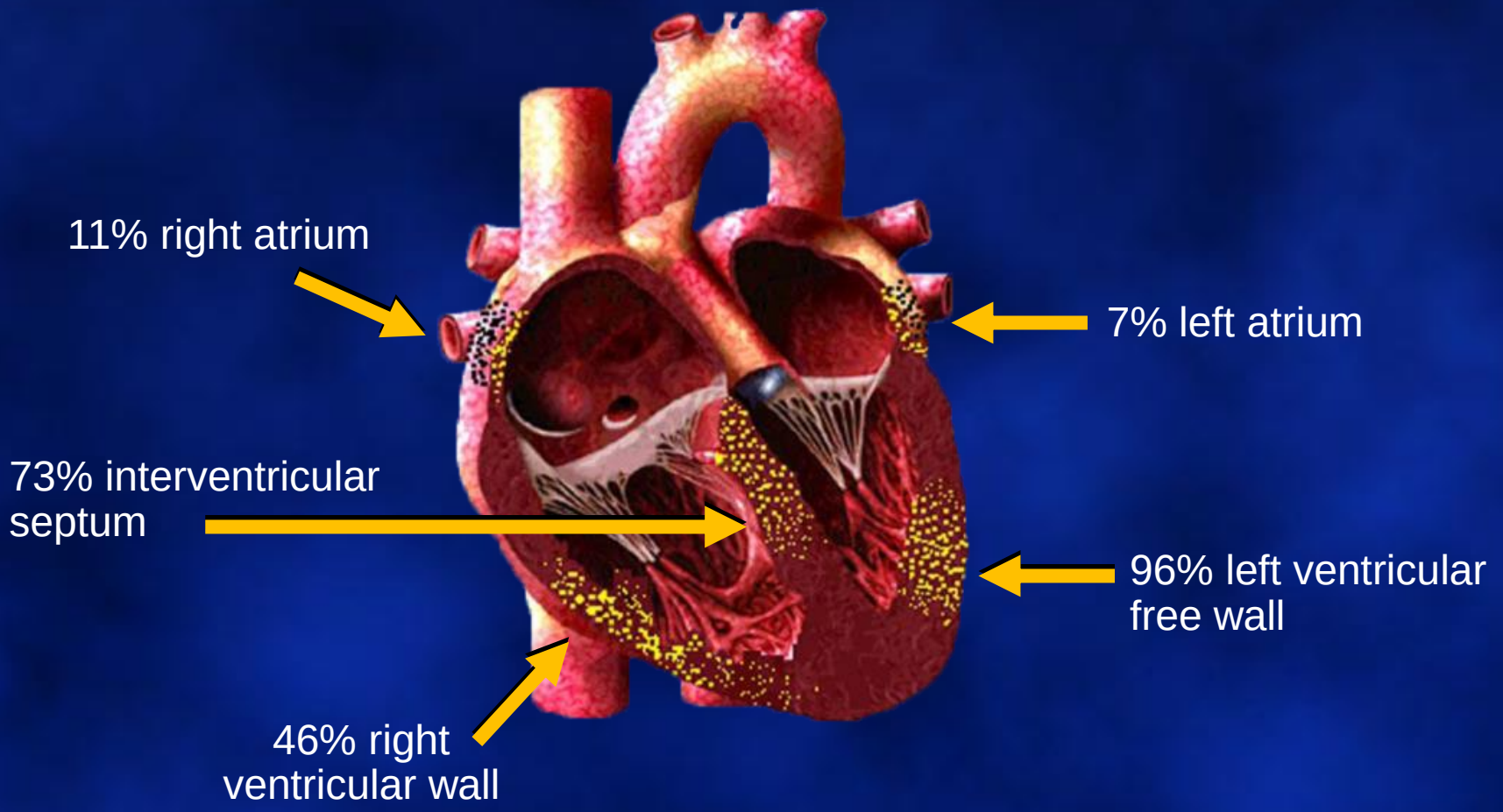
Cardiac Sarcoidosis

- Noncaseating granuloma
- Regional wall motion abnormalities in unusual distribution
- Heart block
- Sudden death



Courtesy William Edwards, MD

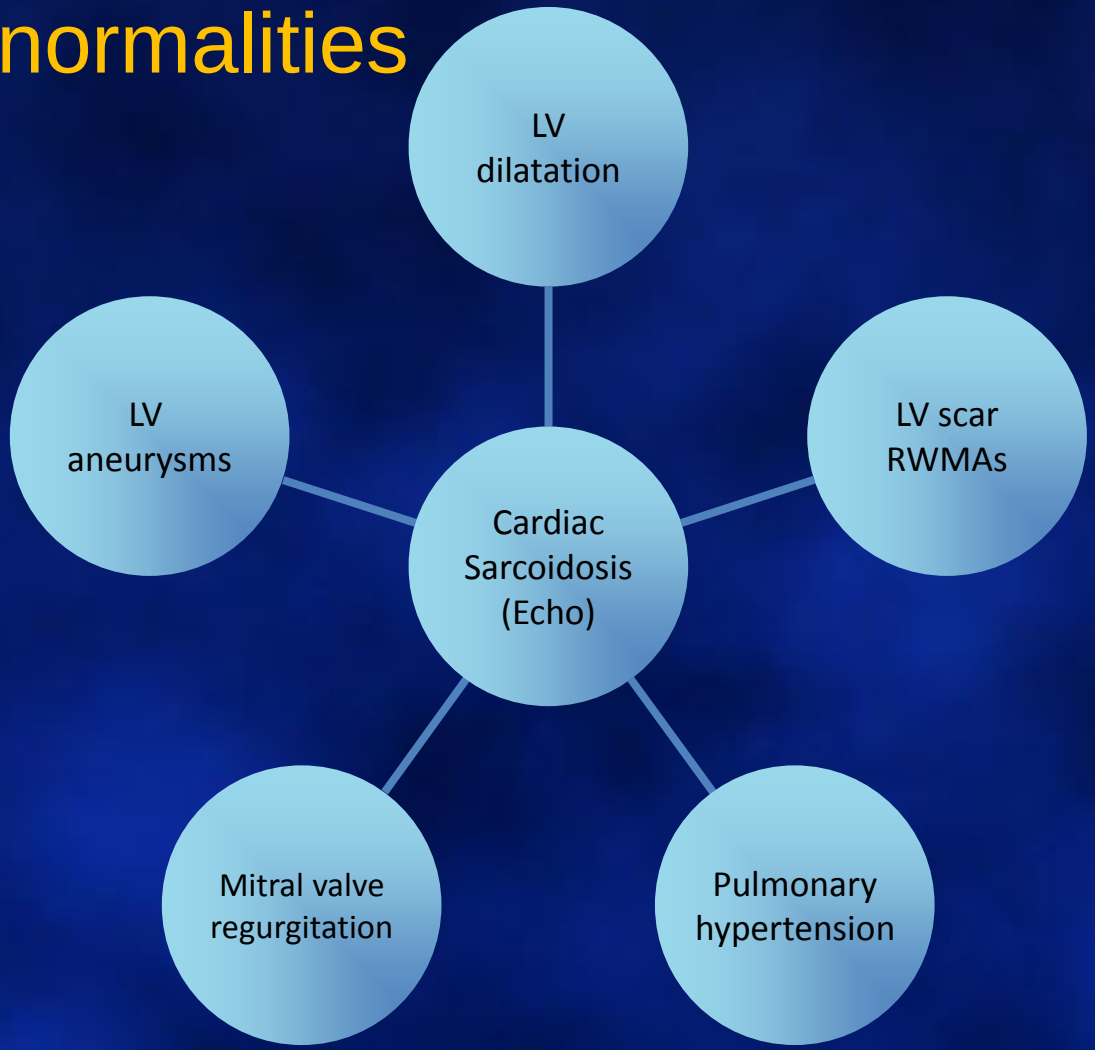
Sarcoidosis – Granulomas



Bargout R: Int J Cardio, 2004

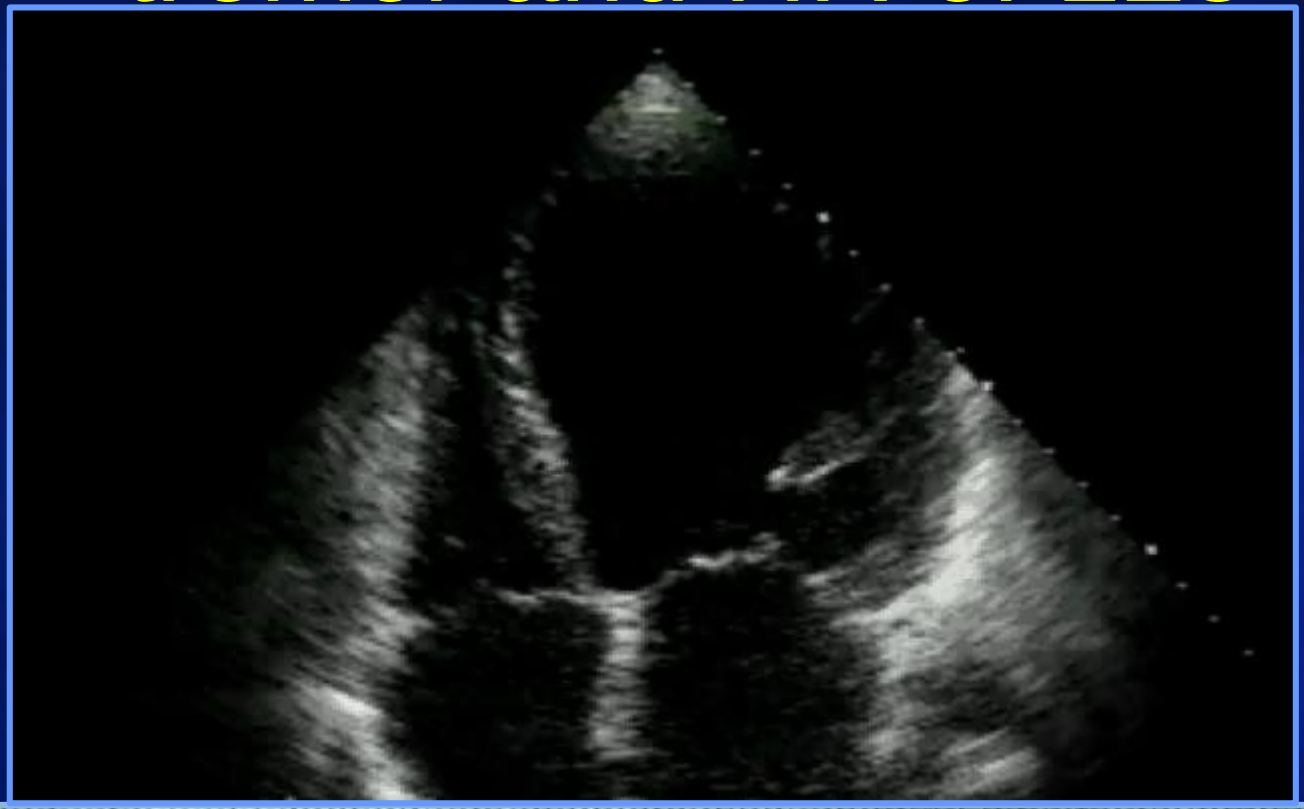
Sarcoidosis – Echo features

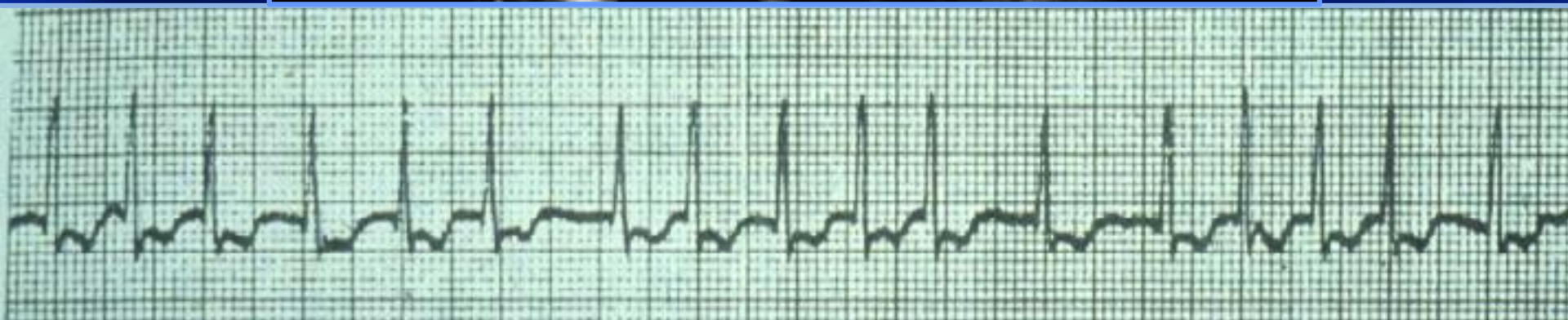
Echo abnormalities are rare



Sekhri V et al. Arch Med Sci 2011

58 yo woman with weight loss, tremor and HR of 125





Hyperthyroidism

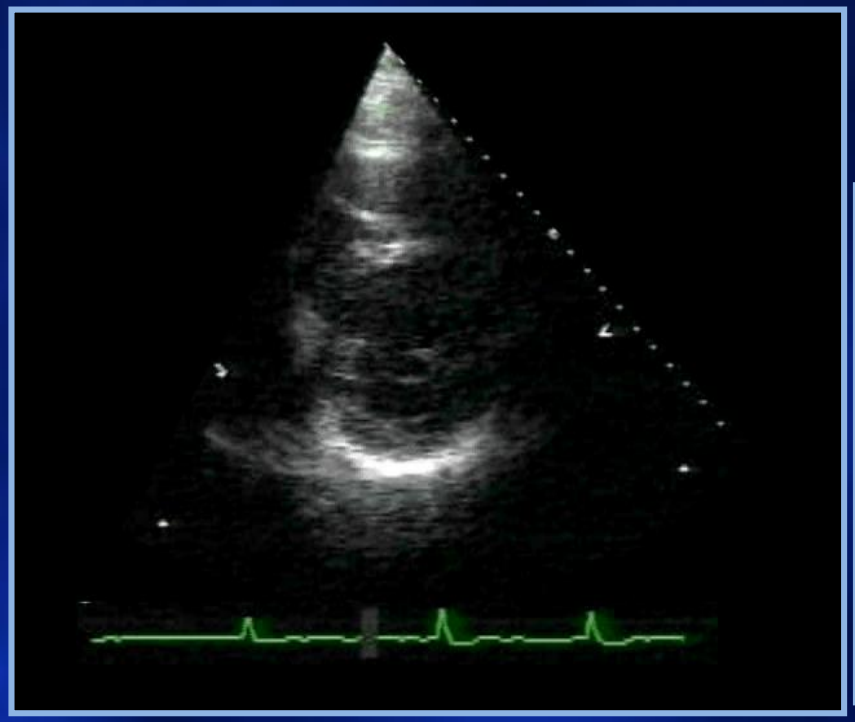
- Atrial fibrillation
  - ↑ **risk of systemic embolism**
  - **cardioversion *after* euthyroid**
- Decreased Peripheral resistance
  - **hypotension**
- Exacerbation of underlying CAD
  - **increased myocardial O2 demand**
- Tachycardia induced cardiomyopathy

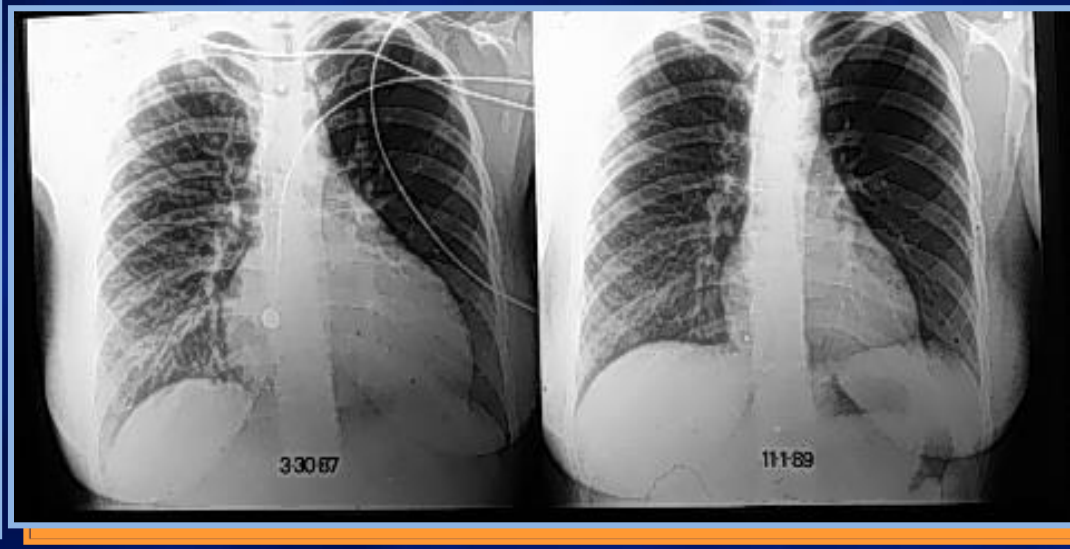
Tachycardia Mediated Cardiomyopathy

- 25% of patients w/ LV dysfunction & AF will have improved EF with rate control
- Usually *unaware* of rhythm
- Resting heart rate - poor indicator of overall rate control
- Consider in all pts with AF & LV dysfunction

Grogan M et al. AJC, 1992.

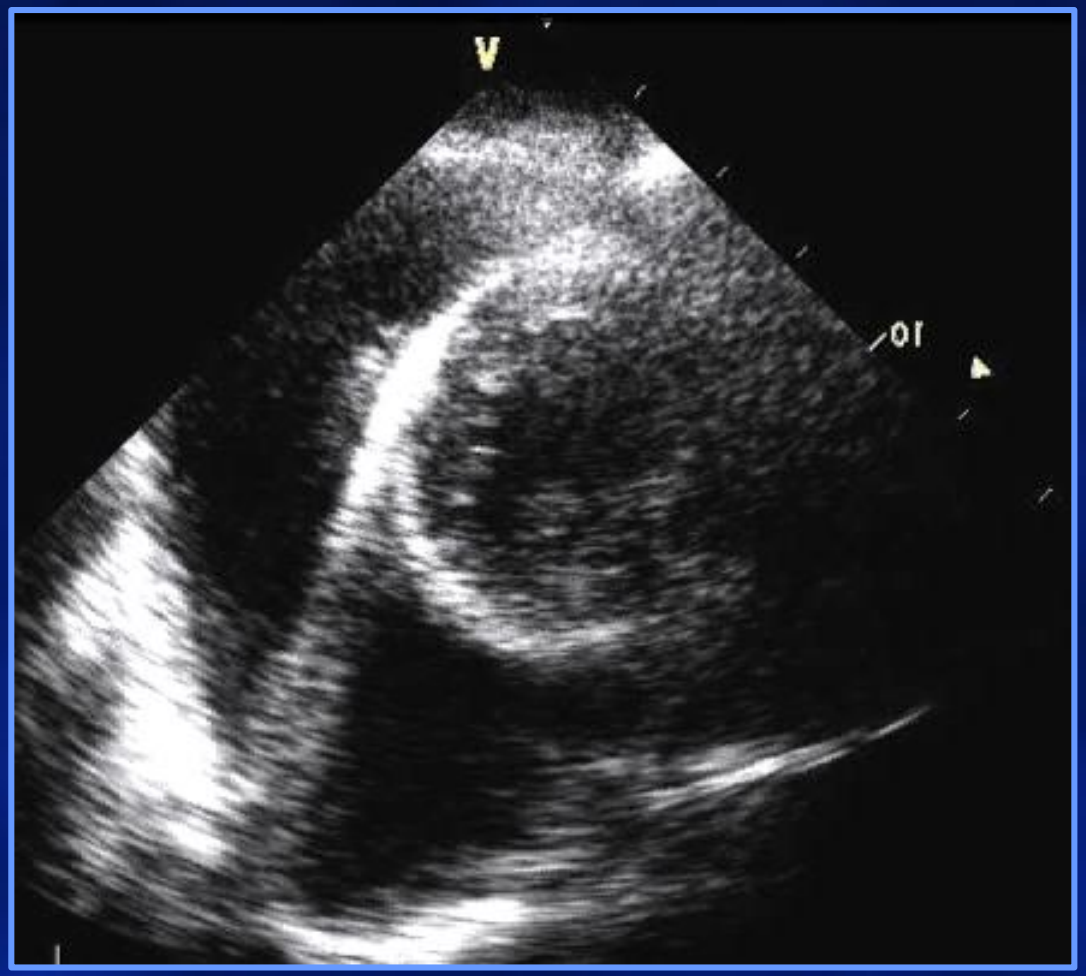
2 Years after Cardioversion and Treatment of Hyperthyroidsin



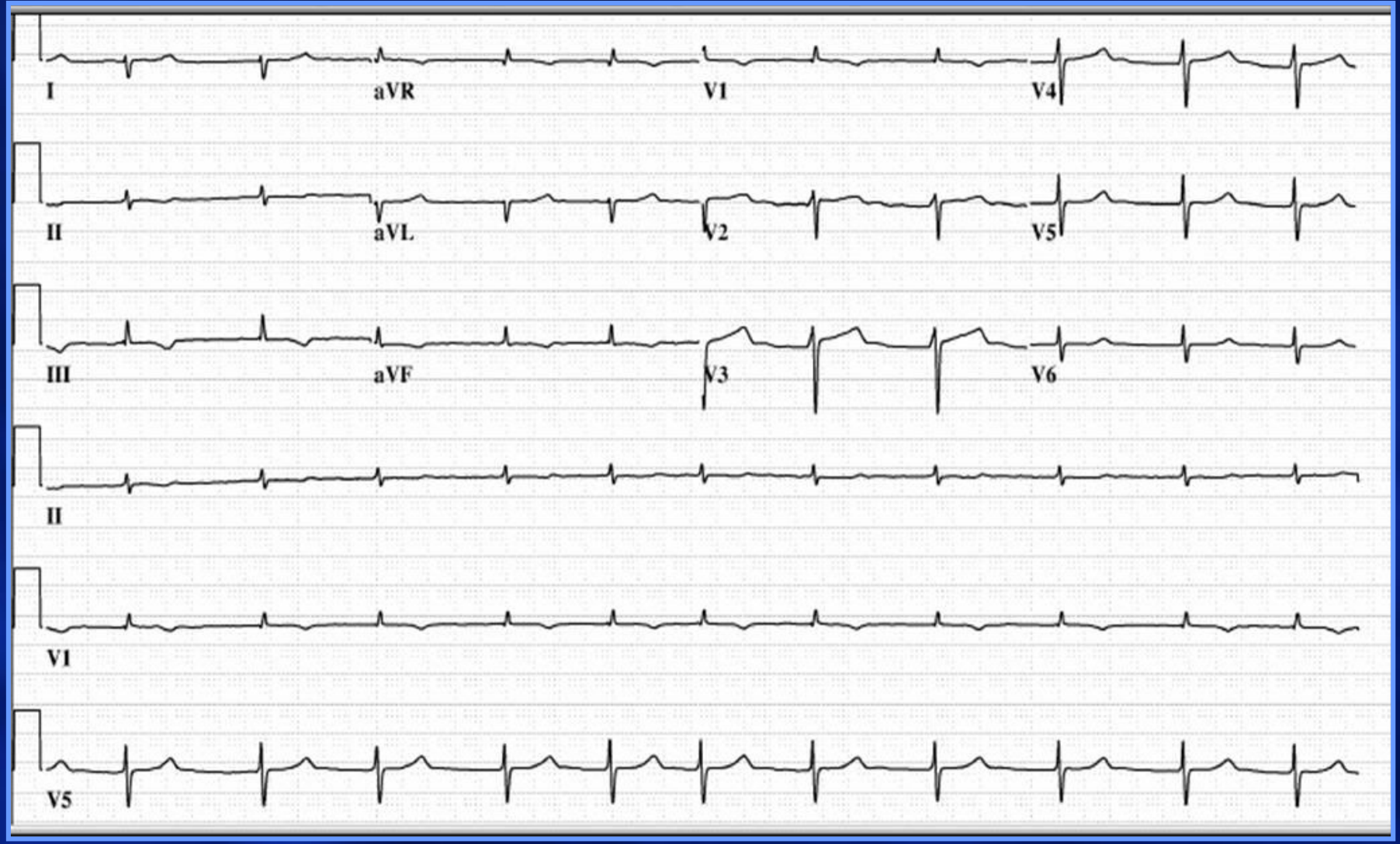


Hypothyroidism:

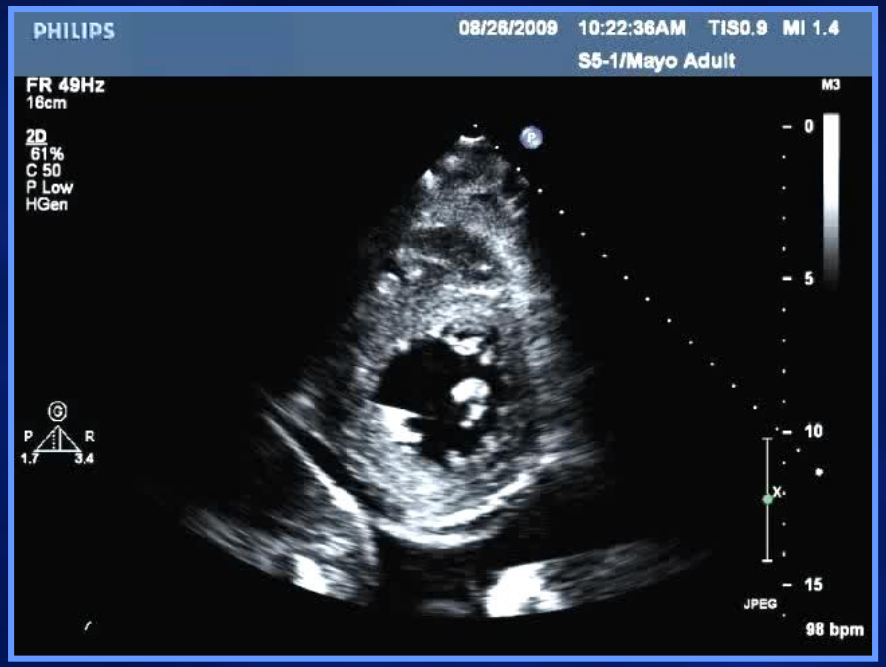
Large Pericardial Effusion

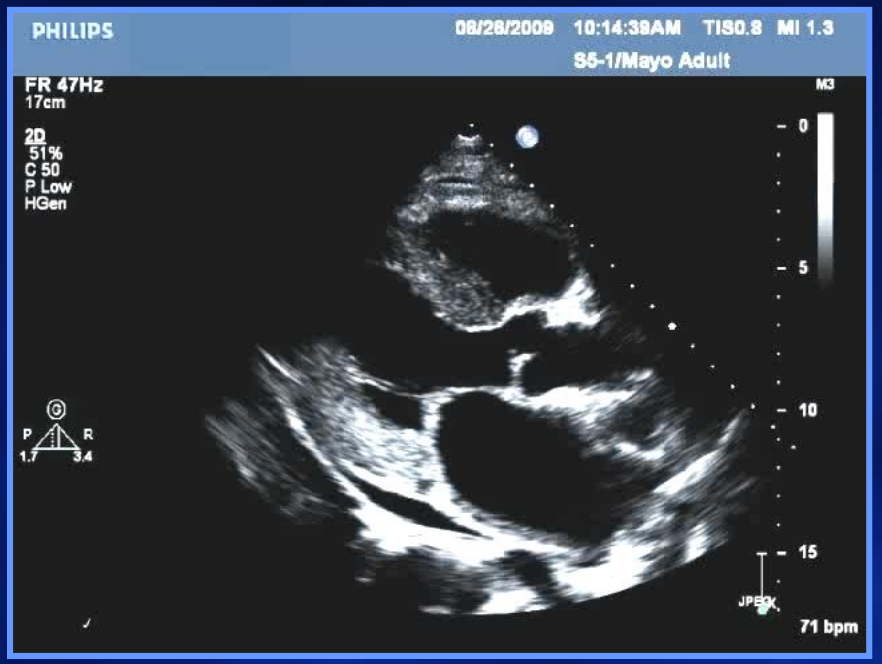


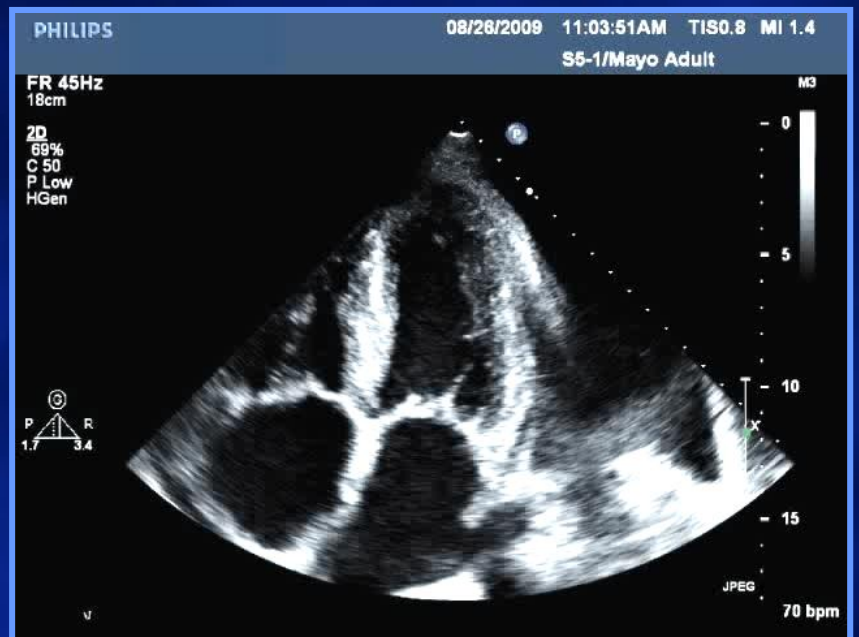
43 year old man

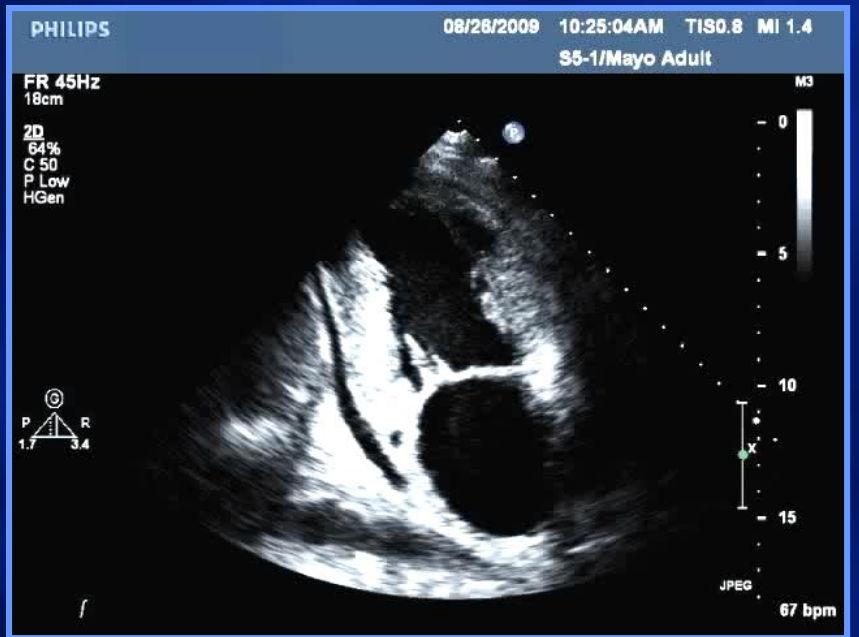


43 year old man with amyloidosis



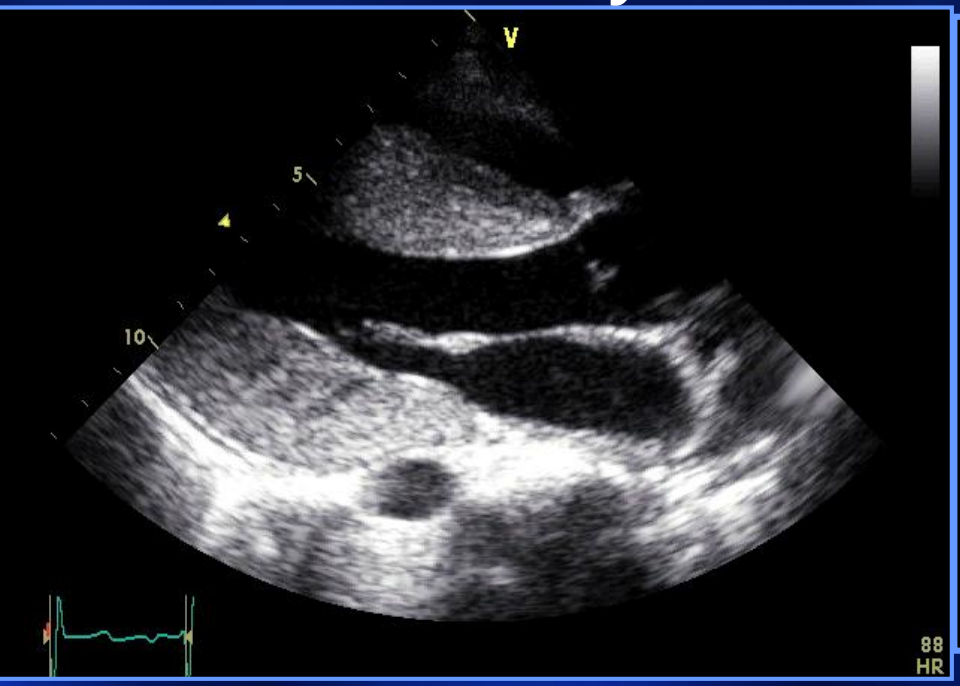


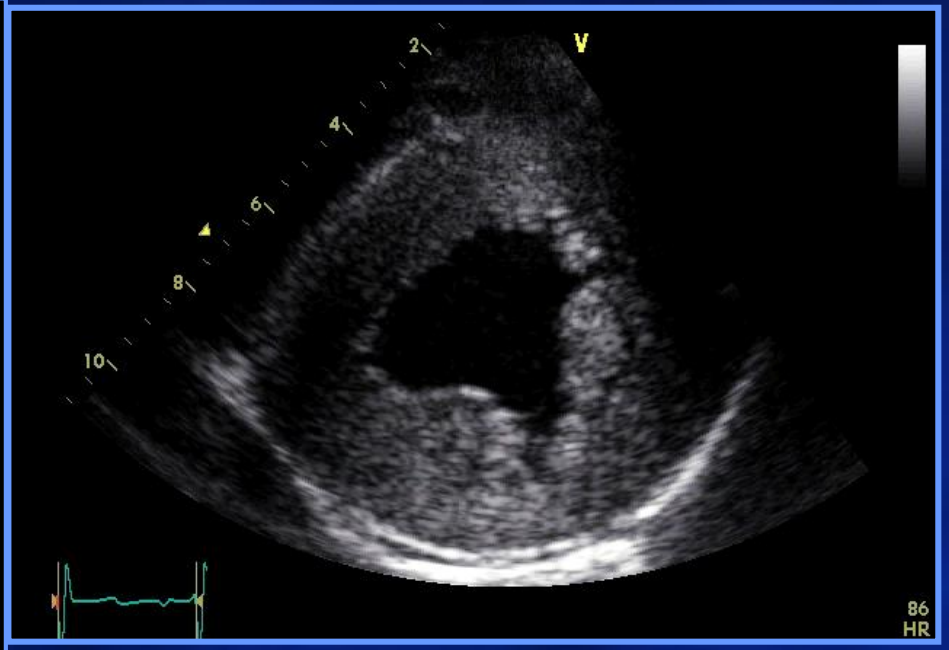




What is the most likely Diagnosis?

- 19 year old male with an abnormal gait, cerebellar dysarthria, areflexia





1. HIV myocarditis
2. Friedrich's Ataxia
3. Hypertrophic obstructive CM
4. Arrhythmogenic right ventricular cardiomyopathy
5. Cardiac amyloidosis

Friedrich's Ataxia

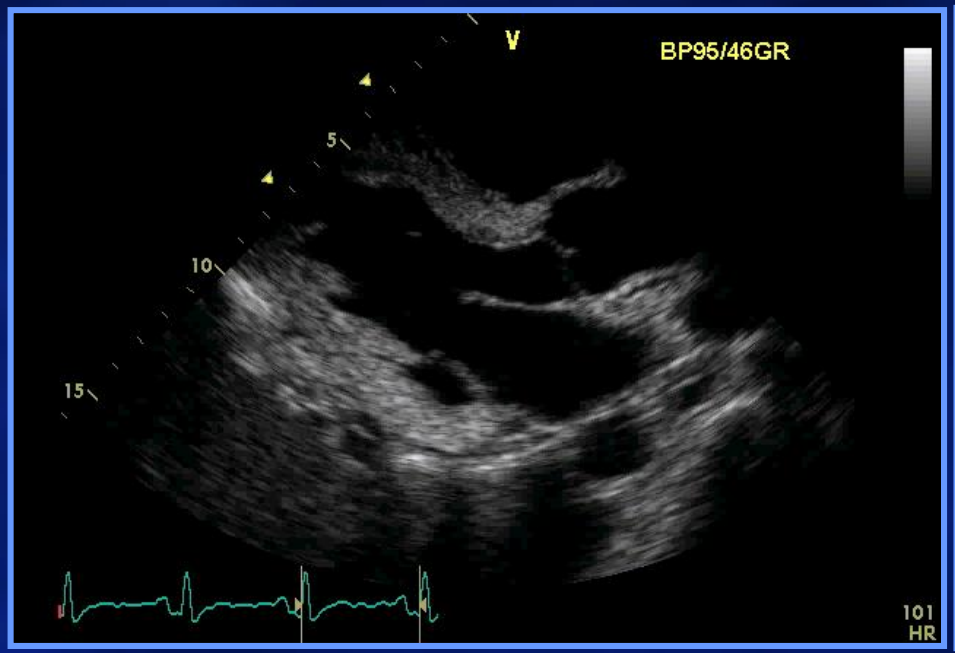
- Rare AR neurodegenerative disorder
  - 1:50,000
- Ataxia, cerebellar dysarthria, areflexia
- Onset < 20 years, relentless course
- Echo features
  - Symmetrical hypertrophied LV
  - Prominent papillary muscles
  - Absence of SAM

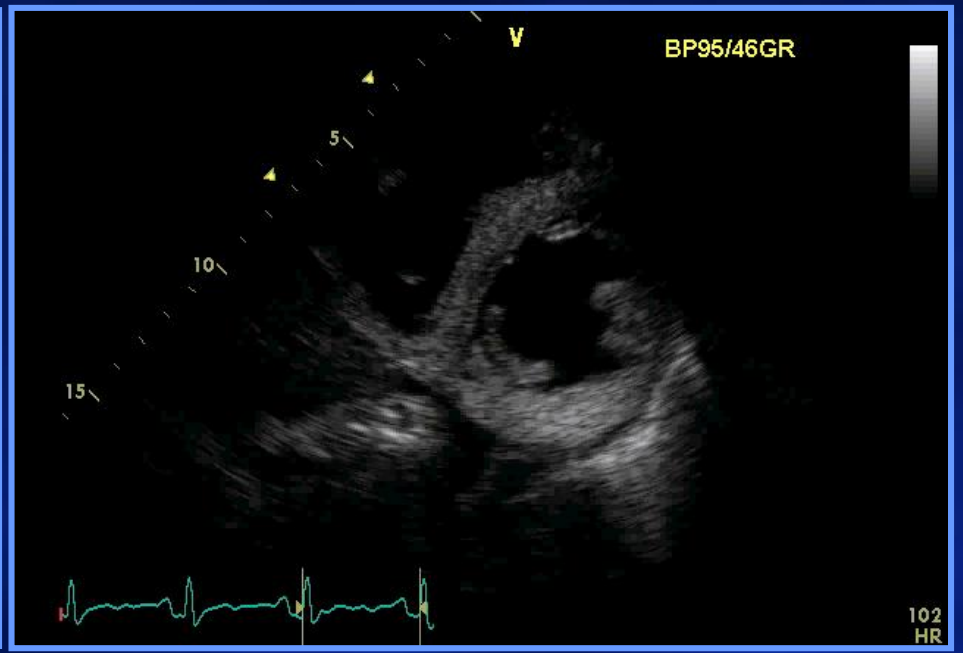
Durr A: NEJM 1996

Mimickers of Amyloid

- Friedrich's Ataxia
- Primary Hyperoxaluria
- Fabry's Disease
- Hypertrophic cardiomyopathy
- Hydroxychloroquine-induced Cardiotoxicity
- Renal Failure

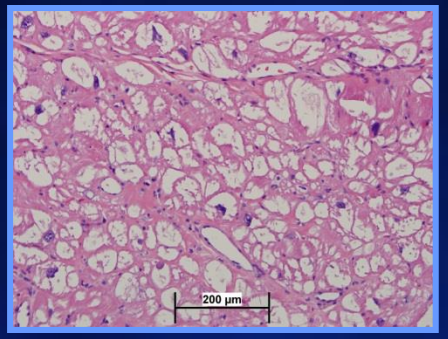
Primary Hyperoxaluria



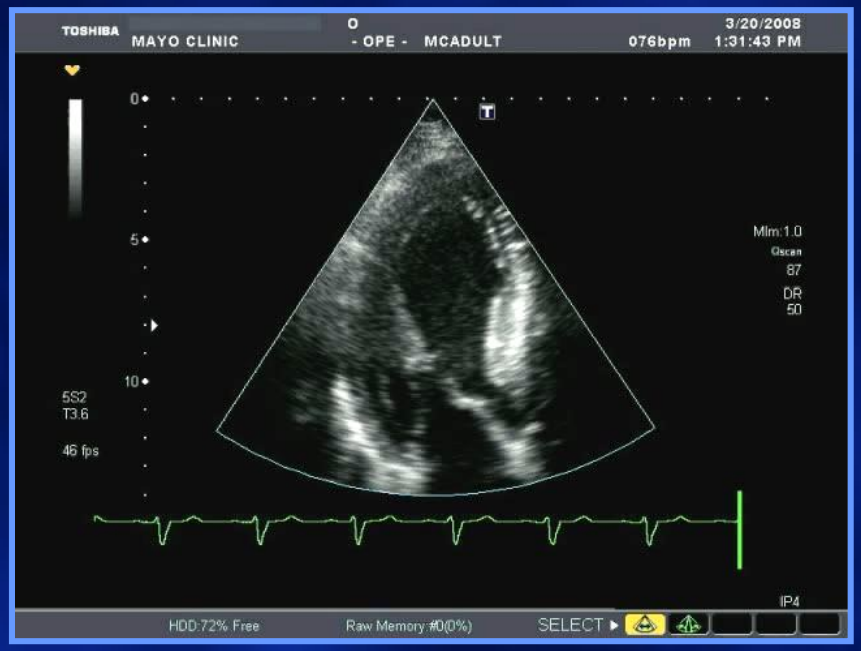


- Rare metabolic disorder with autosomal recessive inheritance
- PHO type 1 (0.11 - 0.26 per 100,000 live births)
- Enzymatic defect resulting in enhanced conversion of glyoxalate to poorly soluble oxalate which is excreted in the urine

Fabry's Disease



- Inherited X-linked recessive
- Lysosomal storage disease
- α-galactosidase A (α-Gal A) enzyme deficiency
- Intralysosomal accumalation of the glycosphingolipid globotriaosylceramide (GL-3)
- "Binary" appearance of walls on echo



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ISSN 0735-1097/06/$32.00
doi:10.1016/j.jacc.2005.11.070

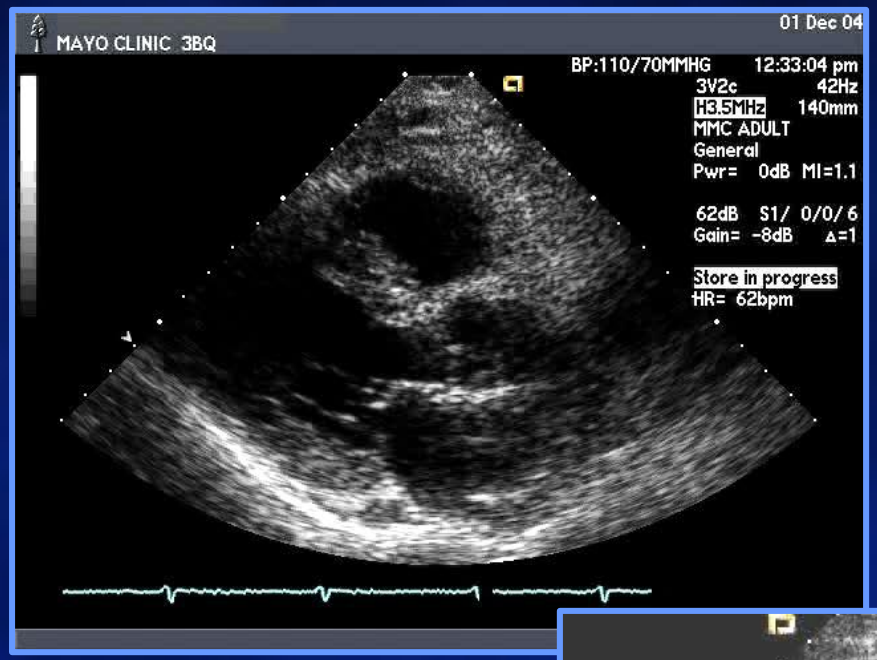
Fabry's Disease Cardiomyopathy

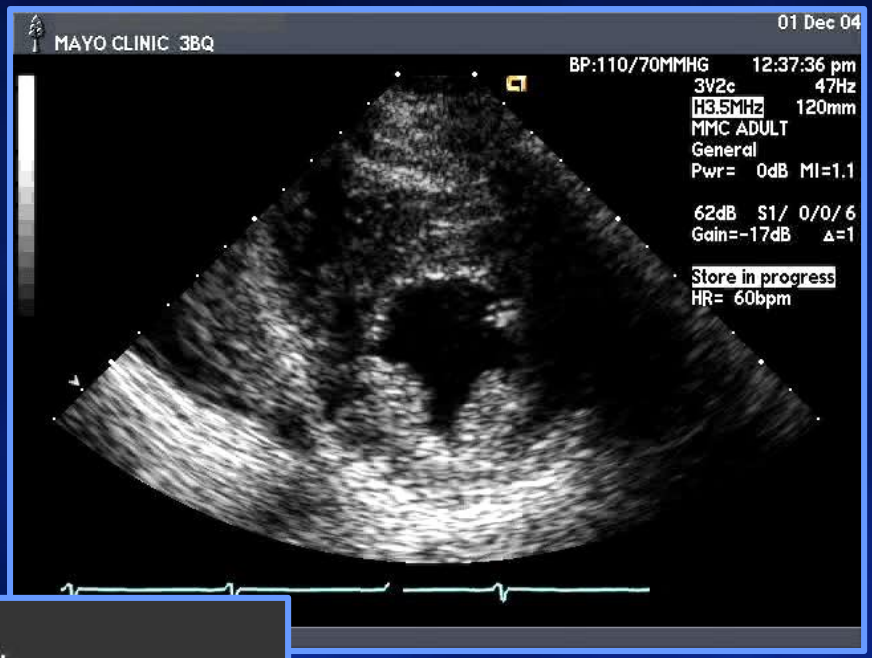
Echocardiographic Detection of

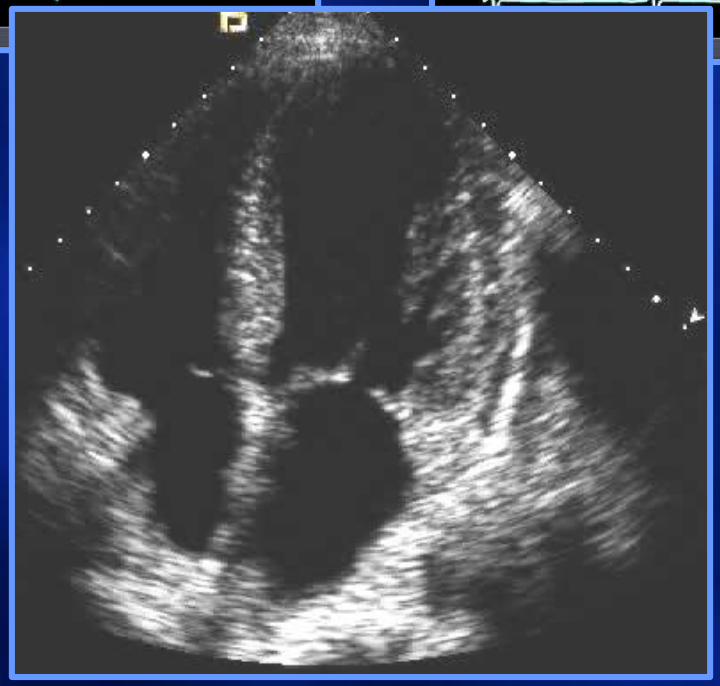
Echocardiography showed in 83% of FC patients (95% of FC patients with LVH) a binary appearance of endocardial border absent in all HCM, hypertensive, and healthy subjects. The sensitivity and specificity of this echocardiographic feature in detecting Fabry patients in study population were 94% and 100%, respectively.

diagnostic hallmark of Fabry's disease cardiomyopathy. (J Am Coll Cardiol 2006;47: 1663–71)

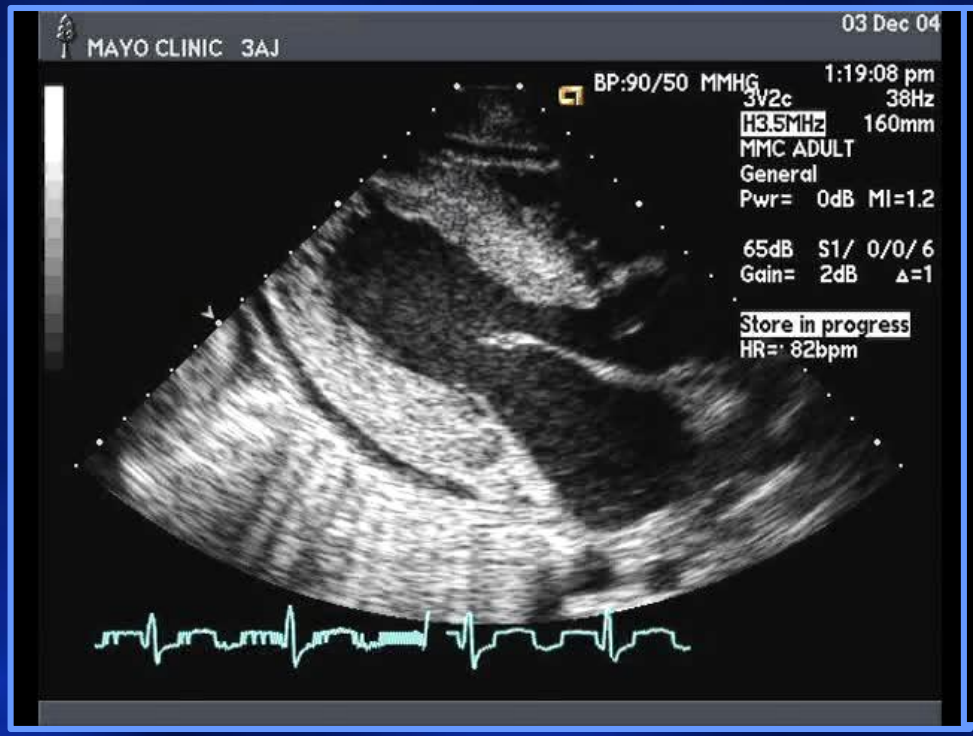
Hydroxychloroquine-induced Cardiotoxicity

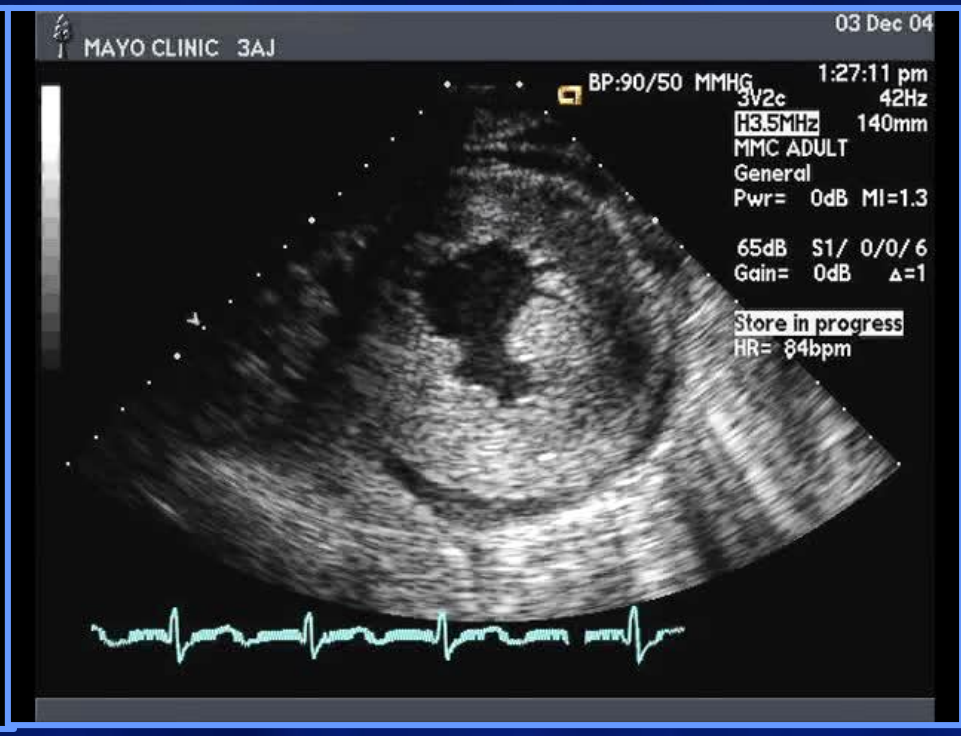






Renal Failure





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QUARTERLY FOCUS ISSUE: HEART FAILURE

State-of-the-Art Paper

Infiltrative Cardiovascular Diseases

Cardiomyopathies That Look Alike

James B. Seward, MD,* Grace Casaclang-Verzosa, MD†

Rochester, Minnesota

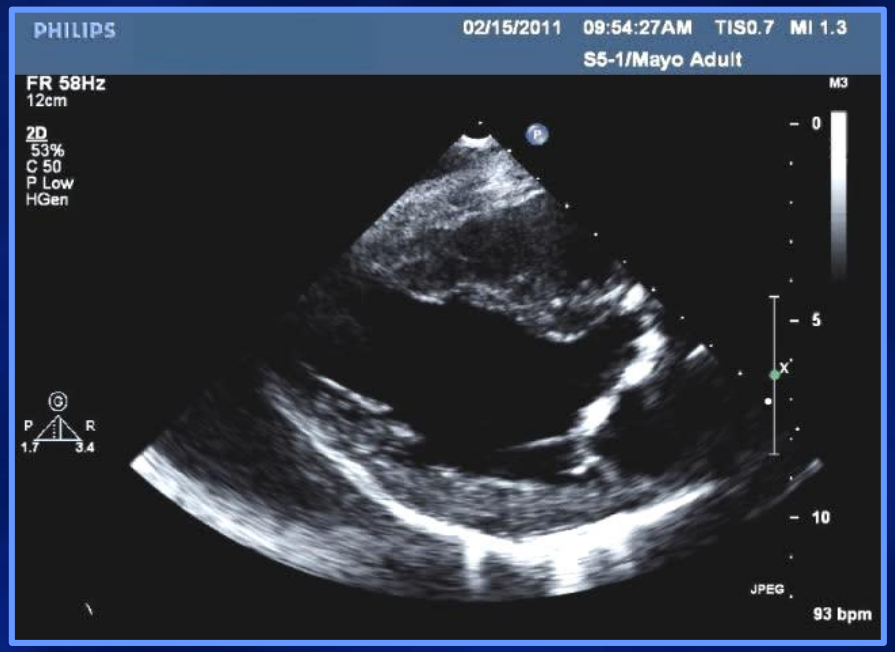
Infiltrative cardiomyopathies are characterized by the deposition of abnormal substances that cause the ventricular walls to become progressively rigid, thereby impeding ventricular filling. Some infiltrative cardiac diseases increase ventricular wall thickness, while others cause chamber enlargement with secondary wall thinning. Increased wall thickness, small ventricular volume, and occasional dynamic left ventricular outflow obstruction (e.g., amyloidosis) can outwardly appear similar to conditions with true myocyte hypertrophy (e.g., hypertrophic cardiomyopathy, hypertensive heart disease). Likewise, infiltrative disease that presents with a dilated left ventricle with global or regional wall motion abnormalities and aneurysm formation (e.g., sarcoidosis) may mimic ischemic cardiomyopathy. Low-voltage QRS complex was the sine qua non of infiltrative cardiomyopathy (i.e., cardiac amyloid). However, low-voltage QRS complex is not a uniform finding with the infiltrative cardiomyopathies. The clinical presentation, along with functional and morphologic features, often provides enough insight to establish a working diagnosis. In most circumstances, however, tissue or serologic evaluation is needed to validate or clarify the cardiac diagnosis and institute appropriate therapy. (J Am Coll Cardiol 2010;55:1769–79)

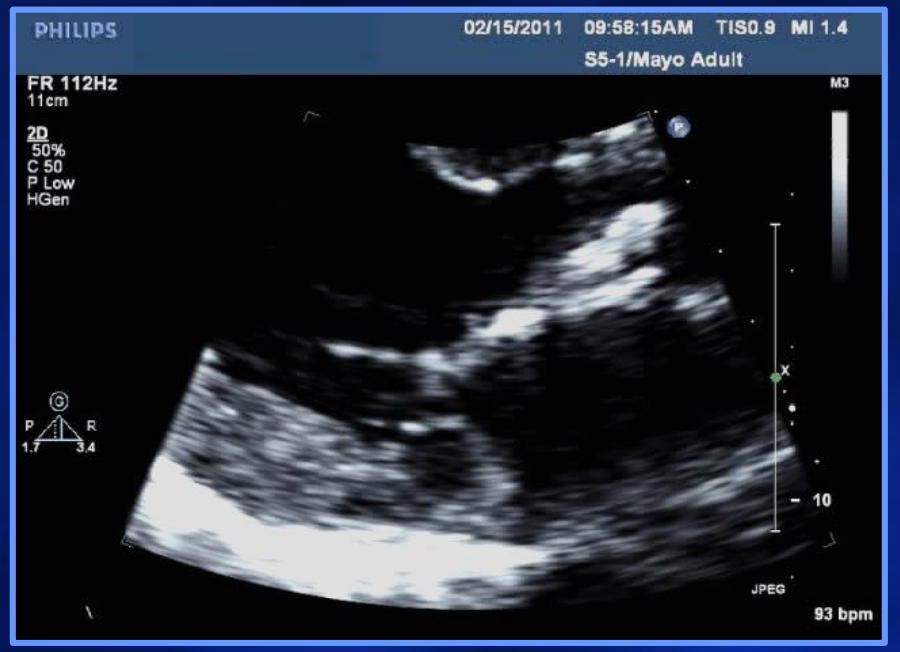
Infiltrative cardiomyopathies are characterized by the deposition of abnormal substances that cause the ventricular walls to become progressively rigid, thereby impeding ventricular filling. Some infiltrative cardiac diseases increase ventricular wall thickness (Table 1), while others cause chamber enlargement with secondary wall thinning (Table 2). The clinical presentation, along with functional and morphologic features, often provides enough insight to establish a working diagnosis. However, in most circumstances, tissue or

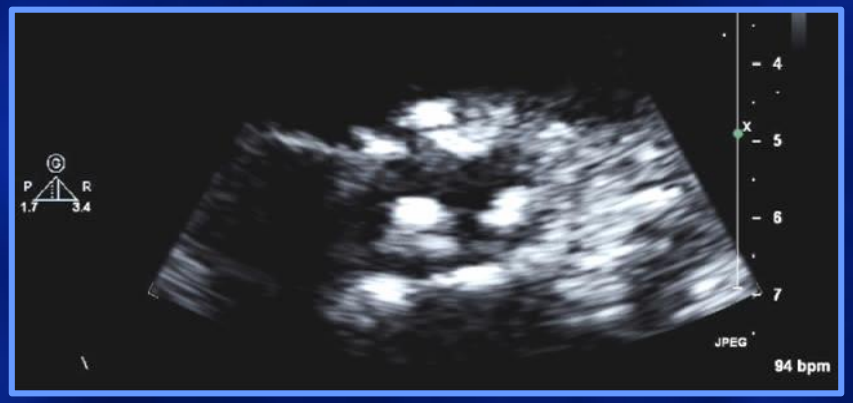
atrial remodeling, which are hallmarks of the restrictive disease process. The chronicity of diastolic dysfunction is best characterized by depressed Doppler myocardial relaxation velocity (mitral annular E tissue velocity) and increased left atrial volume index (1). Systolic dysfunction is commonly measured as a decrease in the ejection fraction or systolic tissue Doppler velocity (2).

The role of computed tomography and cardiac magnetic resonance (CMR) imaging and late gadolinium enhancement (LGE) in providing incremental information for risk

56 y/o Woman with a history of radiation therapy for Hodgkin's lymphoma at age 14







Courtesy of Dr. WK Freeman

Radiation Induced Cardiac Disease

- Pancarditis: pericardial, myocardial, endocardial/valvular (fibroelastosis)
- Acute pericarditis during therapy
- Delayed pericarditis: constriction, pericardial effusion
- Cardiomyopathy: diastolic/systolic dysfunction
- CAD: intimal proliferation, endothelial dysfunction
- Conduction system defects

Radiation Induced Cardiac Disease Risk Factors

- Total radiation dose
- Younger age during radiation therapy
- Higher percentage anteroposterior vs. tangential beam trajectory
- Anthracycline therapy: cardiomyopathy and valvular disease
- Smoking, hyperlipidemia, DM: CAD

Aleman BM, et al. Blood 2007; 109: 1878

Hooning MJ, et al. J Natl Cancer Inst 2007; 99: 365

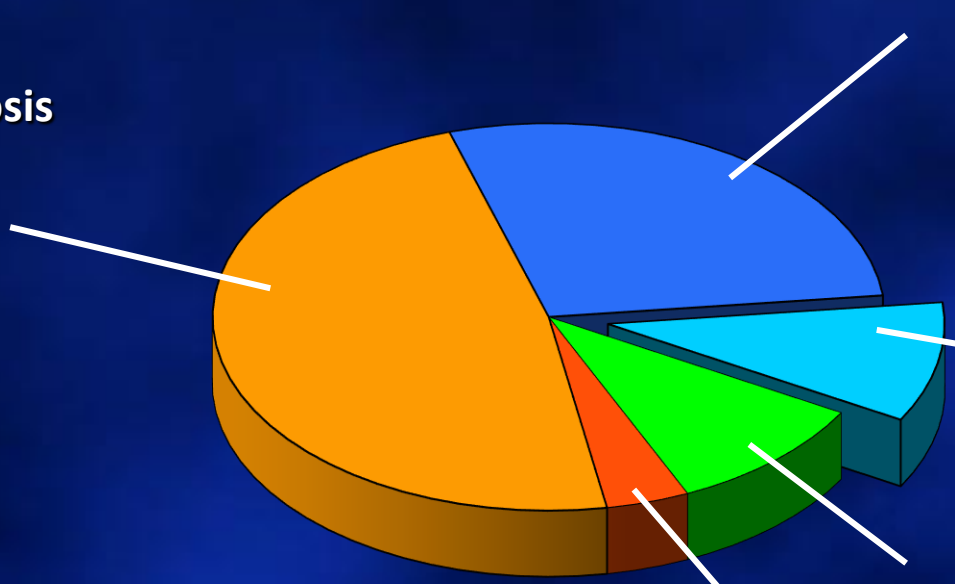
Radiation Therapy for Hodgkin's Lymphoma Cardiovascular Effects in 404 Patients

(Treated 1962-1998)

	Incidence	Median Time After Therapy
Coronary Artery Disease	10.4%	9 Yrs
Carotid ± Subclavian Disease	7.4%	17 Yrs
Significant Valvular Disease	6.2%	22 Yrs

Hull MC, et al. JAMA 2003; 290:2831

Radiation Therapy for Hodgkin's Lymphoma Clinically Significant Valvular Disease



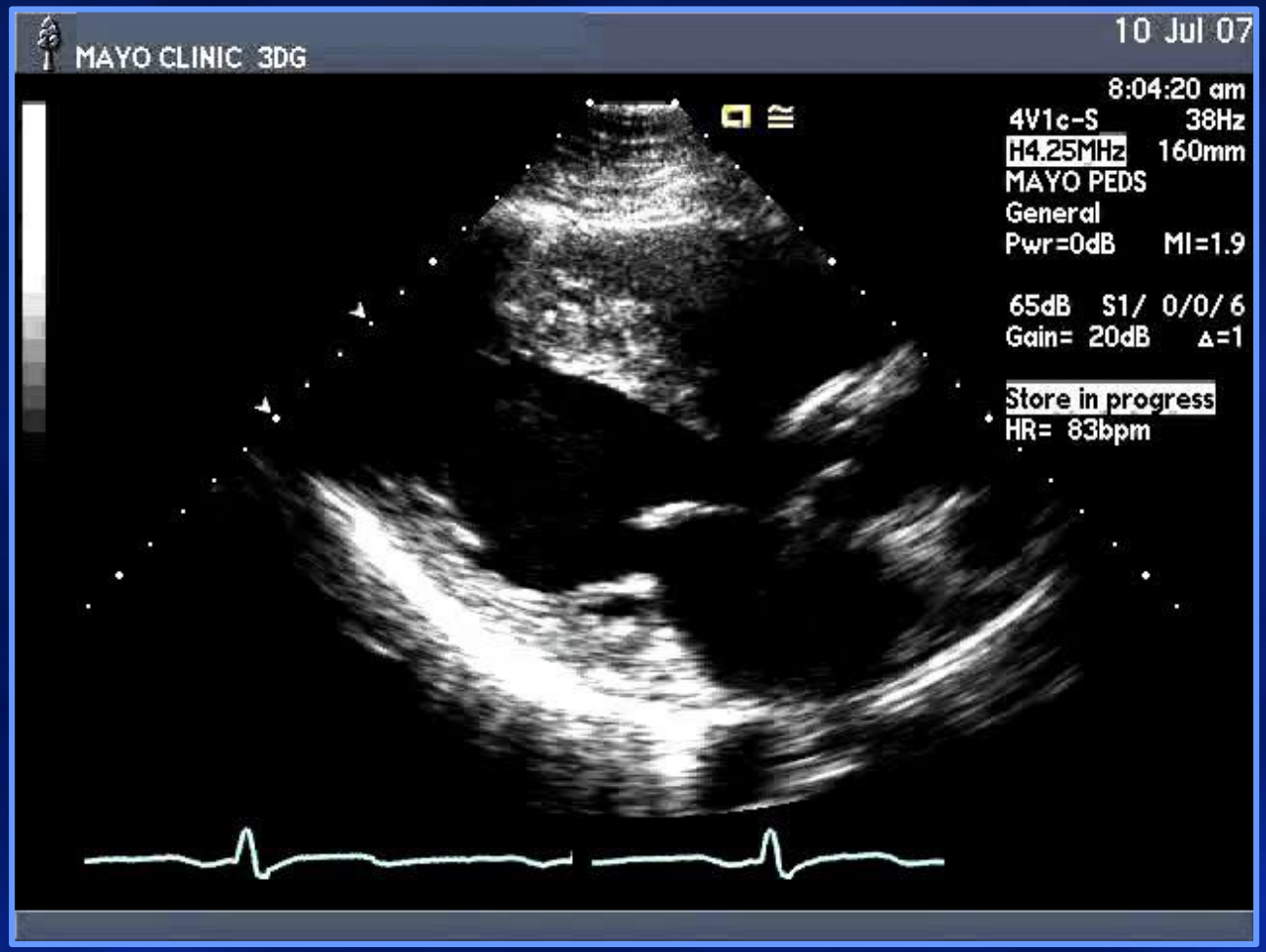
Hull MC, et al. JAMA 2003; 290:2831

Drug-Induced Valvular Disease Echocardiographic Findings

- Thickening and retraction of valve leaflets or cusps
  - No commissural fusion
  - Reduced mobility, restricted closure coaptation
- Thickened, fused, shortened MV/TV chordal support apparatus
- Variable regurgitation, rarely significant stenosis

Mimics Rheumatic Valve Disease

Ergot Induced Valve Disease

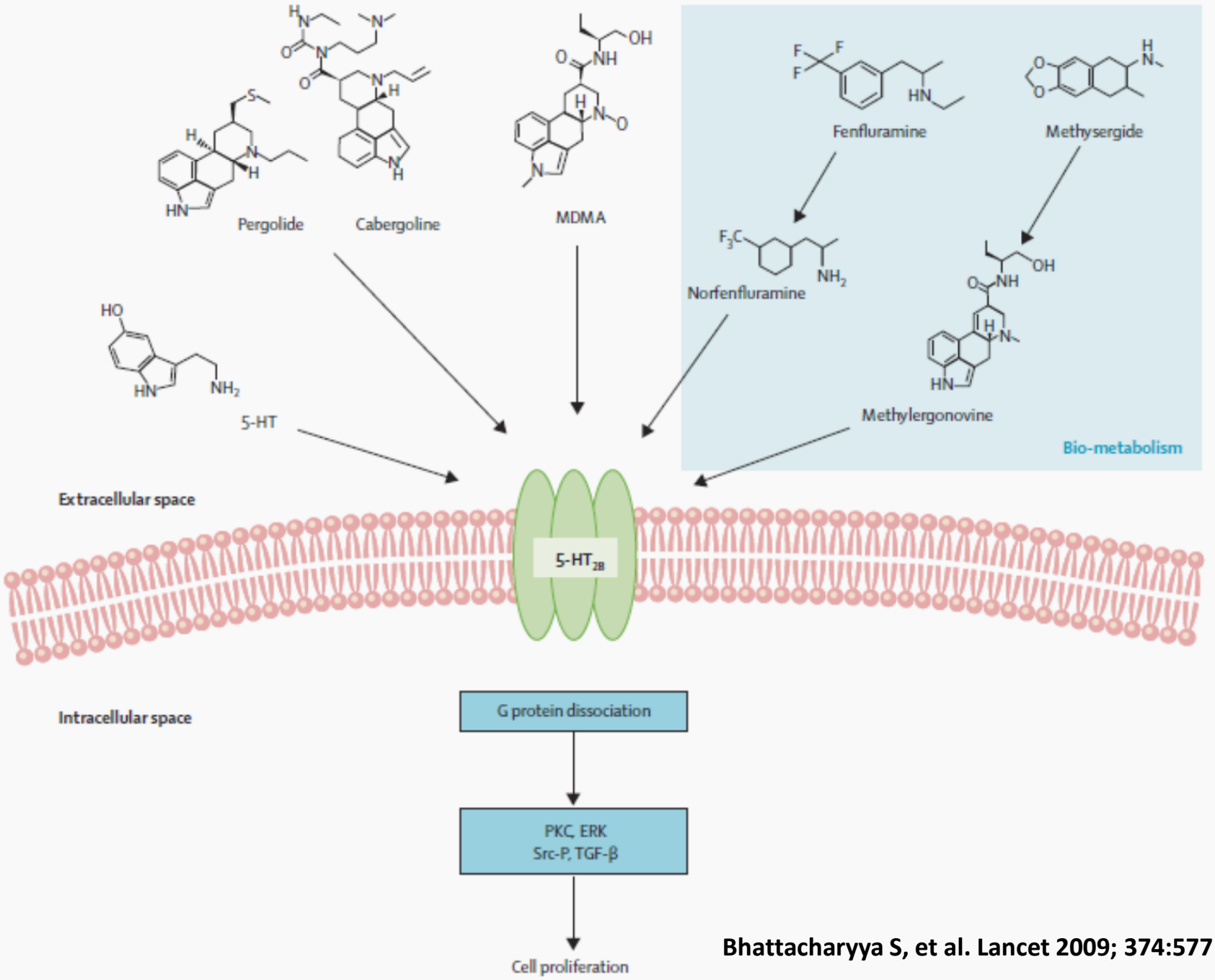


MDMA (3,4-Methylenedioxymethamphetamine) Echo Findings with "Ecstasy" Abuse

	MDMA Users (n=33)	Controls (n=29)
Duration of use	6.1 ± 3.4 yrs	0
Age (yrs)	24.3 ± 3.1	25.6 ± 3.1
MR ≥ Grade 2/4	4 (14%)	0
Restricted MV motion	7 (24%)	0
TR ≥ Grade 2/4	13 (45%)	0
Restricted TV motion	7 (24%)	0
AR ≥ Grade 1/4	4 (14%)	0

- Prevalence of MDMA abuse: 0.4 – 6% worldwide

Droogmans S, et al. Am J Cardiol 2007; 100: 1442

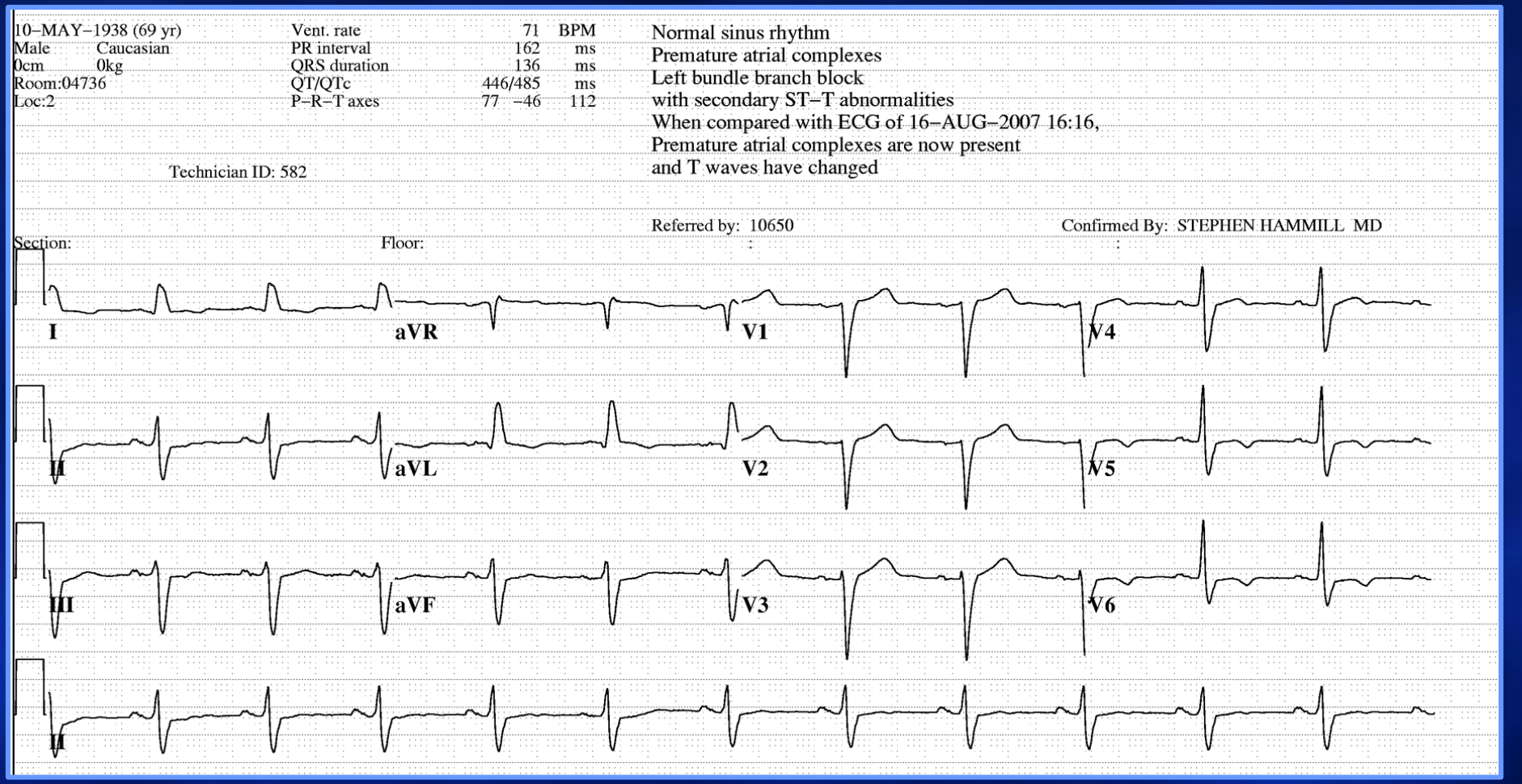


Bhattacharyya S, et al. Lancet 2009; 374:577

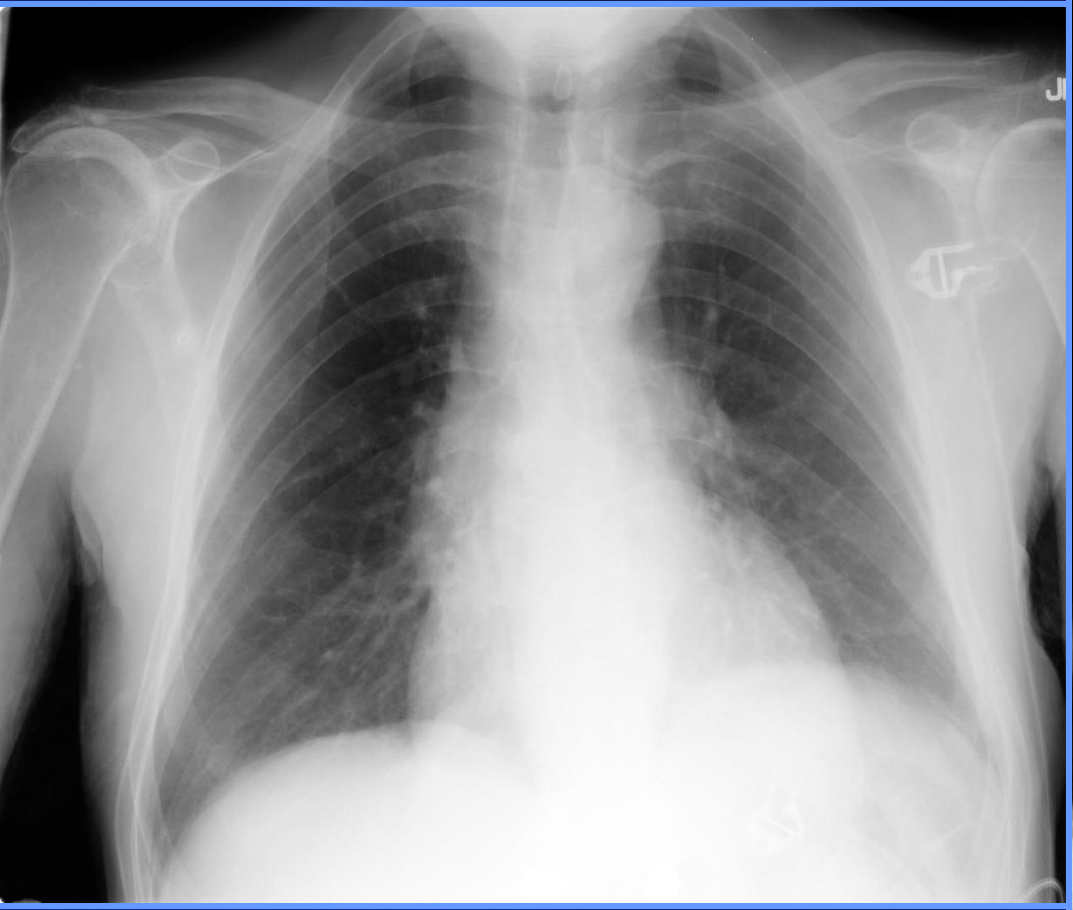
A 60 year old male farmer is referred for evaluation of dyspnea

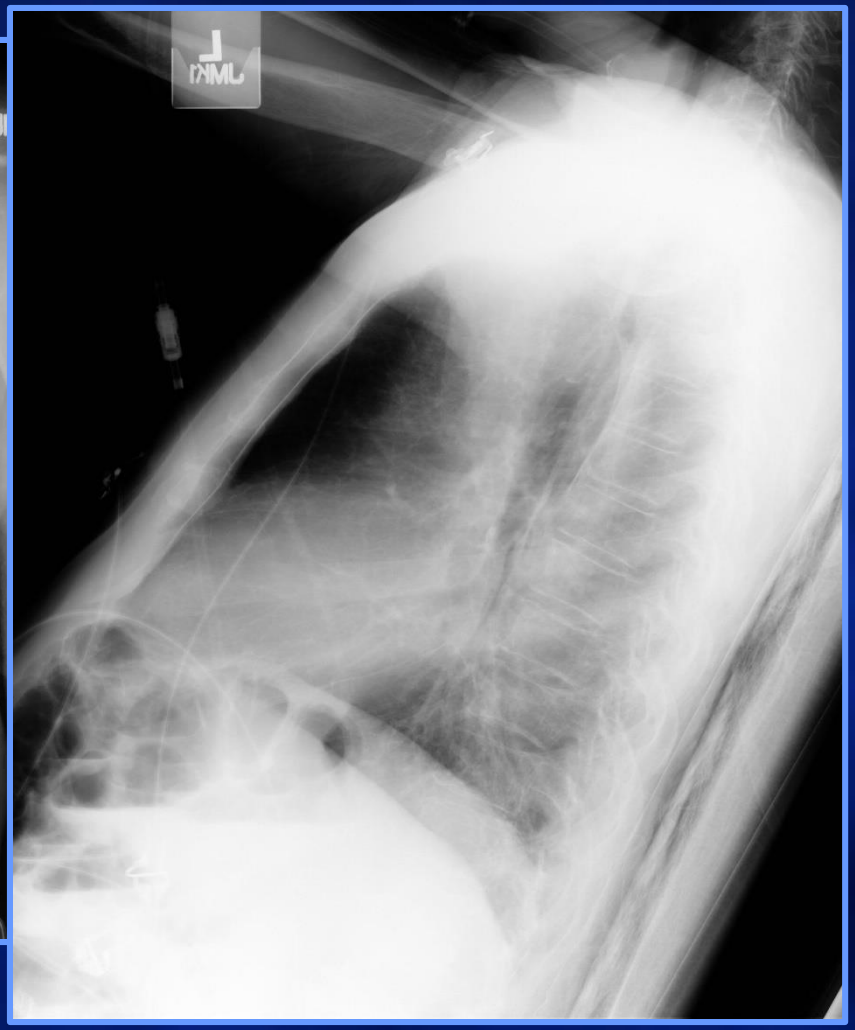
- NYHA Class III symptoms
- PMH: Type 2 DM
- Abnormal LFT's
- Physical Exam:
  - 110/70 mmHg, HR 70 BPM
  - S3 gallop
  - Bronze skin

EKG

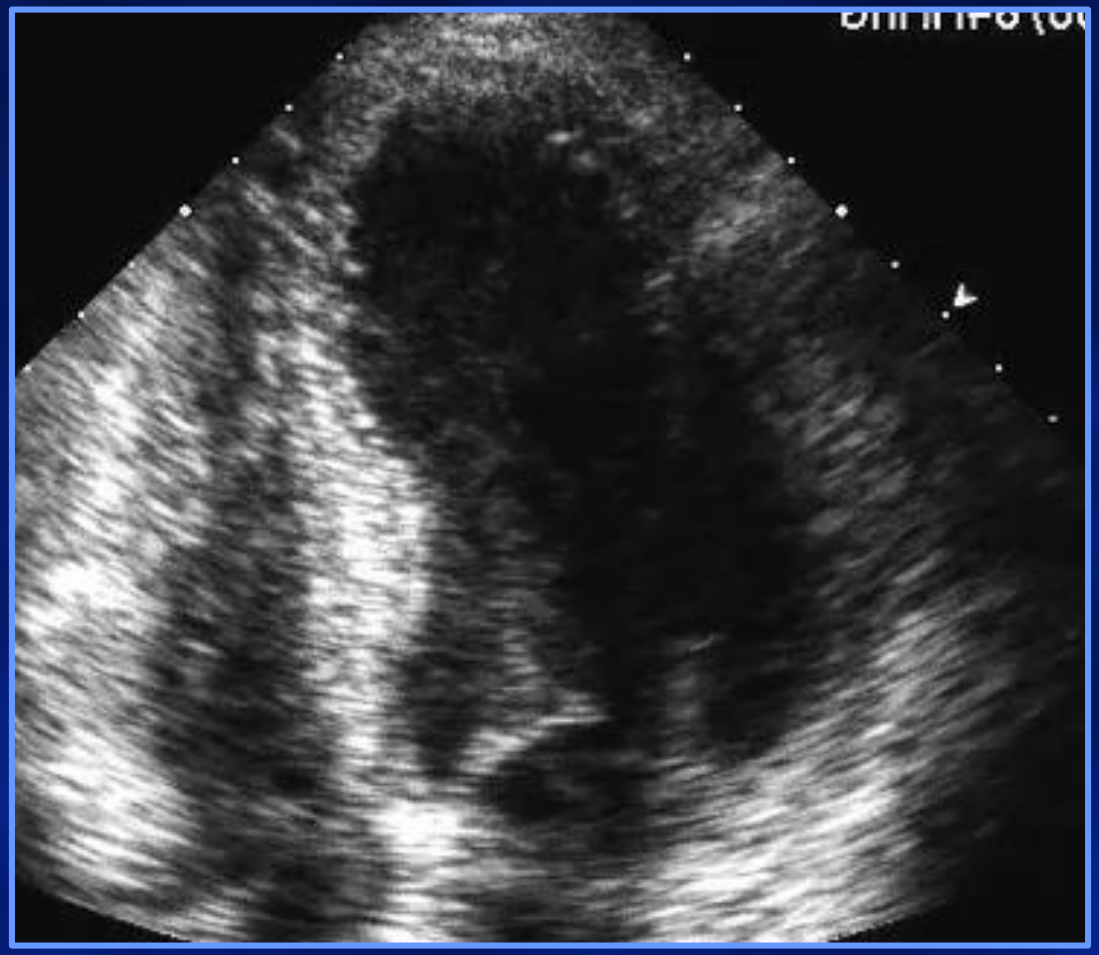

10–MAY–1938 (69 yr)
Male Caucasian
0cm 0kg
Room:04736
Loc:2
Technician ID: 582
Vent. rate 71 BPM
PR interval 162 ms
QRS duration 136 ms
QT/QTc 446/485 ms
P–R–T axes 77 –46 112
Normal sinus rhythm
Premature atrial complexes
Left bundle branch block
with secondary ST–T abnormalities
When compared with ECG of 16–AUG–2007 16:16,
Premature atrial complexes are now present
and T waves have changed
Referred by: 10650
Confirmed By: STEPHEN HAMMILL MD
Section:
Floor:
I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II

CXR

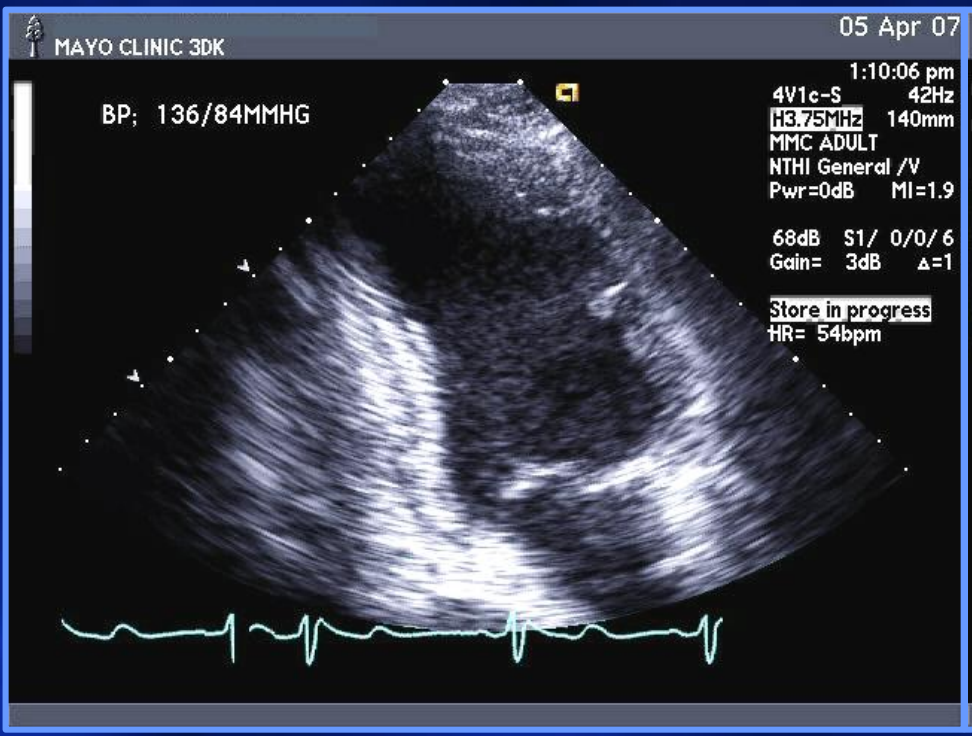


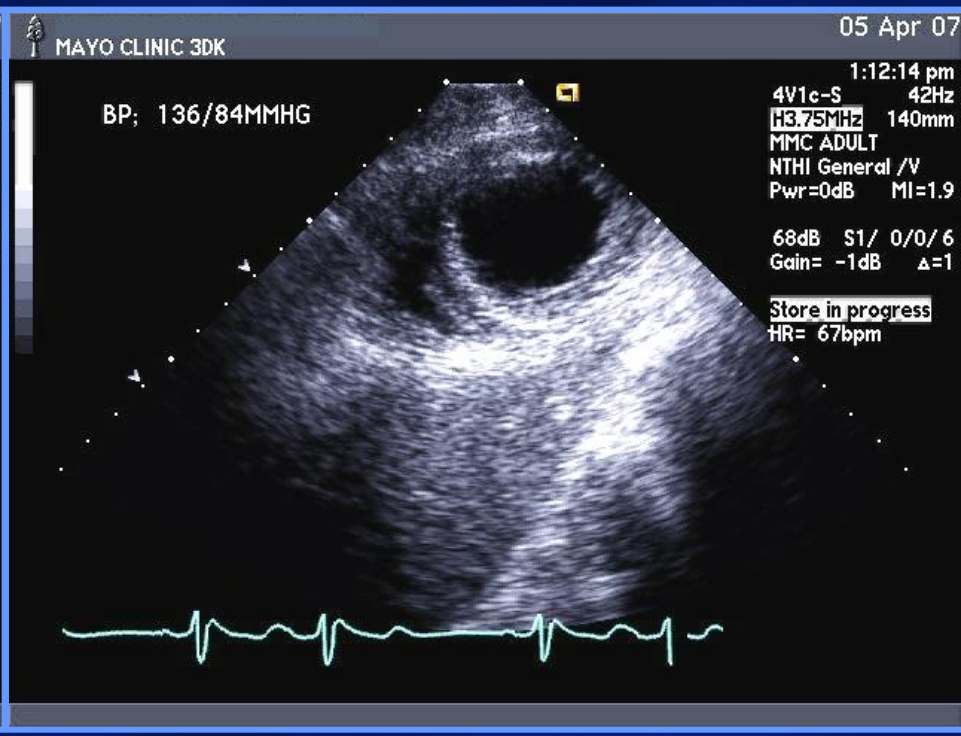


Apical 4 Chamber View

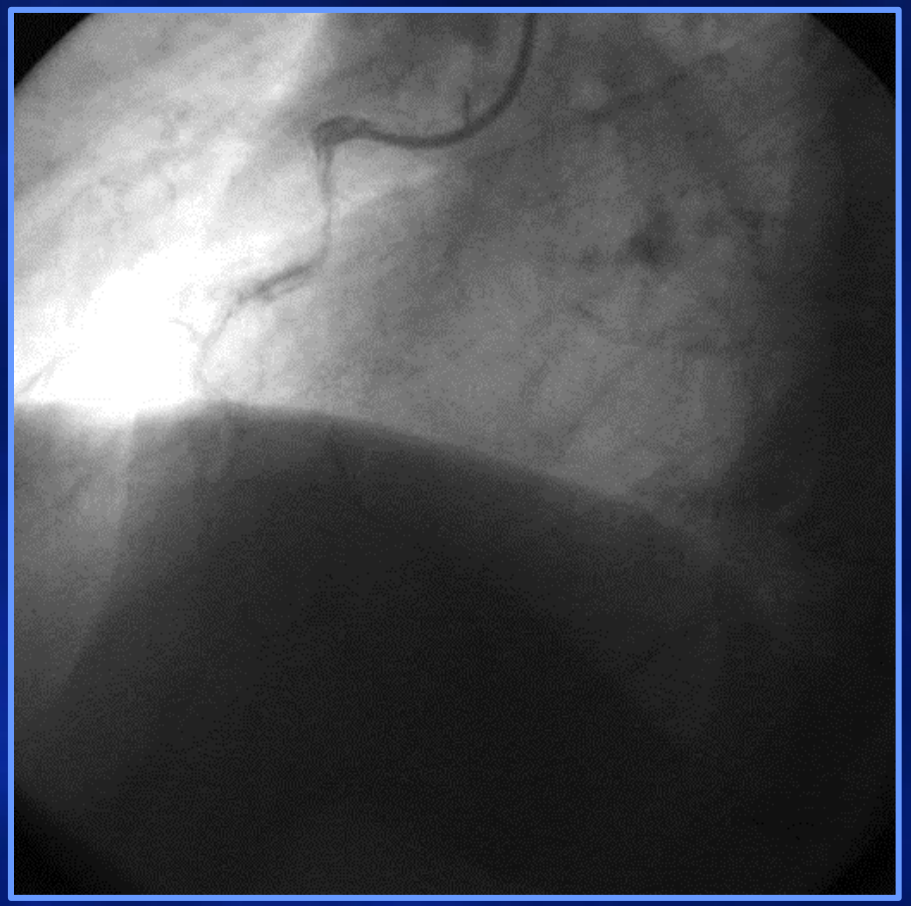


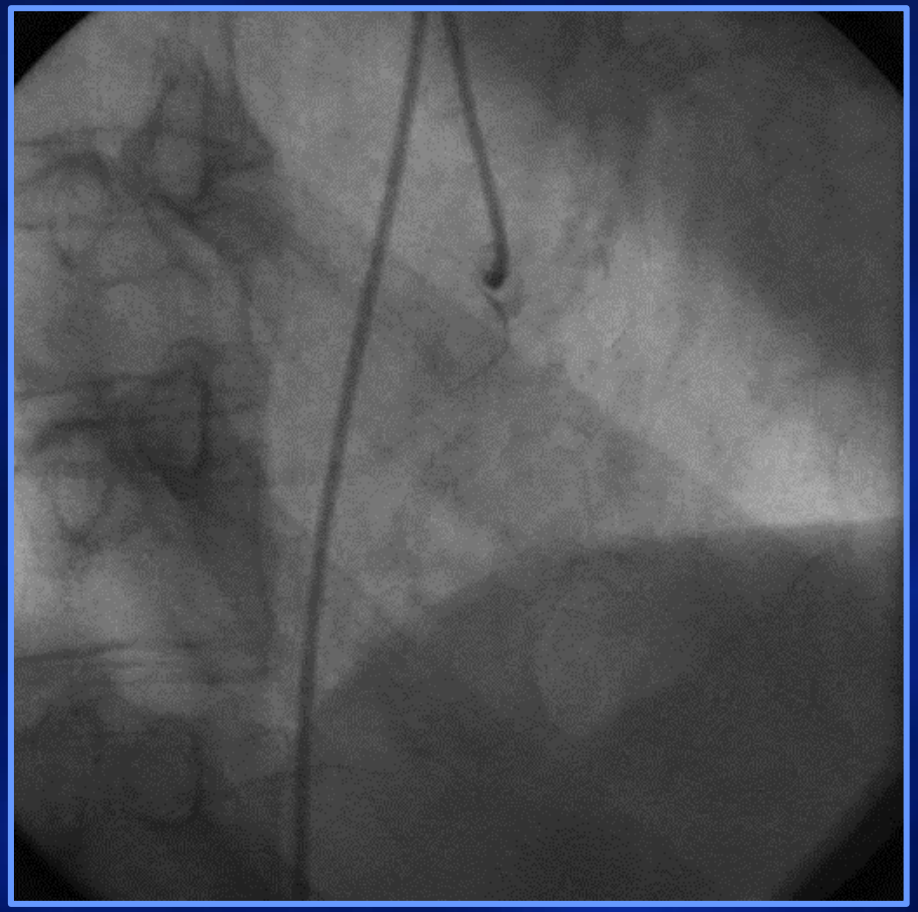
Apical Images



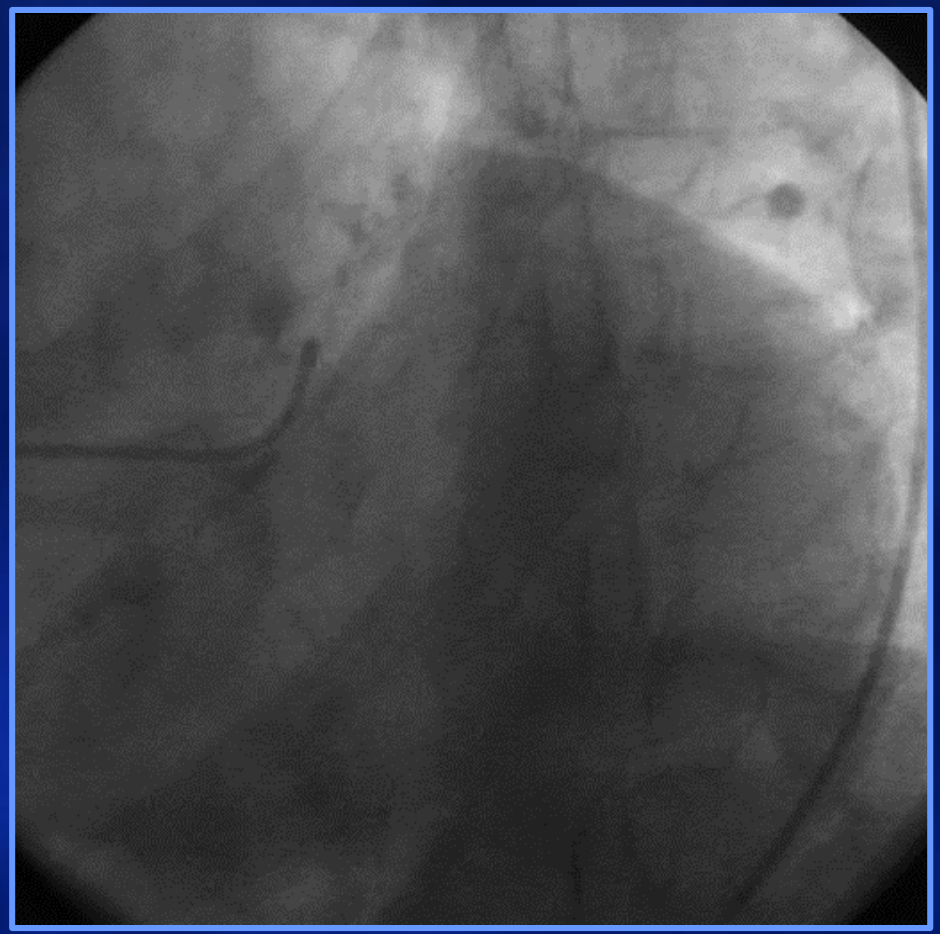


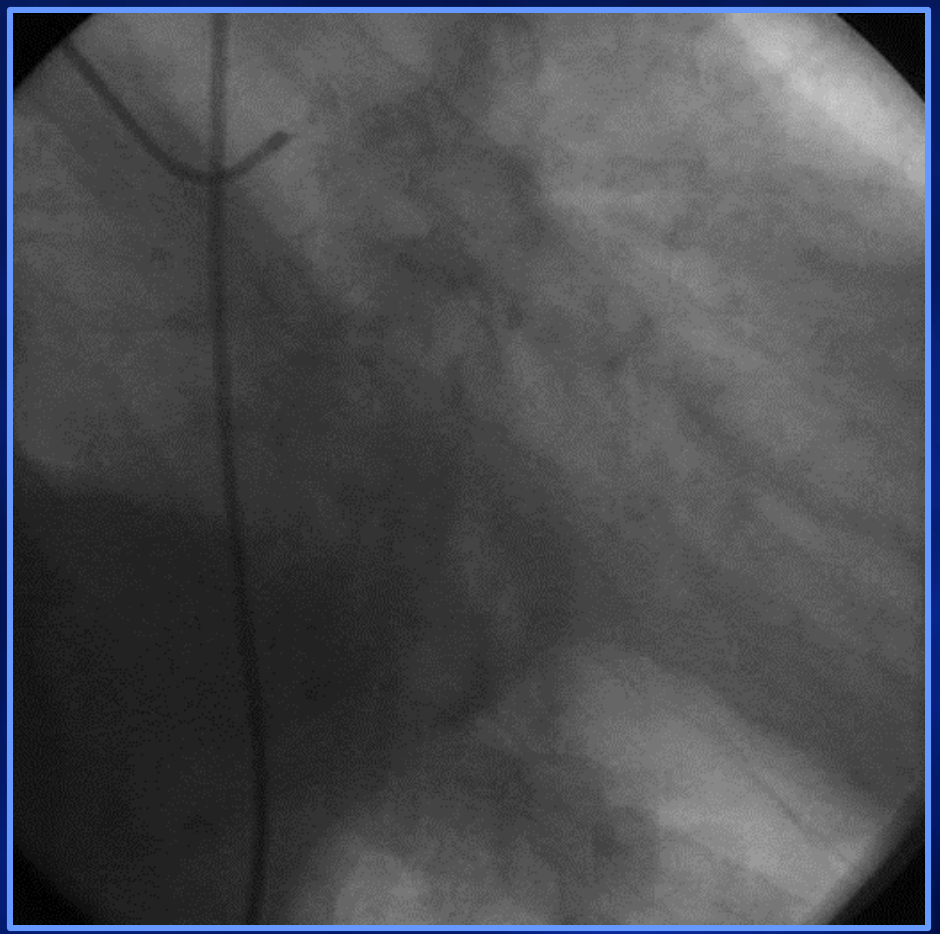
Coronary Angiography





Coronary Angiography

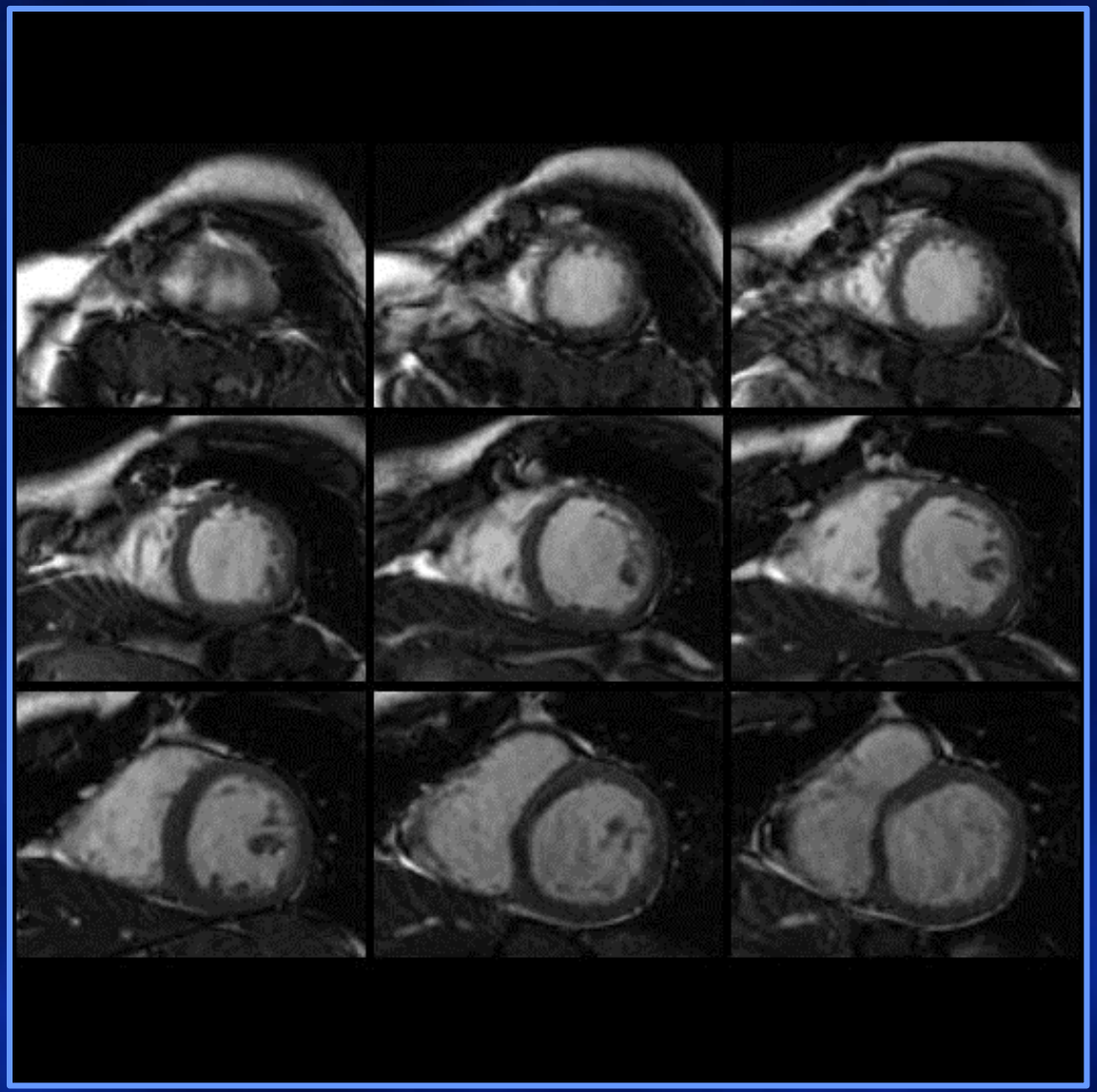




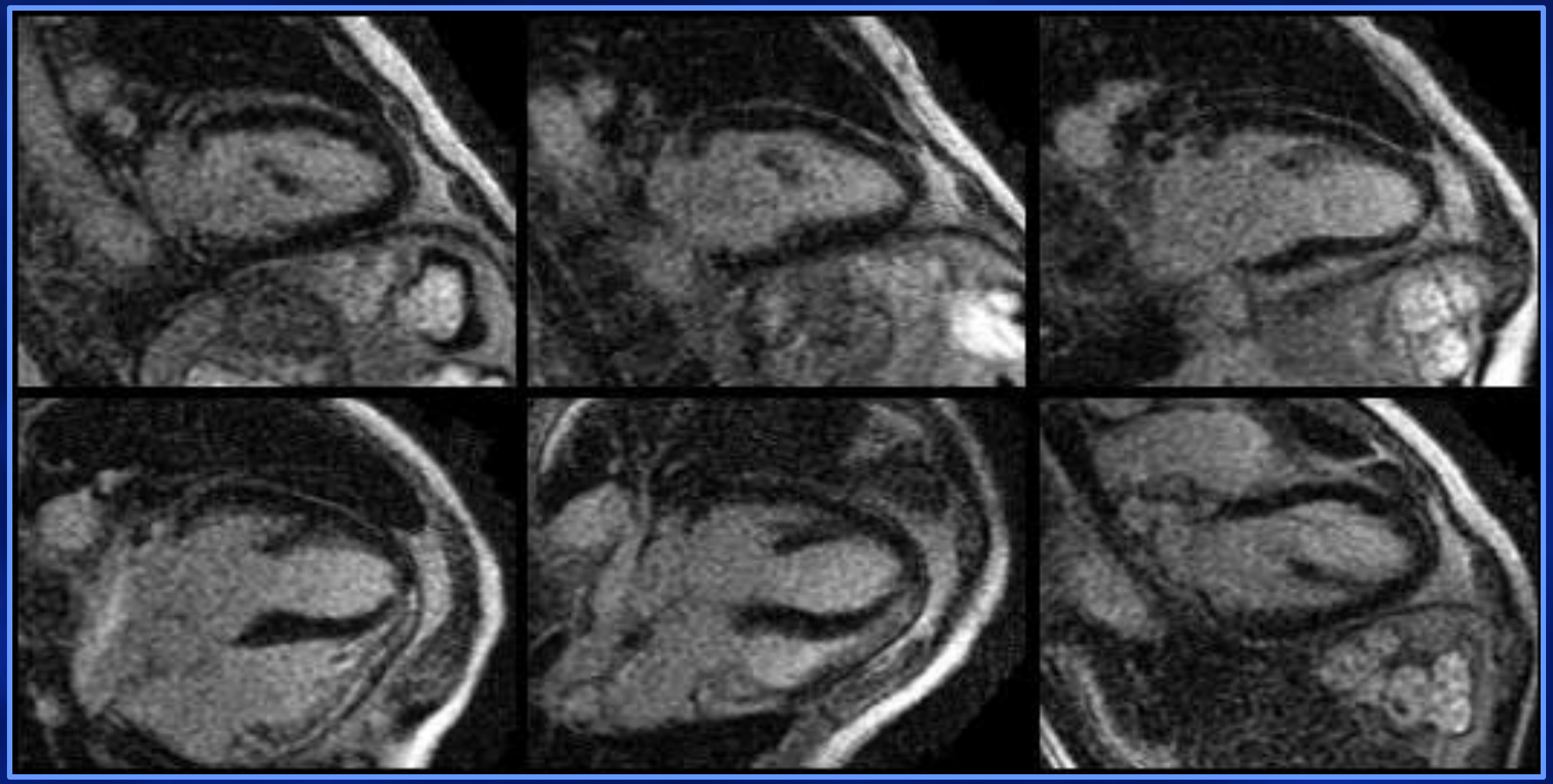
What would you recommend next to help establish the diagnosis?

1. Cardiac Endomyocardial Biopsy
2. Cardiac MRI
3. Cardiac CT
4. Dobutamine Stress Echo

Cardiac Cine-MRI



Contrast MRI: No delayed Hyperenhancement



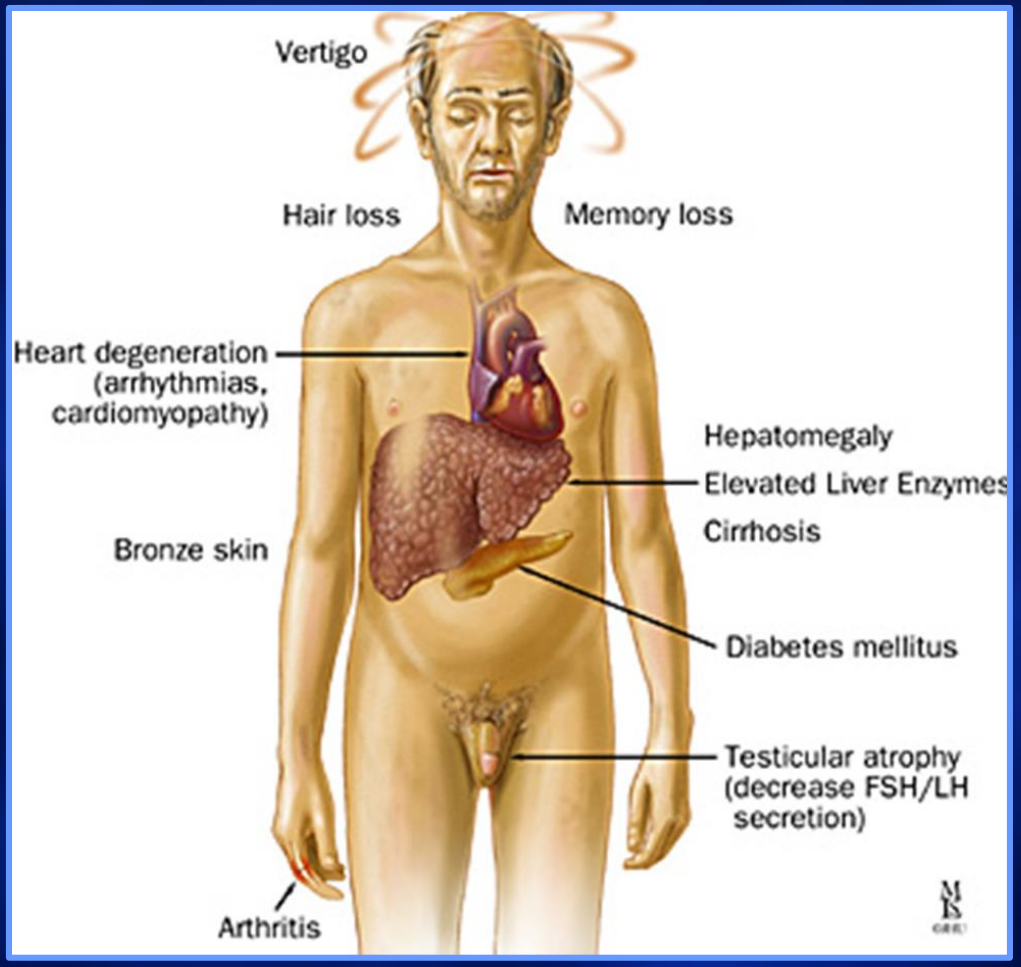
60 year old male farmer with Type 2 DM, bronze skin, and abnormal LFT's

What is the most likely diagnosis?

a. Cardiac hemochromatosis
b. Cardiac amyloidosis
c. Cardiac sarcoidosis
d. Fabry's Disease
e. Carcinoid syndrome

Hemochromatosis

- ↑ total body iron – intracellular deposits in heart, liver, pituitary, pancreas, gonads, skin



Review Article

Iron-Overload Cardiomyopathy: Pathophysiology, Diagnosis, and Treatment

COLM J. MURPHY, MD, FRCPC, AND GAVIN Y. OUDIT, MD, PhD, FRCPC

Edmonton, Alberta, Canada

ABSTRACT

Background: The prevalence of primary (hereditary) hemochromatosis and secondary iron overload (hemosiderosis) is reaching epidemic levels worldwide. Iron-overload leads to excessive iron deposition in a wide variety of tissues, including the heart and endocrine tissues.

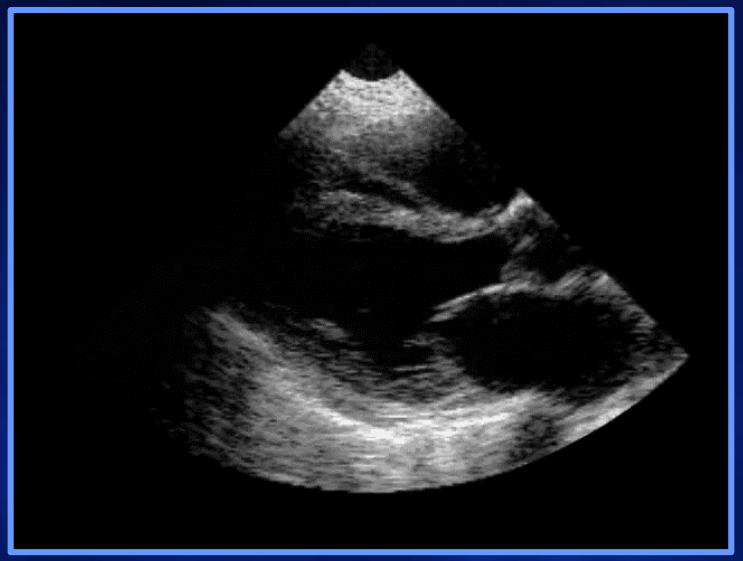
Methods and Results: Iron-overload cardiomyopathy is the primary determinant of survival in patients with secondary iron overload, while also being a leading cause of morbidity and mortality in patients with primary hemochromatosis. Iron-induced cardiovascular injury also occurs in acute iron toxicosis (iron poisoning), myocardial ischemia-reperfusion injury, cardiomyopathy associated with Friedreich ataxia, and vascular dysfunction. The mainstay therapies for iron overload associated with primary hemochromatosis and secondary iron overload is phlebotomy and iron chelation therapy, respectively. L-type Ca^{2+} channels provide a high-capacity pathway for ferrous (Fe^{2+}) uptake into cardiomyocytes in iron-overload conditions; calcium channel blockers may represent a new therapeutic tool to reduce the toxic effects of excess iron.

Conclusions: Iron-overload cardiomyopathy is a an important and potentially reversible cause of heart failure at an international scale and involves diastolic dysfunction, increased susceptibility to arrhythmias and a late-stage dilated cardiomyopathy. The early diagnosis of iron-overload cardiomyopathy is critical since the cardiac dysfunction is reversible if effective therapy is introduced before the onset of overt heart failure. (*J Cardiac Fail 2010;16:888–900*)

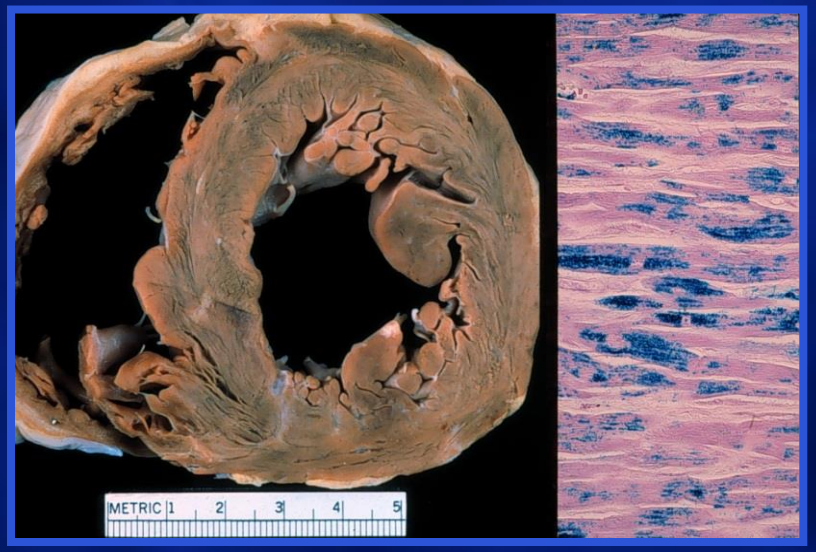
Key Words: Cardiomyopathy, hemochromatosis, oxidative stress, anemia, cardiac MRI, echocardiography.

Hemochromatosis

- Think of this when DCM seen in setting of hepatic dysfunction; diabetes, tanned skin
- Diagnosis is critical, since reversible
  - Males 9:1
  - 2-3/1000 population
  - Ferritin usually > 500, transferrin > 50%
- Normal wall thickness
- Arrhythmias, conduction abnormalities

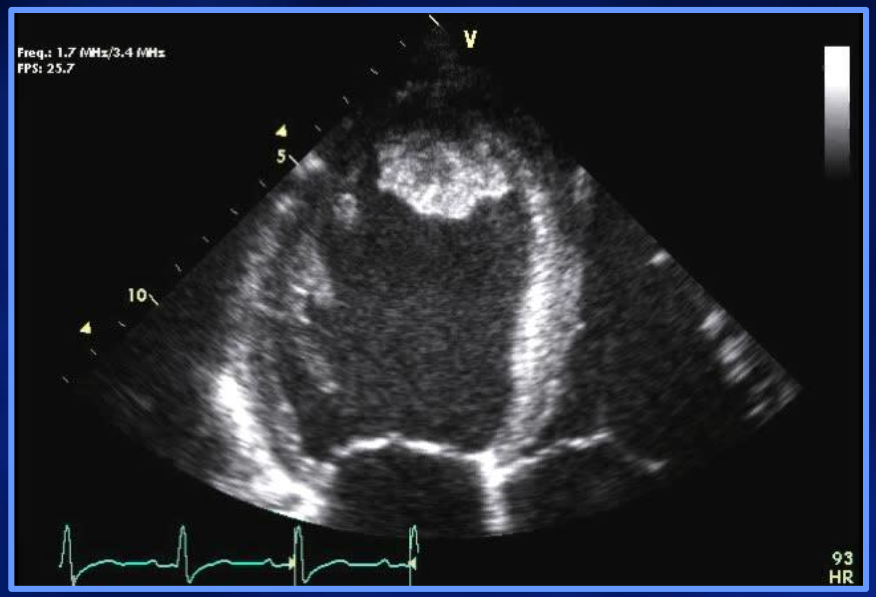


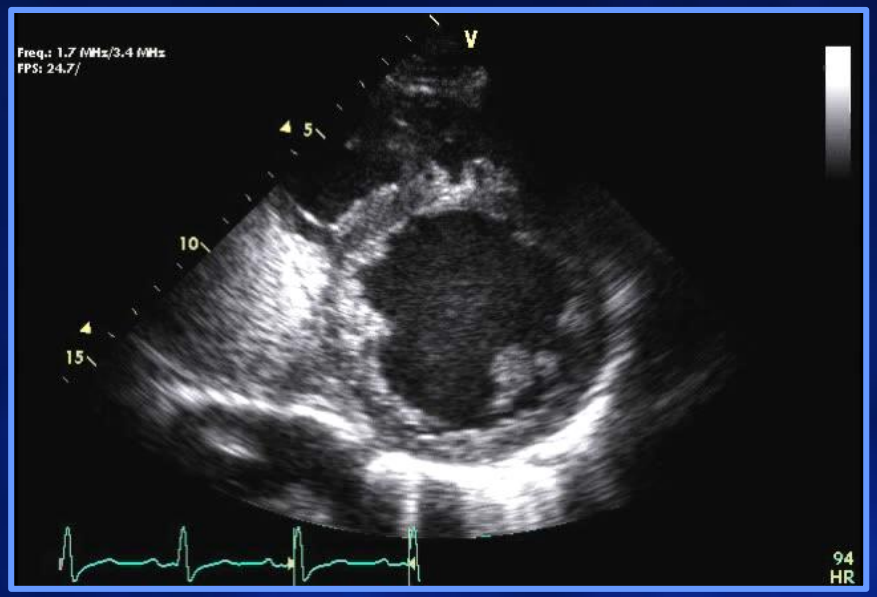
Intracellular iron
– directly toxic to myocytes

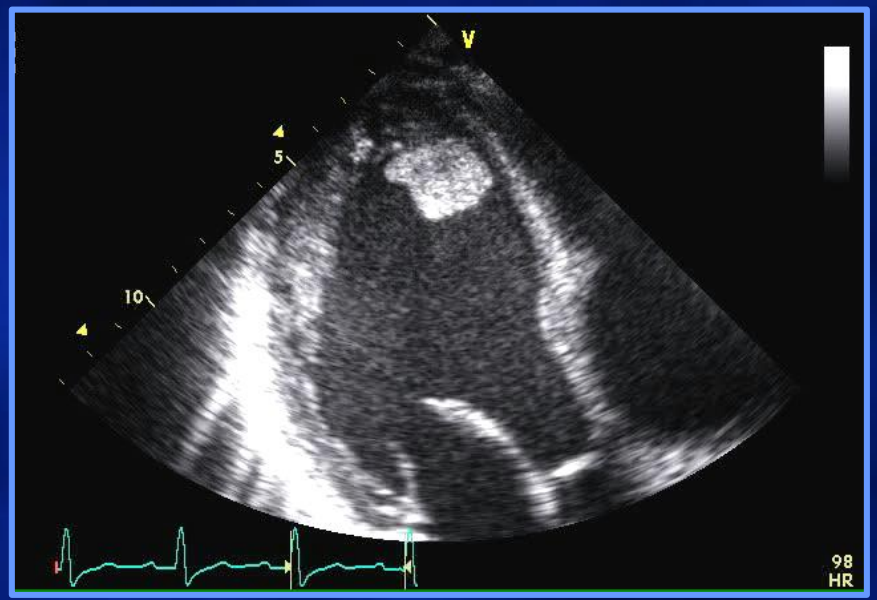


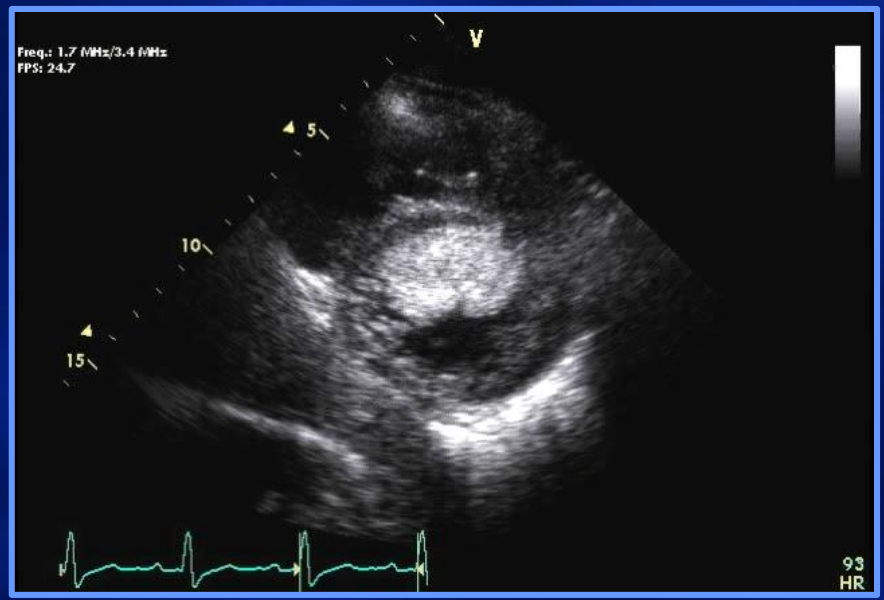
Courtesy of William Edwards, MD

26 year old with Hemochromatosis

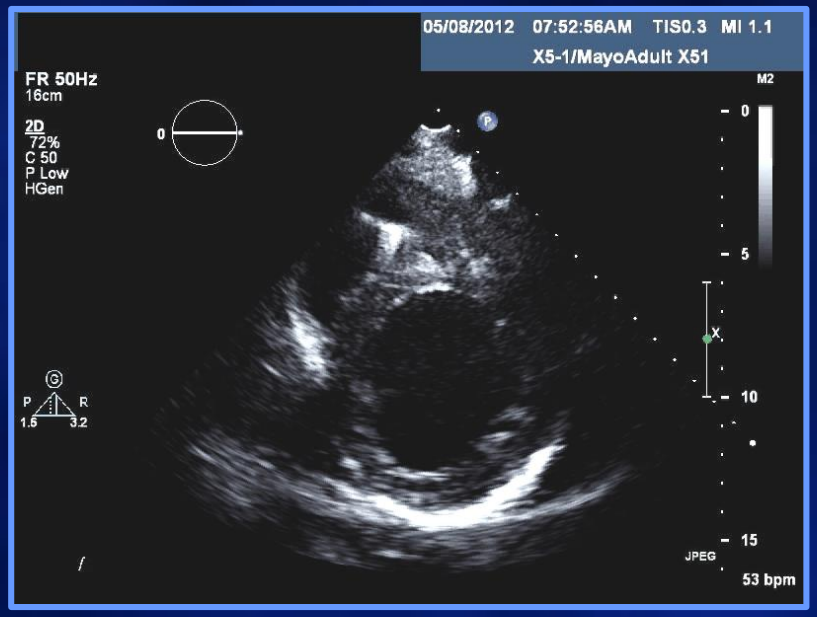


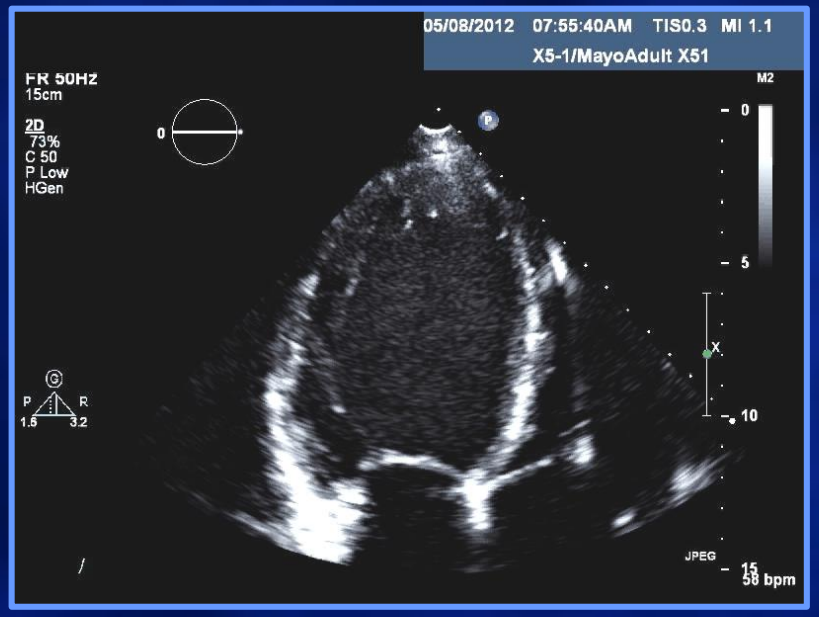


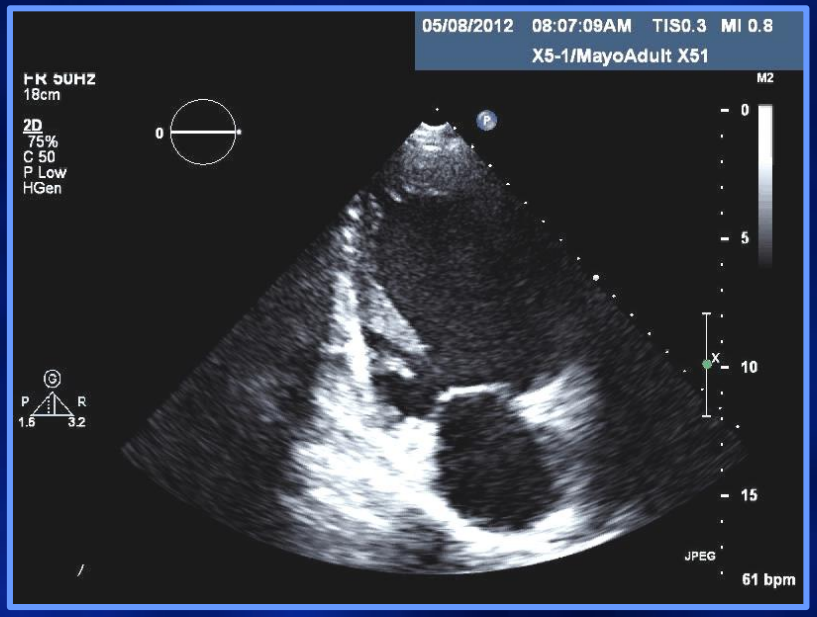




After Tx with Deferoxamine

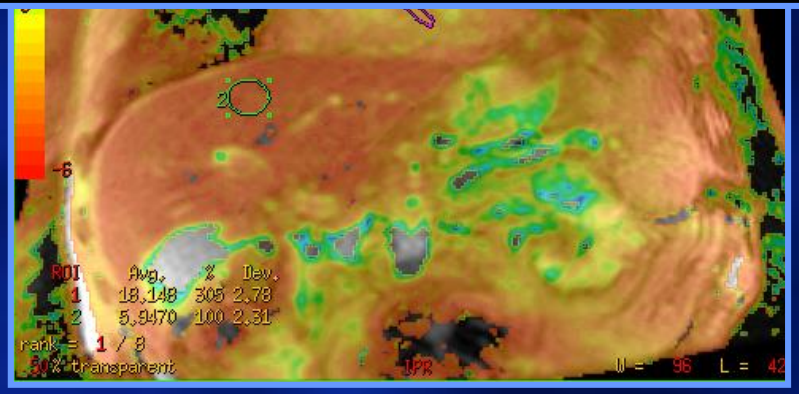






- The evaluation of the T2* relaxation time is an excellent noninvasive correlate of myocardial iron deposition and is a useful technique to follow response to iron-chelation therapy.
- Myocardial T2* has been shown to have no relation to serum ferritin and liver iron overload.
- T2* relaxation time predicts CHF and Arrhythmias

Circulation 2009;120:1961-8
Eur Heart J 2001;22:2171-9.



that suggests hemochromatosis

Take Home Points

- The Iron Heart is a weak heart…
- Hemochromatosis may be a cause of idiopathic dilated cardiomyopathy
  - Reversible with treatment
- Cardiac MRI (T2 relaxation time) is important in helping to establish diagnosis and monitoring treatment effects

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STATE-OF-THE-ART PAPER

Iron Overload Cardiomyopathy

Better Understanding of an Increasing Disorder

Pradeep Gujja, MD,* Douglas R. Rosing, MD,† Dorothy J. Tripodi, RN,†
Yukitaka Shizukuda, MD, PHD*†

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

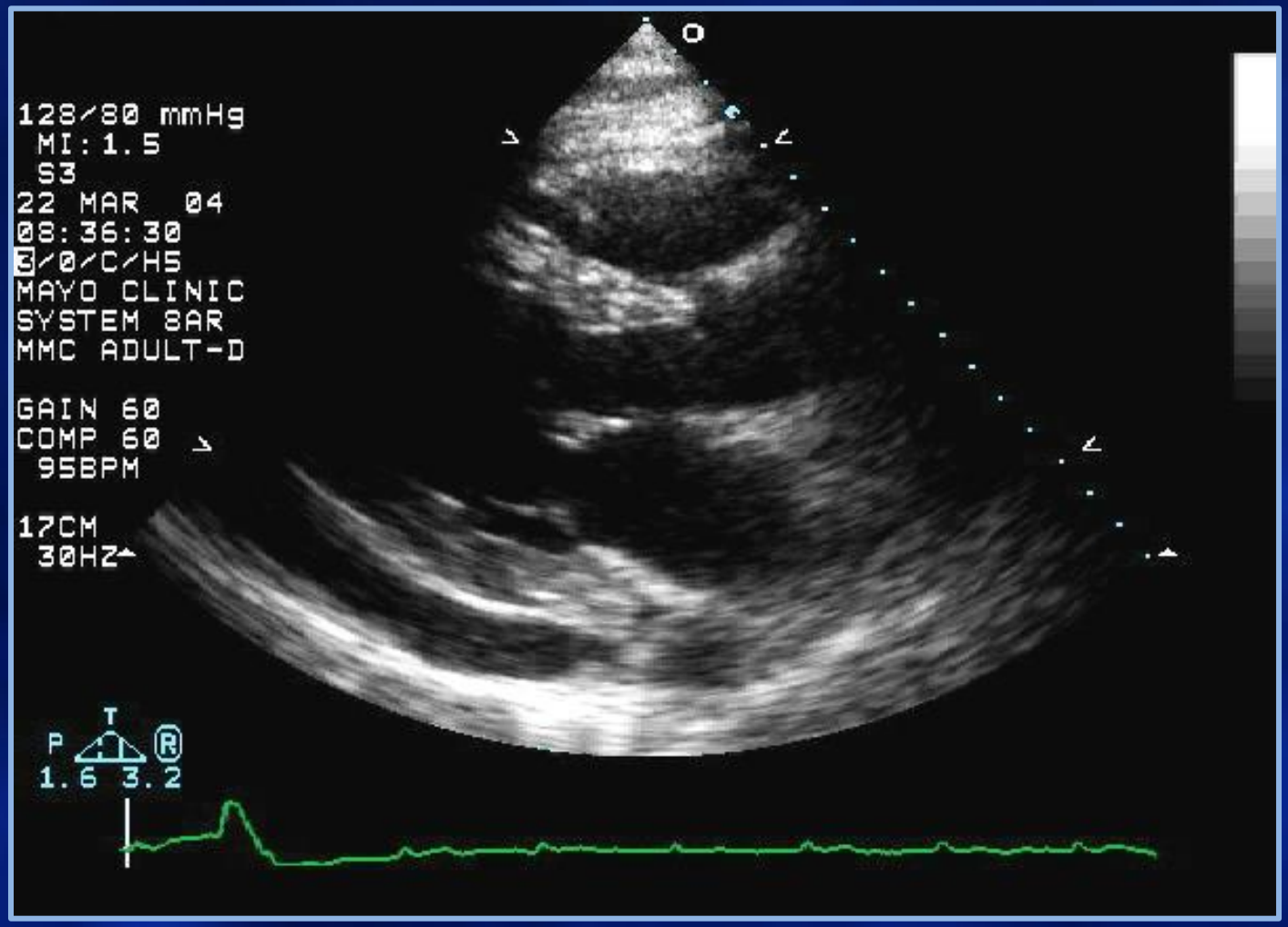
American Heart Association®

Cardiovascular Function and Treatment in β-Thalassemia Major: A Consensus Statement From the American Heart Association

Dudley J. Pennell, James E. Udelson, Andrew E. Arai, Biykem Bozkurt, Alan R. Cohen, Renzo Galanello, Timothy M. Hoffman, Michael S. Kiernan, Stamatios Lerakis, Antonio Piga, John B. Porter, John Malcolm Walker and John Wood
on behalf of the American Heart Association Committee on Heart Failure and Transplantation of the Council on Clinical Cardiology and Council on Cardiovascular Radiology and Imaging

Circulation. 2013;128:281-308; originally published online June 17, 2013;

28 year old male with hemophilia and dyspnea



HIV and Cardiac Disease

- Clinical cardiac involvement - 10% AIDS
  - Myocarditis (50% at autopsy)
  - Ventricular arrhythmias
  - Heart failure (DCM)
  - Pericarditis and effusions
  - Infectious or malignant invasion
  - Diastolic dysfunction
  - Pulmonary Hypertension ?

- Heidenreich PA et al. Pericardial effusion in AIDS. Incidence and survival. Circulation 1995; 92:3229.
- Luginbuhl LM et al. Cardiac morbidity and related mortality in children with HIV infection. JAMA 1993; 269:2869.

Conclusions:

Systemic Diseases and the Echo Boards

- Carcinoid Syndrome
- Hypereosinophilic endomyocardial disease
- Sarcoidosis
- Systemic Lupus Erythematosus
- Scleroderma/Crest: Pulm Hypertension
- Amyloidosis
- Hyper or Hypothyroidism
- Radiation Heart Disease
- Drug Induced Valve Disease
- Hemochromatosis

Thank You!

mankad.sunil@mayo.edu

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Dr. Thais Couthino
Dr. Mark Callahan