Myocardial Diseases: The Cardiomyopathies
Mat Maurer and Charles Marboe

Objectives
At the conclusion of this seminar, learners will be able to:
1. Define the term cardiomyopathy and be able to classify myocardial diseases into major types.
2. Be able to link pathophysiologic mechanism(s) with each type of cardiomyopathy.
3. Delineate physical exam findings in patients with cardiomyopathy.
4. Understand basic tests (EKG, CXR, Echo, Cardiac Catheterization) that are employed to diagnose a cardiomyopathy and be able to define results for a particular type of cardiomyopathy.
5. Delineate conditions that cause reversible cardiomyopathies and those that may require an endomyocardial biopsy for diagnosis.
6. Identify gross anatomic and histologic correlates of the major types of cardiomyopathy.

Etiologies
- Ischemic cardiomyopathy
- Valvular cardiomyopathy
- Hypertensive cardiomyopathy
- Inflammatory cardiomyopathy
- Metabolic cardiomyopathy
- General system disease
- Muscular dystrophies.
- Neuromuscular disorders.
- Sensitivity and toxic reactions.
- Peripartal cardiomyopathy

Definition and Classification
- Cardiomyopathy, literally means “heart muscle disease”
- A classification serves to bridge the gap between ignorance and knowledge

Historical Timeline

WHO / ISFC 1980
- Etiologic
  - Dilated
  - Hypertrophic
  - RV/Dilation
  - Unclassified

WHO 1995
- Functional
  - Dilated
  - Restrictive
- Primary
- Secondary

Genetic 2006
- Genetic
- Primary
- Secondary

Define the Etiology: For Treatment and Prognosis

WHO Classification
- Functional Classification
  1. Dilated Cardiomyopathy
  2. Hypertrophic cardiomyopathy
  3. Restrictive Cardiomyopathy
  4. RV Dysplasia
  5. Unclassified (Obliterative)

Hypertrophic Normal Dilated

**Functional / Morphologic Classification**

<table>
<thead>
<tr>
<th>Type</th>
<th>Definition</th>
<th>Sample Etiologies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertrophic</td>
<td>Left and/or right ventricular hypertrophy</td>
<td>Familial with autosomal dominant inheritance</td>
</tr>
<tr>
<td>Dilated</td>
<td>Dilated left/both ventricle(s) with impaired contraction</td>
<td>Ischemic, idiopathic, familial, viral, alcoholic, toxic, valvular</td>
</tr>
<tr>
<td>Restrictive</td>
<td>Restrictive filling and reduced diastolic filling of one/both ventricles, Normal/near normal systolic function</td>
<td>Idiopathic, amyloidosis, endomyocardial fibrosis</td>
</tr>
</tbody>
</table>

**Dilated vs. Hypertrophic vs. Restrictive**

**ARVD vs. Unclassified**

<table>
<thead>
<tr>
<th>Type</th>
<th>Definition</th>
<th>Sample Etiologies</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARVD</td>
<td>Genetic, muscular disorder of the right ventricle is replaced by fat and fibrosis, and causes abnormal heart rhythm</td>
<td>ARVD</td>
</tr>
<tr>
<td>Unclassified</td>
<td>Genetic disorder, known as &quot;spongiform cardiomyopathy&quot; in which embryonically the myocardium fails to is regress.</td>
<td>Non-compaction</td>
</tr>
</tbody>
</table>

**Morphologic Summary**

**Genetic Classification**

- **Primary**
  - Can be genetic, nongenetic or acquired
  - Solely or predominantly confined to heart muscle and are relatively few in number

- **Secondary**
  - Pathological myocardial involvement as part of a large number and variety of generalized systemic (multi-organ) disorders
Secondary

- Infiltrative
- Storage
- Toxicity
- Endomyocardial
- Inflammatory
- Endocrine
- Cardiofacial
- Neuromuscular/Neurologic
- Autoimmune/Collagen

Diagnostic Tests

- Chest X ray
- EKG
- Echocardiogram
- Blood tests: Na, BUN, Creatinine, BNP
- Exercise tests
- MRI
- Cardiac catheterization
- Endomyocardial Biopsy

EKG

Normal MRI
Diagnoses made by Endomyocardial Bx

1. Myocarditis
   - Giant Cell
   - CMV
   - Toxoplasmosis
   - Chagas disease
   - Rheumatic
   - Lyme

2. Infiltrative
   - Amyloid
   - Sarcoid
   - Hemochromatosis
   - Hypereosinophilic
   - Tumors

3. Toxins
   - Doxorubicin
   - Radiation Injury

4. Genetic
   - Infiltrative
   - Glycogen Storage

Potentially Reversible Dilated Cardiomyopathies

- Ischemic with viable myocardium
- Uncorrected Valvular Disease
- Inflammatory
  - Viral
  - Toxo
  - Lyme
- Toxic
  - Alcohol
  - Cocaine
  - Cobalt
- Hypersensitivity

Endomyocardial Biopsy

Case #1 (DCM): History

- 56-year old female
- Recent URI about 3 weeks
- Progressive effort intolerance
- Increasing shortness of breath and fatigue
- Admitted to the hospital
Case #1 (DCM): Physical Exam

- Well-developed, well-nourished female
- 5 feet 10 inches, weighed 188 pounds.
- BP = 100/70 mmHg, P= 70 bpm, RR =26.
- Skin: warm
- Neck: JVP at 8 cm with prominent “v” wave.
- Cardiac: Regular cardiac rhythm with a S3 gallop but non-displaced PMI
- Lungs: crackles at bases
- Abdomen: soft, nontender without organomegaly
- Ext: No edema.

Case #1 (DCM): EKG

Case #1 (DCM): MRI

Case #1 (DCM): MRI

Case #1(DCM):MRI
Case #1 (DCM): Catherization and Bx

- Catheterization
  - Right atrial pressure = 18
  - Pulmonary artery pressure = 43/29
  - Pulmonary wedge pressure = 27
  - Cardiac output of 3.6 L/min
  - Cardiac index 1.8 L/min/m²
- Biopsy was performed

Case #1 (DCM): Primary Mechanism

Decreased Contractility

Myocarditis

Myocarditis

Inflammatory infiltrate in the myocardium associated with myocyte damage

Giant cell myocarditis
Diagnoses of Dilated Cardiomyopathies made by Endomyocardial Bx

1. Myocarditis
   - Giant Cell
   - CMV
   - Toxoplasmosis
   - Chagas disease
   - Rheumatic
   - Lyme

2. Infiltrative
   - Amyloid
   - Sarcoloma
   - Hemochromatosis
   - Tumors

3. Toxins
   - Doxorubicin
   - Radiation Injury

4. Genetic
   - Infiltrative
   - Glycogen Storage

Chagas Disease: Clinical Manifestations

- **Acute stage:**
  - Usually occurs unnoticed
  - Fever, fatigue, body aches, headache, rash, loss of appetite, diarrhea, and vomiting.
  - Signs: mild enlargement of liver and spleen, swollen glands, and local swelling (a chagoma, Romaña’s sign)

- **Chronic stage:**
  - The symptomatic chronic stage affects digestive system and heart.
  - Cardiomyopathy, which causes heart rhythm abnormalities and can result in sudden death.
  - 1/3 develop digestive system damage (megacolon and mega esophagus).

Chagas Disease: American trypanosomiasis

- Most common cause of heart failure worldwide
- Caused by the protozoan Trypanosoma cruzi.
- Insect vector

Chagas Disease Life cycle

Chagas Disease

Trypanosoma cruzi
Amastigotes

$\text{Trypanosoma} \quad \text{Amastigotes}$
Rheumatic Fever: a pancarditis with involvement of pericardium & epicardium, endocardium (valves), and myocardium.

Rheumatic Fever: Myocardial involvement with an Aschoff body – a cardiac ‘granuloma.’

Sarcoid granulomas with extensive fibrosis

Infiltrative Disorders

Amyloid
Sarcoid - a granulomatous disease
Hemochromatosis
Hypereosinophilic Syndrome
Tumors
12/9/2009

36 year old woman with restrictive hemodynamics and liver disease

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Toxins

- Anthracycline-derivatives such as Doxorubicin
- Radiation injury
- Alcohol (no specific features for diagnosis by biopsy)

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Anthracycline Cardiotoxicity

1. **Acute, within days**: EKG changes, LV dysfunction is usually transient and reversible.
2. **Late-onset**: ventricular dysfunction and arrhythmias; irradiation increases risk.
3. **Dilated cardiomyopathy**: cumulative, dose dependent, irreversible, progressive.
   Overall incidence of severe CHF is 2-3%.
Anthracycline Cardiotoxicity
Pathology
1. Cytoplasmic vacuolation (dilated sarcoplasmic reticulum).
2. Myofibrillar degeneration (loss of myofibrils)
3. Seen in almost all patients receiving doses of > 240 mg/m².
4. Little or no inflammation.
5. End stage: myocyte hypertrophy and interstitial fibrosis

Glycogen storage disease type IV (Andersen disease)
- Autosomal Recessive
- Deficiency of glycogen branching enzyme (GBE1; 1,4-1,6-glucan: 1,4-glucan 6-glycosyl transferase); chr. 3p14
- Abnormal glycogen (polyglucosan) accumulates in tissues
- The clinical presentations are extremely heterogeneous.

Glycogen storage disease type IV (Andersen disease)
- Classic: rapidly progressive liver failure
- Non-progressive hepatic form
- Fatal neonatal neuromuscular disease
- Multisystem: skeletal, cardiac, nerve and liver
Polyglucosan bodies

6 nm fibrils; non-membrane bound

Part Two

Break Time!!!!
Case #2 (RCM): History

- 53 year old male with progressive shortness of breath
- PMHx: HTN, DM, and hypercholesterolemia
- Unlimited exercise tolerance until 6 weeks ago
- Initially SOB on severe exertion and w/ stairs
- Progressed over 6 weeks to minimal exertion
- Symptoms: two pillow orthopnea, frequent paroxysmal nocturnal dyspnea, increasing lower extremity edema and abdominal distention, early satiety and 25 pound weight gain and tight clothes
- NYHA Class III

Case #2 (RCM): Physical Exam

BP=90/60  HR=104 RR=22  T=98.6  SaO2=100%
- Gen: WD/WN, in NAD
- Skin: multiple echymosis
- HEENT: NC/AT; EOMI; PERRL, macroglossia
- Neck: elevated JVP to 12cm with rapid x and y descent
- Chest: Bilateral basilar rales
- Heart: PMI in 5th intercostal space, RRR, S1 + S2, S4,
- Abd: distended, NT; +BS, liver 2 finger breaths below CM and 14 cm in span.
- Ext: 2+ LE edema bilaterally to calf

Case #2 (RCM): Laboratory Data

- Hemoglobin/Hematocrit = 11 / 33
- Blood urea nitrogen 47 mg/dl, Creatinine = 1.4 mg/dl
- B- type naturetic peptide = 875 pg/ml
- Troponin I = 0.2
- 24 hour urine protein 527 mg/dl
- Serum protein electrophesis - small monoclonal protein
- Serum lambda light chains = 23 mg/dl, Kappa = 4.1 mg/dl, ratio = 4.5
Case #2 (RCM):
Cardiac Catheterization
- Left dominant circulation
- Left Main = no disease
- RCA = mild diffuse disease
- LAD = proximal 40% stenosis
- Middle 40% stenosis
- LCx = mild diffuse disease
- Left ventricular function low normal
- Mild mitral regurgitation

Case #2 (RCM):
Pressure Measurements
- Right Atrium = 30 mmHg
- Right Ventricle = 60/30 mmHg
- Pulmonary Artery = 60/35 mmHg
- Pulmonary Wedge = 35 mmHg
- Left Ventricle = 127/30 mmHg
- Aorta = 127/88 mm Hg
- Cardiac Output = 2.4 L/min
- Cardiac Index = 1.2 L/min/m²

Case #2 (RCM) Right Heart Catheterization:
Right Atrial Pressure

Case #2 (RCM): Catheterization:
LV - RV Pressures
What is the Primary Pathophysiologic Mechanism?

1. Increased Blood Volume (Excessive Preload)
2. Increased Resistant to Blood Flow (Excessive Afterload)
3. Decreased contractility
4. Decreased Filling

Cardiac Amyloidosis

Nodular deposits of amyloid in the myocardium

Diffuse deposits of amyloid around individual myocytes

Amyloid deposits are birefringent when the Congo Red stain is viewed with polarized light.
Amyloid infiltration of epicardial fat

Involvement of fat and blood vessel (vein)

These amyloid deposits are reactive by immunoperoxidase staining for Kappa light chains.

Cardiac Amyloid: Electron microscopy is the most sensitive means of diagnosis.

AMYLOID: 7-10 nanometer fibrils haphazardly arranged.

Cardiac Amyloid – An infiltrative process causing diastolic dysfunction.
Case #3 (HCM): History

- 26 year old male
- Presents with episode of syncope
- No history of heart disease
- Family history of uncle and grandmother with premature death in 40-50’s

Case #3 (HCM): Physical Exam

BP = 90/70   P = 60   RR = 18   T= 37°
- Gen: WD/WN, in NAD
- Neck: JVP to 8cm with prominent “v” wave
- Chest: clear lung fields
- Heart: PMI in 5th intercostal space, midclavicular line, RRR, S1 + S2, S4, III/IV holosystolic murmur at apex radiating to axilla
- Abd: mildr right upper quadrant tenderness, liver 14 cm in span.
- Ext: trace ankle edema

Case #3 (HCM): Laboratory Testing

- White blood count = 6.5
- Hemoglobin /Hematocrit = 13 / 39
- Sodium = 135
- Blood urea nitrogen 20 mg/dl, Creatinine = 1.0 mg/dl
- B- type naturetic peptide = 227 pg/ml
Who Does HCM affect?

- 1 in 500 people (most common genetic cardiovascular disease)
  - Incidence is about 0.2% to 0.5% of general population.
- An estimated 600,000 to 1.5 million Americans have HCM.
- HCM can present at anytime in any age of life
- Most people are not aware they have HCM because symptoms can go unnoticed and most people with the disease live healthy, normal lives.
Pathophysiology of HCM

- Systole
  - dynamic outflow tract gradient
- Diastole
  - impaired diastolic filling, ↑ filling pressure
- Myocardial ischemia
  - ↑ muscle mass, filling pressure, O2 demand
  - ↓ vasodilator reserve, capillary density
  - abnormal intramural coronary arteries
  - systolic compression of arteries
- Mitral Regurgitation
- Arrhythmias

Symptoms of HCM

- Chest pain
- Fainting, especially during exercise
- Light-headedness or dizziness, especially after activity or exercise
- Palpitations
- Shortness of breath
- Fatigue, reduced activity tolerance
- Shortness of breath
- Heart failure

HCM: Obstruction and Mitral Regurgitation

Clinical Manifestation of HCM

- Asymptomatic, echocardiographic finding
- Symptomatic
  - dyspnea in 90%
  - angina pectoris in 75%
  - fatigue, pre-syncope
  - syncope ↑ risk of SCD in children and adolescents
  - palpitation, PND, CHF, dizziness less frequent

Presentation of HCM

- Hypertrophic Cardiomyopathy
  - Asymptomatic
  - Sudden death
  - Angina
  - Dyspnea
  - Syncope

Physical exam in HCM

- Apex localized, sustained
- Palpable S4
- Tripple ripple
- Prominent “a” wave
- Rapid upstroke carotid pulse, “jerky” bifid (spike-and-dome pulse)
- Harsh systolic ejection murmur across entire precordium → apex & heart base
- MR: separate murmur: severity of MR related to degree of outflow obstruction
**Genetics of HCM**

- First discovered in the 1950s
- Autosomal dominant trait
  - Mutations in genes that encode one of the sarcomere proteins including
  - >400 mutations in these genes.
  - Frequency
    - 45% of mutations occur in β myosin heavy chain gene
    - 35% involve cardiac myosin binding protein C gene.

**HCM - Genetics**

- Autosomal dominant disease
- Males and females equally affected.
- 50% of the offspring of affected individuals will be at risk for inheriting the gene and developing disease
- In any one family, all members have the same mutation
- Onset of clinical symptoms is delayed until adolescence or early adulthood
- Clinical features somewhat predictive of sudden death
- Certain mutations are highly predictive of sudden death

**HCM Sarcomere Genes**

<table>
<thead>
<tr>
<th>Gene Symbol(s)</th>
<th>Gene Name</th>
<th>Disease Phenotype</th>
<th>Frequency in Patients with HCM</th>
</tr>
</thead>
<tbody>
<tr>
<td>MYH7</td>
<td>β-Myosin heavy chain</td>
<td>Mild or severe DCM, DCMX, non-compaction CM, hypertrophic necrosis</td>
<td>25 - 35%</td>
</tr>
<tr>
<td>MYBP3</td>
<td>Cardiac myosin-binding protein 3</td>
<td>Expression similar to MYH7, late-onset</td>
<td>30 - 50%</td>
</tr>
<tr>
<td>TNNT2</td>
<td>Cardiac tropomyosin 3</td>
<td>Mild hypertrophy, cardiac death, DCM, DCMX</td>
<td>&lt;10%</td>
</tr>
<tr>
<td>TNND</td>
<td>Cardiac troponin 1</td>
<td>Extensive intracellular heterogeneity, no sudden death without severe disease; restricted contractility, increased wall thickness</td>
<td>&lt;10%</td>
</tr>
<tr>
<td>TPM1</td>
<td>Tropomyosin 1</td>
<td>HCM and DCMX, Variable prognosis, sudden death</td>
<td>&lt;10%</td>
</tr>
<tr>
<td>ACTC</td>
<td>α-Cardiac actin</td>
<td>Malignant hypertrophy, Adult onset dilated DCM, low prevalence</td>
<td>&lt;10%</td>
</tr>
<tr>
<td>MYL3</td>
<td>Essential myosin light chain 3</td>
<td>Skeletal myopathy</td>
<td>Rare</td>
</tr>
<tr>
<td>MYL2</td>
<td>Regulatory myosin light chain 2</td>
<td>Skeletal myopathy</td>
<td>Rare</td>
</tr>
<tr>
<td>TNNC1</td>
<td>Troponin C</td>
<td>HCM</td>
<td>Rare</td>
</tr>
</tbody>
</table>

**Other Causes of Left Ventricular Hypertrophy**

- Clinical mimics
  - Glycogen storage,
  - Amyloid
- Genetic
  - Noonan’s
- Exaggerated physiologic response
  - Afro-Caribbean hypertension
  - Old age hypertrophy
  - Athlete’s heart

**Causes of Sudden Death in Young Athletes**

- HCM
  - Can be asymmetric
  - Wall thickness: > 15 mm
  - LA: > 40 mm
  - LVDD: < 45 mm
  - Diastolic function: always abnormal

- Athletic heart
  - Concentric & regresses
  - < 15 mm
  - < 40 mm
  - > 45 mm
  - Normal

**Differential Diagnosis Between HCM and Athlete’s Heart**

- HCM
- Athletic heart

- Can be asymmetric
- Wall thickness: > 15 mm
- LA: > 40 mm
- LVDD: < 45 mm
- Diastolic function: always abnormal

- Concentric & regresses
- < 15 mm
- < 40 mm
- > 45 mm
- Normal
Natural History/Prognosis of HCM

- Annual mortality 3% in referral centers, probably closer to 1% for all patients
- Risk of SCD higher in children may be as high as 6% per year
  - Majority have progressive hypertrophy
  - Adolescents - 4-6% SCD per year
  - Infants (less than 1 yr old), mortality = 50%
- Clinical deterioration usually is slow
- Progression to DCM occurs in 10-15%

Risk Factors for Sudden Death in HCM

- Massive LVH (e.g > 30 mm)
- Family history of sudden death
- Unexplained/recurrent syncope
- Nonsustained VT (Holter Monitoring)
- Drop in blood pressure during exercise
  - ? Genetic mutations prone to SCD

Br Heart J 1994; 72:S13

Risk Stratification in HCM

Management of HCM

Case #4 (ARVD): History

- 48 year old male with recurrent syncope and mild-moderate shortness of breath
- PMHx: None
- Family History: Father, uncle has sudden cardiac death
- Recurrent syncope over last 5-10 years, with episodes notable occurring during physical exertion (e.g. playing tennis)
- Successfully resuscitated during one of these episodes.
- Currently NYHA Class II
- Had extensive evaluation including following.

Case #4 (ARVD): Physical Exam

BP=100/70  HR=60  RR=16  T=98.6°  SaO2=100%
- Gen: WD/WN, in NAD
- Skin: warm
- HEENT: NC/AT; EOMI; PERRL
- Neck: elevated JVP to 12cm with rapid large v wave
- Chest: clear to auscultation
- Heart: PMI in 5th intercostal space, RRR, S1 + S2, RV heave in subxiphoid space, RVS3
- Abd: NT; +BS, liver 2 finger breaths below CM, 14 cm in span and pulsatile
- Ext: 1+ lower extremity edema bilaterally to calf, prominent varicose veins
Case #4 (ARVD): Laboratory Data

• Hemoglobin /Hematocrit = 12 / 36
• Blood urea nitrogen 42 mg/dl, Creatinine = 1.4 mg/dl
• Total bilirubin = 2.2, Direct billirubin 0.6
• Alkaline Phosphatase 124, GGTP = 450
• B- type natriuretic peptide = 875 pg/ml
• Troponin I = <0.02

Case #4 (ARVD): Chest X-Ray

Case #4 (ARVD): EKG

• Incomplete or complete RBBB
• Inverted T waves in the anterior precordial leads
• Localized prolongation of the QRS complex in leads V1 and V2
• Epsilon waves visible as sharp discrete deflections at the terminal portion of the QRS complex in the anterior precordial leads

Case #4 (ARVD): Ventricular Tachycardia

Case #4 (ARVD): MRI

Case #4 (ARVD): Cardiac Catheterization

• Left dominant circulation
• Left Main = no disease
• RCA = proximal 20% stenosis
• LAD = no disease
• LCx = mild diffuse disease
• Left ventricular function low normal
• No mitral regurgitation
• Right Atrium = 12 mmHg
• Right Ventricle = 30/12 mmHg
• Pulmonary Artery = 30/14 mmHg
• Pulmonary Wedge = 12 mmHg
• Left Ventricle = 100/10 mmHg
• Aorta = 104/72 mm Hg
• Cardiac Output = 3.4 L/min
• Cardiac Index = 2.4 L/min/m2
ARVC: Diagnostic Criteria

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>MAJOR CRITERIA</th>
<th>MINOR CRITERIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrhythmogenic</td>
<td>Left bundle branch block (LBBB) on EKG (independently of normal heart rate)</td>
<td>`- Torsade de pointes (TdP) or ventricular tachycardia (VT) on Holter monitoring</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>Familial history of premature deaths associated with ARVC (e.g., young adult men)</td>
<td>`- Family history of sudden death (SUD) associated with suspected ARVC</td>
</tr>
<tr>
<td>Genetics</td>
<td>Four genes identified:</td>
<td>Four genes identified:</td>
</tr>
<tr>
<td></td>
<td>- Rykodine receptor - calcium release channel (RyR2)</td>
<td>- Plakoglobin (JUP) - cytoskeletal/adherens-junction protein</td>
</tr>
<tr>
<td></td>
<td>- Desmoplakin (DSM) - desmosomal protein</td>
<td>- Desmin-related myopathy ARVD7</td>
</tr>
<tr>
<td></td>
<td>- Laminin? ARVD5</td>
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</tr>
</tbody>
</table>

**Biologic Basis/Genetics**

**Arrhythmogenic Right Ventricular Dysplasia (ARVD)**

**Arrhythmogenic Cardiomyopathy: Genetics**

- ~50% are familial with Autosomal Dominant transmission.
- Eight genetic loci identified
- Four genes identified:
  - Rykodine receptor - calcium release channel (RyR2)
  - Plakoglobin (JUP) - cytoskeletal/adherens-junction protein
  - Desmoplakin (DSM) - desmosomal protein
  - Desmin-related myopathy ARVD7
  - Laminin? ARVD5
Extensive fatty replacement of myocardium; extending from the epicardium toward the endocardium.

Arrhythmogenic RV Cardiomyopathy:

**Epidemiology**
- Estimated incidence of 1 in 10,000 in US
- Rare cause of sudden death in US (~3%)
- Male predominance
- Increased incidence in some areas
  - In northern Italy, it is an important cause of sudden death accounting for 13 - 20% of all cases

**Arrhythmogenic Cardiomyopathy**

EKG:
- QRS prolongation > 110 msec;
- T wave inversion V2-3;
- Ventricular arrhythmias with LBBB;
- Frequent extrasystoles (>1000/24 hours).
Cardiac MRI:
- Assess ventricle thickness, contractile function, fatty infiltration.
Echocardiography
- Dilation of the RV and outflow tract.
- Reduced global or regional EF
Ventriculography
- Can be helpful in making diagnosis.
- Measure LV filling pressures and cardiac output.

**Arrhythmogenic Cardiomyopathy: Clinical Manifestations**

- Family history of sudden death or VT
- Presents with ventricular arrhythmias
  - Frequent ectopic ventricular beats with LBBB morphology
  - Repetitive extraventricular beats
  - Nonsustained VT
- Syncope
- Congestive heart failure

**Arrhythmogenic Cardiomyopathy: Risk Factors for Sudden Death**

- History of cardiac arrest or syncope
- Markedly abnormal late potentials on EKG
- Marked RV dilation
- Motion abnormalities on echo or angio
- LV involvement or dilation
- Locus 1q42.43 (ryanodine receptor - ARVD2)
Supplemental Materials

Physiology – From Muscle to Chamber Function

Clinical Manifestations

- Reduced exercise tolerance
- Shortness of breath
- Congestion / Fluid Retention
- Difficulty in sleeping
  - Orthopnea
  - PND
- Weight loss

Signs

- JVP/ HJ reflux
- Rales / Pleural effusions
- Gallops (S3 and S4)
- Hepatomegaly / Ascites
- Edema
- Cool Extremities
- Pulses Alternans / Bifid Pulse

Goals of Treatment

1. Identification and correction of underlying condition causing heart failure.
2. Elimination of acute precipitating cause of symptoms.
4. Improve long term survival.

Treatment by Stage
Ventricular Remodeling

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

Pharmacologic Treatment

- ACE Inhibitors
- Beta Blockers
- Diuretics
- Angiotensin Receptor Antagonists
- Digoxin
- Vasodilators
- Inotropes

Diuretics for Heart Failure

LV Non-Compaction

Nuerohormonal Antagonism

LV Non-compaction histology – Trichrome stain
Noncompaction of the ventricular myocardium

- “Persistence of spongy myocardium”
- Depressed ventricular function, normal LV volume, increased LVEDP, systemic embolism, ventricular arrhythmias
- May be isolated - or - associated with other anomalies: Pulmonary atresia with intact septum; AS (bicuspid); cardiac fibroma; anomalous coronary arteries; common ventricle

Types of Cardiac Amyloid

<table>
<thead>
<tr>
<th>Amyloidosis Type</th>
<th>Protein</th>
<th>Cardiac involvement</th>
<th>Hemodynamic abnormalities</th>
<th>Diagnostic Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary (AC)</td>
<td>Light chain</td>
<td>35%</td>
<td>Hypertrophy, dilatation, arrhythmias</td>
<td>Serum light chain, electrocardiography</td>
</tr>
<tr>
<td>Hereditary (ACS)</td>
<td>Valvular TR</td>
<td>25%</td>
<td>Hypertrophy, dilatation, arrhythmias</td>
<td>TTE, echocardiography, serum amyloid A levels</td>
</tr>
<tr>
<td>Acquired (ACT)</td>
<td>TTR</td>
<td>10%</td>
<td>Hypertrophy, dilatation, arrhythmias</td>
<td>TTE, echocardiography, serum amyloid A levels</td>
</tr>
</tbody>
</table>

Hemodynamic Subtypes of HCM

- Subaortic obstruction
- Cavity obliteration
- Midventricular obstruction

Types of HCM

- Hypertrophic cardiomyopathy: 65%
- Hypertrophic nonobstructive cardiomyopathy: 35%
- Hypertrophic obstructive cardiomyopathy: 10%

Hypertrophic Cardiomyopathy

- Sarcomeric Protein Mutations
- Non-Sarcomeric Mutations
  - AMP-Kinase (PRKAG2)
  - Lam2 (Danan)

Brockenbrough Sign

Cardiac Catheterization of HCM

EKG: HCM

Supplemental Case: Physical Exam

BP = 160/90, HR = 94, RR = 22, T = 98.9'

Well developed, well nourished
Mild - moderately short of breath
JVD at 15 cm, with a large "v" wave
Decreased breath sounds at both bases with overlying rales 1/3 up bilaterally
PMI displaced laterally and inferiorly, regular cardiac rhythm, S3 gallop, III/IV holosystolic murmur
Soft, with mild RUQ tenderness, liver 2 cm below costal margin, 2+ pitting edema to ankles.

Supplemental Case: Laboratory Data

Laboratory analysis showed:

- Hemoglobin of 12.4 gm/dl, hematocrit of 37%
- Serum sodium = 136 meq/L
- BUN = 36 mg/dl
- Creatinine = 1.4 mg/dl
- B-type naturetic peptide = 670 pg/ml
Supplemental Case: EKG

Supplemental Case: CXR

Supplemental Case: History

• 53 year old African American male
• History of HTN for at least 15 years and Diabetes for 10 years
• Now presents with:
  - Exertional intolerance
  - Increasing abdominal girth
  - Peripheral edema
  - Nightly paroxysmal nocturnal dyspnea

Supplemental Case: Echocardiogram

Questions

1. What class of cardiomyopathy (DCM, RCM, HCM) does this patient have?
2. What is the primary pathophysiologic mechanism of heart failure?
3. What is the utility of endomyocardial biopsy?

Endomyocardial Biopsy in IDCM

Normal

DCM: Myocyte hypertrophy with interstitial fibrosis
Endomyocardial Biopsy in IDCM

Myocyte hypertrophy
(very enlarged and irregular nuclei)

Decreased Contractility