HEART DISEASES

APPROVED

CONGENITAL HEART DISEASE

INFLAMMATORY AND VALVULAR HEART DISEASE

ISCHEMIC HEART DISEASE and SUDDEN CARDIAC DEATH

CARDIOMYOPATHY: HYPERTENSIVE, HYPERTROPHIC, AND DILATED
ISCHEMIC HEART DISEASE

ISCHEMIC HEART DISEASE (IHD)
CORONARY HEART DISEASE (CHD)
CORONARY ARTERY DISEASE (CAD)
ATHEROSCLEROTIC HEART DISEASE (ASHD)

Synonymous terms referring to syndromes resulting in and from myocardial ischemia
Percentage Breakdown of Deaths From Cardiovascular Diseases
United States: 2003*

Source: CDC/NCHS and NHLBI. *Preliminary
ISCHEMIC HEART DISEASE

Although atherosclerosis of the coronary arteries is the most common mechanism responsible for myocardial ischemia, other less common mechanisms can also cause ischemia. These include:

• Coronary emboli
• Coronary spasm (incl. toxic)
• Complications of connective tissue disorders
Atherosclerosis Risk Factors:

Genetics
Cigarette smoking
Hypertension
Diabetes mellitus
Dyslipidemias
Inflammation

Know the risk factors of patients.
MAJOR SYNDROMES

ANGINA PECTORIS

STABLE ANGINA

UNSTABLE ANGINA

MYOCARDIAL INFARCT

SUDDEN CARDIAC DEATH

ISCHEMIC CARDIOMYOPATHY

On exertion patient will have chest pain but at night or with nitrates it will go away. Usually due to a critical stenosis, which becomes apparent when the heart needs greater blood flow.

May occur during sleep and does not respond to angina.

When the heart doesn't get good blood and oxygen, the heart doesn't function properly. You will see both functional change and change in heart structure which can affect the mitral valve. If myocardium is ischemic, you can also get mitral regurgitation.
PREVALENCE OF ISCHEMIC HEART DISEASE

13.5 million Americans (7% of adult population) have symptomatic IHD evidenced by:

- Angina Pectoris (50%)
- Previous MI (>50%) … or both

>500,000 deaths/year (one-third of all U.S. deaths) one-third are premature, i.e. before age 75
Sudden Cardiac Death
Definition:

• Natural Unexpected Death Secondary to Cardiac Causes With Rapid Loss of Consciousness

Patient has some cardiac issue that leads to sudden cessation of cardiac function. Arrhythmia, MI, aneurysm

• Risk factors and Existing Disease may be previously documented

Interestingly, you can survive sudden cardiac death. If you are resuscitated or defibrillated, you have survived a sudden cardiac death event. However, most patients will die within 24 hours.
Atherosclerosis: CAD

- 50% of deaths from CAD are SCD

- 50 – 60% of SCD is the first Clinical manifestation of CAD

- 10% of patients with CAD first presentation is SCD
SCD: Incidence

• 300,000-350,000 annually in the U.S.
• 0.1-0.2% per year for > 35 years old
• **Age peaks:**
  – Birth to 6 months (SIDS, congenital)
  – 45-75 years old
    • Teens - 30 yo: incidence is only .001%
• **Gender:**
  – Male: Female 3-7:1 prior to menopause
Etiology: Age Dependent

- > 30 years
  - **Atherosclerosis (ischemia)** ~ 2/3 of SCD
  - **Cardiomyopathies**
    - LVH, HOCM, ARVD, DCM
  - **Myocarditis / Endocarditis / Infectious**
  - **Infiltrative / Storage Disorders**
    - Fabry’s, Hemochromatosis, Sarcoid, Amyloid, Desminopathy
  - **Vascular Disease / Valvular Disease**
    - Aneurysms, Dissections, Cong. Coronary Anomalies
  - **Conduction System/Channelopathies**
    - CHF — may be feature of many prior to “sudden death”
SUDDEN CARDIAC DEATH

ELECTROPHYSIOLOGY: Ventricular Fibrillation, Asystole, PEA

ANATOMIC FINDINGS:

- Acute Coronary Plaque Rupture or Thrombosis (minority of cases)
- Acute or Organizing (clinically silent?) MI (minority of cases)
- No acute lesion but >60% stenosis of a coronary artery, often LAD (1º VF)

If there is asystole, generally you are not going to resuscitate that patient.

Mostly discovered during autopsy

Patient won't know that they have had an MI.
ISCHEMIC HEART DISEASE

The underlying cause of ischemic heart disease is usually atherosclerosis of the coronary arteries.

The most common cause of acute coronary syndromes (unstable angina or acute myocardial infarction) is a sudden increase in luminal narrowing due to thrombosis and/or plaque rupture.
Plaque Rupture and Thrombosis

Acute Arterial Occlusion

Vulnerability to Plaque Rupture

Large Atheromatous Core
Calcification with Erosion
Thin Fibrous Cap/Increased Cap Tension
Inflammation, Foam Cells in Fibrous Cap
Matrix Metalloproteases
Cap Fatigue

If a patient has vulnerable plaques, it's not usually the severity but rather the fact that they have one or more of the conditions on this list, which leads to higher risk of rupture. Can occur at 20-40% stenosis.
Propagation into lumen causes stenosis.

- **Transitional Zone Thrombus**
  - Fibrin
  - Platelets
  - On surface

- **Intraplaque Thrombus**
  - Platelets
  - Red cells
  - Fibrin

- **Intraluminal Thrombus**
  - Fibrin/red cells
  - (Platelets)
Eccentric atherosclerotic plaque with lipid core
Ruptured atherosclerotic plaque with hemorrhage into plaque
Ruptured atherosclerotic plaque with hemorrhage and thrombus on the surface
Ruptured atherosclerotic plaque with hemorrhage and thrombus on the surface.
Plaque Rupture and Thrombosis

Thin cap is ruptured.

Fatty atheromatis material is being exuded into the lumen.
Plaque Calcification

Organizing thrombus.

Calcification down here.
Coronary Artery Calcium Score Combined with Framingham Score for Risk Prediction in Asymptomatic Individuals. JAMA 2004; 291:210-215

**Framingham Score**
is based on the following risk factors: age, gender, diabetes, smoking history, blood pressure, total cholesterol, and LDL cholesterol

**Coronary Artery Calcium Score (CACS)**
is based on CT scan evaluation of coronary calcification

If you have many of these risk factors, you will have a much higher chance of cardiac death. Calcification increases the risk even more.
Triggers of SCD

**Exertion: 6-30%**
- CAD/ plaque rupture; Neurogenic conditioning
- < weekly exercise: 75x risk, > 5/week: 11 x risk
- Overall: 1 SCD per 1,510,000 severe exertions

**Sleep: 12%**
- Increased occurrence for nonstructural disease

**Stress**

**Sexual Activity:**
- Low even with CAD
Ischemia: How does it Kill?

- Arrhythmia (VF/VT) – 2 Phases:
  - Substrate and Trigger
  - 1A: $2 - 10$ minutes post occlusion
    - Altered extracellular $K^+$ affects refractory periods
    - Injury Currents – normal cells reexcite prematurely
  - 1B: $18 - 30$ minutes post occlusion (greater role)
    - Epicardial cells demonstrate depression of excitability before mid and subendocardial cells
    - Electrical signals produced by unequal stretching of cells at border of ischemic zone
Ischemia: How does it Kill?

Later deaths

- Infarcts – Prior scar creates reentry paths
  - Autonomic Denervation
    - Baroreflex Sensitivity: Vagal protection loss
    - Nerve “Sprouting”: sympathetic reinnervation post MI demonstrated with marker studies.

- Ventricular Dysfunction - ↓ LVF, Regurg

Lose the ability of the vagus nerve to tell the heart to chill out.

Overgrowth of sympathetic nerves that stimulate the heart.

When you have death of a bunch of myocardial cells.
MANAGEMENT OF ACS RELATED SUDDEN CARDIAC DEATH

Prevention of IHD (Risk factor control)

Identification of High Risk Patients

Prophylactic drug therapy (β blockers)

Implantable automatic defibrillator

Rapid Resuscitation (each minute of VF decreases survival rate by 7-10%)
ISCHEMIC HEART DISEASE

Pathology of Myocardial Infarcts

Heart will undergo coagulative necrosis first, then there is inflammation then there is cleanup by macrophages and scar formation.
Patient Prognosis is Inversely Related to Infarct Size

Larger Infarcts:
- Higher frequency of arrhythmias
- Higher frequency of hemodynamic complications
- Higher short-term mortality

Cardiogenic Shock is usually associated with infarcts occupying > 30% (mean = 40%) of the Left Ventricle
Gross Pathology: Determinants of Infarct Size

Size of the Vascular Territory involved (Area at Risk)

Larger infarct if the occlusion is proximal rather than distal because it supplies a larger territory.

Duration of Ischemia: Wavefront Phenomenon

Magnitude of Collateral Blood Flow to the Area at Risk

Can slow down the progression of an MI

Metabolic Rate of Myocardium during Ischemia

- Hemodynamic Determinants - Heart rate, Systolic LV pressure, Contractile state
- Myocardial Temperature

How hard was the heart working before losing blood flow? In a person that was sleeping it will take longer for the infarct to develop, than if the person was exercising.
Prior to this people though the whole area perfused by a certain artery dies off at the same time. The Duke researchers showed that it progresses as a wavefront starting from the endocardium, which gets blood flow last, and is under more stress so requires more oxygen. Then the infarct progresses to the epicardium.
1.) They found it takes between 3-6 hours for an infarct to become transmural, which means to cover a majority of the space from the inner to the outer wall.

2.) That's why you rush people in the ER with an infarct to the cath lab because you have a small window where you can save some myocardial tissue. Collaterals can extend this window even more.
Relationship between Collateral Flow and Infarct Size

Collateral flow is highest in the outer layer of the myocardium; if collateral flow is high enough, the infarct will not be transmural regardless of duration.

Gradual stenosis of a coronary artery promotes the development of collateral circulation.

Some patients with virtually complete occlusion of a major coronary artery do not have an infarct.
Collateral Flow in Different Layers (inner third, middle third, outer third) of the Myocardium following Coronary Occlusion
Dating Myocardial Infarcts

• Importance
  – Potential for intervention/myocardium salvage
  – Forensic: Cause of death vs. Contributing Factor
  – Medico-legal: Assess Negligence

• Assessment
  – History: Risk Factors, HPI, Physical Exam, Labs
  – Gross: Autopsy > Surgical Specimens
  – Histology: Routine and Special Stains
MI: Gross Appearance

• **REPERFUSION? – Key question**
  - Pallor vs. Hemorrhage
  - Timing of Reperfusion/Ischemia
  - Border vs. Central Healing

• **Acute findings**
  - **May be absent**
  - Pallor or hemorrhage
    - Inflammation → Myophagocytosis

• **Subacute**
  - Granulation tissue
  - Mummified myocytes

• **Advanced healing – Mature fibrous scar**
  - Fatty change – mesenchymal differentiation
<table>
<thead>
<tr>
<th>Time Interval</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 6 hours</td>
<td><strong>No Change</strong> (Gross or Microscopic)</td>
</tr>
<tr>
<td>6 - 24 hours</td>
<td>+/− “Wavy-fiber Change” Early features of <strong>Coagulative Necrosis</strong> (Cytoplasmic eosinophilia; Nuclear pyknosis followed by karyolysis)</td>
</tr>
<tr>
<td>1 - 4 days</td>
<td>Coagulative Necrosis with <strong>Acute Inflammatory Response</strong> (mostly neutrophils) - maximum influx at 2 - 3 days; neutrophils intact at first, disintegrating by 3 - 5 days</td>
</tr>
<tr>
<td>5 - 7 days</td>
<td><strong>Macrophage Activity</strong> (phagocytic removal of dead myocytes, pigmented macrophages increasing)</td>
</tr>
<tr>
<td>7 - 10 days</td>
<td>Developing peripheral rim of <strong>Granulation Tissue</strong></td>
</tr>
<tr>
<td>1 - 6 weeks</td>
<td>Progressive <strong>Organization</strong> of infarct</td>
</tr>
<tr>
<td>1 - 3 months</td>
<td>Progressive <strong>Collagen Deposition, Mature replacement scar</strong></td>
</tr>
</tbody>
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*Consider Variable Reperfusion, Interventions and Infarct Size*
Dating Myocardial Infarcts

Who cares?
Case

• 47 yo male with a history of hypertension, tobacco abuse presents with reported new onset chest pain.

• He is worked up for cardiac as well as pulmonary and GI disease.

• An ECG and Cardiac enzymes are eventually performed and are noted to be positive 12 hours after admission.

• The patient is taken for cardiac catheterization where a thrombus in the LAD is treated with angioplasty and stenting. Did the right thing, but somewhat delayed.

• The patient has continued low ventricular function and succumbs that night to severe cardiogenic shock.
Now Who Cares?
Who **REALLY** Cares?
Pathology Scenario A
Acute MI

Pallor with hyperemic border
H&E stained section of subendocardium with hypereosinophilic necrotic myocytes, separated from the endocardium by a layer of intact myocytes.

Viable myocardium under endocardium surface because oxygen can directly diffuse into these cells from the ventricular chamber.

More viable cells
Acute MI

Hypereosinophilia

More pink, loss of nuclei,

Contraction bands

Contraction band, can have them in infarcts that aren't completely reperfused.

Contraction bands
RESULT:
Pathology Scenario B
3-4 day old myocardial infarct with early karyolysis and numerous neutrophils
Subacute posteroseptal infarct (yellow discoloration)
Granulation tissue repair at the interface between viable and necrotic myocytes
Organizing anteroseptal MI; healed posteroseptal MI with aneurysmal thinning
Healed posteroseptal MI with aneurysmal thinning

Old infarct that was not recognized by patient or physician
RESULT:

Pathologic findings indicate infarct was maximal size at time of presentation to ER.

Possibly also shows prior large healed infarcts.

“The Miscarriage of Justice”
REPERFUSION

1. Accelerates disintegration of irreversibly injured myocytes (causes contraction band necrosis)

2. May accentuate hemorrhage into areas of microvascular injury (causes hemorrhagic infarct)

3. May or may not cause lethal reperfusion injury

4. Limits myocardial infarct size if early enough

5. Supports slow metabolic and contractile recovery of viable myocytes (stunning)

Cells that are not fully injured become irreversibly injured by reperfusion bc of stimulation of Nitric oxide and physical obstruction.
Acute anteroseptal MI with hemorrhage following late thrombolytic therapy
Interventions to Limit Myocardial Infarct Size

Restoration of Myocardial Perfusion

- Thrombolytic Therapy
- Emergency Coronary Angioplasty

Adjunctive Therapy

- To delay lethal myocyte injury until reperfusion has been achieved
- To prevent lethal reperfusion injury
Myocardial Infarction - Mortality & Morbidity

Acute In-hospital Mortality - 7%
One Year Mortality - 35%

Arrhythmias - 40 - 50 % of deaths

Pump Failure - 40 - 45 % of deaths
  • Cardiogenic Shock
  • Congestive Heart Failure - 20 % of patients surviving MI develop CHF

Other Complications
  • Rupture - LV free wall, interventricular septum, or papillary muscle
  • Mitral insufficiency
  • Ventricular Aneurysm
  • Mural Thrombosis
Acute infarct of the lateral wall of the left ventricle with rupture of the wall
Ruptured papillary muscle following acute MI

Leads to acute mitral regurgitation and patients end up dying of pulmonary edema.
Healed transmural apical infarct of the left ventricle with aneurysm and laminated mural thrombus in the apex
Cardiomyopathies

dysfunction of the heart muscle itself.

- LVEF most powerful risk stratifier
  - $\leq 30\%$ improved survival with ICD placement

- Ischemic:
  - Scarring
    - Arrhythmia
    - Aneurysm
    - CHF
Hypertrophic Cardiomyopathy

- Classic Form – Asymmetric vs Concentric
- Incidence 0.2%
- Genetics: Cardiac sarcomere proteins:
  - β myosin heavy chain
  - Myosin binding protein C
  - Cardiac troponin T and I (↑ SCD)
  - α-tropomyosin
- Frequently autosomal dominant with 55% penetrance by age 30
- Phenotypes may be markedly different

Involves septum more than the ventricle.

Different in terms of extent of fibrosis and enlargement

- These are the athletes that die suddenly.
  - Shows up at a pretty young age.
Hypertrophic Cardiomyopathy: Gross

Asymmetric

Thickness $> 3.0$ cm high risk

*But Majority of SCD at lesser thicknesses

Degree of LVOT obstruction

Treatment is to go in and shave the muscle down.

Large lump of muscle blocks outflow into the aorta.
Hypertrophic Cardiomyopathy

- **Histology:**
  - Myocyte hypertrophy
  - Disarray
  - Fibrosis
  - Small vessel disease

**Degree of hypertrophy and fibrosis is variable**

“Burnt out” phase – fibrosis with wall thinning
Screening?

• Practical only when limited by Family History

• Risk SCD in HS athletes 0.46/100,000

• USAF basic training 1.2/100,000

• Italian study suggests benefits to ECG screening of athletes – Only subset with identifiable hypertrophy prior to risk SCD
Other Hypertrophic CM’s

• **HYPERTENSIVE**
  – **Concentric**, requires ↑ preload
  – Increased susc. to ischemia/hypoxia

• **Storage Disorders** – enzyme deficiencies:
  – Fabry’s disease (α-galactosidase)
  – Pompe’s disease (α-1,4-glucosidase)
  – Other Glycogen Storage Disorders
    • LAMP2 (Danon’s disease)
    • PRKAG2
    • Both associated with VF/VT with hypertrophy and diminished extracardiac lesions

All can lead to hypertrophy and sudden cardiac death.

Often time heart is the only organ affected.
Dilated Cardiomyopathy

- Less well-delineated causes
- Less unexpected sudden death though can occur with arrhythmias

- Myocarditis “inflammatory cardiomyopathy”
  - Enterovirus, Adenovirus, Influenza, HIV
  - Protozoan – Toxoplasma, Trypanosoma (Chagas)

- Toxic: Alcohol, Iron
Cardiomyopathy: ARVD

- Arrhythmogenic Right Ventricular Dysplasia
  - Fibrofatty replacement with thinning
    - “Triangle of Dysplasia”: Inflow, outflow, apex
  - **Frequent VT in young adults**
  - If survive may progresses to RV failure
  - Ultimately involves LV failure

Major and Minor Criteria include Gross, EP, Hx
From gross picture:
- Starts at apex of RV and can spread to LV as well.

ARVD

Transmural replacement with fatty tissue.

No treatment other than giving patient a defibrillator to keep them alive. Some will go to transplant.
Genetic Arrhythmias: No anatomic Cause
Ion channels

- **Long QT Syndrome**: Torsades, SCD in youth
  - 7 mutations identified. Some with associated syndromes
- **Brugada Syndrome**: ↑ST in right leads, RBBB
  - SCD in 20-30’s often during rest/sleep
  - Cardiac sodium channel genes, *SCN5A* (LQT3), *KCNQ1* gene in forms associated with AF
- **Catecholaminergic VT**: Dom and recessive
  - CA⁺⁺ channel protein Ryanodine and CA⁺⁺ regulatory proteins.
  - Stress related trigger

For people who suffer SAD and don't have a cause, they take a blood sample and check for these disorders.
Commotio cordis

- Sudden death following precordial impact
- Impact location – directly over heart
- Impact timing - T wave upstroke in window between 15-30 milliseconds prior to apex
  - Potassium channels may play a role
- 2nd leading cause of SCD in athletes behind HCM
Questions?