

ISCHEMIC HEART DISEASE

I. TERMINOLOGY

A. Ischemic Heart Disease (IHD): a spectrum of clinical cardiac disorders occurring when myocardial oxygen demand exceeds oxygen delivery to the myocardium.

B. Coronary Heart Disease (CHD): myocardial ischemia resulting from decreased blood flow through the coronary arteries; accounts for vast majority of IHD.

II. EPIDEMIOLOGY

A. Incidence: heart disease most common cause of death in the U.S.(approx. 40% of all deaths). IHD accounts for 80% of all cardiac mortality (approx. 550,000 deaths/yr.)

B. Risk Factors: IHD risk factors same as those for atherosclerosis.

III. PATHOPHYSIOLOGY

A. Factors determining myocardial oxygen consumption

1. **Increased Contractility -----> Increased oxygen demand**

a. increased by sympathetic stimulation or catecholamine release - exercise, stress, increased metabolic demands

b. decreased by rest, beta adrenergic blockade, calcium channel blockers.

2. **Increased Heart Rate -----> Increased oxygen demand**

a. increased by sympathetic stimulation or catecholamines

b. decreased by rest, beta adrenergic blockade, calcium channel blockers

3. **Increased Ventricular Wall Tension -----> Increased oxygen demand**

a. increased by

(1) ventricular dilatation - muscle damage, volume overload

(2) increased ventricular pressure - hypertension, outflow obstruction

b. decreased by use of nitrates or calcium channel blockers

(1) reduce preload - decrease ventricular end-diastolic volume by causing venous dilatation with peripheral pooling of blood

(2) reduce afterload - decrease ventricular pressure by causing arterial dilatation

4. **Increased Ventricular Wall Thickness(Hypertrophy) -----> Increased oxygen demand**

5. **Regional Factors**

a. left ventricle has highest oxygen demands

b. subendocardium most susceptible to ischemia

B. Factors determining myocardial oxygen supply

1. **Coronary Artery Blood Flow - single most important factor; in turn depends on:**

a. coronary artery status

(1) **normal** - coronary artery reserve - ability to increase flow to meet the demands of exercise (note: myocardial oxygen extraction is already near maximum at rest)

(2) **pathologic** - coronary artery stenosis

(a) **50-75% reduction in diameter (75-90% reduction in cross-sectional area) - flow adequate at rest, but cannot meet demands of exercise**

(b) **critical stenosis (> 75% reduction in diam., > 90% reduction in CSA) - point at which coronary flow is decreased at rest**

(3) **collateral blood flow - alternative blood supply may develop to an area of poorly perfused myocardium when stenosis of the supplying vessel develops gradually; this collateral blood supply may be protective when the usual feeding vessel becomes totally occluded**

b. hemodynamic factors

(1) systemic blood pressure

(2) aortic valve status

2. **Oxygen carrying capacity of blood - e.g.. may be decreased in anemia, carbon monoxide poisoning**

IV. PATHOLOGY OF ISCHEMIC HEART DISEASE

A. Coronary artery lesions

1. **Atherosclerosis: accounts for $\geq 90\%$**

a. sites

- (1) epicardial portion of vessel
- (2) LAD > distal RCA > L CIRC
- b. pathology of plaques
 - (1) often mainly fibrous, little lipid
 - (2) usually $\geq 75\%$ stenosis of at least one vessel
- c. what triggers acute event?
 - (1) thrombosis due to complication/acute change in plaque (ulceration, fissure)
 - (2) hemorrhage into plaque
 - (3) vasospasm
 - (4) hypotensive episode
- d. sites: epicardial portion of artery; proximal LAD > distal RCA > proximal L CIRC
- 2. Thrombosis: thrombosis superimposed on atherosclerosis leads to sudden, complete occlusion in huge majority of cases
- 3. Vasospasm:
 - a. may cause acute decrease in coronary flow in atherosclerotic or normal vessels
 - b. probable mechanism of ischemia in Prinzmetal's angina and cocaine abuse
- 4. Uncommon causes of decreased coronary flow - together account for < 10% of cases
 - a. emboli
 - b. arteritis
 - c. coronary artery dissection/aneurysm
 - d. ostial stenosis (e.g. syphilis)
 - e. anomalous coronary anatomy

B. Locations of infarcts

1. LV >> RV; RV infarction can occur with massive infarct also involving LV, but isolated RV infarction is very rare

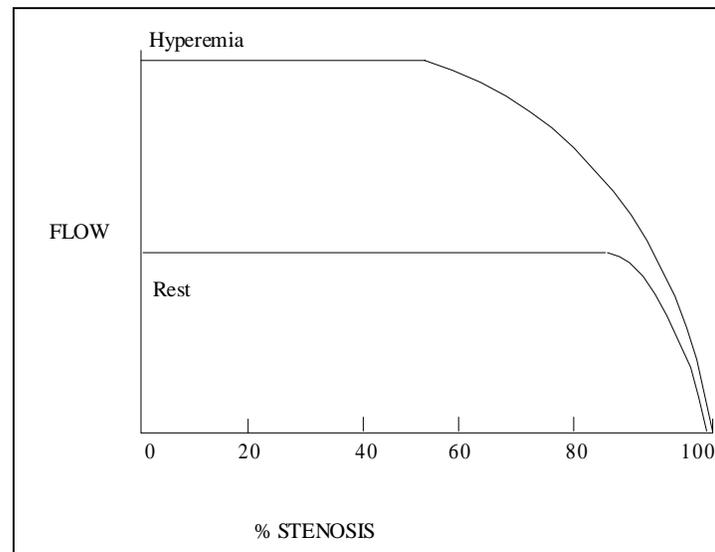
<u>Occlusion Site</u>	<u>Infarct Site</u>	<u>Frequency</u>
LAD	anterior LV near apex; anterior 2/3's of septum	40 - 50%
RCA	posterior LV; posterior 1/3 of septum (\pm RV)	30 -40%
L CIRC	lateral LV	15 - 20%

Note: Occlusions involving the left main coronary artery or the presence of triple vessel disease are likely to cause the most extensive infarction and, therefore, have the gravest clinical implications.

3. Infarction at a Distance/Paradoxical Infarction - gradual occlusion of one coronary artery leads to development of collateral flow from a second vessel to its normal area of supply; when this second coronary becomes occluded infarction occurs in the region originally supplied by the first coronary artery

C. Size of infarct

1. 2 classes based on thickness of wall involved
 - a. subendocardial - < 50% of wall thickness
 - (1) most susceptible region to ischemia (note: narrow rim of preserved fibers just beneath endocardium)
 - (2) may occur with hypotension or vasospasm superimposed on atherosclerosis
 - b. transmural - > 50% of wall thickness; subendocardium always included
2. Collateral flow limits size of infarct
3. Extension of an infarct - increase in amount of necrotic muscle due to reduction in oxygen supply to a larger area occurring at a later time
4. Expansion of an infarct - attenuation of necrotic muscle fibers causes apparent



**enlargement of the originally infarcted area
without death of any additional muscle**

D. Gross/Microscopic Appearance

1. Types of necrosis

a. coagulation necrosis

(1) appearance: homogeneous deep pink cells; outlines preserved; loss of cross-striations; karyolysis

(2) setting: persistent lack of perfusion

b. contraction band necrosis

(1) appearance: transverse deep pink bands; blood extravasation

(2) site: periphery of infarct

(3) setting: ischemia followed by reperfusion; irreversibly injured cells are reperfused and die in hyper-contracted state

2. Time course

a. depends on size of infarct

b. all changes proceed from periphery inward

3. Sequence of morphologic changes:

<u>Time After Occlusion</u>	<u>Gross Path</u>	<u>Microscopic Path</u>
0-6 hours*	None	? Wavy fiber change
6-12 hours	None	Early coagulation necrosis (hypereosinophilia)
12-24 hours	Pallor + Congestion	Continuing coagulation necrosis; peripheral neutrophil infiltrate
24-72 hours	Yellow	Total coagulation necrosis with loss of nuclei and cross-striations; dense neutrophil infiltrate
3-7 days	Soft yellow center Hyperemic border Slight shrinkage	Macrophages replace neutrophils; necrotic muscle resorbed from periphery inward; granulation tissue at periphery
10-21 days	Gray, translucent Shrinkage	Macrophages; granulation tissue; fibrosis progressing from periphery inward
6 wks- 1 yr	Scar, Full tensile strength at one year	Replacement of cardiac muscle by fibrous tissue

*Early ischemic change (less than 6 hours) can be detected by histochemistry (tetrazolium test for lactate dehydrogenase) and electron microscopy.

Histologic Progression of Myocardial Infarction								
Time	Necrotic Muscle	PMN's	Blood Vessels	Macrophages	Eos	PC/LC	Fiber Removal	Collagen
12 hours	++	±	0	0	0	0	0	0
1 day	+++	+	0	0	0	0	0	0
2 days	++++	+++	0	0	0	0	0	0
3 days	++++	++++	0	0	0	0	0	0
5 days	++++	++++	+	+	0	0	+	0
7 days	+++	++	++	++	+	+	+++	+
2 Wk	++	+	+++	+++	++	++	++++	++
3 Wk	+	+	++++	++++	+	++	+++	++
4 Wk	+	0	++++	+++	0	++	++	+++
2 Mos	+	0	+++	++	0	++	+	+++
3 Mos	+	0	++	+++	0	++	+	++++
6 Mos	0	0	+	+	0	+	0	++++
1 Yr or more	0	0	+	+	0	0	0	++++

PMN's = Polymorphonuclear leukocytes; Eos = eosinophils; PC/LC = plasma cells/lymphocytes.
Composite of data from Mallory GK, White PO, Salcedo-Seiger J The speed of healing of myocardial infarction: A study of the pathologic anatomy in 72 cases AM Heart J 16:647, 1939; Lodge-Patch I The aging of cardiac infarcts and its influence on cardiac rupture AM Heart J 13:37, 1951; and Fishbein MC, MacClean D, Maroko PR The histopathologic evolution of myocardial infarction, Chest 73:843, 1976.

V. CLINICAL SPECTRUM OF ISCHEMIC HEART DISEASE

A. Angina Pectoris: severe chest pain caused by transient myocardial ischemia; without clinical, laboratory or pathologic evidence of infarction

1. Stable/typical/exertional angina pectoris

a. most common form

b. pain related to exertion, excitement, stress

c. pathogenesis - stenosing coronary atherosclerosis

d. diagnosis - ST segment depression on EKG; no evidence of myocardial necrosis by lab testing

e. management - relieved by rest and vasodilators

2. Prinzmetal's/variant angina pectoris

a. pain occurs at rest

b. pathogenesis - coronary artery spasm

c. diagnosis - ST segment elevation on EKG

d. management - relieved by vasodilators

3. Unstable/crescendo angina pectoris

a. angina of increasing frequency, duration, severity and requiring less and less exertion to precipitate each attack

b. pathogenesis - progressive atherosclerotic narrowing; possible superimposed platelet aggregation/thrombosis

B. Sudden Cardiac Death

1. Fatal arrhythmia (often ventricular fibrillation) without evidence of myocardial necrosis; usually defined as death within 1 hour of onset of acute symptoms

2. Pathogenesis

a. IHD is major cause - atherosclerosis with critical stenosis in ≥ 1 major vessel \pm acute coronary changes; ? role of vasospasm

b. other causes much less common

(1) aortic stenosis

(2) conduction system pathology

(3) mitral valve prolapse

- (4) myocarditis
- (5) hypertrophic cardiomyopathy
- (6) electrolyte disorders

C. Myocardial Infarction (MI): sudden episode of myocardial necrosis caused by occlusion of an epicardial coronary artery (see below)

1. **Symptoms:** Crushing substernal chest pain, nausea, vomiting, diaphoresis, anxiety.
2. **Diagnosis**
 - a. **Electrocardiogram (EKG) - Q waves, ST segment and T wave changes**
 - b. **Cardiac enzymes – Troponins, CK, LDH, SGOT**
3. **Clinical Course/Complications**
 - a. **Uncomplicated 10-20%**
 - b. **Arrhythmias**
 - (1) **commonest complication (75-95%)**
 - (2) **variable severity - lead to sudden death in 25% of all acute MI's (esp. ventricular fibrillation, asystole)**
 - c. **Congestive heart failure/pulmonary edema (60%)**
 - d. **Cardiogenic Shock (10%) - 70% mortality rate; cause of most in hospital deaths**
 - e. **Mural thrombosis/embolization (15-40%) - major risk is CNS embolus**
 - f. **Cardiac rupture (5%)**
 - (1) **timing - peak at 2 to 10 days post infarction (time of maximal wall softening)**
 - (2) **sites**
 - (a) **free wall ---> hemopericardium/tamponade**
 - (b) **papillary muscle ---> mitral regurgitation**
 - (c) **septum ---> L to R shunt, congestive failure**
 - g. **Ventricular aneurysm - ballooning of fibrous scar; thrombosis common**
 - h. **Pericarditis**
 4. **Mortality**
 - a. **Sudden death (pre-hospital) - 25%; arrhythmias**
 - b. **In hospital - 10%; arrhythmias; congestive failure**
 - c. **Annual (after 1st year) - 10%**
5. **Treatment**
 - a. **Management of stable IHD**
 - (1) **eliminate risk factors: hypertension, hypercholesterolemia, smoking.**
 - (2) **reduce myocardial oxygen demand:**
 - (a) **by decreasing heart rate, preload, afterload**
 - (b) **beta blockers, calcium channel blockers, and vasodilators**
 - (3) **reduce risk of thrombosis: antiplatelet agents, anticoagulants.**
 - (4) **urgically correct lesions: coronary artery bypass grafting, angioplasty, laser**
 - b. **Management of acute myocardial infarction**
 - (1) **limit infarct size**
 - (a) **restore coronary blood flow**
 - **thrombolysis: streptokinase, tissue plasminogen activator.**
 - **percutaneous transluminal coronary angioplasty (PTCA)**
 - **coronary artery bypass grafting (CABG)**
 - (b) **decrease oxygen demand**
 - **eliminate pain**
 - **decrease heart rate, preload, afterload**
 - (2) **prevention and control of arrhythmias**

D. Chronic Ischemic Heart Disease/Ischemic Cardiomyopathy:

1. **Slowly progressive congestive heart failure secondary to progressive ischemic damage to the myocardium; ± history of prior myocardial infarction(s)**
2. **Pathogenesis - coronary atherosclerosis**
3. **Pathology**
 - a. **diffuse myocardial atrophy, brown atrophy**
 - b. **diffuse interstitial fibrosis with larger patchy foci of scarring**
 - c. **myocytolysis**