ISCHAEMIC HEART DISEASE AND MYOCARDIAL INFARCTION.

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I. NORMAL CARDIAC STRUCTURE

A. Anatomy

1. Location and dimensions.

   a. The heart, lying in the middle mediastinal compartment, is enclosed within the pericardial sac. It is the muscular pump for blood. The pericardial sac lined by a serosal membrane, contains up to 30 ml of clear serous fluid, which acts as a lubricant.

   b. Normally, the heart is roughly the size of a fist and weighs about 250 to 300 g in women and 300 to 350 g in men; this weight varies, however, with age, & 250-300 grm in female, nutritional status, and the amount of epicardial (pericardial) fat deposits.
2. **Chambers of the heart.** The heart is divided into four chambers right and left sides, with two chambers (an atrium and a ventricle) on each side.

   a. Blood that has circulated through the body enters the right atrium, from superior and inferior vena cava passes into the right ventricle, and then is delivered to the pulmonary circulation, where it is oxygenated through pulmonary artery.

   b. After oxygenation, blood returns to the heart, entering at the left atrium through pulmonary vein. Blood then passes into the left ventricle and then to the aorta, from which it is circulated to the tissues of the body.
c. The ventricular chambers vary greatly in thickness. The left ventricle normally is about 1.3-1.5 mm thick, whereas the right ventricle is about 0.3-0.5 mm thick.

d. The transport of blood is regulated by cardiac valves: two loose flap-like arterioventricular valves, tricuspid on right and mitral on the left. The two semi lunar valves with three leaflets each. The pulmonary and aortic valves guarding the outflow tracts. The normal circumferences of vulvar opening measures about 12cm in tricuspid, 8.5 in pulmonary, 10cm in mitral and 7.5 in aortic valve.
3. **Blood supply to the heart.** This blood supply is provided chiefly by the two major coronary arteries.

a. **The left coronary artery** originates from the aorta in the sinus of Valsalva, behind the left coronary leaflets. Shortly after its origin, the left coronary artery divides into two main branches.
(1) The first branch, the left anterior descending coronary artery (commonly supplies the left ventricular apex, the medial half of the anterior surface of the left ventricle, a portion of the medial anterior wall of the right ventricle, and the anterior two-third portion of the interventricular septum.

(2) The other branch, the left circumflex coronary artery, supplies blood to the anterolateral wall of the left ventricle and a portion of the posterior wall of the left ventricle and posterior thival of interventricular septum.
b. The right coronary artery originates from the aorta, behind the right coronary leaflet. It supplies a large part of the right ventricle as it passes to the right and then posteriorly along the posterior-inferior heart surface. The right coronary artery commonly provides circulation to the posterior portion of the interventricular septum, to adjacent parts of the posterior left ventricle, and sometimes to the apex of the left ventricle. It also supplies the right atrium.

c. “Dominance” of the coronary circulation is determined by the coronary artery that supplies the posterior descending coronary artery. The coronary arteries are arranged in a right dominant distribution in 70% to 80% of cases.

d. Collateral blood flow. Because the coronary artery “watersheds” are highly variable, coronary blood flow distribution may be slightly different from one person to the next. This distribution becomes important in considering potential pathways for collateral blood flow in coronary artery atherosclerotic diseases.
There are three anatomic pattern of distribution of the coronary supply depending upon which of the coronary arteries cross the crux which is the region on the posterior surface of the heart where all the four cardiac chamber and the interarterial and interventricular septum meet. These

1. Right coronary artery preponderance – most common. Here the right coronary artery supplies blood to the whole of right ventricle, posterior half of the interventricular septum and a part of the posterior wall of the left ventricle by crossing the crux.
2. Balanced cardiac circulation is the next most common frequent where right and left ventricles receive blood supply entirely from right and left coronary arteries respectively. The posterior part of the interventricular septum is supplied by a branch of the right coronary while the anterior part by a branch of left coronary artery.

3. Left coronary artery preponderance. The least fragment where left coronary artery supply blood the entire left ventricle, whole interventricular septum and also supplies blood to part of the posterior wall of right ventricle by crossing the crux.

Coronary vein run parallel to the major coronary arteries to collect blood and drain into coronary sinus.
B. Histology. The cardiac wall has three layers.

1. Endocardium. The endocardium, which lines the inner surface of the heart, consists of a single, thin layer of endothelium overlying a continuous basement membrane covering the inner chambers, cardiac valves, chordae tendonaes and the papillary muscle.

2. Myocardium. The myocardium, the intermediate layer, consists of a unique form of striated muscle termed cardiac muscle, which is embedded in a connective tissue framework with numerous capillaries.
3. **Epicardium.** The epicardium (also called the pericardium) is the outermost cardiac layer, it is lined by a thin layer of mesothelium that rests on a layer of connective tissue, which merges with the connective tissue of the myocardium.

**ISCHAEMIC HEART DISEASE** (also called **coronary artery disease**) is a collective term for various diseases characterized by inability of the coronary arteries to deliver adequate oxygen to meet the needs of the myocardium. The degree of coronary insufficiency, the rapidity of onset, and the degree of collateral circulation determine the nature of the resulting disease; that is, chronic ischaemic heart disease, angina pectoris, myocardial infarction, or sudden death.
A. **Incidence and mortality**

Ischaemic heart disease is by far the most common form of cardiac disease in the industrialized world, where it is the number one cause of death. It is uncommon, however, in less developed areas of the world, such as Africa and China.

B. **Aetiology and risk factors**

I. **Artherosclerosis** of the coronary arteries is by far the leading cause of ischaemic heart disease seen in >90%. The risk factors identified for atherosclerosis essentially are the risk factors for ischaemic heart disease. Table 1 lists the modifiable and unmodifiable risk factors.

1. **Distribution:** Atherosclerotic lesions in coronary arteries are distributed in one or more of the three major coronary arterial trunks, the highest incidence being in the anterior descending branch of the left coronary, followed in decreasing frequency, by the right coronary artery and still less in circumflex branch of the left coronary. About one-third of cases have single-vessel disease, most often left anterior descending arterial involvement; another one-third have two-vessel disease, and the remainder have three major vessel disease.
2. **Location**: Almost all adults show atherosclerotic plaques scattered throughout the coronary arterial system. However, significant stenotic lesions that may produce chronic myocardial ischaemia show more than 75% (three-fourth) reduction in the cross-sectional area of a coronary artery of its branch. The area of severest involvement is about 3 to 4 cm from the coronary ostia, more often at or near the bifurcation of the arteries, suggesting the role of haemodynamic forces in atherogenesis.

3. **Fixed atherosclerotic plaques**: The atherosclerotic plaques in the coronaries are more often eccentrically located bulging into the lumen from one side (Colour plate XIII: CL50). Occasionally, there may be concentric thickening of the wall of the artery. Atherosclerosis produces gradual luminal narrowing that may eventually lead to 'fixed' coronary obstruction. The general features of atheromas of coronary arteries are similar to those affecting elsewhere in the body and may develop similar complications like calcification, coronary thrombosis, ulceration, haemorrhage, rupture and aneurysm formation.
II. Superadded changes in Coronary Atherosclerosis

1. **Acute changes in chronic atheromatous plaque:** Though chronic fixed obstructions are the most frequent cause of IHD, acute coronary episodes are often precipitated by sudden changes in chronic plaques such as plaque haemorrhage, fissuring, or ulceration that results in embolisation of atheromatous debris. Acute plaque changes are brought about by factors such as sudden coronary artery spasm, tachycardia, intraplaque haemorrhage and hypercholesterolaemia.

2. **Coronary artery thrombosis:** Transmural acute myocardial infarction is often precipitated by partial or complete coronary thrombosis. The initiation of thrombus occurs due to surface ulceration of fixed chronic atheromatous plaque, ultimately causing complete luminal occlusion. The lipid core of plaque, in particular, is highly thrombogenic. Small fragments of thrombotic material are then dislodged which are embolised to terminal coronary branches and cause microinfarcts of the myocardium.
3. **Local platelet aggregation and coronary artery spasm:** Some cases of acute coronary episodes are caused by local aggregates of platelets on the atheromatous plaque, short of forming a thrombus. The aggregated platelets release vasospasmic mediators such as thromboxane A2 which may probably be responsible for coronary vasospasm in the already atherosclerotic vessels.
III. Non-atherosclerotic Causes.

a. **Coronary artery spasm** (i.e. spasm of morphologically normal coronary arteries), which may result in variant angina.

b. **Coronary arteritis** (usually caused by polyarteritis nodosa), syphilitic aortitis (which causes obliteration of the coronary orifice), and other inflammatory conditions that significantly impair coronary artery perfusion.

c. **Conditions that increase cardiac work load and oxygen demand** (e.g. increased heart rate, hyperthyroidism catecholamine treatment) or decrease oxygen delivery to the heart (e.g., anemia, hypotension, carbon monoxide poisoning).

d. **Anomalous origin of left coronary artery.**

e. **Chest trauma** (rare cause).

f. **Stenosis of coronary ostia** – can result from extension of syphilitic aortitis or from aortic atherosclerotic plaque encroaching the opening.

g. **Embolism** – rare.

h. **Thrombotic disease** – as hypercoagulability as in shock, polycythaemia, sickle cell disease thrombotic thrombocytopenic purpura.

i. **Aneurysms** – Extension of dissecting aneurysm of the aorta into the coronary along may produce thrombotic coronary occlusion.

j. **Compression** – due to primary or secondary tumor.
C. **Pathogenesis.** Regardless of the eventual outcome, ischemic heart disease almost always begins with atherosclerotic changes in the coronary circulation.

1. Atherosclerosis of the coronary arteries develops like that of other large arteries of the body.

2. Severe or fatal disease often involves a 70% or greater decrease in the diameter of at least one of the major coronary vessels (usually more than one), which correlates with a 90% reduction of its normal cross-sectional area and, thus, a critical decrease in blood flow. Typically, the most severe narrowing occurs in the proximal 2 cm of the left anterior descending coronary artery followed by the anterior and left circumflex coronary arteries.

3. Sudden thrombotic occlusion, probably due to rupture of an atheromatous plaque, appears to be the precipitating event of most acute myocardial infarcts. Endothelial injury and platelet aggregation play a central role in most cases.
D. **Clinicopathological entities**

1. **Chronic ischaemic heart disease**, ischaemic cardiomyopathy or myocardial fibrosis are the terms used for focal or diffuse fibrosis in the myocardium characteristically found in elderly patients of progressive IHD. Such small areas of fibrous scarring are commonly found in the heart of patients who have history of episodes of angina and attacks of MI some years back. The patients generally have gradually developing CHF due to decompensation over a period of years. Occasionally, serious cardiac arrhythmias or infarction may supervene and cause death. ? Etropathogenesis pathologic change.

2. **Angina pectoris** is a clinical syndrome of IHD resulting from transient myocardial ischaemia. It is characterized by raroxyosomal pain in the substrenal or precordial region of the chest which is aggravated by an increase in the demand of the heart and relieved by a decrease in the work of the heart. Often, the pain radiates to the left arm, neck, jaw or right arm.
There are 3 overlapping clinical pattern of angina pectoris with some differences in their pathogeneisis:

i. Stable or typical angina

ii. Prinzmetal's variant angina

iii. Unstable or crescendo angina
i. **Stable or typical angina** is the most common pattern. Stable or typical angina is characterized by attacks of pain following physical exertion or emotional excitement and is relieved by rest. The pathogenesis of condition lies in chronic stenosing coronary atherosclerosis that cannot perfuse the myocardium adequately when the workload on the heart increases. During the attacks, there is depression of ST segment in the ECG due to poor perfusion of the subendocardial region of the left ventricle but there is no elevation of enzymes in the blood as there is no irreversible myocardial injury.
ii. **Prinzmetal's variant angina** is characterized by pain at rest and has no relationship with physical activity. The exact pathogenesis of Prinzmetal's angina is not known. It may occur due to sudden vasospasm of a coronary trunk induced by coronary atherosclerosis, or may be due to release of humoral vasoconstrictors by mast cells in the coronary adventitia. ECG shows ST segment elevation due to transmural ischaemia. These patients respond well to vasodilators like nitroglycerin.

iii. **Unstable or crescendo angina** also referred to as 'pre-infarction angina' or 'acute coronary insufficiency', this is the most serious pattern of angina. It is characterized by more frequent onset of pain of prolonged duration and occurring often at rest. It is thus indicative of an impending myocardial infarction. Multiple factors are involved in its pathogenesis which include: stenosing coronary atherosclerosis, complicated coronary plaques (e.g. superimposed thrombosis, haemorrhage, rupture, ulceration etc), platelet thrombi over atherosclerotic plaques and vasospasm of coronary arteries. More often, the lesions lie in a branch of the major coronary trunk so that collaterals prevent infarction.
Table 1. **Risk factors for Ischaemic Heart Disease (IHD)**

<table>
<thead>
<tr>
<th>Unmodifiable Risk Factors</th>
<th>Modifiable Risk Factors</th>
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<tbody>
<tr>
<td>• Older age (peak ages 65 to 74 years)</td>
<td>Hypertension</td>
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<tr>
<td>• Male gender (prior to age 74 years)</td>
<td>Cigarette smoking</td>
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<tr>
<td>• Family history of premature IHD</td>
<td></td>
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<tr>
<td>• Hypercholesterolemia</td>
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<td>• Diabetes mellitus</td>
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<td>• Obesity</td>
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<tr>
<td>• Physical inactivity</td>
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<tr>
<td>• Psychological factors</td>
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<td>• (“Type A personality”)</td>
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3. **Acute myocardial infarction** refers to irreversible myocardial injury from prolonged ischaemia. The result is coagulative necrosis of the myocardial fibers, with loss of the normal conductive and contractile properties of the affected myocardial tissue. Infarction most frequently involves the left ventricle because its workload is greater than that of the other heart chambers. When right ventricular infarction occurs, it almost always represents an extension of severe left ventricular infarction.
a. **Clinical features**

(1) Myocardial infarction most often is characterized by a sudden onset of chest pain that is similar to the pain of angina but more severe and prolonged, generally lasting more than 15 to 20 minutes, and is unrelieved by nitroglycerin. The discomfort may occur when the patient is relatively inactive and even may awaken the patient from sleep. Sweating, nausea, and vomiting often are present. In many patients, a period of unstable angina precedes acute myocardial infarction.

(2) In some cases, myocardial infarction may be clinically silent or associated with only mild discomfort—particularly in diabetics and in patients who have undergone cardiac transplantation.
b. **Diagnosis.**

With acute myocardial infarction, usually two out of three of the following are present: impressive clinical history of chest pain, ischaemic ECG abnormalities, and elevated cardiac enzymes. The serum levels of creatine kinase (CK) is a highly sensitive marker of myocardial infarction. CK peaks at 12 to 24 hours after infarction. Changes in the serum levels of lactic dehydrogenase (LDH) are also helpful. The serum LDH level remains elevated after the serum CK has subsided (decreased).
c. **Classification.**

Myocardial infarcts commonly are described in two ways: according to the degree of ventricular wall involvement and according to the location within the heart of the specific artery involved.
(1) **Depth of mural involvement**

(a) Most infarcts are transmural, involving at least one-third to half of the ventricular wall thickness. Transmural infarcts usually correspond with the distribution of one of the major coronary vessels, often with associated coronary thrombosis, and they may result in shock, the formation of aneurysms, or cardiac rupture.

(b) Infarcts that involve the inner one-third to half of the ventricular wall are described as subendocardial, or nontransmural. Subendocardial infarcts usually are circumferential; often result from hypoperfusion states (e.g. shock), and rarely result in aneurysms, pericarditis, or rupture. Although severe coronary atherosclerosis usually is present, thrombosis generally is absent.
d. **Pathology.**

(1) **Appearance during the first week postinfarction**

(a) **Macroscopic appearance**

(i) The first grossly visible change—pallor of myocardium—is visible about 15 to 24 hours postinfarction. Hemorrhage may be prominent in patients treated with thrombolytic therapy.

(ii) At 2 to 3 days, the infarct becomes mottled and more circumscribed.

(iii) From 3 to 7 days postinfarction, the necrotic area becomes progressively more apparent, with a soft, yellow-brown central area and a hyperemic border.
(b) Microscopic appearance (Figure 1)
(i) The first histologic sign of infarction, seen at 5 to 12 hours, is the appearance of coagulation necrosis, including loss of cross-striations, cytoplasmic hyaline change and eosinophilia, clumping of nuclear chromatin (nuclear pyknosis), and karyorrhexis. “Wavy myocardial fibers” may be found earlier.

(ii) At 12 to 24 hours, intercellular edema and focal hemorrhages appear, and neutrophils are first seen at the periphery of the infarct.

(iii) Over the next several days, coagulative necrosis becomes more extensive as does the neutrophilic infiltrate.

(iv) At 3 to 7 days, the neutrophilic infiltrate abates, and the number of mononuclear cells progressively increases. Macrophages engulf and destroy the necrotic myocytes.

(v) At the end of the first week, new capillaries and fibroblasts (granulation tissue) are seen at the periphery of the infarct.
(c) **Electron microscopic appearance.** Changes in myocardial cells, including swelling of the mitochondria and endoplasmic reticulum, nuclear pyknosis and early degeneration of the sarcolemma, can be seen within 1 hour after the onset of ischaemia.
(2) **Appearance at 2 and 3 weeks postinfarction.** Removal of necrotic muscle fibers continues. Macrophages in the necrotic zone contain abundant lipofuscin granules from phagocytosis of necrotic myocytes and erythrocytes. Collagenation of the infarct continues.

(3) **Appearance at 7 weeks postinfarction.** The entire infarct has been transformed into a fibrous scar. Occasional viable myofibers may be seen in the scar.

e. **Complications** of myocardial infarction that produce histologic findings also may produce clinical manifestations. Other complications, such as ventricular arrhythmias, do not demonstrate histologic findings.
(1) Arrhythmias, the most common complications, may result from ischaemia, hypoxia, sympathetic and parasympathetic stimulation, lactic acidosis, hemodynamic abnormalities, or electrolyte imbalances. Several types of arrhythmias may follow myocardial infarction. The most serious, ventricular arrhythmias, probably are the most common cause of sudden cardiac death in the first hour after infarction.

(2) **Heart failure** develops when the infarct involves 20% to 25% of the left ventricle. Scar tissue over the infarcted areas results in decreased contractility and abnormal ventricular wall motion, with subsequent reduction of cardiac output. Infarction involving 40% or more of the left ventricle leads to cardiogenic shock, which is the most common cause of death among hospital patients with acute myocardial infarcts.
(3) **Rupture of the myocardium** at the site of infarction can occur at any time within about 3 weeks after onset of the infarct, but it tends to occur most frequently between 2 and 10 days postinfarction, when the infarcted zone has minimal structural strength. After cardiogenic shock and arrhythmias, cardiac rupture is the most common cause of death postinfarction, being responsible for up to 20% of all fatal infarcts.

(a) Intrapericardial hemorrhage can result, leading to cardiac tamponade, if the rupture is through any portion of the ventricular wall other than the septum.

(b) Rupture of the ventricular septum can cause a left-to-right intracardiac shunt.

(c) Rupture of the papillary muscle of the left ventricle results in mitral insufficiency.
(4) **Thromboembolism.** Mural thrombi can form on the disrupted endocardial surface over areas of myocardial infarction. Because these thrombi are quite friable prior to fibrous organization, portions of a thrombus may break off and enter the peripheral circulation as emboli. They most frequently lodge in arterial vessels that supply the brain, kidneys, spleen, intestine and extremities and may result in infarction.

(5) **Fibrinous pericarditis** can develop soon after infarction in the region overlying the necrosis, or it may become generalized.

(6) **Ventricular aneurysm** is a late complication that occurs in 12% to 20% of patients. It develops when the fibrous scar that forms after infarction has insufficient structural strength to withstand the intraventricular chamber pressure. The scar stretches, resulting in extreme thinning of the ventricular wall with progressive convex deformity of the external cardiac surface. Stasis of blood within the aneurysm results in mural thrombi in 50% of patients, because the affected segment of myocardium cannot contract in phase with the remaining normal ventricle.
(f) **Prognosis and treatment**

(1) Prognosis. Most patients who develop an acute myocardial infarct have an uncomplicated course. Currently, the overall mortality rate for patients who reach the hospital is 3% to 30%. Among patients who develop cardiogenic shock, the mortality rate is greater than 70%.