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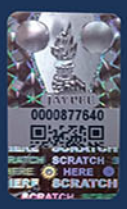

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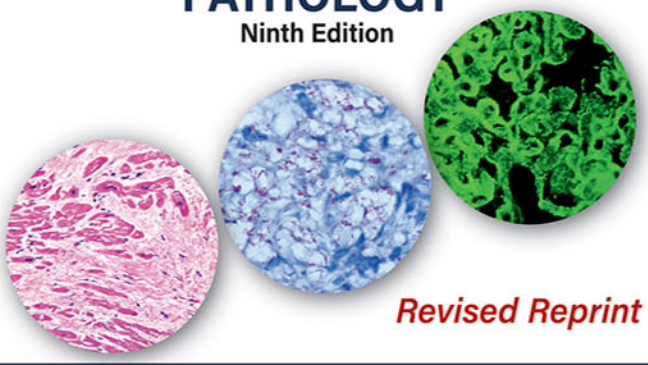

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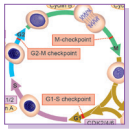

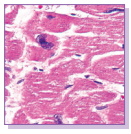

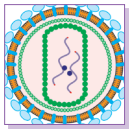

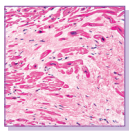

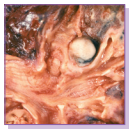

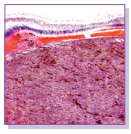

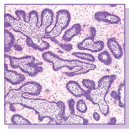

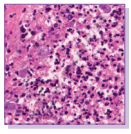

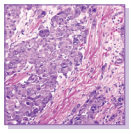

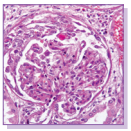

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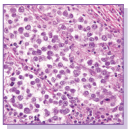

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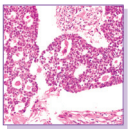

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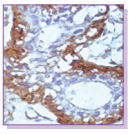

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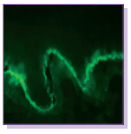

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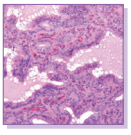

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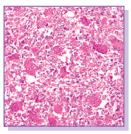

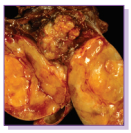

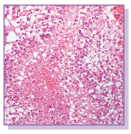

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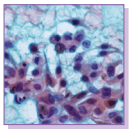
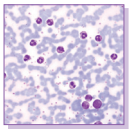




CHAPTER 17

The Heart*

Chapter Orientation

The heart is the most important organ in the body for preservation of life. It is a muscular pump that ejects blood into the vascular tree with sufficient pressure to maintain optimal circulation to various organs and tissues. Thus, the heart and blood vessels together function as cardiovascular unit for meeting the perfusion requirements of the body. Currently, cardiovascular diseases (CVDs) are the most prevalent disorders, accounting for maximum number of deaths worldwide, more so due to industrialisation, urbanisation, and associated lifestyle changes. Predominant forms of CVDs are rheumatic valvular disease, hypertension, coronary heart disease, and stroke.

From point of view of pathologic study of diseases of the heart, they are best understood in the context of its normal structure and function, and then learn diseases relating to three anatomic elements that comprise the heart, namely the endocardium, the myocardium and the pericardium. However, such compartmental heart diseases are generally not always possible because many heart diseases do not remain confined to a single anatomic boundary of the heart, but may involve other layers of the heart as well.

In view of this, heart diseases are described under following headings on the basis of rational combination of anatomic region involved and the functional impairment produced: 1) normal structure and function, 2) heart failure, 3) congenital heart diseases, 4) ischaemic heart disease, 5) rheumatic fever and rheumatic heart disease, 6) non-rheumatic endocarditis, 7) valvular diseases and deformities, 8) other myocardial diseases, 9) pericardial disease, 10) tumours of the heart, and 11) pathology of cardiovascular interventions.

NORMAL STRUCTURE

ANATOMY AND PHYSIOLOGY

Average weight of the heart in an adult male is 300-350 gm while that of an adult female is 250-300 gm. Heart is divided into four chambers: a right and a left atrium both lying superiorly, and a right and a left ventricle both lying inferiorly which are larger. The atria are separated by a thin interatrial partition called *interatrial septum*, while the ventricles are separated by thick muscular partition called *interventricular septum*. The thickness of the right ventricular wall is 0.3 to 0.5 cm, while that of the left ventricular wall is 1.3 to 1.5 cm. The blood in the heart chambers moves in a carefully prescribed pathway: venous blood from systemic circulation → right atrium → right ventricle → pulmonary arteries → lungs → pulmonary veins → left atrium → left ventricle → aorta → systemic arterial supply **(Fig. 17.1)**.

The transport of blood is regulated by cardiac valves: two loose flap-like atrioventricular valves, tricuspid on the right and mitral (bicuspid) on the left; and two semilunar valves with three leaflets each, the pulmonary and aortic valves, guarding the outflow tracts. Average normal circumference of the valvular openings measures about 12 cm in tricuspid, 8.5 cm in pulmonary, 10 cm in mitral and 7.5 cm in aortic valve.

Wall of the heart consists mainly of the *myocardium* which is covered externally by thin membrane, the *epicardium* or visceral

**Core (Must know)* | *Non-core (Desirable to know)* | *Competencies for Undergraduate Readers from India, as per the National Medical Commission*

Describe the etiology, types, stages, pathophysiology, pathology and complications of heart failure (PA27.3)	Written/Viva voce
Describe the etiology, pathophysiology, pathology, gross and microscopic features, criteria and complications of rheumatic fever (PA27.4)	Written/Viva voce
Describe the epidemiology, risk factors, etiology, pathophysiology, pathology, presentations, gross and microscopic features, diagnostic tests and complications of ischaemic heart disease (PA27.5)	Written/Viva voce
Describe the etiology, pathophysiology, pathology, gross and microscopic features, diagnosis and complications of infective endocarditis (PA27.6)	Written/Viva voce
Describe the etiology, pathophysiology, pathology, gross and microscopic features, diagnosis and complications of pericarditis and pericardial effusion (PA27.7)	Written/Viva voce
Interpret abnormalities in cardiac function testing in acute coronary syndromes (PA27.8)	Practical/Skill
Classify and describe the etiology, types, pathophysiology, pathology, gross and microscopic features, diagnosis and complications of cardiomyopathies (PA27.9)	Written/Viva voce
Describe the etiology, pathophysiology, pathology features and complications of syphilis on the cardiovascular system (PA27.10)	Written/Viva voce

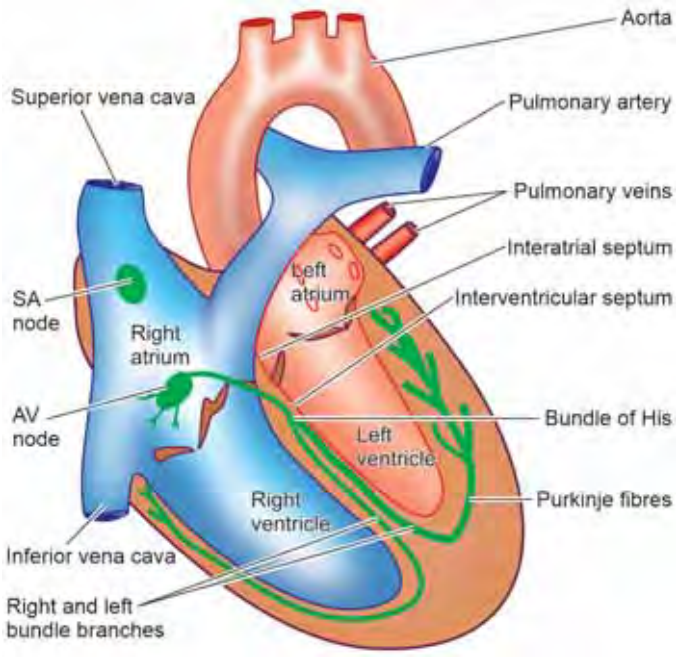


Figure 17.1 The normal anatomic structure of the heart. (SA, sinoatrial; AV, atrioventicular).

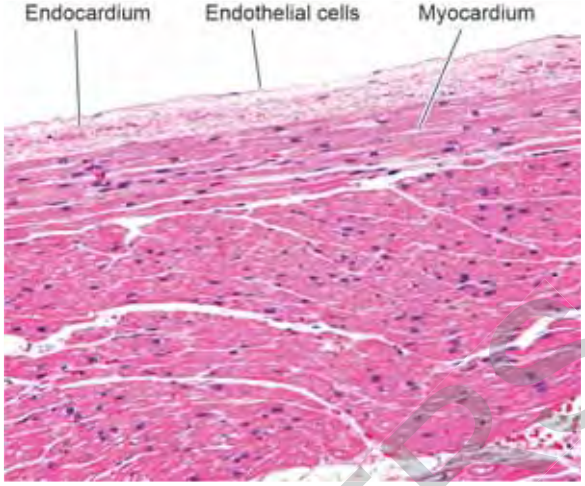


Figure 17.2 Normal microscopic structure of the heart. The endocardium is a thin layer composed of loose connective tissue. The myocardium is composed of striated muscle cells, arranged in syncytium. (Reproduced with permission from *Atlas of Histopathology* by Ivan Damjanov 2012, Jaypee Brothers Medical Publishers Pvt Ltd, New Delhi).

pericardium, and lined internally by another thin layer, the *endocardium* **(Fig. 17.2)**:

- The **myocardium** is the muscle tissue of the heart composed of syncytium of branching and anastomosing, transversely striated muscle fibres arranged in parallel fashion. The space between myocardial fibres contains a rich capillary network and loose connective tissue. The myocardial fibres are connected to each other by irregular joints called as *intercalated* discs. They represent apposed cell membranes of individual cells which act as tight junctions for free transport of ions and action potentials. The cardiac myocyte is very rich in mitochondria which are the source of large amount of ATP required for cardiac contraction. The cardiac muscle fibre has abundant sarcoplasmic reticulum corresponding to endoplasmic reticulum of other cells. Transverse lines divide each fibre into *sarcomeres* which act as structural and functional subunits. Each sarcomere consists of prominent central *dark A-band* attributed to thick myosin filaments and flanked on either side by *light I-bands* consisting of thin actin filament. The actin bands are in the form of twisted rods overlying protein molecules called *tropomyosin*. These protein molecules are of 3 types: *troponin-I, troponin-T, and troponin-C.* Troponin molecules respond to calcium ions in cyclical contraction-relaxation of myocardial fibres. Myocardial fibres are terminally differentiated cells and do not regenerate but there is recent evidence that new cardiac myocytes can be formed from stem cells recruited from the circulation.
- The **conduction system** of the heart located in the myocardium is responsible for regulating rate and rhythm of the heart. It is composed of specialised Purkinje fibres which contain some contractile myofilaments and conduct action potentials rapidly. The conduction system consists of 4 major components:

1. The *sinoatrial (SA) node* is located in the posterior wall of the right atrium adjacent to the point at which the superior vena cava enters the heart. It is also called cardiac pacemaker since it is responsible for determining the rate of contraction for all cardiac muscle.
2. The *atrioventricular (AV) bundle* conducts the impulse from the SA node to the AV node.
3. The *atrioventricular (AV) node* is located on the top of the interventricular septum and receives impulses from the SA node via AV bundle and transmits them to the bundle of His.
4. The *bundle of His* extends through the interventricular septum and divides into right and left bundle branches which arborise in the respective ventricular walls. These fibres transmit impulses from the AV node to the ventricular walls.

- The **pericardium** consists of a closely apposed layer, *visceral pericardium or epicardium,* and an outer fibrous sac, the *parietal pericardium*. The two layers enclose a narrow pericardial cavity which is lined by mesothelial cells and normally contains 10-30 ml of clear, watery serous fluid. This fluid functions as lubricant and shock absorbent to the heart.
- The **endocardium** is the smooth shiny inner lining of the myocardium that covers all the cardiac chambers, the cardiac valves, the chordae tendineae and the papillary muscles. It is lined by endothelium with connective tissue and elastic fibres in its deeper part.
- The **valve cusps and semilunar leaflets** are delicate and translucent structures. The valves are strengthened by collagen and elastic tissue and covered by a layer of endothelium (valvular endocardium).

MYOCARDIAL BLOOD SUPPLY

The cardiac muscle, in order to function properly, must receive adequate supply of oxygen and nutrients. Blood is transported to myocardial cells by the coronary arteries which originate immediately above the aortic semilunar valve. Most of blood flow to the myocardium occurs during diastole. There are three major coronary trunks, each supplying blood to specific segments of the heart **(Fig. 17.3)**:

1. The **anterior descending branch of the left coronary artery,** commonly called **LAD** (left anterior descending coronary) supplies most of the apex of the heart, the anterior surface of the left ventricle, the adjacent third of the anterior wall of the right ventricle, and the anterior two-third of the interventricular septum.
2. The **circumflex branch of the left coronary artery,** commonly called **LCX** (left circumflex coronary) supplies the left atrium and a small portion of the lateral aspect of the left ventricle.
3. The **right coronary artery,** abbreviated as **RCA** supplies the right atrium, the remainder of the anterior surface of the right

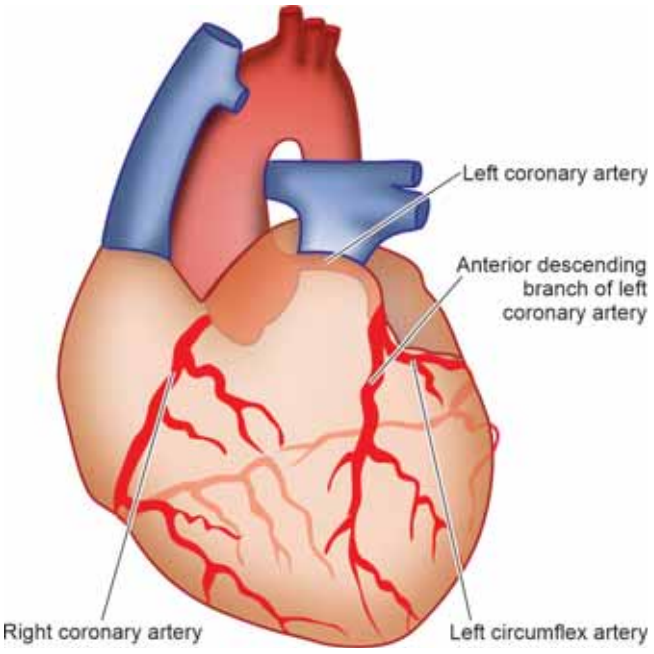


Figure 17.3 Distribution of blood supply to the heart.

ventricle, the adjacent half of the posterior wall of the left ventricle and the posterior third of the interventricular septum.

Coronary veins run parallel to the major coronary arteries to collect blood after the cellular needs of the heart are met. Subsequently, these veins drain into the *coronary sinus*.

Before describing diseases of the heart, it may be mentioned here that ***pattern of heart diseases*** in developing and developed countries is distinct due to differences in living standards:

- **In children**, valvular diseases are common all over the world. But in developing countries including India, *infectious origin*, particularly rheumatic valvular disease, is the dominant cause compared to higher prevalence of *congenital valvular disease* in developed countries.
- **In adults**, *cardiovascular diseases* due to ischaemic heart disease and hypertensive cardiomyopathy are the major cardiac diseases in adults in high-income group countries compared to low-income group countries. Overall, cardiovascular disease is the leading cause of premature death in men as well as women in the developed countries of the world, accounting for about one-fourth of all deaths.

KEY POINTS **Normal Structure**

- Average weight of the heart is 300-350 gm in adult male and 250-300 gm in adult female.
- Thickness of the right ventricular wall is 0.3-0.5 cm while that of the left ventricular wall is 1.3-1.5 cm.
- Average normal circumference of the valvular openings measures about 12 cm in tricuspid, 8.5 cm in pulmonary, 10 cm in mitral and 7.5 cm in aortic valve.
- Wall of the heart consists mainly of the *myocardium* which is covered externally by the *epicardium*, and lined internally by the endocardium.
- There are three major coronary trunks, each supplying blood to specific segments of the heart: left anterior descending coronary (LAD), left circumflex coronary (LCX) and right coronary artery (RCA).

HEART FAILURE

Heart failure is defined as the pathophysiologic state in which impaired cardiac function is unable to maintain an adequate circulation for the metabolic needs of the tissues of the body. It may be *acute* or *chronic*. The term congestive heart failure (CHF) is used for the chronic form of heart failure in which the patient has evidence of congestion of peripheral circulation and of lungs (page 161). CHF is the end-result of various forms of serious heart diseases.

ETIOLOGY

Heart failure may be caused by one of the following factors, either singly or in combination:

1. INTRINSIC PUMP FAILURE The most common and most important cause of heart failure is weakening of the ventricular muscle due to disease so that the heart fails to act as an efficient pump. The various diseases which may culminate in pump failure by this mechanism are as under:

i) Ischaemic heart disease
ii) Myocarditis
iii) Cardiomyopathies
iv) Metabolic disorders, e.g. beriberi
v) Disorders of the rhythm, e.g. atrial fibrillation and flutter.

2. INCREASED WORKLOAD ON THE HEART Increased mechanical load on the heart results in increased myocardial demand resulting in myocardial failure. Increased load on the heart may be in the form of pressure load or volume load.

i) Increased pressure load may occur in the following states:
a) Systemic and pulmonary arterial hypertension
b) Valvular disease, e.g. mitral stenosis, aortic stenosis, pulmonary stenosis
c) Chronic lung diseases

ii) Increased volume load occurs when a ventricle is required to eject more than normal volume of the blood resulting in cardiac failure. This is seen in the following conditions:
a) Valvular insufficiency
b) Severe anaemia
c) Thyrotoxicosis
d) Arteriovenous shunts
e) Hypoxia due to lung disease

3. IMPAIRED FILLING OF CARDIAC CHAMBERS Decreased cardiac output and cardiac failure may result from extracardiac causes or defect in filling of the heart:

i) Cardiac tamponade, e.g. haemopericardium, hydropericardium
ii) Constrictive pericarditis

TYPES OF HEART FAILURE

Heart failure may be acute or chronic, right-sided or left-sided.

ACUTE AND CHRONIC HEART FAILURE

Depending upon whether the heart failure develops rapidly or slowly, it may be acute or chronic.

Acute heart failure Sudden and rapid development of heart failure occurs in the following conditions:

i) Larger myocardial infarction
ii) Valve rupture
iii) Cardiac tamponade
iv) Massive pulmonary embolism
v) Acute viral myocarditis
vi) Acute bacterial toxaemia

In acute heart failure, there is sudden reduction in cardiac output resulting in systemic hypotension, but oedema does not occur. Instead, a state of cardiogenic shock and cerebral hypoxia develops.

Chronic heart failure More often, heart failure develops slowly as observed in the following states:

i) Myocardial ischaemia from atherosclerotic coronary artery disease
ii) Multivalvular heart disease
iii) Systemic arterial hypertension
iv) Chronic lung diseases resulting in hypoxia and pulmonary arterial hypertension
v) Progression of acute into chronic failure

In chronic heart failure, compensatory mechanisms like tachycardia, cardiac dilatation and cardiac hypertrophy try to make adjustments so as to maintain adequate cardiac output. This often results in well-maintained arterial pressure and there is appearance of oedema.

LEFT-SIDED AND RIGHT-SIDED HEART FAILURE

Though heart as an organ eventually fails as a whole, but functionally the left and right heart act as independent units. From clinical point of view, therefore, it is helpful to consider failure of the left and right heart separately. The clinical manifestations of heart failure result from accumulation of excess fluid *upstream* to the left or right cardiac chamber whichever is initially affected **(Fig. 17.4)**:

Left Heart Failure

It is initiated by stress to the left heart. The major causes are as follows:

i) Systemic hypertension, most common (discussed below)
ii) Mitral or aortic valve disease (stenosis)
iii) Ischaemic heart disease
iv) Myocardial diseases, e.g. cardiomyopathies, myocarditis
v) Restrictive pericarditis

The clinical manifestations of left-sided heart failure result from decreased left ventricular output and hence there is accumulation of fluid *upstream* in the lungs. Accordingly, the major pathologic changes are as under:

i) Pulmonary congestion and oedema causes dyspnoea and orthopnoea (page 161).
ii) Decreased left ventricular output causing hypoperfusion and diminished oxygenation of tissues, e.g. in kidneys causing ischaemic acute tubular necrosis (page 679), in brain causing hypoxic encephalopathy (page 900), and in skeletal muscles causing muscular weakness and fatigue.

HYPERTENSIVE HEART DISEASE Hypertensive heart disease or hypertensive cardiomyopathy results from systemic hypertension of prolonged duration and manifests by left ventricular hypertrophy. Even mild hypertension (blood pressure higher than 140/90 mmHg) of sufficient duration may induce hypertensive heart disease. It is the second most common form of heart disease after IHD. As already discussed, hypertension predisposes to atherosclerosis (page 399). Therefore, most patients of hypertensive heart disease have also advanced coronary atherosclerosis and may develop progressive IHD.

Amongst the causes of death in hypertensive patients, cardiac decompensation leading to CHF accounts for about one-third of the patients; other causes of death in these cases are IHD, cerebrovascular stroke, renal failure following arteriolar nephrosclerosis, dissecting aneurysm of the aorta and sudden cardiac death.

Pathogenesis Pathogenesis of systemic hypertension is discussed in Chapter 23 (page 688). Here, pathogenesis of left ventricular

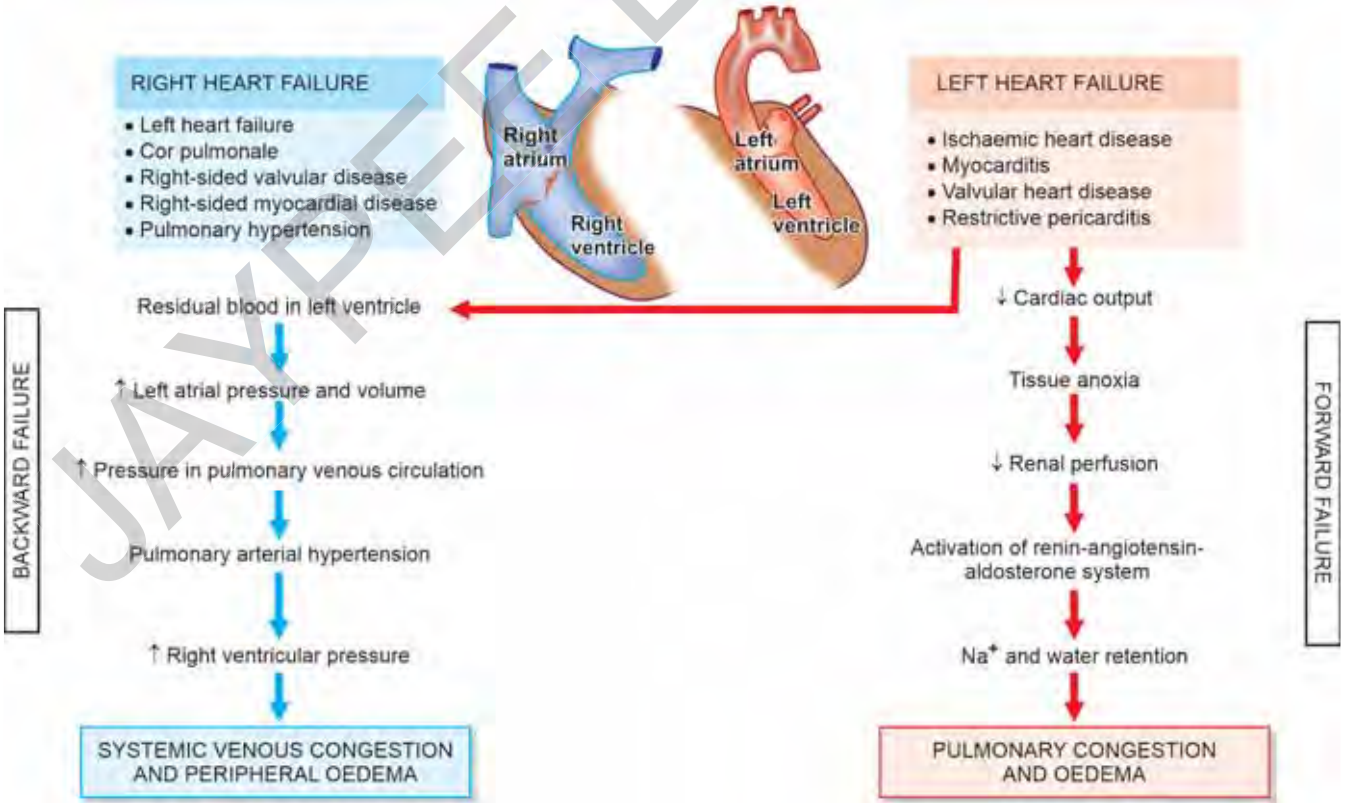


Figure 17.4 Schematic evolution of congestive heart failure and its effects.

hypertrophy (LVH) which is most commonly caused by systemic hypertension is described.

Stimulus to LVH is pressure overload in systemic hypertension. Both genetic and haemodynamic factors contribute to LVH. The stress of pressure on the ventricular wall causes increased production of myofilaments, myofibrils, other cell organelles and nuclear enlargement. Since the adult myocardial fibres do not divide, the fibres are hypertrophied. However, the sarcomeres may divide to increase the cell width.

LVH can be diagnosed by ECG. With aggressive control of hypertension, the left ventricular mass can regress. Abnormalities of diastolic function in hypertension are more common in hypertension and are present in about one-third of patients with normal systolic function.

Right-sided Heart Failure

Right-sided heart failure occurs more often as a consequence of left-sided heart failure. However, some conditions primarily affect the right ventricle, producing right-sided heart failure. These are:

i) As a consequence of left ventricular failure.
ii) Cor pulmonale or pulmonary heart disease in which right heart failure occurs due to intrinsic lung diseases, most common (discussed below).
iii) Pulmonary or tricuspid valvular disease.
iv) Pulmonary hypertension secondary to pulmonary thromboembolism.
v) Myocardial disease affecting right heart.
vi) Congenital heart disease with left-to-right shunt.

Whatever be the underlying cause, the clinical manifestations of right-sided heart failure are upstream of the right heart such as systemic (i.e. blood from vena cavae) and portal venous congestion, and reduced cardiac output. Accordingly, the pathologic changes are as under:

i) Systemic venous congestion in different tissues and organs, e.g. subcutaneous oedema on dependent parts, passive congestion of the liver, spleen, and kidneys (page 165), ascites, hydrothorax, congestion of leg veins and neck veins.
ii) Reduced cardiac output resulting in circulatory stagnation causing anoxia, cyanosis and coldness of extremities.

COR PULMONALE Cor pulmonale (*cor*=heart; *pulmonale*=lung) or pulmonary heart disease is the right heart disease resulting from disorders of the lungs. It is characterised by right ventricular dilatation or hypertrophy, or both. Thus, cor pulmonale is the right-sided counterpart of the hypertensive heart disease that affects left heart predominantly.

Depending upon the rapidity of development, cor pulmonale may be acute or chronic:

- *Acute cor pulmonale* occurs following massive pulmonary embolism resulting in sudden dilatation of the pulmonary trunk, conus and right ventricle.
- *Chronic cor pulmonale* is more common and is often preceded by chronic pulmonary hypertension (page 466). Following chronic lung diseases can cause chronic pulmonary hypertension and subsequent cor pulmonale:

i) Chronic emphysema
ii) Chronic bronchitis
iii) Pulmonary tuberculosis
iv) Pneumoconiosis
v) Cystic fibrosis
vi) Hyperventilation in marked obesity (Pickwickian syndrome)
vii) Multiple organised pulmonary emboli.

Pathogenesis Chronic lung diseases as well as diseases of the pulmonary vessels cause increased pulmonary vascular resistance. The most common underlying mechanism causing increased pulmonary blood pressure (pulmonary hypertension) is by pulmonary vasoconstriction, activation of coagulation pathway and obliteration of pulmonary arterial vessels. Pulmonary hypertension causes pressure overload on the right ventricle and hence right ventricular enlargement. Initially, there is right ventricular hypertrophy, but as cardiac decompensation sets in and right heart failure ensues, dilatation of right ventricle occurs.

The sequence of events involved in the pathogenesis of cor pulmonale is summarised in **Fig. 17.5**.

In summary, in early stage the left heart failure manifests with features of pulmonary congestion and decreased left ventricular output, while the right heart failure presents with systemic venous congestion and involvement of the liver and spleen. CHF, however, combines the features of both left and right heart failure.

COMPENSATORY MECHANISMS: CARDIAC HYPERTROPHY AND DILATATION

In order to maintain normal cardiac output, several compensatory mechanisms play a role as under:

- Compensatory enlargement in the form of *cardiac hypertrophy, cardiac dilatation, or both.*
- *Tachycardia* (i.e. increased heart rate) due to activation of neurohumoral system, e.g. release of norepinephrine and atrial natriuretic peptide, activation of renin-angiotensin-aldosterone mechanism.

According to *Starling law* on pathophysiology of heart, the failing dilated heart, in order to maintain cardiac performance, increases the myocardial contractility and thereby attempts to maintain stroke volume. This is achieved by increasing the length of sarcomeres in dilated heart. Ultimately, however, dilatation decreases the force of contraction and leads to residual volume in the cardiac chambers causing volume overload resulting in cardiac failure that ends in death **(Fig. 17.6)**.

CARDIAC HYPERTROPHY

Hypertrophy of the heart is defined as an increase in size and weight of the myocardium. It generally results from increased pressure load while increased volume load (e.g. valvular incompetence) results in hypertrophy with dilatation of the affected chamber due to regurgitation of the blood through incompetent valve. The atria may also undergo compensatory changes due to increased workload.

Initially, the hypertrophy of the myocardial fibres is adaptive response to maintain cardiac function. However, sustained stress

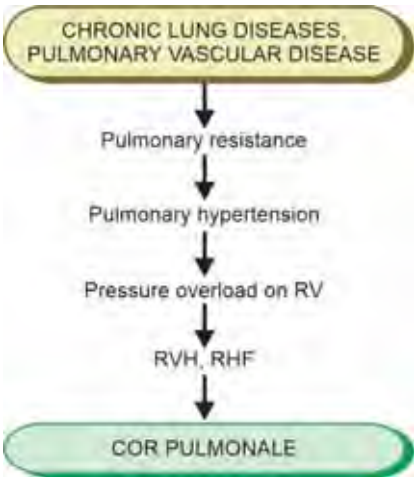


Figure 17.5 Pathogenesis of cor pulmonale. (RV, right ventricle; RVH, right ventricular hypertrophy, RHF, right heart failure).

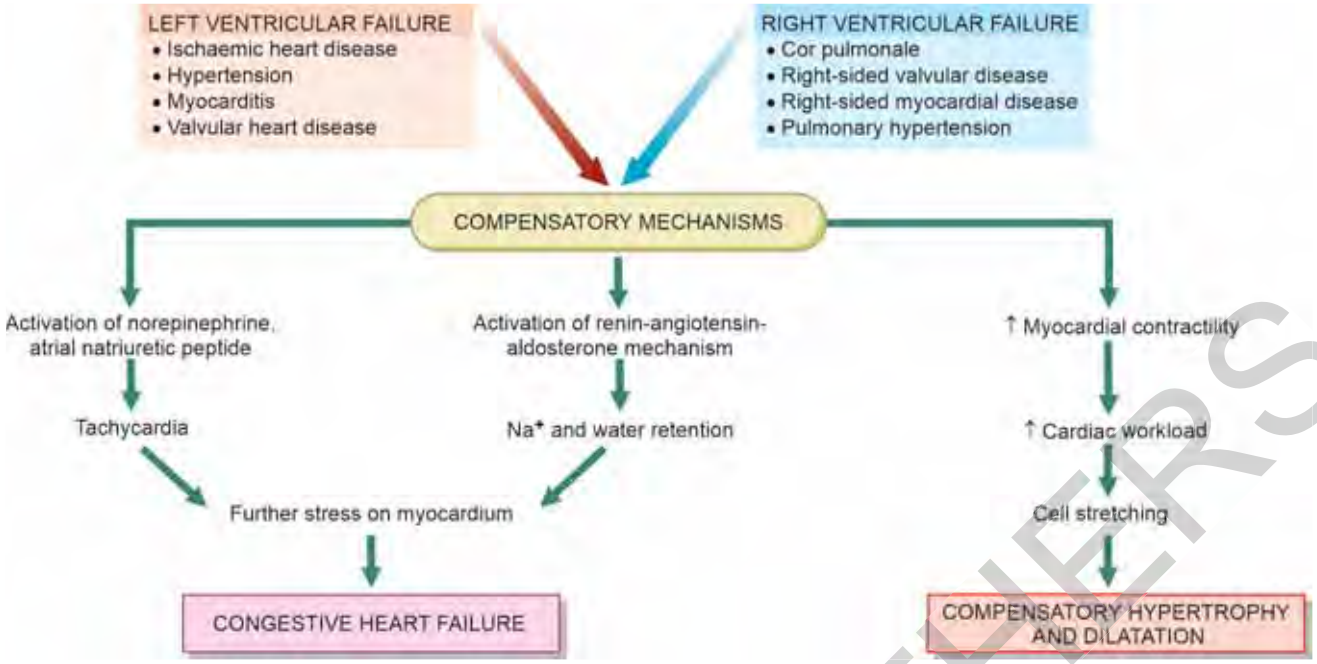


Figure 17.6 Schematic pathophysiology of compensatory mechanisms in cardiac failure.

leads to pathological hypertrophy by involvement of numerous mediators such as changes in gene transcription, signalling proteins, protein synthesis, calcium handling, metabolism, oxidative stress and inflammation.

CAUSES Hypertrophy with or without dilatation may involve predominantly the left or the right heart, or both sides.

Left ventricular hypertrophy Common causes are as under:

i) Systemic hypertension, most common
ii) Aortic stenosis and insufficiency
iii) Mitral insufficiency
iv) Coarctation of the aorta
v) Occlusive coronary artery disease
vi) Congenital anomalies like septal defects and patent ductus arteriosus
vii) Conditions with increased cardiac output, e.g. thyrotoxicosis, anaemia, arteriovenous fistulae.

Right ventricular hypertrophy Most of the causes of right ventricular hypertrophy are due to pulmonary arterial hypertension. These are as follows:

i) Cor pulmonale from chronic lung diseases (e.g. chronic emphysema, bronchiectasis, pneumoconiosis, pulmonary vascular disease etc), most common
ii) Pulmonary stenosis and insufficiency
iii) Tricuspid insufficiency
iv) Mitral stenosis and/or insufficiency
v) Left ventricular hypertrophy and failure of the left ventricle

CARDIAC DILATATION

Quite often, hypertrophy of the heart is accompanied by cardiac dilatation. Stress leading to accumulation of excessive volume of blood in a chamber of the heart causes increase in length of myocardial fibres and hence cardiac dilatation as a compensatory mechanism.

CAUSES Accumulation of excessive volume of blood within the cardiac chambers from the following causes may result in dilatation of the respective ventricles, or both:

i) Valvular insufficiency (mitral and/or aortic insufficiency in left ventricular dilatation, tricuspid and/or pulmonary insufficiency in right ventricular dilatation)
ii) Left-to-right shunts, e.g. in VSD
iii) Conditions with high cardiac output, e.g. thyrotoxicosis, arteriovenous shunt
iv) Myocardial diseases, e.g. cardiomyopathies, myocarditis
v) Systemic hypertension

PATHOLOGY

Hypertrophy of the myocardium without dilatation is referred to as *concentric,* and when associated with dilatation is called *eccentric* **(Fig. 17.7).**

Grossly, the most significant finding is marked hypertrophy of the heart, chiefly of the left ventricle **(Fig. 17.8)**. The weight of the heart increases to 500 gm or more (normal weight about 300 gm).

✠ *In LVH,* thickness of the left ventricular wall increases from its normal 13 to 15 mm up to 20 mm or more. The papillary muscles and trabeculae carneae are rounded and prominent. Initially, there is *concentric hypertrophy* of the left ventricle (without dilatation). But when decompensation and cardiac failure supervene, there is *eccentric hypertrophy* (with dilatation) with thinning of the ventricular wall and there may be dilatation and hypertrophy of right heart as well, i.e. biventricular hypertrophy.

✠ *In RVH* due to acute cor pulmonale, there is characteristic ovoid dilatation of the right ventricle, and sometimes of the right atrium. In chronic cor pulmonale, there is increase in thickness of the right ventricular wall from its normal 3 to 5 mm up to 10 mm or more, i.e. right ventricular hypertrophy (RVH). Often, there is dilatation of the right ventricle too.

Microscopically, there is increase in size of individual muscle fibres. There may be multiple minute foci of degenerative changes and necrosis in the hypertrophied myocardium **(Fig. 17.9).** These changes appear to arise as a result of relative hypoxia of the hypertrophied muscle as the blood supply is inadequate to meet the demands of the increased fibre size. Ventricular hypertrophy renders the inner part of the myocardium more liable to ischaemia.

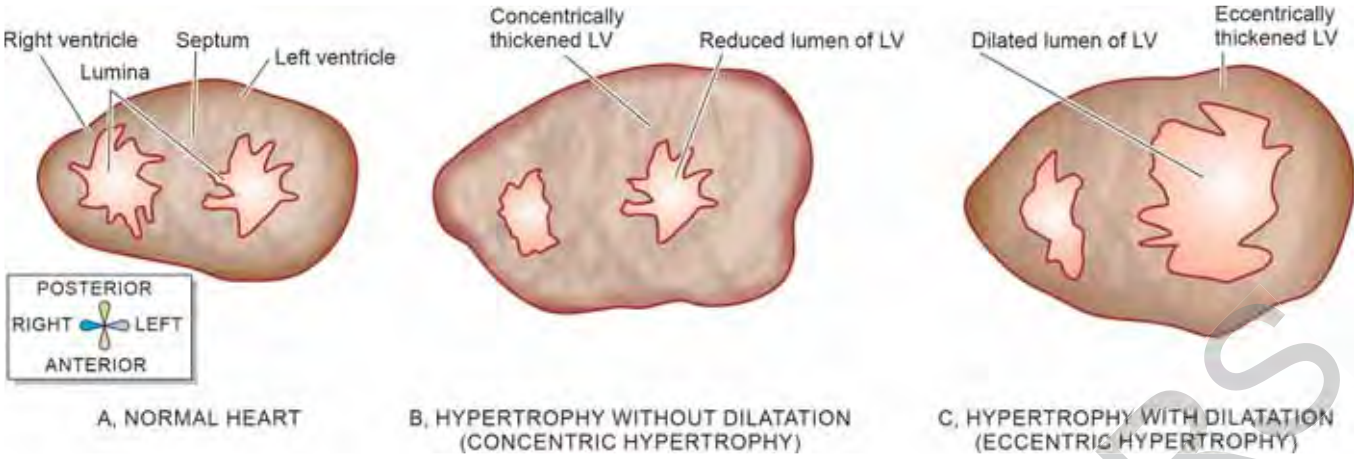


Figure 17.7 Schematic diagram showing transverse section through the ventricles with left ventricular hypertrophy (concentric and eccentric). (LV, left ventricle) .

Electron microscopy reveals increase in the number of myofilaments comprising myofibrils, mitochondrial changes and multiple intercalated discs which are active sites for the formation of new sarcomeres. Besides, the nucleic acid content determinations have shown increase in total RNA and increased ratio of RNA to DNA content of the hypertrophied myocardial fibres.

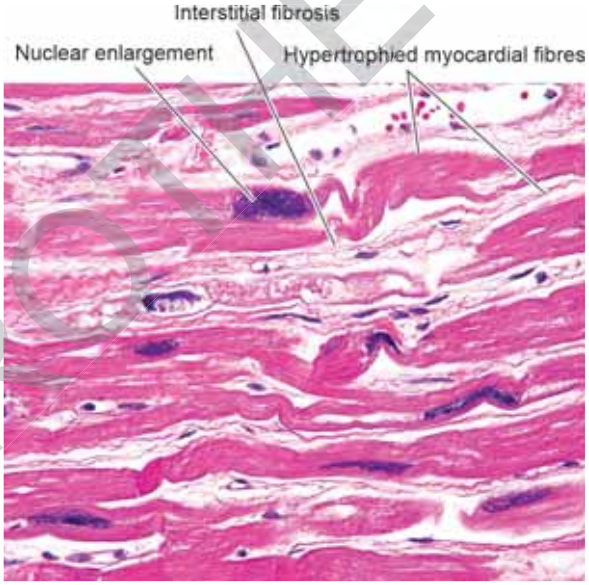


Figure 17.9 Cardiac hypertrophy. Longitudinally sectioned cardiac myocytes are thick with enlarged, hyperchromatic vesicular nuclei and abundant cytoplasm. (Reproduced with permission from *Atlas of Histopathology* by Ivan Damjanov 2012, Jaypee Brothers Medical Publishers Pvt Ltd, New Delhi).

KEY POINTS | **Heart Failure**

- Heart failure is a pathophysiologic state of impaired cardiac function when it is unable to maintain the metabolic needs of the tissues of the body.
- Heart failure may be caused by intrinsic pump failure, increased pressure or volume overload, or impaired filling.
- Heart failure may be acute or chronic, left-sided or right-sided, backward.
- Hypertensive heart disease resulting from systemic hypertension of prolonged duration is most common cause of left heart failure and left ventricular hypertrophy (LVH).

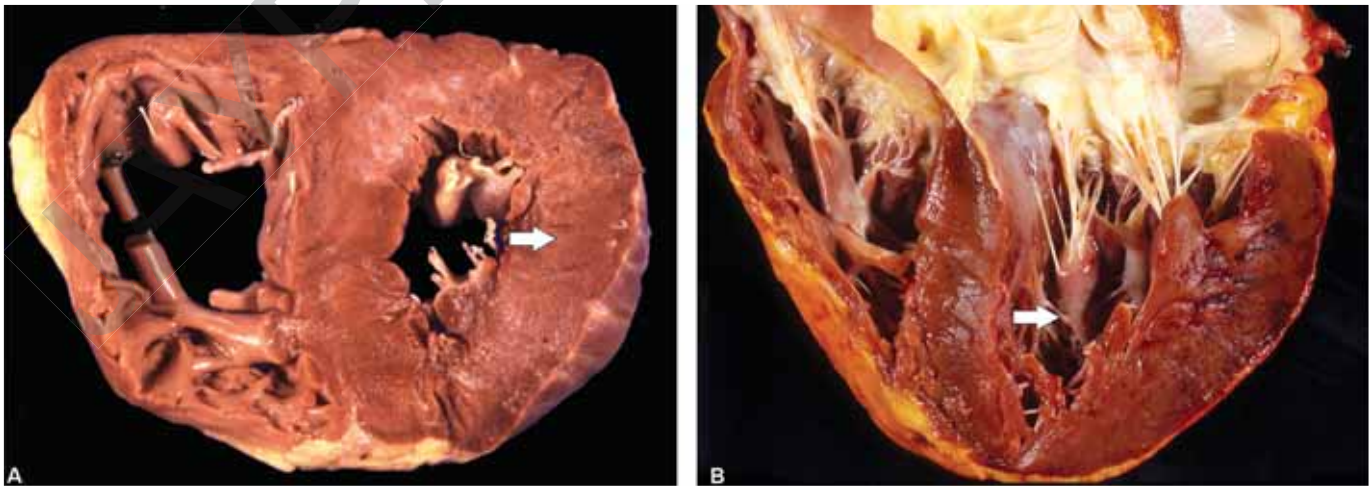


Figure 17.8 A, *Concentric cardiac hypertrophy*. Weight of the heart in this hypertensive deceased is increased. The opened up chambers show concentric thickening of left ventricular wall (white arrow) with obliterated lumen (hypertrophy without dilatation). B, *Eccentric cardiac hypertrophy*. The heart is heavier. Free walls of both left and right ventricles are thickened (biventricular hypertrophy) while the lumen is dilated (white arrow) (hypertrophy with dilatation). (Images courtesy by Dr Ivan Damjanov, Department of Pathology and Laboratory Medicine, The University of Kansas School of Medicine, Kansas, USA).

- In LVH, initially there is concentric hypertrophy of the left ventricle (without dilatation). But when decompensation and cardiac failure supervene, there is eccentric hypertrophy (with dilatation).
- Cor pulmonale or pulmonary heart disease is most common cause of right heart failure and right ventricular hypertrophy (RVH) resulting from disorders of the lungs.
- Right heart failure may be acute or chronic; the latter is more common. There is thickened right ventricular wall, often with dilatation.
- In both LHF and RHF, compensatory mechanisms are its enlargement in the form of cardiac hypertrophy (concentric or eccentric), cardiac dilatation, or both; eventually there is biventricular enlargement.

CONGENITAL HEART DISEASE

Congenital heart disease is the abnormality of the heart present from birth. It is the most common and important form of heart disease in the early years of life and is present in approximately 1% of neonates. The incidence is higher in premature infants. The cause of congenital heart disease is unknown in majority of cases. Congenital heart disease is attributed to multifactorial inheritance involving genes and chromosomes. Other factors which may cause *in utero* foetal injury resulting in congenital malformations of the heart include environmental influence and maternal factors during pregnancy such as her diet, use of medications, heavy alcohol consumption, rubella infection etc.

CLASSIFICATION Congenital anomalies of the heart may be either *shunts* (left-to-right or right-to-left), or defects causing *obstructions* to flow. However, complex anomalies involving *combinations* of shunts and obstructions are also often present.

A simple classification of important and common examples of these groups is given in **Table 17.1;** five most common in the list are VSD, ASD, PDA, pulmonary stenosis and tetralogy of Fallot.

TABLE 17.1 Classification of congenital heart diseases.

I.	MALPOSITIONS OF THE HEART
II.	SHUNTS (CYANOTIC CONGENITAL HEART DISEASE)
	A. *Left-to-right shunts (Acyanotic or late cyanotic group)* 1. Ventricular septal defect (VSD), *most common* 2. Atrial septal defect (ASD) 3. Patent ductus arteriosus (PDA) B. *Right-to-left shunts (Cyanotic group)* 1. Tetralogy of Fallot 2. Transposition of great arteries 3. Persistent truncus arteriosus 4. Tricuspid atresia and stenosis
III.	OBSTRUCTIONS (OBSTRUCTIVE CONGENITAL HEART DISEASE)
	1. Coarctation of aorta 2. Aortic stenosis and atresia 3. Pulmonary stenosis and atresia

I. MALPOSITIONS OF THE HEART

Dextrocardia is the condition when the apex of the heart points to the right side of the chest. It may be accompanied by situs inversus, i.e. all other organs of the body are also transposed in similar way and thus heart is in normal position in relation to them. However, isolated dextrocardia is associated with major anomalies of the heart such as transposition of the atria in relation to ventricles or transposition of the great arteries.

II. SHUNTS (CYANOTIC CONGENITAL HEART DISEASE)

A shunt may be left-to-right side or right-to-left side of the circulation.

A. LEFT-TO-RIGHT SHUNTS (ACYANOTIC OR LATE CYANOTIC GROUP)

In conditions where there is shunting of blood from left-to-right side of the heart, there is volume overload on the right heart producing pulmonary hypertension and right ventricular hypertrophy. At a later stage, the pressure on the right side is higher than on the left side creating late cyanotic heart disease. The important conditions included in this category are described here:

VENTRICULAR SEPTAL DEFECT Ventricular septal defect (VSD) is the most common congenital anomaly of the heart and comprises about 30-40% of all congenital heart diseases. The condition is recognised early in life. The smaller defects often close spontaneously, while larger defects remain patent and produce significant effects.

Depending upon the location of the defect, VSD may be of the following types:

1. In 90% of cases, the defect involves *membranous septum* and is very close to the bundle of His **(Fig. 17.10)**.
2. The remaining 10% cases have VSD immediately below the pulmonary valve (*subpulmonic*), below the aortic valve (*subaortic*), or exist in the form of multiple defects in the muscular septum.

PATHOLOGY The *effects* of VSD are produced due to left-to-right shunt at the ventricular level, increased pulmonary flow and increased volume in the left side of the heart. These effects are as under:

i) Volume hypertrophy of the right ventricle.
ii) Enlargement and haemodynamic changes in the tricuspid and pulmonary valves.
iii) Endocardial hypertrophy of the right ventricle.
iv) Pressure hypertrophy of the right atrium.
v) Volume hypertrophy of the left atrium and left ventricle.
vi) Enlargement and haemodynamic changes in the mitral and aortic valves.

ATRIAL SEPTAL DEFECT Isolated atrial septal defect (ASD) comprises about 10% of congenital heart diseases. The condition remains unnoticed in infancy and childhood till pulmonary hypertension is induced causing late cyanotic heart disease and right-sided heart failure.

Depending upon the location of the defect, there are 3 types of ASD:

i) Fossa ovalis type or ostium secundum type is the most common form comprising about 90% cases of ASD. The defect is situated in the region of the fossa ovalis **(Fig. 17.11)**.

ii) Ostium primum type comprises about 5% cases of ASD. The defect lies low in the interatrial septum adjacent to atrioventricular valves. There may be cleft in the aortic leaflet of the mitral valve producing mitral insufficiency.

iii) Sinus venosus type accounts for about 5% cases of ASD. The defect is located high in the interatrial septum near the entry of the superior vena cava.

PATHOLOGY The *effects* of ASD are produced due to left-to-right shunt at the atrial level with increased pulmonary flow. These effects are as follows:

i) Volume hypertrophy of the right atrium and right ventricle.

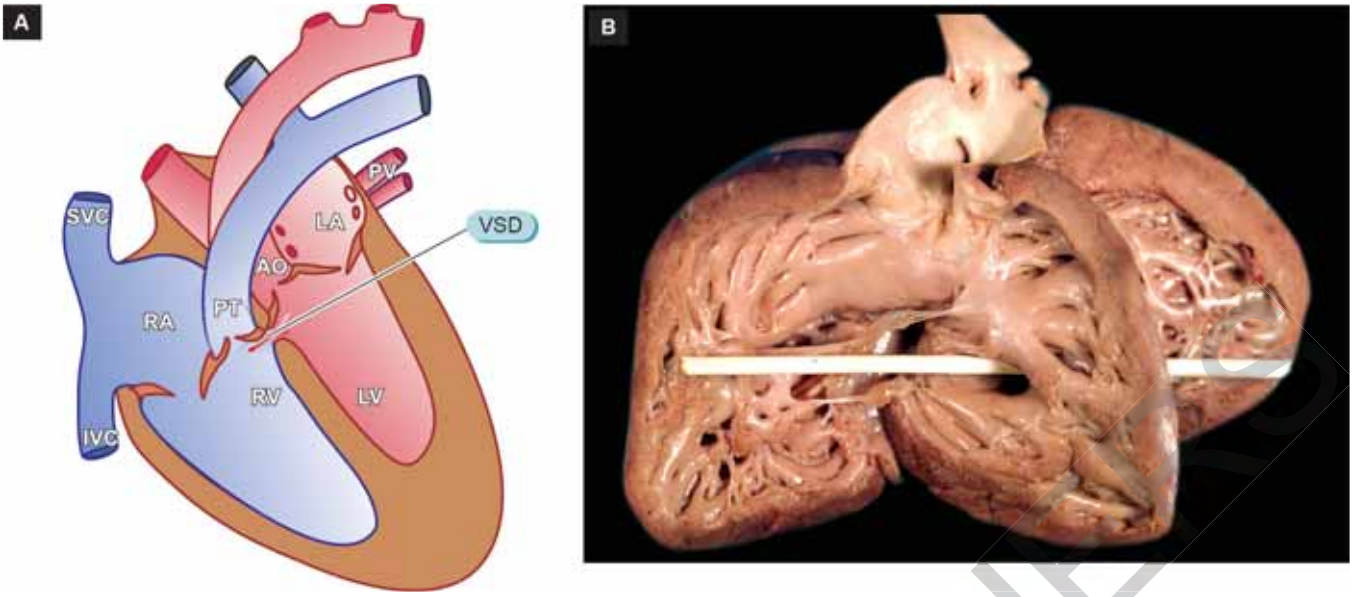


Figure 17.10 Ventricular septal defect. A, Schematic representation. B, The opened up chambers of the heart show a communication in the interventricular septum superiorly (white pipe). (LA, left atrium; LV, left ventricle; AO, aorta; PV, pulmonary valve; PT, pulmonary trunk; RA, right atrium; RV, right ventricle; SVC, superior vena cava; IVC, inferior vena cava; VSD, ventricular septal defect). (Gross image courtesy by Dr Ivan Damjanov, Department of Pathology and Laboratory Medicine, The University of Kansas School of Medicine, Kansas, USA).

ii) Enlargement and haemodynamic changes of tricuspid and pulmonary valves.
iii) Focal or diffuse endocardial hypertrophy of the right atrium and right ventricle.
iv) Volume atrophy of the left atrium and left ventricle.
v) Small-sized mitral and aortic orifices.

PATENT DUCTUS ARTERIOSUS (PDA) The ductus arteriosus is a normal vascular connection between the aorta and the bifurcation of the pulmonary artery. Normally, the ductus closes functionally within the first or second day of life. Its persistence after 3 months of age is considered abnormal. Prostaglandins, especially PGE2, maintain the patency of the ductus; continued synthesis of PGE2 after birth in infants with respiratory distress syndrome in infants is associated with PDA. Thus, inhibition of PGE2 synthesis by administration of indomethacin causes pharmacologic closure of PDA. PDA constitutes about 10% of congenital malformations of the heart and great vessels. In about 90% of cases, it occurs as an isolated defect, while in the remaining cases it may be associated with other anomalies like VSD, coarctation of aorta and pulmonary or aortic stenosis. A patent ductus may be up to 2 cm in length and up to 1 cm in diameter **(Fig. 17.12)**.

PATHOLOGY The *effects* of PDA on heart occur due to left-to-right shunt at the level of ductus resulting in increased pulmonary flow and increased volume in the left heart. These effects are as follows:
i) Volume hypertrophy of the left atrium and left ventricle.

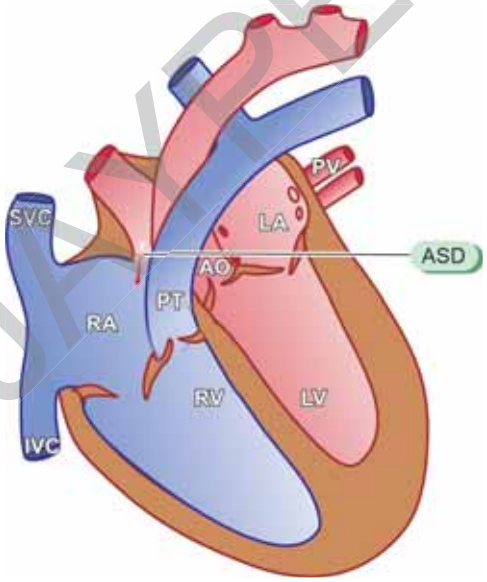


Figure 17.11 Atrial septal defect fossa ovalis type, a schematic representation. (LA, left atrium; LV, left ventricle; PV, pulmonary vein; AO, aorta; PT, pulmonary trunk; RA, right atrium; RV, right ventricle; SVC, superior vena cava; IVC, inferior vena cava; ASD, atrial septal defect).

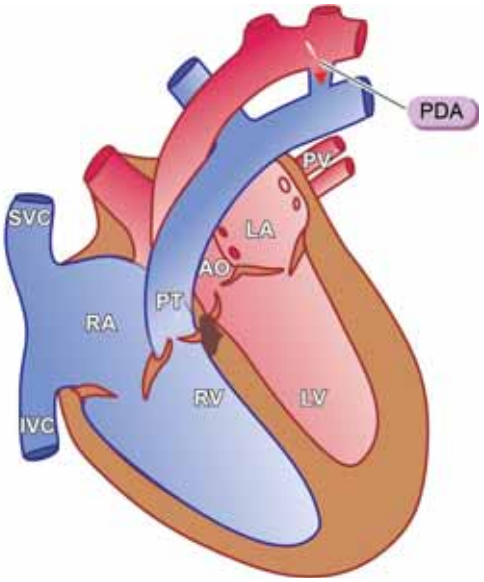


Figure 17.12 Patent ductus arteriosus, a schematic representation. (LA, left atrium; LV, left ventricle; PT, pulmonary trunk; PV, pulmonary vein, AO, aorta; RA, right atrium; RV, right ventricle; SVC, superior vena cava; IVC, inferior vena cava; PDS, patent ductus arteriosus).

ii) Enlargement and haemodynamic changes of the mitral and pulmonary valves.
iii) Enlargement of the ascending aorta.

B. RIGHT-TO-LEFT SHUNTS (CYANOTIC GROUP)

In conditions where there is shunting of blood from right side to the left side of the heart, there is entry of poorly-oxygenated blood into systemic circulation resulting in early cyanosis. The examples described below are not pure shunts but are combinations of shunts with obstructions but are described here since there is functional shunting of blood from one to the other side of circulation.

TETRALOGY OF FALLOT Tetralogy of Fallot is the most common cyanotic congenital heart disease, found in about 10% of children with anomalies of the heart.

PATHOLOGY The four features of tetralogy are as under* **(Fig. 17.13)**:
i) Ventricular septal defect (VSD) *('shunt')*
ii) Displacement of the aorta to right so that it overrides the VSD
iii) Pulmonary stenosis *('obstruction')*
iv) Right ventricular hypertrophy

The severity of the clinical manifestations is related to two factors: extent of pulmonary stenosis and the size of VSD. Accordingly, there are two forms of tetralogy: cyanotic and acyanotic.

a) Cyanotic tetralogy Pulmonary stenosis is greater while the VSD is mild so that there is more resistance to the outflow of blood from right ventricle resulting in right-to-left shunt at the ventricular level and cyanosis. The *effects* on the heart are as follows:
i) Pressure hypertrophy of the right atrium and right ventricle
ii) Smaller and abnormal tricuspid valve
iii) Smaller left atrium and left ventricle
iv) Enlarged aortic orifice

b) Acyanotic tetralogy The VSD is larger and pulmonary stenosis is mild so that there is mainly left-to-right shunt with increased pulmonary flow and increased volume in the left heart but no cyanosis. The *effects* on the heart are as under:
i) Pressure hypertrophy of the right ventricle and right atrium
ii) Volume hypertrophy of the left atrium and left ventricle
iii) Enlargement of mitral and aortic orifices

III. OBSTRUCTIONS (OBSTRUCTIVE CONGENITAL HEART DISEASE)

Congenital obstruction to blood flow may result from obstruction in the aorta due to narrowing (*coarctation of aorta*), obstruction to outflow from the left ventricle (*aortic stenosis and atresia*), and obstruction to outflow from the right ventricle (*pulmonary stenosis and atresia*).

COARCTATION OF AORTA The word 'coarctation' means contracted or compressed. Coarctation of aorta is localised narrowing in any part of aorta, but the constriction is more often just distal to ductus arteriosus (*postductal or adult*), or occasionally proximal to the ductus arteriosus (*preductal or infantile type*) in the region of transverse aorta:

PATHOLOGY The two common forms of coarctation of the aorta are as under:

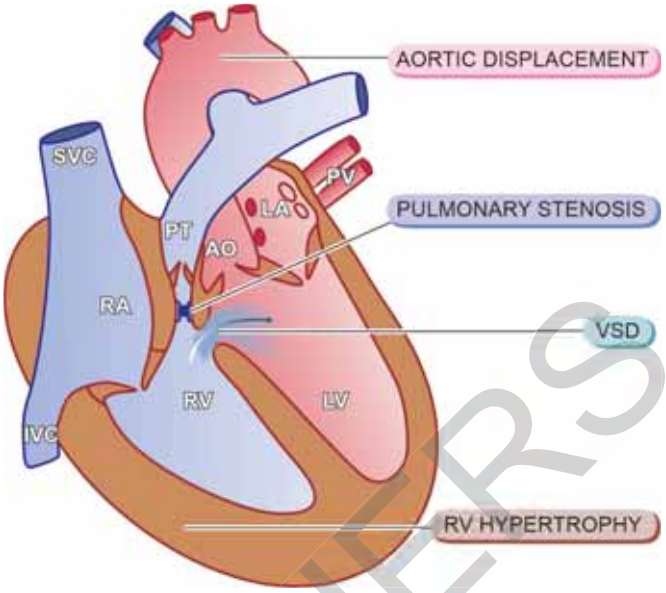


Figure 17.13 Tetralogy of Fallot, a schematic representation. (LA, left atrium; LV, left ventricle; PT, pulmonary trunk; PV, pulmonary vein; AO, aorta; RA, right atrium; RV, right ventricle; SVC, superior vena cava; IVC, inferior vena cava; PDA, patent ductus arteriosus; VSD, ventricular septal defect).

i) Postductal or adult type The obstruction is just distal to the point of entry of ductus arteriosus which is often closed **(Fig. 17.14)**. In the stenotic segment, the aorta is drawn in as if a suture has been tied around it. The aorta is dilated on either side of the constriction. The condition is recognised in adulthood, characterised by hypertension in the upper extremities, weak pulses and low blood pressure in the lower extremities and effects of arterial insufficiency such as claudication and coldness. In time, there is development of collateral circulation between pre-stenotic and post-stenotic arterial branches so that intercostal arteries are enlarged and palpable and may produce erosions on the inner surface of the ribs.

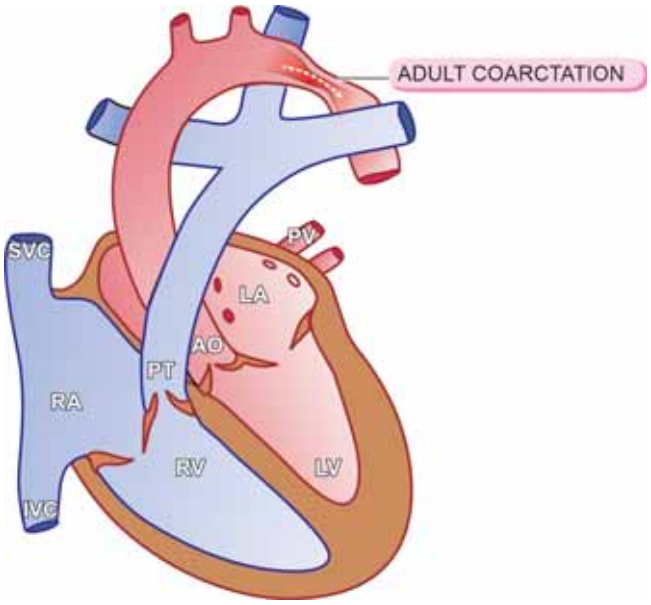


Figure 17.14 Postductal or adult type coarctation of the aorta, a schematic representation. (LA, left atrium; LV, left ventricle; PT, pulmonary trunk; PV, pulmonary vein; AO, aorta; RA, right atrium; RV, right ventricle; SVC, superior vena cava; IVC, inferior vena cava).

*Easy way to remember from acronym *PROV*e = *P*ulmonary stenosis, *R*ight ventricular hypertrophy, *O*verriding of aorta, *V*entricular septal defect.

ii) Preductal or infantile type The manifestations appear early in life. The narrowing is proximal to the ductus arteriosus which usually remains patent. The narrowing is generally gradual and involves larger segment of the proximal aorta. There is often associated interatrial septal defect. Preductal coarctation results in right ventricular hypertrophy while the left ventricle is small. Cyanosis develops in the lower half of the body while the upper half remains unaffected since it is supplied by vessels originating proximal to the coarctation. Children with this defect have poor prognosis.

AORTIC STENOSIS AND ATRESIA The most common congenital anomaly of the aorta is bicuspid aortic valve which does not have much functional significance, but predisposes it to calcification (page 451). Congenital aortic atresia is rare and incompatible with survival. Aortic stenosis may be acquired (e.g. in rheumatic heart disease, calcific aortic stenosis) or congenital.

PATHOLOGY Congenital aortic stenosis may be of three types: valvular, subvalvular and supravalvular.

i) Valvular stenosis The aortic valve cusps are malformed and are irregularly thickened. The aortic valve may have one, two or three such maldeveloped cusps.

ii) Subvalvular stenosis There is thick fibrous ring under the aortic valve causing subaortic stenosis.

iii) Supravalvular stenosis The most uncommon type, there is fibrous constriction above the sinuses of Valsalva.

In all these cases, there is pressure hypertrophy of the left ventricle and left atrium, and dilatation of the aortic root.

PULMONARY STENOSIS AND ATRESIA Isolated pulmonary stenosis and atresia do not cause cyanosis and hence are included under acyanotic heart diseases.

PATHOLOGY

Pulmonary stenosis It is the commonest form of obstructive congenital heart disease comprising about 7% of all congenital heart diseases. It may occur as a component of tetralogy of Fallot or as an isolated defect. Pulmonary stenosis is caused by fusion of cusps of the pulmonary valve forming a diaphragm-like obstruction to the outflow of blood from the right ventricle and dilatation of the pulmonary trunk.

Pulmonary atresia There is no communication between the right ventricle and lungs so that the blood bypasses the right ventricle through an interatrial septal defect. It then enters the lungs via patent ductus arteriosus.

KEY POINTS **Congenital Heart Disease**

- Congenital heart diseases are anomalies of the heart present since birth and are seen in ~1% of neonates. These anomalies may be either shunts (left-to-right or right-to- left), or defects causing obstructions to flow.
- Left-to-right shunts are acyanotic group of heart diseases, e.g. ventricular and atrial septal defects, and patent ductus arteriosus.
- Right-to-left shunts are cyanotic group of heart disease; examples are tetralogy of Fallot, transposition of great arteries, persistent truncus arteriosus and tricuspid atresia and stenosis.
- Obstructive congenital heart diseases are coarctation of aorta, and stenosis and atresia of aorta or pulmonary artery.
- Most common forms of congenital heart diseases are VSD, ASD, PDA, pulmonary stenosis and tetralogy of Fallot.

ISCHAEMIC HEART DISEASE

Ischaemic heart disease (IHD) is defined as acute or chronic form of cardiac disability arising from imbalance between the myocardial supply and demand for oxygenated blood. Since narrowing or obstruction of the coronary arterial system due to atherosclerosis is the most common cause of myocardial anoxia, the alternate terms *'coronary artery disease (CAD)'* and *'atherosclerotic cardiovascular disease'* are used synonymously with IHD.

Globally, it is estimated that IHD or CAD affects ~3-4% of world's population. It is the leading cause of death in high-income countries accounting for about a quarter of all deaths, and somewhat lower incidence is observed in low- and middle-income countries. A rising trend in incidence in the countries with increasing urbanisation and emerging economies is attributed to increased consumption of the energy-rich Western diet and thus higher prevalence of major risk factors for IHD such as obesity, lipid abnormalities, type 2 diabetes mellitus, and hypertension. In general, men develop IHD earlier than women and death rates are also slightly higher for men than for women until the menopause.

ETIOPATHOGENESIS

IHD is invariably caused by disease affecting the coronary arteries, the most prevalent being atherosclerosis accounting for more than 90% cases, while other causes are responsible for less than 10% cases of IHD. Therefore, it is convenient to consider the etiology of IHD under three broad headings:

i) coronary atherosclerosis;
ii) superadded changes in coronary atherosclerosis; and
iii) non-atherosclerotic causes.

I. CORONARY ATHEROSCLEROSIS

Coronary atherosclerosis resulting in 'fixed' obstruction is the major cause of IHD in more than 90% cases. The general aspects of atherosclerosis as regards its etiology, pathogenesis and the morphologic features of atherosclerotic lesions have already been dealt with at length in Chapter 16 (page 398). Here, a brief account of the specific features in pathology of lesions in *atherosclerotic coronary artery disease* in particular is presented.

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 (LAD), followed in decreasing frequency, by the right coronary artery (RCA), and still less in circumflex branch of the left coronary (CXA). 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 has *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 or 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 Atherosclerotic plaques in the coronaries are more often eccentrically located bulging into the lumen from one side **(Fig. 17.15)**. 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 (page 404).

II. SUPERADDED CHANGES IN CORONARY ATHEROSCLEROSIS

The attacks of *acute coronary syndromes,* which include acute myocardial infarction, unstable angina and sudden ischaemic death, are precipitated by certain changes superimposed on a pre-existing fixed coronary atheromatous plaque. These changes are as under:

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 result in thrombosis and 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 vessel.

III. NON-ATHEROSCLEROTIC CAUSES

Several other coronary lesions may cause IHD in less than 10% of cases. These are as under:

1. Vasospasm It has been possible to document vasospasm of one of the major coronary arterial trunks in patients with no significant atherosclerotic coronary narrowing which may cause angina or myocardial infarction.

2. Stenosis of coronary ostia Coronary ostial narrowing may result from extension of syphilitic aortitis or from aortic atherosclerotic plaques encroaching on the opening.

3. Arteritis Various types of inflammatory involvements of coronary arteries or small branches like in rheumatic arteritis, polyarteritis nodosa, thromboangiitis obliterans (Buerger disease), Takayasu disease, Kawasaki disease, tuberculosis and other bacterial infections may contribute to myocardial damage.

4. Embolism Rarely, emboli originating from elsewhere in the body may occlude the left coronary artery and its branches and produce IHD. The emboli may originate from bland thrombi, or from vegetations of bacterial endocarditis; rarely fat embolism and air embolism of coronary circulation may occur.

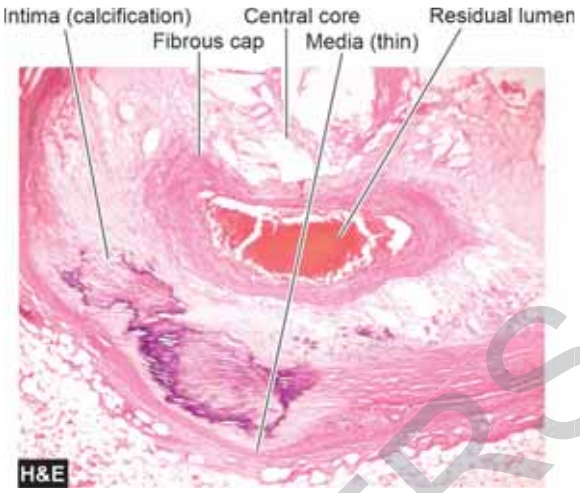


Figure 17.15 Left anterior descending (LAD) coronary artery showing critical narrowing with eccentric luminal obliteration due to atheromatous plaque having a hard sclerotic and calcified core. The residual lumen is reduced to a slit-like.

5. Thrombotic diseases Another infrequent cause of coronary occlusion is from hypercoagulability of the blood such as in shock, polycythaemia vera, sickle cell anaemia and thrombotic thrombocytopenic purpura.

6. Trauma Contusion of a coronary artery from penetrating injuries may produce thrombotic occlusion.

7. Aneurysms Extension of dissecting aneurysm of the aorta into the coronary artery may produce thrombotic coronary occlusion. Rarely, congenital, mycotic and syphilitic aneurysms may occur in coronary arteries and produce similar occlusive effects.

8. Compression Compression of a coronary from outside by a primary or secondary tumour of the heart may result in coronary occlusion.

EFFECTS OF MYOCARDIAL ISCHAEMIA

Development of lesions in the coronaries is not always accompanied by cardiac disease. Depending upon the suddenness of onset, duration, degree, location and extent of the area affected by myocardial ischaemia, the spectrum of changes and clinical features may range from an asymptomatic state at one extreme to immediate mortality at another end **(Fig. 17.16)**:

A. Asymptomatic state
B. Angina pectoris (AP)
C. Acute myocardial infarction (AMI)
D. Chronic ischaemic heart disease (CIHD)
E. Sudden cardiac death

The term *acute coronary syndromes* include a triad of acute myocardial infarction, unstable angina and sudden cardiac death.

ANGINA PECTORIS

Angina pectoris is a clinical syndrome of IHD resulting from transient myocardial ischaemia. It is characterised by paroxysmal pain in the substernal 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. It is more common in men past 5th decade of life.

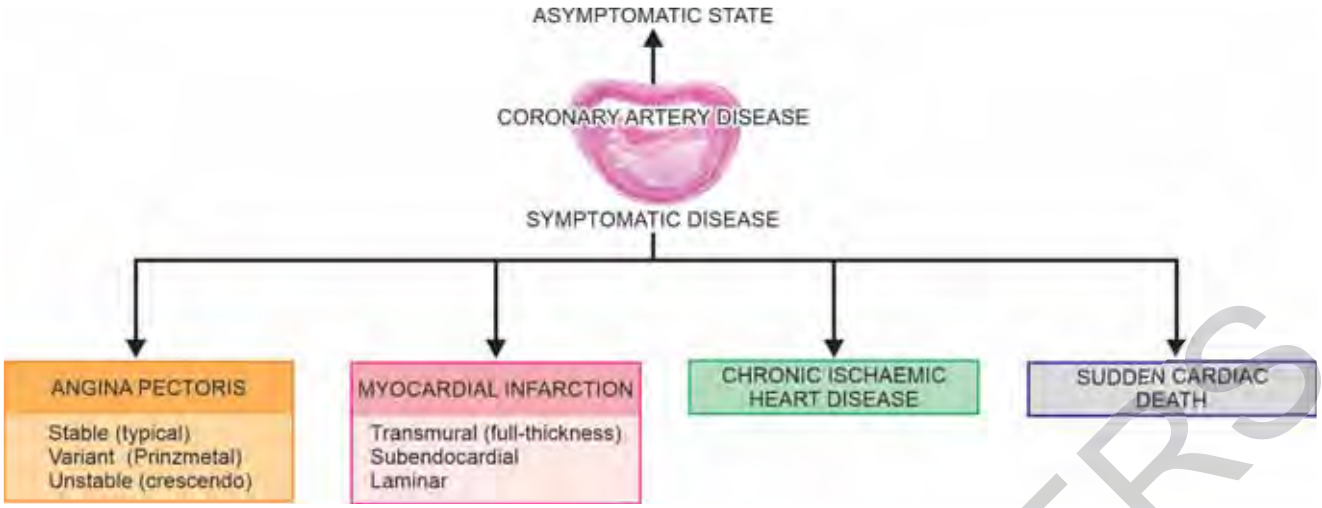


Figure 17.16 Spectrum of coronary ischaemic manifestations.

There are 3 overlapping clinical patterns of angina pectoris with some differences in their pathogenesis:

i) Stable or typical angina
ii) Prinzmetal variant angina
iii) Unstable or crescendo angina

STABLE OR TYPICAL ANGINA This is the most common pattern. Stable or typical angina is characterised 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.

PRINZMETAL VARIANT ANGINA This pattern of angina is characterised by pain at rest and has no relationship with physical activity. The exact pathogenesis of Prinzmetal 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.

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 characterised by more frequent onset of pain of prolonged duration and occurring often at rest. It is thus indicative of an impending acute myocardial infarction. Distinction between unstable angina and acute MI is made by ST segment changes on ECG—acute MI characterised by ST segment elevation while unstable angina may have non-ST segment elevation MI. *Multiple factors* are involved in the pathogenesis of unstable angina 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.

ACUTE MYOCARDIAL INFARCTION

Acute myocardial infarction (AMI) is the most important and feared consequence of coronary artery disease. Many patients may die within the first few hours of the onset, while remainder suffer from effects of impaired cardiac function. A significant factor that may prevent or diminish the myocardial damage is the development of collateral circulation through anastomotic channels over a period of time. A regular and well-planned exercise programme encourages good collateral circulation and improved cardiac performance.

INCIDENCE AMI accounts for 10-25% of all deaths, more so out of hospital. There is a decline in mortality for hospital in-patients from 10 to ~5%. Due to the dominant etiologic role of coronary atherosclerosis in AMI, its incidence correlates well with the incidence of atherosclerosis in a geographic area.

Age AMI may virtually occur at all ages, though the incidence is higher in the elderly. About 5% of heart attacks occur in young people under the age of 40 years, particularly in those with major risk factors to develop atherosclerosis like hypertension, diabetes mellitus, cigarette smoking and dyslipidaemia including familial hypercholesterolaemia.

Sex Males throughout their life are at a significantly higher risk of developing AMI as compared to females. Women during reproductive period have remarkably low incidence of AMI, probably due to the protective influence of oestrogen. The use of oral contraceptives is associated with high risk of developing AMI. After menopause, this gender difference gradually declines but the incidence of disease among women never reaches that among men of the same age.

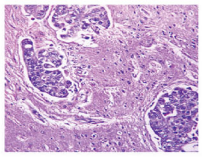
ETIOPATHOGENESIS The etiologic role of severe coronary atherosclerosis (more than 75% compromise of lumen) of one or more of the three major coronary arterial trunks in the pathogenesis of about 90% cases of AMI is well documented by autopsy studies as well as by coronary angiographic studies. A few notable features in the development of acute MI are as under:

1. Myocardial ischaemia Myocardial ischaemia is brought about by one or more of the following mechanisms:

i) Diminished coronary blood flow, e.g. in coronary artery disease, shock.
ii) Increased myocardial demand, e.g. in exercise, emotions.
iii) Hypertrophy of the heart without simultaneous increase of coronary blood flow, e.g. in hypertension, valvular heart disease.

2. Role of platelets Rupture of an atherosclerotic plaque exposes the subendothelial collagen to platelets which undergo aggregation, activation and release reaction. These events contribute to the build-up of the platelet mass that may give rise to emboli or initiate thrombosis.

3. Acute plaque rupture In general, slowly-developing coronary ischaemia from stenosing coronary atherosclerosis of high-grade



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A Gold Medallist in academics from Panjab University, Dr Mohan has served as former founding Professor and Head, Department of Pathology at Government Medical College and Hospital, Chandigarh, India for about 22 years until his superannuation in July 2015. An alumnus of Postgraduate Institute of Medical Sciences (PGIMS), Rohtak, Haryana, India, he initially worked on the faculty of his alma mater in various capacities until 1993. Dr Mohan has over 45 years of rich professional experience in teaching and diagnostic pathology, has published over 300 scientific articles in national and international indexed journals, and has authored 8 books. He was Editor-in-Chief of Indian Journal of Pathology and Microbiology (2003-07), and President of Indian Association of Pathologists and Microbiologists (2008). Besides other awards and honours, he was conferred Haryana Vigyan Ratna (2010-11), in recognition of his outstanding contribution to medical science and education, and Lifetime Achievement Award conferred by National Medicos Organisation in 2018. His keen interests in teaching, perfectionist attitude, and meticulous approach have won him love and adoration from his students and colleagues, and are best reflected in his works in books.

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