CHAPTER VII

CARDIO-VASCULAR SYSTEM

Introduction. The **primary function** of the cardio-vascular system is to provide an adequate supply to all cells of the body, of materials needed for their proper function and that carries away the waste products of their metabolism. It is a well-organised transport system of the body by which the blood being circulated within a closed system under different **pressure gradients,** created by the pumping mechanism where heart acts as the central pump (FIG. 129). The cardio-vascular system includes (*i*) **heart,** (*ii*) **arteries,** (*iii*) **capillaries** and (*iv*) **veins.** They all differ in structures as well as in functions. The volume of blood in our body is limited, but it has to perform unlimited amount of work continuously. This naturally leads to the conclusion that the same quantity of blood must be used over and over again. In other words, *blood must circulate.* One simple example will clarify. The total blood volume can carry about 1,200 ml of O_2, and this amount can meet the oxygen needs of the body for about five minutes only. So blood must be re-oxygenated and sent back to the tissues at every five minutes. Many other similar examples indicate that blood must circulate continuously in a cyclical manner, doing the same job repeatedly.

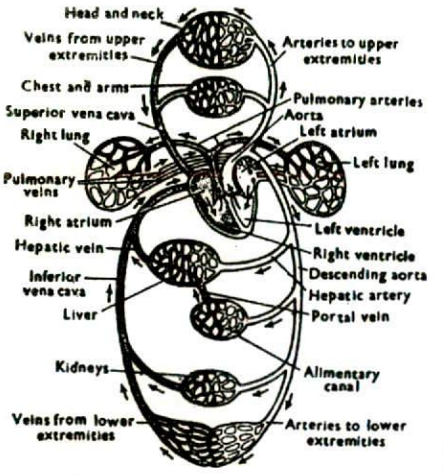


FIG. 129. Diagram illustrating the arrangement of the different parts of the circulatory system.

Blood gets reduced in the tissues and oxygenated in the lungs. Consequently, it has to pass alternately through lungs and tissues, doing opposite functions at these two places. Hence, circulatory system has been divided into two functionally opposite parts: (1) The **systemic circulation** (Greater circulation with high resistance circuit)—passing through the tissues. (2) The **pulmonary circulation** (Lesser circulation with low resistance circuit)—passing through the lungs. The two systems again meet in the heart (FIG. 130).

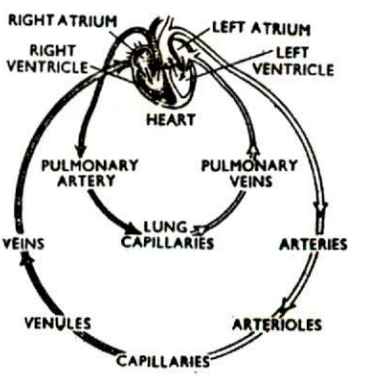


FIG. 130. Schematic representation of the relationship between systemic and pulmonary circulation.

The **main functions of circulation** are to make available to the tissues its different metabolic needs and on the

other hand to carry away from the tissues the CO_2 and other metabolic waste products for elimination from the body. These are done in two ways: (1) By maintaining an efficient circulation, so that blood supply to every part of the body—in rest and activity—may be assured. (2) By maintaining an optimum blood pressure which is essential for capillary exchange.

Anatomical considerations of heart. The heart is roughly *heart*-shaped* structure and rests obliquely in the thoracic cavity (FIG. 131). The anterior surface of the heart faces the sternum, the posterior surface—the base of the cone faces the vertebral column and the inferior or diaphragmatic surface rests on the diaphragm. The heart has got

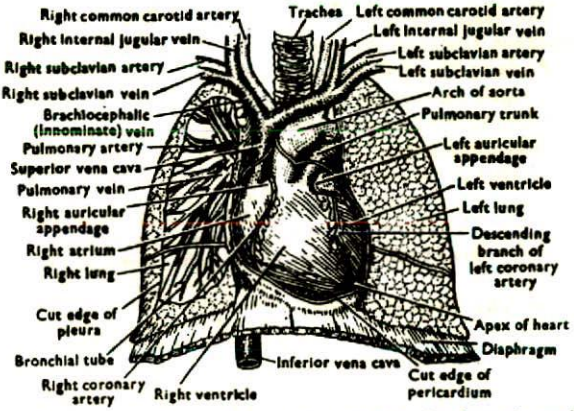


FIG. 131. Anatomical position of the heart in the thoracic cavity.

four chambers (FIG. 132): **two ventricles** and **two atria****—both **right** and **left.** The two left chambers are separated from the two right ones, by a continuous partition, the atrial portion of which is called the *interatrial septum* (fibrous) while the ventricular part is known as the *interventricular septum* (upper one-fourth fibrous, lower three-fourths muscular). From the left ventricle arises the *aorta*, carrying oxygenated blood to the tissues. From the right ventricle, which is *less muscular than the left*, arises the *pulmonary trunk*, carrying reduced blood to the lungs. The right atrium receives all the venous blood from the body through three veins : the *inferior* and the *superior venae cavae*, and the *coronary sinus*. The left atrium receives all the oxygenated blood from the lungs through *pulmonary veins*.†

Thus the four chambers of heart perform four different functions. The course of circulation is as follows (FIGS. 129 & 130). The left ventricle propels oxygenated blood to the tissues. Here, it gives up

* Like 'heart' of playing cards.

** Atrium is sometimes called *auricle*. Strictly speaking, the auricles mean the ear-like flaps protruding from the atria, although atria and auricles are often used synonymously.

† The term *artery* means a vessel which carries blood away from the heart. The term *vein* indicates a vessel carrying blood towards the heart. In the systemic circulation arteries carry oxygenated blood (arterial blood) and the veins carry reduced blood (venous blood). But in the pulmonary circulation their functions are opposite.

oxygen and becomes reduced. The reduced blood comes back to the heart through the veins and is received by the right atrium. From the right atrium it passes into the right ventricle, which then propels it into the lungs. Here, it becomes re-oxygenated, and is returned to the left atrium through the pulmonary veins. From here it enters the left ventricle and is pumped out into the *greater circulation* again. In this way circulation goes on. The *systemic circulation*, therefore, begins in the left ventricle and ends in the right atrium. The *pulmonary circulation* starts in the right ventricle and ends in the left atrium (FIG. 130). The right half of the heart is concerned with reduced blood, while the left half with oxygenated blood. Two technical terms are used in connection with heart, e.g., systole and diastole. The term **systole** means contraction and **diastole** means relaxation.

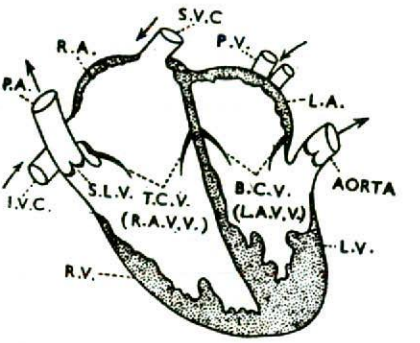


FIG. 132. Showing the chambers, valves and vessels of heart. T.C.V. (R.A.V.V.)—Tricuspid Valve (Right Atrioventricular Valve); B.C.V. (L.A.V.V.)—Bicuspid Valve (Left Atrioventricular Valve); R.V.—Right Ventricle; L.V.—Left Ventricle; R.A.—Right Atrium; L.A.—Left Atrium; S.V.C.—Superior Vena Cava; I.V.C.—Inferior Vena Cava; P.A.—Pulmonary Artery; P.V.—Pulmonary Vein; S.L.V.—Semilunar Valve.

Valves of the heart (FIGS. 132 & 133). There should not be any admixture between arterial and venous blood. In other words, *circulation must be strictly one way*. This is done by the action of valves. There are four sets of valves in the heart. The right atrioventricular opening is guarded by **tricuspid** valve (*anterior* (infundibular), *posterior* (marginal) and *medial* (septal) cusps), the left opening by the **mitral** (due to its resemblance to a bishop's mitre) or **bicuspid** valve (*anterior* (aortic) and *posterior* cusps). The openings of the aorta and pulmonary artery are guarded by **semilunar** valves (three cusps).

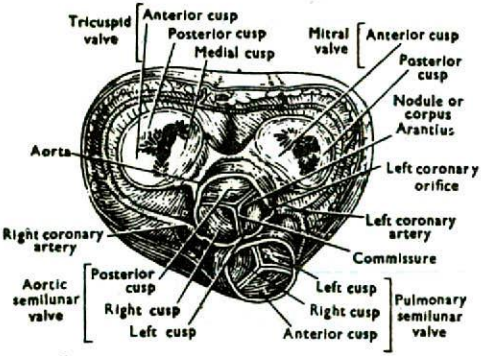


FIG. 133. Diagrammatic representation of open A.V. valves of the heart in *diastole* (atria removed) permitting blood flow into ventricles.

The cusps of tricuspid valve and mitral valve are triangular in shape and are attached at their bases to the margins of fibrous connective tissue encircling the atrioventricular orifices. These valves open when the blood passes from the atria to the ventricles. The apices of the valves are projected within the ventricles during flowing of blood into ventricles. But the apices are restricted to bulge within the atrium during ventricular contraction by the presence of

chordae tendineae which attach the apical end of the valve and the **papillary muscle** in the ventricular wall at the other (FIG. 134). During ventricular contraction the pressure of blood forces the cusps into apposition and closes the orifice and the chordae tendineae prevent the cusp to go inside the atria or allowing blood to be ejected back into the atria. During the contraction of ventricular walls, the papillary muscles contract simultaneously and do not assist to close the valves. These muscles also pull vanes of the valves inwards toward the ventricles to prevent excessive backward bulging of the valves toward the atria. If one of the papillary muscles is paralysed or if a chorda tendinea is ruptured under certain abnormal conditions (i.e., ischaemia), the valves bulge far backwards.

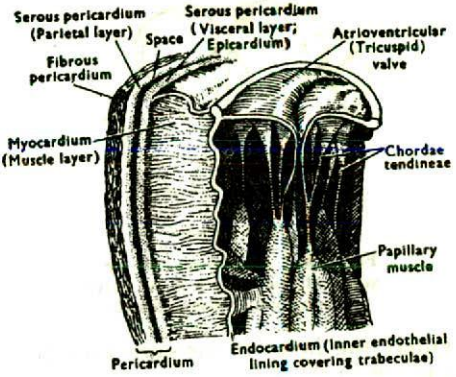


FIG. 134. Diagram shows the arrangement of A.V. valves and their attachment with chordae tendineae and papillary muscles.

The larger and stronger **aortic semilunar valve** (*right* (anterior), *left* and *posterior* (right) cusps) guards the orifice between the left ventricle and the systemic aorta, whereas the **pulmonary (pulmonic) semilunar valve** (*anterior* (left), *right* and *left* (posterior) cusps) guards the opening between the right ventricle and the pulmonary trunk. *Thicker nodules* or **corpora Arantii** are attached at the centre of free margin of each semilunar pocket. **Sinuses of Valsalva** or *aortic sinuses* are present between aortic wall and cusps of the valve (FIG. 133). During **ventricular contraction** the intraventricular pressure rises and the push opens the valves. During **ventricular relaxation** the blood begins to flow back and the cusps are thus kept in apposition and the orifice is closed (FIG. 135).

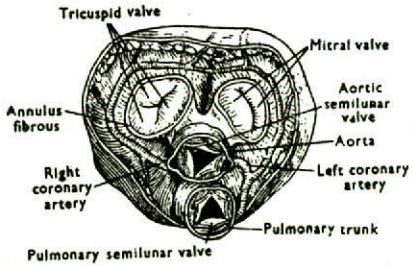


FIG. 135. Diagram showing the heart after removal of atria in *systole* with open semilunar valves.

Action of the valves. The atrioventricular (A.V.) valves open towards the ventricles and close towards the atria. The semilunar (S. L.) valves open away from the ventricles and close towards the ventricles. So that when atria contract, atrioventricular valves open and blood passes into the ventricles (FIG. 136). When ventricles contract, atrioventricular valves close, but semilunar valves open. This prevents regurgitation of blood into the atria but allows it to flow out of the ventricles (FIG. 137). *In this way circulation becomes one way.*

Heart is a miracle of constants. The two ventricles contract

simultaneously, as also the two atria. The same amount of blood passes out of the ventricles at the same time during systole. The same amount of blood

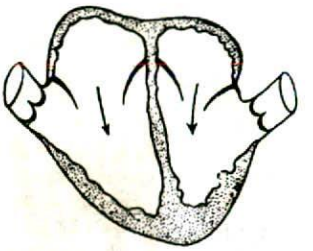


FIG. 136. Condition of heart when atria contract. A. V. valves open, S. L. valves closed.

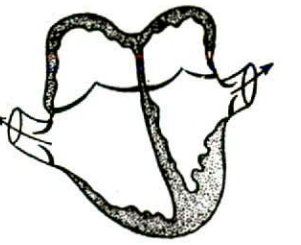


FIG. 137. Heart during ventricular contraction. A. V. valves shut, S. L. valves open.

enters the heart at the same time during diastole. Any discrepancy in the time or in the quantitative relations may ultimately cause heart failure.

Histology of cardio-vascular system. The aorta divides successively into branches of gradually diminishing calibre. It, at first, breaks up into a number of big *arteries*, each one of which divides into a number of smaller arteries. Each small artery gives rise to a bunch of **arterioles** (0·2 mm outside diameter). Blood flows from the arteriole into a **metarteriole** and then into the **capillaries** (7–9 μ in diameter). Zweifach has shown that the metarterioles lead into **thoroughfare (preferential) channels** which lead into **venules.** The **true capillaries** which are shorter in length arise from the metarterioles, arterioles and thoroughfare channels (FIG. 138). In each capillary there is a *precapillary sphincter* which is under the control of the sympathetic nervous system. By means of this sphincter blood flow through the capillary may be adjusted. *At each division, the vascular bed enlarges and blood pressure falls*—because the total cross-section of the branches is greater than the parent vessel. The capillaries collect into **venules,** venules into **veins** and ultimately come back to the heart through the two venae cavae.

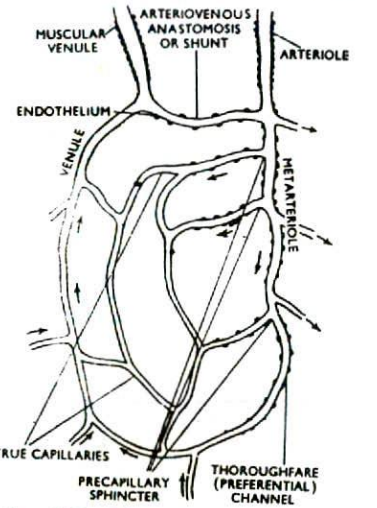


FIG. 138. Diagrammatic representation of the structural pattern of the capillary bed.

The whole circulatory system is built up on the same histological plan. There are *three layers:* the outer layer is made up of fibrous tissue (collagen) and elastic tissue **(tunica adventitia** or **externa)**, the middle layer of plain muscles and a network of elastic fibres **(tunica media)** and the inner layer of endothelium surrounded by an elastic layer **(tunica intima** or **interna)** (FIGS. 139 & 140). But all the layers are not found equal proportions in all the vessels (FIG. 141). In the **heart,** tunica adventitia is

represented by the **fibrous pericardium;** the media by cardiac muscle and the intima, by the **endocardium.**

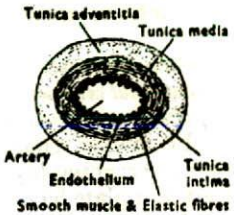


FIG. 139. Diagram showing the cross-section through an artery.

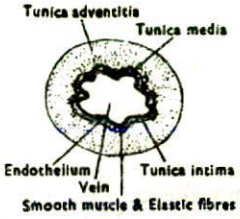


FIG. 140. Diagram representing the cross-section through a vein.

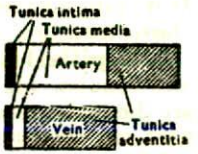


FIG. 141. Diagram shows the comparative thickness of different layers in artery and vein.

Histological characteristics of the different vascular systems are described below: **Arteries.** In the arteries, all the layers (FIG. 142) are present. The two outer layers are very thick, because it has to withstand considerable blood pressure. The *tunica media* consists chiefly of circularly arranged smooth muscle cells. The *tunica adventitia* is composed chiefly of white fibrous connective tissue that run parallel to the long axis of the blood vessels and a definite external elastic membrane is present very close to the media. This outer coat is comparatively non-elastic and limits the stretching of the artery and thus prevents undue distention and rupture. A special system of vessels—the *vasa vasorum*—passes into the arterial wall to supply blood to these layers. The *tunica intima* consists of a single layer of endothelium, set upon a basement membrane of elastic tissue—known as the *internal elastic membrane* (*elastic lamina*). This lamina is thrown into folds to prevent injury to the endothelial lining as may occur owing to pulsation. Besides these, there is also an inner endothelial lining which is *subendothelial layer* of delicate fibro-elastic (areolar) connective tissue.

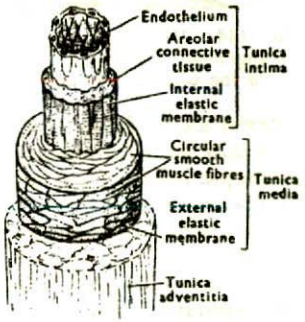


FIG. 142. Diagrammatic structure of arterial wall.

Arterioles. The arterioles have got relatively thick walls and narrow lamina. These vessels are rich in vasomotor innervation and are capable of distributing blood to the different portions of the body by vasodilatation and vasoconstriction. Pressure and flow of the vascular systems are principally maintained through modifying the lumen of the arterioles.

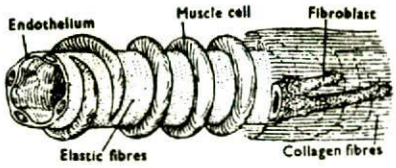


FIG. 143 Diagrammatic representation of the structure of an arterial wall showing endothelium, muscle cells, elastic fibres, etc.

The arterioles also possess three layers (Fig. 143). The *tunica intima* consists of endothelial lining and internal elastic membrane.

But it is devoid of subendothelial fibro-elastic connective tissue. The *tunica media* is composed of one to five layers of muscle cells and contains scattered elastic fibrils. The *tunica adventitia* is also present and is very thin. It is composed of loose connective tissue. There is no definite external elastic membrane.

Capillaries. These make a connective link in between the arterioles and venules. They are linked by a single layer of *flat endothelial cells* which are the major component of the wall (FIG. 144). The capillary endothelium does not directly touch the elements of other tissues and is always separated from a supporting bed of the connective tissue by an intervening layer —the *basal lamina.* Each endothelial cell consists of curved thin plate having an ovoid or elongated nucleus. The cells are generally stretched and

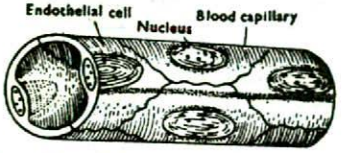


FIG. 144. Diagram representing the arrangement of endothelial cells along the wall of a blood capillary.

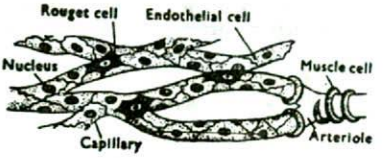


FIG. 145. Diagram showing Rouget cells and capillary networks where oxygen and nutrient materials are received.

tapered along the axis of the capillary. The capillaries are also surrounded by a thin layer of delicate collagenous and reticular fibres. These are also accompanied by fixed macrophages, fibroblasts, undifferentiated mesenchymal cells and a few cells belonged to accompanying nerve fibres. Besides these, there are peculiar type of cells with long branching processes that surround the capillary walls. These cells are known as **Rouget cells.** These cells (FIG. 145) were known to function as contractile elements of the capillaries. But recent observations claim that the contractility of the capillaries are independent of Rouget cells.

The average diameter of the capillaries is 7–9 μ and just allowing blood corpuscles to pass through. In resting state the most of the capillaries remain closed and during functional state all of the capillaries mostly open up. According to Zweifach, the arteriovenous shunt is always present in a capillary bed (*vide* page 230).

Recent electron microscopic studies have added a considerable knowledge on the structure of capillaries. According to Fawcett and others, the capillaries can be grouped into (*i*) **muscular type** and (*ii*) **fenestrated type.** The *muscular type* (FIG. 146) comprises the capillaries of the cardiac muscle, smooth muscle, lung, central nervous system and also other

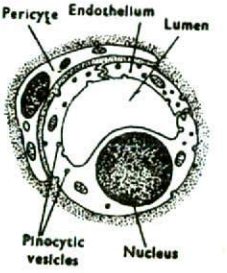


FIG. 146. The *muscular type* of capillary showing thick endothelium with pinocytic vesicles (diagrammatic).

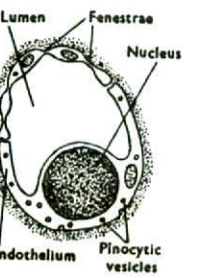


FIG. 147. The *fenestrated type* of capillary showing relatively thin endothelium with *Fenestrae* (diagrammatic).

tissues, which have got uninterrupted endothelial cell of approximately equal thickness with occasional luminal bulges due to location of cell nuclei. The *fenestrated type* (FIG. 147) comprises the capillaries of many endocrine glands, intestinal mucosa, renal glomerulus and certain other organs. In this type the endothelial linings are not continuous and attenuated with numerous pores ranging from 300 to 500 Å. The pores or circular fenestrations are not completely open but are covered by a diaphragm thinner than the cell membrane (FIG. 147). The glomerular capillaries of the kidney have got large pores which are enveloped by the continuous basal lamina. These large pores are very important in production of glomerular filtrate. From electron microscopic studies, it reveals that all capillaries have got numerous small vesicles along the luminal and basal surfaces of the endothelial cells. These vesicles are known as **pinocytic vesicles** or **caveolae intracellulares.** These vesicles are presumably formed by the invagination of the cell membrane and are involved in the transport of fluid across the cell membrane.

Sinusoids. Sinusoids and sinusoidal capillaries are not true capillaries and they have got relatively large calibre (30 μ) with irregular and tortuous walls. Continuous endothelial lining is absent. There is also some incomplete lining of phagocytic cells. Due to absence of basal lamina, the blood gets direct contact with the tissue cells.

Sinusoids differ from the capillaries on the following points:

(*i*) Capillaries have got complete endothelial lining whereas the sinusoids have got irregular linings of both endothelial and phagocytic cells. Basal lamina is absent and blood can have direct contact with the tissue cells within the sinus.

(*ii*) The capillaries are surrounded by thin layer of connective tissue but the sinusoids are lined by a network of reticular fibres.

(*iii*) Capillaries always make a connecting link in between the arteries and veins whereas the sinusoids always make connecting link with the same type of vessels.

(*iv*) Sinusoids are of comparatively large calibre (30 μ) and, the velocity of flow is very slow.

Veins. In veins all the three layers are present but the intima and media are comparatively thinner than those of arteries only due to reduction of muscular and elastic components. Though the walls are very thin yet the vessels are very strong due to presence of connective tissue components.

In *tunica intima*, the endothelial cells are less elongated than those of the arteries. A little connective tissue along with a few fine elastic fibres are present. In *tunica media*, there is little elastic tissue and muscle. There is also considerable collagen fibres. The *tunica adventitia* is much developed and much thicker than the tunica media due to presence of muscle, collagen and elastic fibres. Structures of the veins all throughout are not same and differ from one place to another. Some veins do not possess smooth muscle. These are the cerebral veins, meningeal veins, retinal veins, etc.

Valves of the veins. Valves are present in most of the veins particularly of those of the lower limb. These valves prevent backflow from the heart. These are **semilunar pocket** like flaps (FIG. 148) formed by the local folding of the intima.

Blood vessels of blood vessels (vasa vasorum). Large arteries and veins of diameter above 0·1 mm are generally supplied with nutrient

blood vessels which arise from the adjacent small arteries. In large arteries the vasa vasorum penetrates or may penetrate all the layers of the blood vessels and ends ultimately with the lumen of the artery. In true sense, the vasa vasorum actually supplies the tunica adventitia and the external part of the tunica media.

Lymphatics of blood vessels. Lymphatic vessels are also present abundantly in the adventitial and periadventitial tissue.

Factors that maintain circulation

1. **Pumping action of the heart.** This is the main motive force of circulation.

2. **Elastic recoil of the arteries.** Ventricles contract during systole and relax during diastole. So during systole certain amount of blood is being led directly into the aorta and thus the vessel is stretched (potential energy is gained). But due to elasticity of blood vessel wall, the aorta recoils during diastole of the ventricle and thus blood moves forward (due to change of potential energy into kinetic energy for flow) towards the periphery as the backward movement is restricted due to presence of semilunar valves.

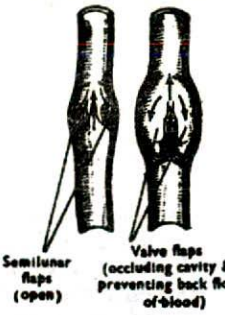


FIG. 148. Diagram depicts the action of valves.

3. **Pressure gradient.** Blood pressure gradually falls from the left to the right side of the heart. In the big *arteries* the average pressure is **120 mm of Hg;** in the *arterioles* the pressure sharply falls to about **50-60 mm of Hg;** in the *capillaries* the pressure is about **15 mm of Hg;** in the veins the pressure falls further, while near the heart the pressure is 0 mm of Hg or even negative. Due to this pressure gradient blood passes from the higher to the lower pressure, i.e., from the left to the right side of the heart.

4. **Respiration.** During inspiration intrathoracic pressure falls and intra-abdominal pressure rises. Hence, with each inspiration, venous blood is sucked up by the thorax and is pumped out by the abdomen. In this way respiration helps venous return and acts as a great force in maintaining circulation.

5. **Muscular exercise.** When muscles contract, they squeeze the capillaries and veins, and thus help venous return. This is aided by the valves of veins, which prevent the passage of blood back towards the capillary bed (FIG. 149).

6. **Effect of gravity.** Above the level of heart, it helps venous return. But below the level of heart, it works against it.

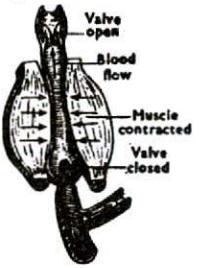


FIG. 149. Showing the action of valves of a vein during muscular exercise.

SPECIAL JUNCTIONAL TISSUES OF THE HEART

Cardiac muscle consists essentially of certain specialised structures which are responsible for initiation and transmission of cardiac impulses at a higher rate than the rest of the muscle. Those specialised cardiac tissues operate such mechanism *are collectively known as the* **junctional tissues** *of heart* (FIG. 150). They comprise the following structures: (1) **Sino-atrial** (S. A.) **node.** (2) **Atrioventricular** (A. V.) **node.** (3) **Bundle of His**

(atrioventricular bundle). (4) The **right** and **left** branches of the bundle —ending in the (5) **Purkinje fibres.**

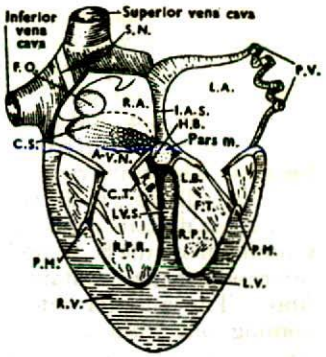


FIG. 150. Diagrammatic representation of location and distribution of specialised nodal tissues and conducting tissues in human heart.
S.N.=sinus node; F.O.=foramen ovale; C.S.=coronary sinus; R.A.=right atrium; L.A.=left atrium; I.A.S.=interatrial septum; P.V.=pulmonary vein; Pars m.=pars membranacea; A.V.N.=atrioventricular node; H.B.=bundle of His; P.M.=papillary muscle; R.B.=right branch of bundle of His; L.B.=left branch of bundle of His; I.V.S.=interventricular septum; C.T.=chordae tendineae; F.T.=*false tendon* of Purkinje network; R.V.=right ventricle; L.V.=left ventricle; R.P.R.=ramification of Purkinje fibres within right ventricle; R.P.L.=ramification of Purkinje fibres within left ventricle. (*Used with permission*).

From Marshall, Jean M. : The heart. In Mountcastle, Vernon B., editor: Medical physiology, ed. 12, St. Louis, 1968, The C. V. Mosby Co. ; redrawn from Schutz, E. : Physiologie des Herzens, Berlin, 1958, Springer-Verlag.

Histology of the cardiac muscle has been described on pp. 60–62. The sino-atrial and atrioventricular nodes and bundle of His are composed of specialised cardiac tissue (FIG. 151) and contain high amount of glycogen. These have got more sarcoplasm than the rest of the cardiac muscle fibres. *Purkinje fibres* also contain high amount of glycogen in their sarcoplasm. The atrial muscle fibre is connected with the ventricular muscle fibre only through the bundle of His because a fibrous tissue ring keeps the atrial muscle separated from the ventricular muscle. Damage of bundle of His causes dissociation of atrial and ventricular rhythm.

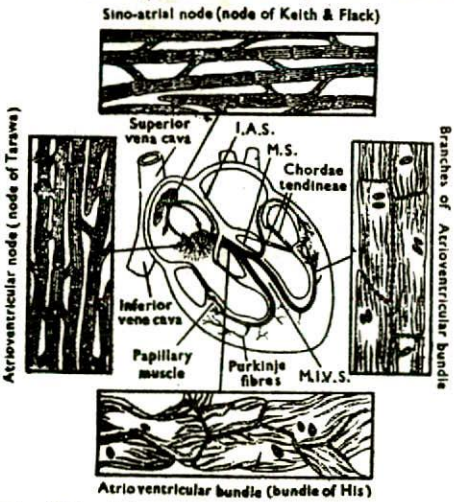


FIG. 151. Diagrammatic representation of different specialised cardiac tissues. I.A.S.=interatrial septum, M.S.=membranous septum, M.I.V.S.=muscular interventricular septum.

1. **Sino-atrial node** (Keith and Flack, 1907). It is situated in the right atrium at the junction of superior vena cava and the right auricular appendage (FIG. 131). It extends downwards along the *sulcus terminalis* for about 2 cm (three-fourths of an inch). It is broader at the top and tapering below, and measures about 5×20 mm. **Histology.** It is made up of modified cardiac muscle fibres. The fibres are thin (one-third the size of cardiac muscle fibres), elongated, tapering at the ends, longitudinally striated and intercrossing with one another in a plexiform manner.

This nodal tissue possesses relatively few myofibrils and also it is claimed to consist of a dense network of small Purkinje fibres. Some investigators

believe that the transmission of cardiae impulse from the S. A. node to the A. V. node is mostly facilitated by the presence of Purkinje fibres in the atria. No pathways of special fibres have yet been satisfactorily demonstrated until recently in the walls of the atria.

From electrophysiological studies, Carvalho and others (1959) have suggested that the possibility of preferential channels for impulse conduction in both dog and rabbit atria. They have recorded the Purkinje-like action potential from single fibres within a band of tissues—the **sinus ring bundle.** This sinus ring bundle encircles the venae cavae and one branch of the bundle goes to the sinus region very close to the A. V. node. Goldman (1970) has described that there are **three internodal atrial pathways** originating from the S. A. node go to the A. V. nodal region ((Fig. 152). These internodal tracts contain Purkinje type of fibres. The anterior internodal tract after coming out from the S. A. node curves round the superior vena cava and anterior wall of the right atrium. Here it bifurcates into two branches, one of which goes to the left atrium and other goes to the anterior superior region of the A. V. node. The middle internodal tract and posterior internodal tract after coming out from the S. A. node curve behind the superior vena cava and end in the superior margin and posterior margin of the A. V. node respectively. In between three internodal tracts there are interconnecting fibres which merge just above the A. V. node and also by-pass this node. In between the muscle cells, many nerve cells are found which act as relay stations for the vagus only. Excitor sympathetic fibres are also found here.

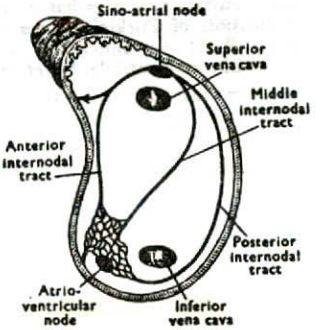


Fig. 152. Diagram shows the internodal pathways of impulse-conducting systems from S.A. node to A.V. node (after Goldman).

Functions. It generates the normal cardiac impulse at the rate of 70 to 80 per minute in the adult and acts as the **pacemaker** of heart and the rhythm originated from this region is generally designated as **sinus rhythm.**

2. **Atrioventricular node** (Tawara, 1906). It is situated in the right atrium at the posterior part of the interatrial septum close to the opening of the coronary sinus. It measures about 2×5 mm. The presence of the atrioventricular node was first identified by Kent in 1892 and afterwards His in 1893 described a band of modified muscle fibres to course from the atrium to the ventricle. Tawara (1906) described in details the presence of this specialised tissue in many species of animals. **Histology.** The cells of the A. V. node are cardiac muscle fibres but have a few myofibrils. It also consists of Purkinje fibres which form a dense network. The node is extended into the common—the atrioventricular bundle (bundle of His). **Functions.** (*a*) It receives the impulse originating from the S. A. node and transmits it to the ventricles through the bundle of His. (*b*) It acts as **reserve pacemaker.** The rhythm that is originated in the A. V. node is known as **nodal rhythm.** (*c*) It also initiates the cardiac impulse, but at a slower rate (40 to 60 per minute). In abnormal conditions, when the S. A. node fails, the A. V. node generates the impulse (***nodal rhythm***).

The sino-atrial node is a right-sided structure, being the remnant of tissues at the entrance of the primitive right great vein, which in the higher animals, becomes transformed into superior vena cava. Hence, it is supplied by the right vagus nerve and is situated in the right atrium, near the superior vena cava. The A. V. node, on the other hand, is a left-sided structure being developed from similar tissues of the primitive left great vein which in the mammalian heart becomes the coronary sinus. Hence, it is supplied by the left vagus nerve.

3. **Bundle of His.** *Course*—The main trunk of this bundle is continuous with the A. V. node and passes upwards until it reaches the posterior margin of the membranous part of the interventricular septum and then forwards below it. It measures about 20 mm long.

4. **Bundle branch.** Just above the muscular part of the septum, the bundle divides into right and left branches. The right bundle branch is longer than the left one. The left bundle branch bifurcates into superior and inferior divisions. It pierces the *membranous septum*; enters the left ventricle and passes along the muscular septum towards the apex. The left branch ends in the Purkinje systems of the ventricular subendocardial tissue (Fig. 153). The right branch passes down the right side of the septum. These branches remain just under the endocardium. They are finally distributed through the terminal arborisations of a special type of cardiac muscle fibres, known as the *Purkinje fibres*. The main bundle (bundle of His), its right and left branches and the finer ramifications of the latter remain ensheathed in a special connective tissue covering and thus separated from the surrounding cardiac muscles. **Histology.** The bundle is about 1–2 mm thick, consisting of fusiform parallel fibres with scanty striations. They are rich in glycogen. The fibres gradually increase in size as one proceeds onwards, and merges with the Purkinje fibres. **Functions.** (1) *Conduction*—Its normal function is to conduct the atrial impulse into the ventricles. (2) *Rhythmicity*—When the S. A. and A. V. nodes fail, the bundle can originate cardiac impulse. But the rate is very slow, about 36 per minute.

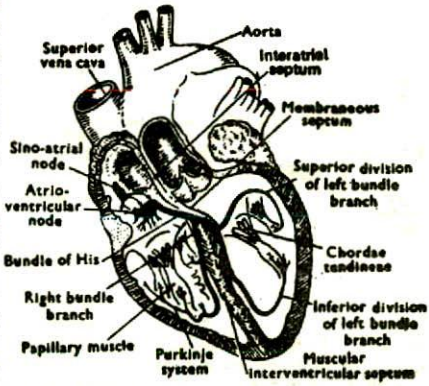


Fig. 153. Diagrammatic representation of conducting system of heart muscle.

5. **Purkinje fibres.** The Purkinje fibres which arise from the branches of the bundle of His, spread from the interventricular septum directly to the papillary muscle and then to the lateral walls of the ventricle ending ultimately within the subendocardial network. Purkinje (1845) first observed the presence of these fibres in the subendocardial tissue of the ungulate heart. Purkinje fibres have got a larger diameter (50 to 70-μ) than the ordinary cardiac muscle fibre (15 μ). It also contains relatively more sarcoplasm with large amount of glycogen. Myofibrils in the fibre are present mostly in the periphery of cells and the central space is occupied by glycogen. **Functions.** Main function of these fibres is to conduct impulse quickly to every part of the ventricular muscle fibre. These fibres also can initiate impulse (30–35 per min.) in case of atrioventricular dissociation.

This specialised conducting tissue—the Purkinje fibres has been demonstrated only in the ventricles of the birds and mammals. In fishes, amphibia and reptiles these are not usually present and conduction is made through the ordinary cardiac muscle fibre. It is claimed that these fibres are relatively poor in carnivores, mammals and primates but highly developed in ungulates. These fibres ramify into the subendocardial network and ultimately loose their special characteristics gradually and become ordinary cardiac muscle fibres.

Origin of the heart beat

Initiation of impulse and localisation of pacemaker. By separating atria from the ventricles of excised hearts, William Harvey in 1628 had shown that the atrial rhythm was higher than the ventricular rhythm. Keith and Flack (1907) have described that from the S. A. node the heart beat first starts. If the impulse conduction from this area is cut off by giving a Stannius ligature between the sinus and atrium of the frog heart (first Stannius ligature), the heart beat does not cease but a new slower rhythm develops within a few seconds from a new pacemaker area. This indicates that the S. A. node (sinus) is not the only pacemaker area, there is other pacemaker area—the A. V. node which can maintain the beat in its absence. If second ligature is applied in the same heart in between the atrium and ventricle then ventricle begins to beat at a more slower rate indicating that ventricle can function as pacemaker in the absence of S. A. node or A. V. node. Now it shows that the three separate components of the heart beat at a descending order of frequency are represented by the sequence: *sinus→atrium→ventricle*. In normal heart the S. A. node controls the rest of heart muscle by its higher rhythmical activities.

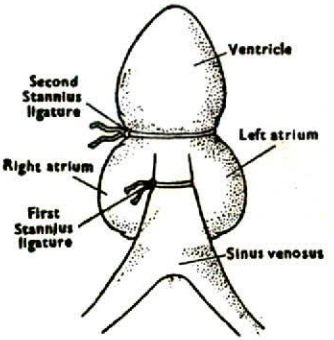


FIG. 154. Diagram showing the location of first and second Stannius ligatures in the frog heart.

This classical experiment described above cannot be possible in mammalian heart because, S. A. node and A. V. node are both present in the atrium. So by simple ligature the S. A. node cannot be separated from the A. V. node by first Stannius ligature. Ventricle however can be separated from the atrium by the second Stannius ligature (FIG. 154).

Experimental localisation of the pacemaker can be done by many other ways. If cold or warm saline is applied to the sinus region of the amphibian heart then rhythm is altered. If the S. A. node is damaged by **thermocautery** then the heart rate slows. With the advent of recording the transmembrane potential simultaneously from the S. A. node, the A. V. node and ventricle in intact beating heart, a more precise localisation of the pacemaker has been possible.

Spread of cardiac impulse

Conduction over atrial muscle. Cardiac impulse originated at the S. A node is transmitted over both the atria like concentric waves and thus the P wave is produced in E.C.G. (Electrocardiogram). The spread of electrical impulse through the S. A node is very slow (0·05 m per sec.) but the same through the junctional tissues that connect the node to the atrial musculature or to the A. V. node is higher (1 m per sec.). According to Carvalho et al and also others, the impulse from the S. A. node may be transmitted directly to the A. V. node through the internodal atrial bundle (FIG. 155).

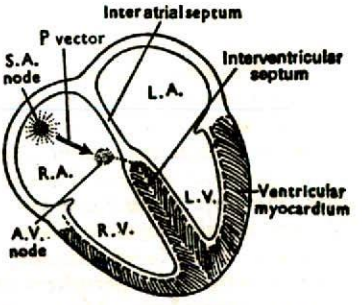


FIG. 155. Diagrammatic representation of atrial activation showing the transmission of impulse.

Conduction over A. V. node. There is also a considerable delay of 0·07 sec. to 0·1 sec. in transmission of impulse in the A. V. node before excitation spreads over the ventricle. This A. V. nodal delay allows the atrial systole to complete before the ventricle is excited. This delay is observed maximally at the junctional region between the atrium and atrioventricular node. The conduction velocity of impulse at this region is approximately 0·05 m per sec.

This delay in conduction across the A. V. node was explained by assuming (*i*) normal conduction velocity over long pathways in the A. V. node, (*ii*) a prolonged refractory period within the nodal tissue. Recent observation of Hoffman and Cranefield has claimed that there is a decremental conduction across the atrial-nodal border region. They have further described that the resting potential of the fibres of atrial-nodal border and of the upper atrioventricular node is lower than that of the atrial or ventricular muscle fibres. The size of the border fibres is smaller than that of the atrial fibres and even the size is gradually increased from the atrial-nodal border region onward to the bundle of His. Besides these, the border fibres have numerous interconnections. The smaller size and the profuse branching of the fibres in the border region as well as in the upper atrioventricular node are presumably the causes of this slow decremental conduction. Because the velocity of conduction is proportional to the diameter of the fibres. The delay is however minimised by sympathetic activity and the same is increased by vagal stimulation.

Besides nodal delay in the A. V. node, the impulse is transmitted through this region in one direction only. Because if the ventricle is stimulated, the impulse fails to reach the A. V. nodal region in retrograde fashion.

Conduction over bundle of His and the right and left bundle branches. Beyond the atrioventricular region, the impulse is transmitted along the bundle branch at a higher velocity (4–5 m per sec.). The impulse from the bundle of His passes quickly through the right and left bundle branches and ultimately reaches the Purkinje fibres and ventricular muscle fibres as well. Passage of impulse through the bundle of His and its branches is not encountered in the E.C.G.

Conduction through Purkinje systems. The impulse, after passing through the right and left bundle branches, passes into the Purkinje fibres and also its multiple ramifications within the subendocardial surfaces of both ventricles. The impulse then travels from the endocardium to the epicardium of ventricular muscle perpendicularly.

Conduction through ventricular muscle. In human beings, the midportion of the interventricular septum is activated normally in a left to right direction. So the depolarisation of the ventricular muscle begins at the left side of the interventricular septum because the Purkinje fibres arise more proximally from the left bundle branch than from the right bundle branch and activates the left side of the septum initially. After midseptal activation from the left to the right direction (Fig. 156), the impulse comes down the septum to the apex of the heart and next portions of myocardium that is activated is the anteroseptal region of the ventricular myocardium (Fig. 157). The impulse then proceeds along the right and left ventricular walls to the atrioventricular groove. The spread of excitation through the ventricle proceeds from the endocardium to the epicardium and thus the

whole of the right and left ventricular walls are depolarised (FIG. 158) producing the QRS complex in E.C.G. The portions of the ventricles that

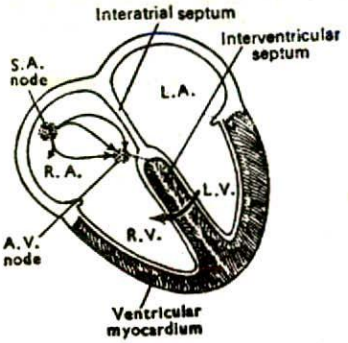


FIG. 156. Diagram depicts beginning of ventricular complex showing midseptal activation from the left to right direction.

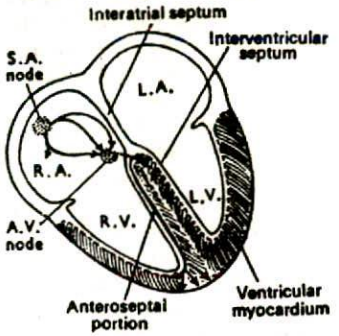


FIG. 157. Diagrammatic representation of early activation of anteroseptal portion of the ventricular myocardium.

are excited lastly are the posterobasal regions of the left ventricle, the pulmonary conus, and the uppermost portion of the interventricular septum (FIG. 159).

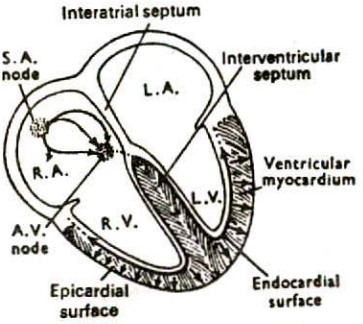


FIG. 158. Showing activation of maximal portion of left and right ventricular myocardium (diagrammatic).

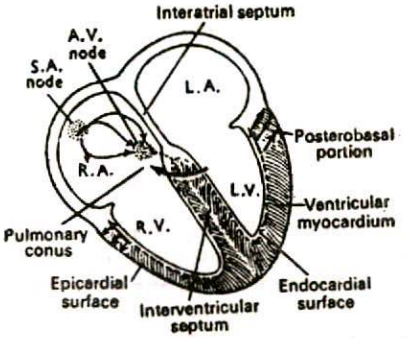


FIG. 159. Diagrammatic representation of late activation of posterobasal region of left ventricle, uppermost region of interventricular septum and pulmonic conus.

Cell-to-cell conduction. Earlier conception was that there is protoplasmic continuity between cells of the cardiac muscle and thus impulse is transmitted through the intercellular bridges. But electron microscopic studies reveal that there is no such bridges or protoplasmic continuity, the cells are bounded on all sides by membranes of high resistance. Transmission of impulse through this membrane is impossible. But the intercalated disc which crosses the short axes of the cells offers very low resistance and impulses reaching the intercalated disc are quickly propagated to the cells. So the syncitium-like properties of cardiac muscle are due to presence of low resistance intercalated discs (FIG. 160 and *vide* page 62).

Intracellular conduction. Through the specialised areas of the intercalated discs, the impulse ultimately reaches the cell membrane—*sarcolemma.* From here, the impulse is transmitted quickly through the *transverse tubules* (T tubules)—*sarcolemmal invagination.* This T tubule passes through the Z-line and here it is in close apposition with the *sarcoplasmic reticulum* that is present in the area in between the Z-lines. So the impulse from the cell wall is transmitted through the transverse tubules and then through the sarcoplasmic reticulum, and reaches ultimately to the contractile units of the muscle (FIG. 160).

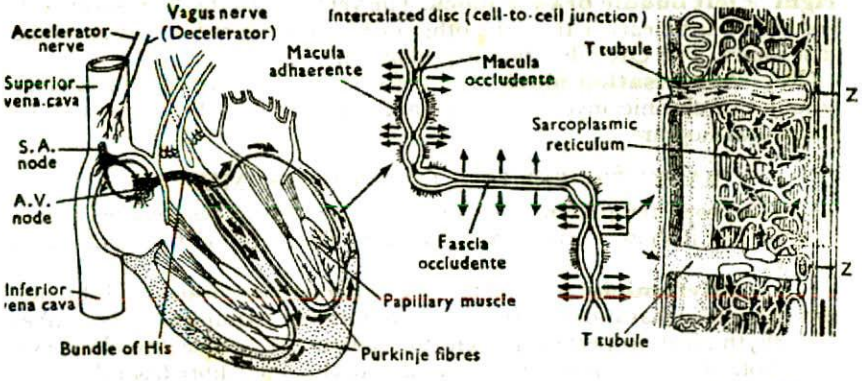


FIG. 160. Diagrammatic representation of cell-to-cell conduction and intracellular conduction in cardiac muscle fibres.

If the bundle of His is damaged experimentally in animals or in disease in man, the atria and ventricles are completely dissociated and they beat quite independently. The impulse is transmitted through the right and left branches of the bundle of His to the right and left ventricles respectively. If any branch of the bundle of His is damaged, conduction of the impulses is retarded on the damaged side. The anterior part of the septal region is excited first, then the apex and lastly the base of the heart. The time taken by the impulse to spread from the bundle of His through its branches to the apex is 0·013 sec. At first the endocardial surface and then the pericardial surface of the ventricles are stimulated. The impulse then spreads from apex to base by the Purkinje fibres.

Heart block. Defective production of the sino-atrial impulse or its conduction in the heart is called *heart block*. There may be four main types according to site of damage.

I. The S. A. node may fail to generate the impulse occasionally, so that the whole heart misses one beat. This is called **sino-atrial heart block** (FIG. 195).

II. The impulse may be normally generated but its transmission into the ventricles is faulty. The defect lies in the A. V. node or in the main bundle before division or in both. This is called **atrioventricular heart block.** This may be of three grades: (1) The impulse is transmitted but is merely delayed. The P–R interval in E.C.G. is prolonged (FIG. 196). (2) The impulse occasionally fails to reach the ventricles, so that the atria contract but the ventricles do not. This type of block is often found to have some

regular rhythm, viz., every 2nd or 3rd or 4th impulse is conducted. So that for every two or three or four atrial beats there will be one ventricular beat. In this way 2 : 1, 3 : 1, 4 : 1, etc., block is produced. (3) The sino-atrial impulse does not reach the ventricles at all, so that atria and ventricles dissociate and beat at their own rhythms—atria at the rate of 60, ventricles about 36 per minute. The pulse rate at ventricular rhythm will be 36 per minute. This is called **idioventricular rhythm.** The first two grades are often called *incomplete heart block;* the third grade *complete heart block* (FIG. 197).

III. One branch of the bundle may be defective producing either **right** or **left bundle branch block.** The ventricle on the normal side will contract a little earlier than the other one producing reduplication of the first sound. The QRS duration is prolonged.

IV. **Arborisation block.** The defect lies in the Purkinje fibres. This is found in chronic myocardial damage and can only be detected with Electrocardiogram.

BASIC PROPERTIES OF CARDIAC MUSCLE

The properties present in other muscles are also shown by the cardiac muscle. But it shows certain *special features.* They are briefly summarised below:

1. **Rhythmicity.** One of the main characteristic features of the cardiac muscle is that it can initiate its own impulse rhythmically. This inherent rhythmical property is present throughout the cardiac muscle as evident from the electrophysiological studies of the single fibre from the S. A. node, A. V. node, atrial muscle, Purkinje fibre and also from the ventricular muscle fibre. If a strip of muscle fibre from the atrium or ventricle is perfused in normal physiological solution with proper ionic concentrations, pH, temperature, etc., then it beats rhythmically, proving the presence of pacemaker activity. It has been discussed earlier that the rate of rhythmicity in the S. A. node is 70 to 80 per minute, in A. V. node 40 to 60 per minute, in atrium 60 per minute, in ventricle 20 to 40 per minute. Due to higher rhythmical property of the S. A. node, it controls the rest of cardiac muscle and thus heart beats at the rhythm of the S. A. node. When the S. A. node fails, the A. V. node takes the charge and if it fails, the atrium and afterwards ventricle take the charge of maintaining heart beat.

Transmembrane potentials, recorded simultaneously from the single fibre of the S. A. node, A. V. node and ventricle during normal beating, vary in their successive phases from those are recorded separately in isolated preparation. Difference in membrane potential recorded in between outside and inside cell membrane is known as **transmembrane potential.** Transmembrane potential can be recorded by inserting micro-electrode (0·2 μ) directly into the single cell and the indifferent electrode is kept outside the cell. As soon as the micro-electrode penetrates the cell membrane and if the indifferent electrode is kept outside the cell, a potential difference ranging from −80 to −90 mV will be shown in the galvanometer. The resting transmembrane potential, thus recorded in the S. A. node, is −80 mV (FIG. 161), but the same, in the A. V. node, atrial muscle (FIG. 166) and ventricular muscle (FIG. 167), is −90 mV. This resting membrane potential will be maintained until the resting state is disturbed by propagated impulse. With the onset of excitation, the steady state is changed rapidly and the membrane potential attains to +20 mV. After reaching at this level, it maintains

steady state for a while and gets down gradually to its initial resting state (FIG. 161). The upward deflection is the *depolarisation phase* as the membrane permeability to Na^+ is altered due to excitation. In resting state the extracellular Na^+ concentration is higher than that of the intracellular and the permeability of Na^+ to the cell membrane is hastened during excitation. So during depolarisation, there is an influx of Na^+ and this process is maintained until it reaches +20 mV. Here Na^+ entry is decreased and K^+ begins to come out from the cell. This phase is known as *repolarisation*. Heart remains in a state of systole at this stage. K^+ efflux decreases after reaching the resting level and reorientation of ions (K^+ and Na^+) takes place at this stage by 'pumping', against electrochemical gradient and by metabolic energy. This phase is known as *slow diastolic depolarisation*. This phase coincides with the period of diastole. This process is very slow and due to reorientation of ions, the threshold potential (−60 mV) is slowly achieved and the membrane is further depolarised and the process is repeated. This process once started is maintained in the cardiac muscle until death ensues. How this process is initially being started in embryonic cardiac tissue is not yet fully known but it is presumed that certain hypoxic state may have been the cause of excitability in the embryonic stage. This slow diastolic depolarisation phase is the characteristic of pacemaker activity. This slow diastolic depolarisation phase of transmembrane potentials is absent in other than pacemaker area if the same is recorded simultaneously from single cell in a pacemaker-dominated heart. This phase is however present in a transmembrane potential recorded from any isolated preparation of cardiac muscle.

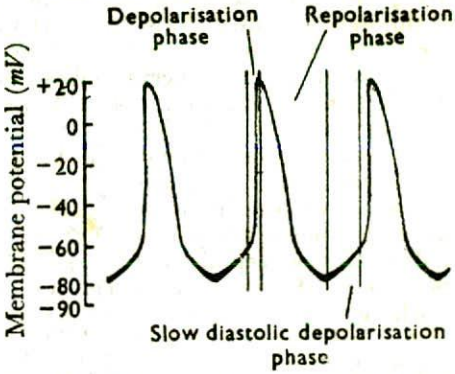


FIG. 161. Diagrammatic representation of the transmembrane action potential recorded from the single fibre of the S. A. node.

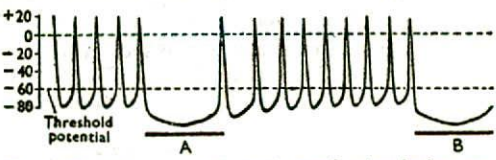


FIG. 162. Showing effect of vagal stimulation on transmembrane potential of the S. A. node. It shows the increase of diastolic phase and also increase of resting potential. A, B indicate the period of vagal stimulation (diagrammatic).

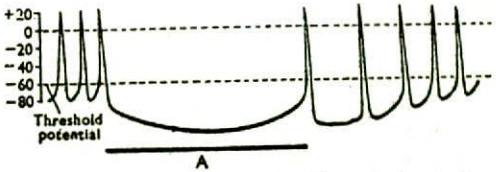


FIG. 163. Showing effects of prolonged stimulation at 'A' on the same fibre as shown in FIG. 162. Note hyperpolarisation during vagal stimulation. Threshold potential (T. P.) is achieved very slowly even after discontinuing the vagal stimulation.

Cardiac rhythm is altered following stimulation of vagi or sympathetic nerve supplying the heart. The cause of the slowered heart rate following vagal stimulation is presumably due to

prolongation of the slow diastolic depolarisation phase and also due to hyperpolarisation for increased permeability of K^+ to the cells. The rate of firing is decreased and longer time interval is required to achieve the level of threshold potential (Figs. 162 & 163). Strong vagal stimulation causes the complete disappearance of spontaneous discharge for some time. These effects are in the vagal nerve endings due to liberation of acetylcholine, which causes hyperpolarisation of the cell membrane by increasing the K^+ permeability. On the other hand, cardiac sympathetic nerve stimulation or administration of adrenaline induces the membrane potential to fall more rapidly and the rate of spontaneous discharge increases greatly (Fig. 164). On gradual lowering of temperature the spontaneous rhythmicity of

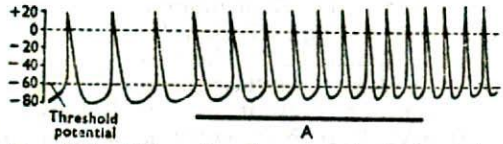


Fig. 164. Effects of cardiac sympathetic stimulation on the pacemaker action potentials of the sinus venosus of the heart muscle showing increase in slope of pacemaker potential, decrease of slow diastolic depolarisation phase. Threshold potential is quickly achieved (diagrammatic).

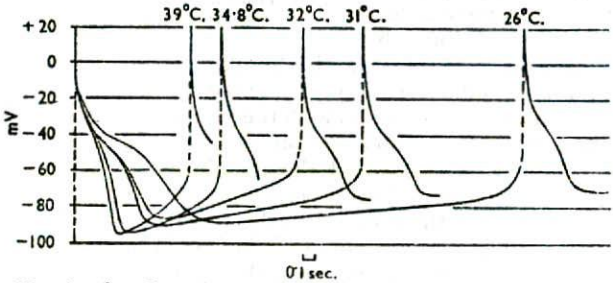


Fig. 165. Showing the effect of graded hypothermia on the transmembrane potential, recorded from spontaneous spacemaker in a Purkinje fibre (diagrammatic).

the spacemaker area is depressed. The slow diastolic depolarisation phase of the muscle fibre is prolonged. The slope of the slow diastolic depolarisation phase is decreased. The resting transmembrane potential is decreased (Fig. 165).

Characteristic features of transmembrane potential recorded simultaneously from the S. A. node, atrial muscle, Purkinje fibres and ventricular muscle in normal beating heart. Transmembrane potential recorded from the single cell of S. A. node shows certain characteristic features which are absent in the same of the atrial muscle, Purkinje fibres and ventricular muscle fibres. In the transmembrane potential of S. A. node, there are slow depolarisation phase, repolarisation phase and also slope of slow diastolic depolarisation phase (Fig. 161). The peak of the action potential is rounded and the repolarisation is slow but uninterrupted. But in atrial and ventricular muscle fibres and also in Purkinje fibres, the depolarisation phase is very sharp, the peak is mostly pointed. Besides these, there are interrupted fall of repolarisation phase and the slope in the diastolic depolarisation phase is absent. Thus in S. A. node-dominated heart, pacemaker activity of the atrial muscle (Fig. 166), ventricular muscle (Fig. 167) and Purkinje fibres are depressed due to higher rhythmical activity of the S. A. node and this is evident from the absence of slope of

slow diastolic depolarisation phase in those muscles. If the transmembrane potential is recorded in isolated fibres, then the slope of slow diastolic

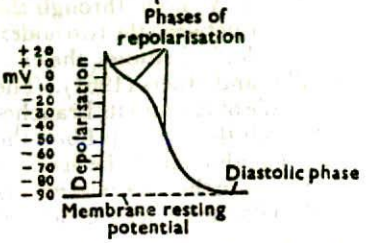


FIG. 166. Graphical tracing of transmembrane action potential recorded from atrial muscle cell (diagrammatic).

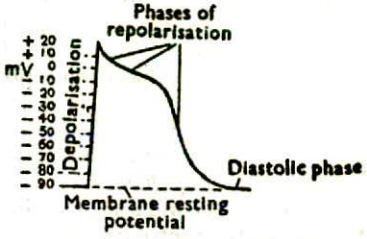


FIG. 167. Graphical tracing of transmembrane action potential recorded from ventricular muscle cell (diagrammatic).

depolarisation phase or the instability of the membrane resting potential is observed. This indicates that in the S. A. node-dominated heart, before achieving the threshold potential, the cell membrane of the atrial muscles, Purkinje fibres or the ventricular muscle fibres are depolarised by the propagated impulse of the S. A. node.

Relationship between transmembrane potential and electrocardiogram. There is a direct relationship between the transmembrane potential recorded from the single ventricular muscle fibre by micro-electrode technique and the unipolar electrocardiogram recorded from an electrode placed on the surface of the heart in close proximity to the micro-electrode. It shows that the R wave of the electrocardiogram (E.C.G.) synchronises with the upstroke of the depolarisation wave of the transmembrane potential. During the plateau of the repolarisation phase of transmembrane potential, the base line of the electrocardiogram returns quickly to the *isoelectric line* followed by smaller biphasic T waves. This T wave actually represents the repolarisation wave of the ventricle. The E.C.G. actually represents the electrical activities of multicellular units but not of unicellular unit. For this reason the amplitude and shape of the R and T waves of an electrocardiogram are mostly dependent upon the amount of electrical activities offered by the multicellular units and also upon the different configurations of the membrane potentials of the multicellular units than that of an individual cell unit (FIG. 168).

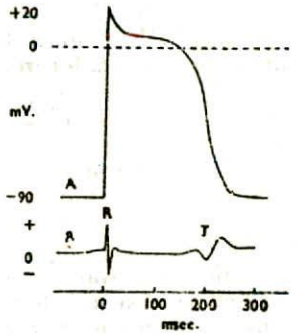


FIG. 168. Graphical representation showing tracings of relationship between transmembrane action potential (A) and unipolar electrocardiogram (B) recorded simultaneously in a strip of parallel ventricular muscle fibres. In A, R wave is practically synchronous with upstroke (depolarisation) transmembrane action potential. In B, following R wave there is a slow return of base line of E.C.G. to zero line and T wave which is slower and smaller than R wave is correlated with repolarisation of transmembrane action potential. T wave also is a negative-positive deflection. *From Marshall, Jeen M.: The heart. In Mountcastle, Vernon B., editor, Medical physiology, ed. 12, St. Louis, 1968. The C. V. Mosby Co.* (*Used with permission*).

2. **Conductivity.** Conduction of impulse through different parts of the heart has already been discussed in detail. The impulse originated at the S. A. node spreads over the atria and reaches the A. V. node through the internodal fibres. There is no special connecting tissue between the two nodes, demonstrated histologically but from electrophysiological studies, the existence of such tissue has been reported by Carvalho and others (1961). The A. V. node transmits the impulse through the bundle of His and its branches to the ventricles. From the apex of the heart through the Purkinje fibres the impulse is conducted to the base (*vide* page 237). Conduction in the *bundle of His* and the *Purkinje fibres* is 1 metre per second, still less in the *ventricular muscles* 0·4 metre per second and least in the S. A. node 0·05 metre per second and A. V. node 0·1 metre per second.

3. **Excitability** and **Contractility.** Like other muscles, the cardiac muscle is excitable by adequate stimuli and responds by contraction. The fundamental contractile unit of the cardiac muscle is myofibril which contains the protein units, *actin* and *myosin*. During contraction these two units are associated in presence of ATP and thus the fibre is shortened, but during rest these are dissociated again with the resynthesis of ATP. Myosin itself is an enzyme 'ATP-*ase*' capable of dephosphorylation of ATP. Ca^{++} ion activates the ATP-*ase* activity—favouring prompt association of *actomyosin* and ADP complex. Excess calcium always keeps the muscle unit in contracting state **(calcium rigor)** due to association of more contractile units. K^+ ions do not favour association of actin and myosin (Szent-Györgyi and Hajdu, 1952). So if excess K^+ is added in the extracellular fluid then the heart muscle gradually stops in diastole.

4. **All-or-none response.** If a quiescent heart muscle is stimulated at widely spaced electrical shocks of increasing strength then muscle contracts as a whole only when the threshold strength is reached. But there was no such increasing amplitude of contraction with increasing intensities of stimulation. This was observed by Bowditch (1871). Single skeletal muscle fibre behaves like this but if the entire muscle is stimulated with graded intensities of stimuli then graded responses are encountered.

5. **Staircase.** In a Stannius preparation if the ventricular muscle is stimulated with inducted current, the first few contractions gradually increase in size and then it becomes steady. This is known as **treppe** or **staircase phenomenon.** This staircase phenomenon is only observed in quiescent heart but not in active normal heart. Bowditch (1871) have described that contractions of ventricular muscle following a stoppage are weaker, but the heart regains its full strength gradually in the subsequent contractions, which on the record form a kind of staircase. In other words, every contraction leaves a condition more favourable than it found, but this favourable condition deteriorates in time. From the experiments on staircase phenomenon of Hajdu and Szent-Györgyi (1952) it can be suggested that it is caused by the decrease of internal potassium. After analysis of ion Hajdu (1953) has reported that this favourable condition following a contraction is mostly related with the release of potassium from the cell, which re-enters during rest at a speed depending on the condition of the membrane. Equilibrium of these two processes will decide the internal ion content and through this, the height of tension. His quantitative measurement leaves very little doubt that the change in tension during the staircase is related to the change in the internal ionic content. Visco-elastic properties or the

accumulation of metabolic products have got little role on the staircase phenomena. Besides this, change in internal ionic content acts on the contractile proteins directly rather than indirectly through some other mechanism. He has further claimed that actomyosin goes from full dissociated (uncontracted) to full associated (contracted) form if there is a change of 10% or even less in the ionic concentration. Loss of 3 mEq potassium out of 106·8 mEq internal Na and K, increases tension from 0–100% (FIG. 169).

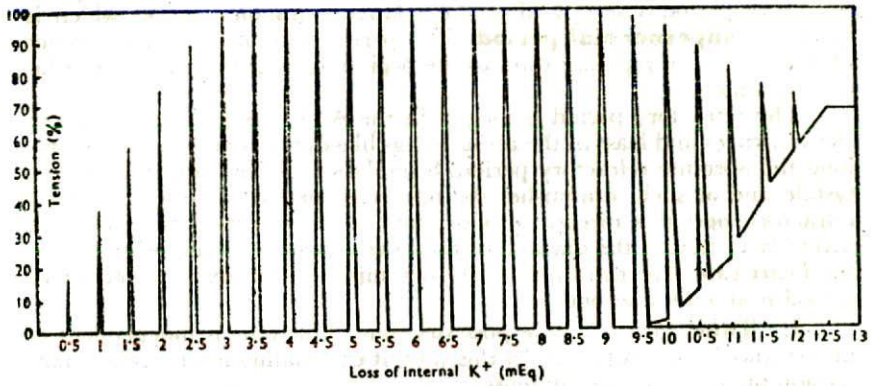


FIG. 169. Graphical representation of staircase phenomena in cardiac muscle fibres showing the height of contraction with the increased loss of internal potassium (after Hajdu).

With digitalis the staircase phenomenon is shortened by blocking K^+ reentry into the cells so that intracellular K^+ concentration is decreased very rapidly. Thus it can be assumed that during quiescent state excess K^+ is accumulated within the cell and the association of actin and myosin is being depressed. With the excitation, a reduction in intracellular K^+ accompanied with successive increased contractions are taken place. Height of contraction is associated with the parallel loss of intracellular K^+. Maximum tension is developed after the loss of 3 mEq of intracellular K^+. But heart muscle remains in contracting states following release of intracellular K^+ more than 10 mEq.

6. **Refractory period.** This is another characteristic property of the heart muscle. *The refractory period of the heart is long and can be divided into three parts:* (1) **Absolute refractory period**—*This period extends throughout the whole period of contraction.* Any stimulus, however strong, will fail to elicit a response if it falls within this period. For this reason, *heart muscle cannot be tetanised. This long refractory period ensures enough time for recovery of the cardiac muscle. This is the reason why cardiac muscle cannot be fatigued.* This period coincides the period

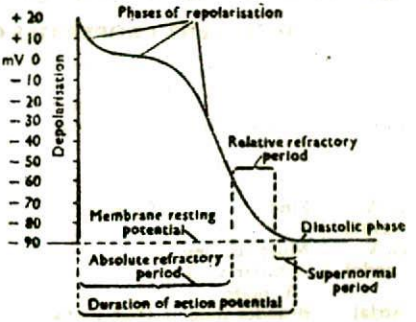


FIG. 170. Diagrammatic tracing showing the different phases of transmembrane potential, refractory periods of a single ventricular muscle fibres following excitation.

from the onset of depolarisation phase to the repolarisation up to the threshold potential (FIG. 170). (2) **Relative refractory period**—This starts immediately after the absolute refractory period and involves the first part of relaxation. Only a very strong stimulus will be effective. This period begins when the transmembrane potential during repolarisation phase has just reached the threshold potential (—60 mV) and ends just before the repolarisation phase is ceased. (3) There is another type of refractory period observed after the relative refractory period which is known as **supernormal period.** This period is limited from the point of termination of repolarisation to the beginning of slow diastolic repolarisation phase.

The refractory period is longest in the A. V. node, intermediate in the ventricles and least in the atria. Drugs like digitalis and quinidine prolong the absolute refractory period. Stimulation of the vagus reduces the systole and as such, diminishes the refractory period. The length of the refractory period is directly proportional to the duration of systole and inversely to that of the diastole of the heart. Hence, it will depend upon the heart rate. For rates up to 100 per minute, the absolute refractory period is about 0·2 second.

7. **Tone.** Heart muscle possesses tone. This tone is independent of nerves and can be adjusted. In this way, it can maintain a fairly constant tension upon its varying contents.

It has been observed that the different properties of cardiac muscles are not developed in all the tissues of heart in the same order. Certain properties have developed specially in certain tissues while others are not. It is also seen that these functions are related to the size and chemical composition of the muscle cells. Hence, cardiac muscle can be divided into four groups: (*a*) The smallest fibres with least glycogen at the nodes. (*b*) The broader fibres with more glycogen in the ventricles. (*c*) The still broader fibres with more glycogen in the atria. (*d*) The broadest fibres with abundant glycogen in the Purkinje fibres, bundle of His and its branches. As the size of the fibres increases, the rate of conduction and the glycogen content also increase. But the duration of systole, the refractory period and the rhythmicity increase in the reverse order.

DIFFERENT PROPERTIES OF CARDIAC MUSCLE FIBRES

Fibres	Size of fibre	Glycogen content	Rate of conduction (metre)	Length of Systole (Refractory period)	Rhythmicity
S. A. nodal	Fine.	Present.	0·05 per sec.	Highest.	Highest.
A. V. nodal	More or less similar to S. A. node.	,,	0·1 ,, ,,	Lower than S. A. node.	Lower than S. A. node.
Atrial	Broader than ventricular.	Higher than ventricular.	1·0 ,, ,,	Lower than ventricular.	Lower than ventricular.
Ventricular	Broader.	Higher than nodal.	0·4 ,, ,,	Lower than nodal.	Lower than nodal.
Purkinje	Broadest.	Same as that of atrial.	1·0 ,, ,,	Same as that of atrial.	Same as that of atrial.

CARDIAC CYCLE

Definition. Changes that occur in the heart during one beat, are repeated in the same order in the next beat. This cyclical repetition of the various changes in heart, from beat to beat, is called **cardiac cycle.**

Cardiac cycle time. *This is the time required for one complete cardiac cycle.* With the normal heart rate of 75 per minute, this time will be 60/75 = **0·8 sec.** It means that every event in the cycle will be repeated at the interval of 0·8 sec. It is obvious that the *cardiac cycle time will be inversely proportional to the heart rate.*

Interrelations of the various events in the cardiac cycle. In the cardiac cycle there are four main events: **atrial systole, atrial diastole, ventricular systole,** and **ventricular diastole.** All the other changes are subsidiary to them.

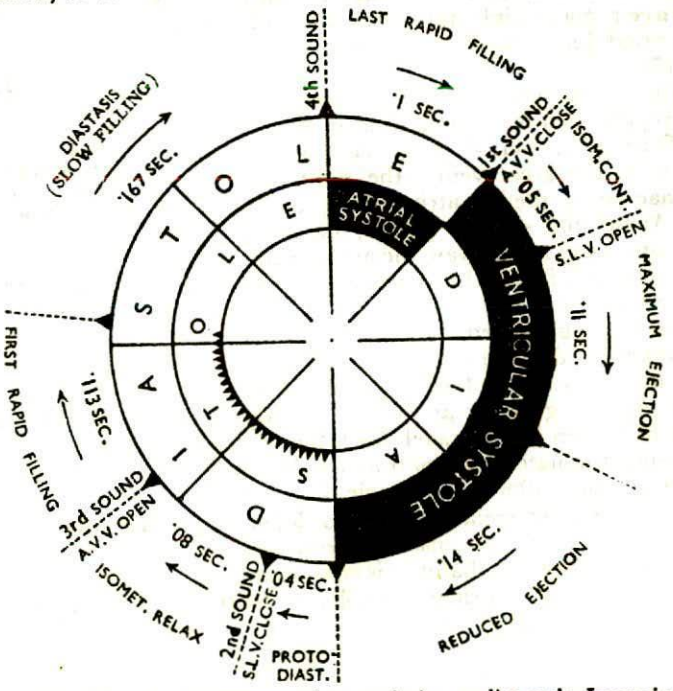


FIG. 171. Showing the sequence of events during cardiac cycle. Inner ring represents atrial events, outer ring ventricular events. The events are to be followed in clockwise manner.

Atrial systole initiates the cycle, because the pacemaker S. A. node is situated in it. It lasts for **0·1 sec.** and is followed by atrial diastole, lasting for **0·7 sec.** At the end of diastole, the atrial systole returns, and in this way, the atrial cycle goes on (total duration **0·8 sec.**).

At the end of atrial systole, ventricular systole starts—duration **0·3 sec.** This is immediately followed by ventricular diastole—duration **0·5 sec.** At the end of diastole, ventricular systole repeats and thus the ventricular cycle goes on (total duration **0·8 sec.**).

In order to follow the march of events during the cardiac cycle and their interrelations, the FIG. 171 should be carefully studied. In it, there are two concentric rings, divided into *eight* equal parts. The whole circle represents one complete cardiac cycle, so that each of its eight divisions represents 0·1 sec. The inner ring represents the atrial events, the outer ring ventricular events.

Let us follow the inner ring first. The *one* shaded division in it denotes atrial systole (0·1 sec.). During this period the atria contract and expel their contents into the respective ventricles. The left atrium, being further away from the S. A. node, contracts a little after the right atrium. But practically their contractions are simultaneous. The force of contraction is stronger in the first half than in the second. Because during first half or at initial stage the **intra-atrial pressure** remains high and during last half the same is decreased due to expulsion of blood to the ventricle (FIG. 172).

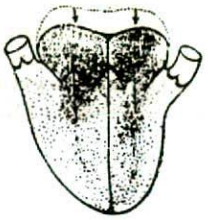


FIG. 172. Heart during atrial systole. Atria shorten, A.V.V. —open. S. L. V.— closed.

After atrial systole, comes its diastole (0·7 sec.), being represented by *seven* unshaded divisions in the ring. During this period the atria relax and receive blood from the great veins—the right atrium from the venae cavae, the left atrium from the pulmonary veins. At the end of this period, the atrial systole comes again and in this way, the atrial events go on.

Let us now follow the ventricular events in the outer ring. There are *three* shaded divisions on it, representing ventricular systole (0·3 sec.). It is followed by *five* unshaded divisions, indicating ventricular diastole (0·5 sec.). On comparing the two rings, it would be found that ventricular systole commences at the end of atrial systole. The reason for this is very clear. The impulse originating at the S. A. node, will certainly overtake the atrium first, then it will travel down the junctional tissues, enter the ventricles and stimulate their contraction. Naturally then, ventricular systole will always come after atrial systole.*

From these interrelations we can deduce one **fundamental rule** of cardiac action that—*the systoles of atrium and ventricle will never overlap*. In other words, when one chamber is contracting, the other must be relaxing.

At the onset of ventricular systole, the **first sound** occurs. It is caused by the sudden closure of the A. V. valves due to sharp rise of intraventricular pressure. The semilunar valves open a little later, because, until the intraventricular pressure goes above that in the aorta and pulmonary artery, the semilunar valves will not open. Thus, at the beginning of ventricular systole, there is a brief period during which both the valves are closed and the ventricles are contracting as closed cavities (FIG. 173). No blood passes out and therefore, no shortening of the cardiac muscle will occur. Hence, this period is called **isometric contraction period** (0·05 sec.). It is marked at the onset by the closure of the A. V. valves (e.g., the first sound) and at the termination by the opening of the semilunar valves.

* The time relations are so adjusted that the atrioventricular conduction time of the impulse (P–R interval of *Electrocardiogram*) is a little longer (0·16 sec.) than the duration of atrial systole (0·1 sec.). This explains why ventricular systole must always come after atrial systole normally.

At the end of this period, the semilunar valves open and the **ejection period** starts, (0·25 sec.). During this period, blood is expelled from the ventricles—from the left ventricle into the systemic aorta, from the right into the pulmonary trunk. In the first part of this period (0·11 sec.) the outflow is very rapid. Hence, it is known as the **maximum ejection period** (FIG. 174). In the last part (0·14 sec.) the rate of outflow slows down. Hence, it is called the **reduced ejection period** (FIG. 175). Here, the ventricular systole ends and diastole begins.

Let us follow the outer ring further. It will be seen that after the three shaded divisions, come the *five* clear divisions—representing the duration of ventricular diastole (0·5 sec.). As soon as ventricles relax, the intraventricular pressure starts falling. The blood columns in the aorta and pulmonary trunk try to roll back towards ventricles but are stopped by the sharp closure of the semilunar valves. This produces the **second sound** of heart. Thus the onset of ventricular systole is marked by the first sound and its termination by the second sound (approximately).

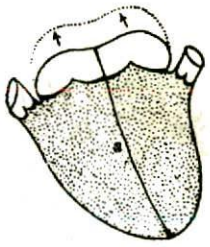


FIG. 173. Heart; during isometric contraction phase. Atria relaxing. Both valves closed. No shortening of ventricles.

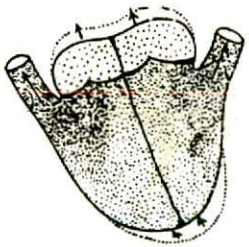


FIG. 174. Heart, during maximum ejection period. A. V. V.—closed. S. L. V. —open. Atria relaxing. Ventricles shortening.

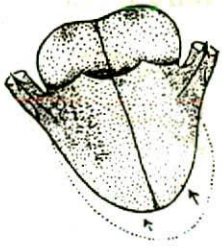


FIG. 175. Heart, during reduced ejection period. A.V.V.—closed. S. L. V.—open. Ventricles much shortening. Atria—full.

On comparing the two rings, it will be seen that the last one division (0·1 sec.) of ventricular diastole is overlapped by atrial systole. In other words, when atria are contracting, the ventricles are still in diastole and are having the last part of their filling. It will be seen further that the first four divisions of ventricular diastole coincide with the corresponding four divisions of the atrial diastole. From this we can come to another **fundamental rule** of cardiac action that—*the diastole of the two chambers will always partly overlap*. In the left half of the FIG. 171 unshaded division will be found. In other words, both the chambers are in diastole here. This is called the **diastole of the whole heart** (0·4 sec.).

Let us again follow the ventricular diastole on the outer ring. As mentioned above, the second sound occurs at the end of ventricular systole. But this statement is not exact, because, till the falling of intraventricular pressure goes below the intra-aortic pressure, the semilunar valves will not close. Consequently, there will be a short interval between the onset of diastole and the closure of the semilunar valves (i.e., the second sound). This period is called the **protodiastolic period** (0·04 sec.). From this it is clear that the second sound does not occur just at the end of ventricular systole but a little afterwards (i.e., after the protodiastolic period).

Although the semilunar valves have closed, yet the A. V. valves are still not open. Because, the falling intraventricular pressure takes a little time to go below that of the atria, so that the A. V. valves may open. Consequently, there will be a brief interval during which both the valves remain closed and ventricles are relaxing as closed cavities. Since no blood enters the ventricles there will be no lengthening of cardiac muscle fibres. Owing to this, it is called the **isometric relaxation period** (0·08 sec.—Fig. 176).

At the end of isometric relaxation period, the A. V. valves open. Blood rushes into the ventricles and ventricular filling begins. The first part of this period is known as the **first rapid filling phase** (0·113 sec.). Because, as soon as the A. V. valves open, blood accumulating so long in the atria, rushes into the ventricles. The steep fall of the intraventricular pressure during the isometric relaxation period, makes the inflow all the more intense. Although the duration is brief yet the largest part of ventricular filling takes place during it. Due to rapid rush of blood a sound is produced, known as the **third sound** of heart (Fig. 177).



Fig. 176. Heart, during isometric relaxation period. Both valves closed. Ventricles relaxing. No blood entering, hence no lengthening of ventricles.

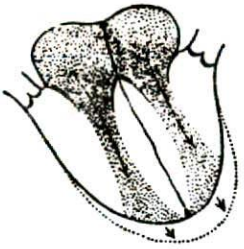


Fig. 177. Heart, during first rapid filling phase. A.V.V. —open. Blood rushing into the ventricles. Ventricles relaxing and lengthening. S.L.V.—closed.

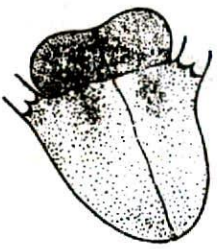


Fig. 178. Heart, during diastasis. A.V.V.—Floating in neutral position. S.L.V.—closed. Both atria and ventricles filled up.

In the next phase of diastole, the rate of filling slows down. The ventricles are already full to a large extent and ventricular pressure slowly rises. Consequently, the rate of inflow from the atria will be gradually slower. This period is called **diastasis** or **slow inflow phase** (0·167 sec.). Although this is the longest phase of ventricular diastole, yet the amount of filling during this period is minimum. If one looks into the heart (Fig. 178) during this time, one will find that, the whole atrioventricular canal contains a continuous column of blood, more or less stagnant, in which the cusps of the A. V. valves are passively floating. After this period comes the last part of ventricular diastole represented by the last unshaded division on the outer ring. It is obvious that this phase corresponds with atrial systole. Due to atrial contraction, blood rushes into the ventricles and ventricular filling again becomes rapid. This phase—the **last rapid filling phase** (0·1 sec.) is responsible for the last part of ventricular filling. Due to rapid rush of blood, again a sound is produced—known as the **fourth sound** of heart. Thus the onset of filling period is marked by the third sound and its termination by the fourth sound. Here the ventricular

diastole ends. They are completely filled up, the impulse from the S. A. node arrives in the mean time and the ventricles plunge into systole again. Thus the cycle goes on.

Summary of the sequence of events in cardiac cycle. The **atrial systole** is the first event (0·1 sec.). It initiates the cardiac cycle, because the pacemaker S. A. node is situated here. Due to higher atrial pressure, the first half of atrial systole is stronger than that of the last half. After systole comes the **atrial diastole** (0·7 sec.). These two alternately follow each other and constitute the atrial cycle (0·8 sec.).

Just after the atrial systole, the **ventricular systole** (0·3 sec.) begins and is immediately followed by its diastole (0·5 sec.). These two events repeat alternately and make up the ventricular cycle (0·8 sec.).

At the onset of ventricular systole, the A. V. valves close producing the **first sound.** The semilunar valves open a little later. The interval between the closing of the A. V. valves and opening of the semilunar valves, is called the **isometric contraction period** (0·05 sec.). During this period ventricles contract as closed cavities and intraventricular pressure steeply rises.

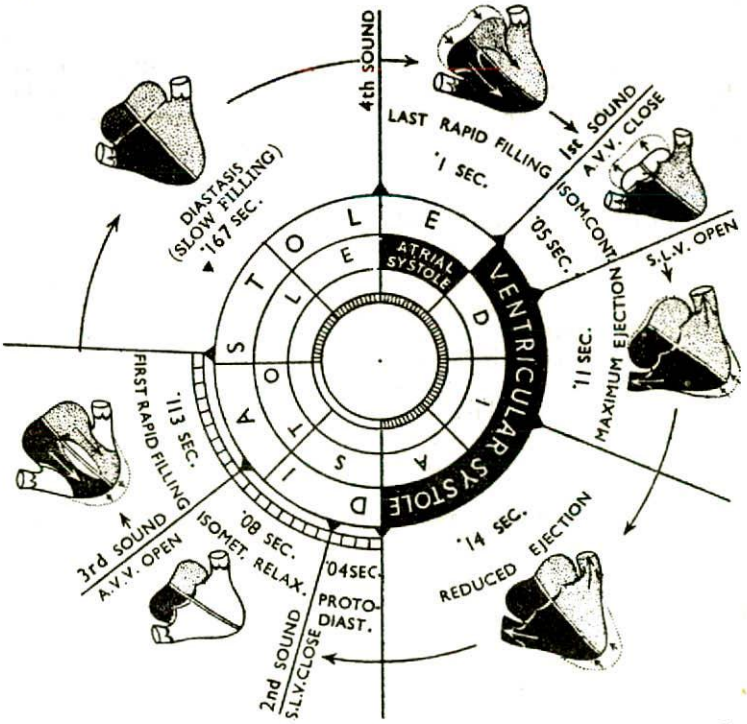


FIG. 179. Represents the interrelations of the important events of the cardiac cycle. Condition of heart corresponding to each important phase is also shown.

After this phase, comes the **ejection period**—when blood is pumped out of the ventricles. The first part of this period, when the outflow is

very rapid, is called the **maximum ejection period** (0·11 sec.). The second part, when the rate of flow slows down, is known as the **reduced ejection period** (0·14 sec.). Here, ventricular systole ends and diastole begins.

At the beginning of ventricular diastole, the semilunar valves close producing the **second sound.** There is a brief interval between the beginning of diastole and the closure of the semilunar valves—known as the **protodiastolic period** (0·04 sec.). So that, second sound occurs actually after this period. The A. V. valves open a little after the closing of the semilunar valves. The interval between these two is called the **isometric relaxation period** (0·08 sec.). During this period ventricles relax as closed cavities and intraventricular pressure steeply falls. At the end of this period, the intraventricular pressure goes below that of the atria and the A. V. valves open. Atrial blood rushes into the ventricles—producing the **third sound.** Here, ventricular filling begins. The first part of filling is very rapid, being known as the **first rapid filling phase** (0·113 sec.). The maximum filling takes place during this brief period. The intermediate part of filling is very slow and is known as **diastasis** or **slow inflow phase.** Although this is the longest phase (0·167 sec.), yet the amount of filling is minimum. The last part of diastole corresponds with atrial systole. Due to active contraction of the atria, filling becomes very rapid. This **last rapid filling phase** (0·1 sec.) is responsible for the last part of ventricular filling. Due to rapid rush of blood, another sound is produced—the so-called **fourth sound** of heart. Here, ventricular diastole ends and systole commences again. In this way the cycle continues (Fig. 179).

TIME RELATIONS OF THE VARIOUS EVENTS

It has been noted that the cardiac cycle time is inversely proportional to heart rate. But all the phases of cardiac cycle do not proportionally vary. *The duration of diastole varies much more than that of systole.* For instance, with a rate of 120 per minute the cardiac cycle time will be 0·5 sec. The systolic period will be reduced to 0·23 sec. and diastolic period to 0·27 sec. With a rate of 60 per minute the cycle time is 1 sec. Here, the systole will be 0·33 sec. and diastole 0·67 sec. Thus when the rate rises from 60 to 120 per minute the systole diminishes only by 0·1 sec., whereas diastole diminishes by 0·4 sec. *In other words, heart rate varies more at the expense of diastole than that of systole.*

Summary of the time relations. With 0·8 sec. as the cardiac cycle time (heart rate 75 per minute), the time relations of the various events are given below:

I. Atrial events:

(*a*) Atrial Systole		0·1 sec.
1. First Phase (at rise of pressure)	0·05 sec.	
2. Second Phase (at fall of pressure) ..	0·05 sec.	
(*b*) Atrial Diastole		0·7 sec.
Total		0·8 sec.

II. Ventricular events:

(*a*) Ventricular Systole		0·3 sec.
1. Isometric Contraction Period	0·05 sec.	
2. Maximum Ejection Period	0·11 sec.	
3. Reduced Ejection Period	0·14 sec.	
Total Ejection Period (0·25 sec.)		
(*b*) Ventricular Diastole		0·5 sec.
1. Protodiastolic Period	0·04 sec.	
2. Isometric Relaxation Period	0·08 sec.	
3. First Rapid Inflow	0·113 sec.	
4. Diastasis or Slow Inflow Phase	0·167 sec.	
5. Last Rapid Inflow (Atrial Systole)	0·100 sec.	
Total Ventricular filling time (0·38 sec.)		
Total		0·8 sec.

PRESSURE AND VOLUME CHANGES IN THE HEART AND BLOOD VESSELS

Methods of study

Pressure change. *In animals*—**Optical method of Wiggers.** A vertical glass tube filled with an anticoagulant solution is used as a cannula. One end of it is introduced into the chamber whose pressure is to be recorded. The other end of the cannula is covered with a tense elastic membrane, upon which a small mirror is set. A beam of light is so arranged that it is reflected by the mirror and falls on a moving photographic plate. The pressure changes in the chamber are transmitted through the solution in the cannula and moves the mirror. The oscillations of the reflected beam are recorded on the moving photographic plate.

In man—(1) **Cournand's method.** Pressure changes in the right atrium and ventricle have been directly measured in man by introducing a thin rubber tube into the antecubital vein and gradually pushing it up through the corresponding bigger veins into the right atrium and then into the right ventricle. The pressure changes are transmitted through this tube and are recorded by suitable apparatus. (2) **From the jugular pulse tracing** indirect information about the pressure changes in the right atrium can also be obtained.

Volume change. *In animals* it can be studied by Cardiometer (Fig. 180). This is a rounded funnel in which the heart is placed in such a way that the ventricles remain inside and atria outside the funnel—the fitting being made airtight around the atrioventricular groove. When ventricles

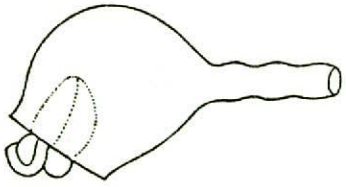


Fig. 180. Henderson's Cardiometer.

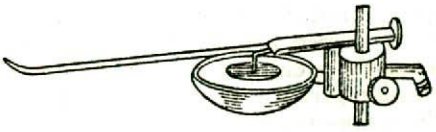


Fig. 181. Marey's Tambour

contract, pressure in the funnel falls; when it relaxes, pressure rises. These pressure changes are transmitted into a Tambour (Fig. 181) or a piston recorder through rubber tubings and are recorded on a moving drum.

with such studies the following facts about the pressure and volume changes are known.

Intraventricular pressure changes. The ventricular curve in FIG. 182 is to be carefully followed. The following pressure changes are found on it:

DURING VENTRICULAR SYSTOLE

1. In the isometric contraction period both valves remain closed, blood cannot run out and ventricles forcibly contract upon the locked-up blood. Hence, intraventricular pressure sharply rises.

2. In the next phase, maximum ejection period comes. Since blood is running out, pressure should fall in the ventricles. But the force of contraction is stronger than the rate of outflow, hence intraventricular pressure continues to rise for a brief while, but at a much slower rate than before. Gradually, the force of contraction and the rate of outflow equalise. Hence, a horizontal plateau is produced at the summit.

3. In the next phase—the reduced ejection phase—the force of contraction is much reduced and is proportionally less than the rate of outflow. Hence, intraventricular pressure gradually falls.

DURING VENTRICULAR DIASTOLE

1. In the protodiastolic period the pressure continues to fall as in the previous stage.

2. In the isometric relaxation period the ventricles are actively relaxing as closed cavities and the intraventricular pressure sharply drops. This continues until the A. V. valves open.

3. As soon as the A. V. valves open atrial blood rushes into the ventricles. But the rate of relaxation being more than filling, ventricular pressure continues to fall slowly to some extent.

4. Then comes the period of diastasis or slow inflow phase. Ventricles are no more relaxing, blood accumulates in it and pressure slowly rises.

5. In the last phase—corresponding to atrial systole—blood is pumped into the ventricles and ventricular pressure shows a small but sudden rise. Then ventricular systole comes again and the changes repeat.

Intra-atrial pressure changes. In the atrial curve of FIG. 182 there are three positive waves 1, 2 and 3, and three negative waves.

(1) During atrial systole, intra-atrial pressure rises causing the first positive wave. In the later part of systole, the pressure falls. Because, most of the atrial fibres have started relaxing. (2) During atrial diastole, the atria relax and pressure should continue to fall. But instead of that, there occurs a sharp rise causing the second positive wave. This corresponds to the isometric contraction period of the ventricles. As soon as ventricles contract, the A. V. valves become shut and bulge into the atrial cavity in a dome-shaped manner. Hence, intra-atrial pressure suddenly rises. (3) Then the pressure very sharply falls and corresponds to the maximum ejection period of the ventricles. This sudden fall is due to the following three reasons: (*a*) Atrial relaxation continues. (*b*) As the ventricular muscles shorten, the A. V. ring is pulled down, so that atrial cavity enlarges. (*c*) Due to reduction of ventricular volume, mediastinal pressure falls. Owing to this negative pressure—the thin-walled atria dilate and atrial pressure falls. (4) In the later part of ventricular systole, intra-atrial pressure slowly rises causing the third positive wave. This is due to accumulation

of blood in the atria, A. V. valves remaining closed. This rise slowly continues until the A. V. valves open (i.e., up to the end of isometric relaxation period). (5) During isometric relaxation period, the A. V. ring rises up and is an additional cause for pressure rising. (6) As soon as the A. V. valves open, atrial blood rushes into the ventricles, so that atrial pressure falls. The fall continues till about the middle of ventricular diastole. Then as ventricles fill up (diastasis), atrial pressure slowly rises. After this, atrial systole comes again.

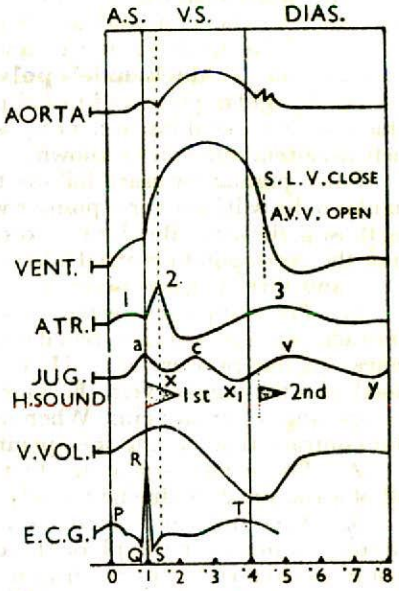


FIG. 182. Relation between Pressure, Volume and Electrical changes in Heart, Aorta and Jugular Vein during the Cardiac cycle of 0·8 sec. duration corresponding to heart rate of 72 per minute.

A.S.—Atrial Systole; V.S.—Ventricular Systole; DIAS.—Ventricular Diastole; AORTA—Pressure changes in Aorta; VENT.—Pressure changes in Ventricles; ATR.—Pressure changes in Atria; JUG.—Jugular Venous pulse; V. VOL.—Volume Curve of left Ventricle; E.C.G.—Electrocardiogram; S.L.V. CLOSE—Closure of Semilunar Valves; A.V.V. OPEN—Opening of Atrioventricular Valves.

Intra-aortic pressure changes (Aortic curve—FIG. 182). 1. During isometric contraction of the ventricles, a slight rise of the intra-aortic pressure takes place due to the bulging-out of the semilunar valves.

2. With the opening of the S. L. valves, blood enters the aorta and aortic pressure smoothly rises and falls—running parallel to the intraventricular pressure. The fall of intra-aortic pressure in the reduced ejection phase is due to three causes: (*a*) Ventricle is contracting less forcibly than before, so that a comparatively less amount of blood is entering the aorta now. (*b*) More blood is running out into the periphery than is entering the aorta from the ventricles. (*c*) Reflex vasodilatation through sino-aortic nerves, thus reducing the peripheral resistance and facilitating better ventricular emptying.

3. With the onset of diastole, ventricular pressure sharply falls causing a backward flow of the aortic blood towards ventricles. Owing to this, aortic pressure drops causing the *incisura*. It corresponds to the *dicrotic notch* of the radial pulse. The blood column is reflected back by the sudden closure of the semilunar valves, thus causing a sharp rise in the aortic pressure. This is the cause of the *dicrotic wave* on the radial pulse. After this, aortic pressure shows a few elastic oscillations (after vibrations) caused by the recoil of the aortic wall.

4. The aortic pressure then slowly falls due to the continuous passage of blood to periphery (propelled by elastic recoil of the vessels). The fall continues till ventricles contract again.

Jugular pressure tracing (Venous pulse—FIG. 182). The pressure changes in the right jugular vein will give a good idea as to those in the right atrium, because the right jugular vein is the direct continuation of the superior vena cava. It may be studied in a number of ways: (*a*) A small metal cup is placed on the vein. The cup communicates through a rubber tube with *Marey's tambour* (FIG. 181)—As the vein pulsates pressure changes take place in the cup and are transmitted to Marey's tambour. The recorder of the tambour moves and the oscillations are recorded on a moving drum. (*b*) **Mackenzie's polygraph.** This is an instrument by which tracing of jugular pulse and radial pulse can be obtained simultaneously. This is a very useful instrument by which the pressure changes as well as their time-relations can be known.

Since jugular pressure follows the atrial pressure, it is obvious that jugular pulse will have three positive waves and three negative waves following those in the atria. But due to its distance, the waves will come a little later than the corresponding atrial waves. The three positive waves are called, *a*, *c*, *v* and three negatives ones as *x*, x_1, *y*. The waves are as follows:

1. The first positive wave—*a* is due to atrial systole. As atrial muscles contract, pressure in it rises, blood in the jugular vein cannot enter the atria, hence, jugular pressure rises. [It is not due to the regurgitation of atrial blood into the jugular vein. Because a sleeve of atrial muscles surrounds the openings of great veins. When atria contract, these sleeves of muscles also contract thus closing the openings of great veins like a purse string.]
2. This is followed by the first negative wave—*x*. This is due to the fall of atrial pressure during the adynamic phase of atrial systole.
3. After this, the second positive wave—*c* comes during isometric contraction phase. In this phase there is bulging of the A. V. valves into the atrium causing rise of intra-atrial pressure. The *a*–*c* interval indicates the conduction time of the bundle of His and corresponds to the P–R interval of the Electrocardiogram. [The *c* wave begins 0·1 sec. before the primary wave of the radial pulse.]
4. x_1 is the second negative wave after *c*. It is due to the corresponding fall of pressure in the atrium.
5. *v* is the third positive wave, caused by the gradual filling of the atria and the return of the A. V. ring to its original position. The summit of the *v* wave indicates the end of ventricular systole.
6. The third negative wave *y* sets in after the opening of the A. V. valves and is caused by the corresponding fall in the atrial pressure.

Many informations regarding the conditions of heart in health and disease may be obtained from the jugular tracing.

Ventricular volume changes. The volume changes of the ventricles are to some extent the reverse of its pressure changes. The following phases are seen: (1) During atrial systole, ventricular volume increases due to rapid filling. This rise is maintained during the isometric contraction phase of the ventricles, because no blood is going out. (2) As soon as ejection starts, ventricular volume smoothly and continuously falls up to the end of systole. (3) In the isometric relaxation period, volume remains same, because no blood is entering. (4) In the next phase ventricular filling starts and its volume rises rapidly corresponding to the first rapid filling period. (5) After this, during diastasis or slow inflow phase, ventricular volume very slowly increases (FIG. 182).

MOVEMENTS OF HEART

1. **Movements during cardiac action. Apex beat.** *It is the outward thrust, felt at the left fifth intercostal space about* 1·27 *cm. (half an inch) inside the midclavicular line.* It takes place at the beginning of ventricular systole and is synchronous with the first sound of heart. It is caused by the following factors: (*a*) Ventricular muscles are arranged in a complex spiral manner. During contraction heart becomes rigid, assuming the form of a rounded cone. The apex is rotated anteriorly and to the right due to the contraction of the spiral fibres. This causes a sharp impact of the apex against the chest wall. (*b*) The entry of blood in the aorta makes the aortic arch more obtuse and helps to push the apex more anteriorly. These two factors cause apex beat.

2. **Movements during respiration.** The pericardium is fixed above with the root of the great vessels and below with the central tendon of diaphragm. During inspiration, diaphragm descends and pulls down the heart. The heart becomes narrow and long, and the apex rotates clockwise. During expiration diaphragm ascends and reverse movements take place.

3. **Movements of heart due to alteration of position of the body.** (*a*) When lying in the left lateral position, the heart is displaced to the left and comes closer to the chest wall. (*b*) In the right lateral position, the apex beat moves more medially. (*c*) Anything which presses the diaphragm upwards (such as flatulence or lying in the prone position) makes the heart assume a more horizontal position. Due to this, flatulence causes cardiac embarrassment. (*d*) In sitting position, the heart is horizontal but more or less normal.

HEART SOUNDS

There are two classical sounds of heart, known as the **first** and the **second** sounds (Fig. 184). They can be easily detected with a Stethoscope. Two other sounds have also been described—the **third** and the **fourth**—which, though difficult to detect clinically, are constantly found in graphic records. The first and the second sounds are close to each other. After the second sound there is a longer pause. The sequence is like this: first sound→second sound→pause; first sound→second sound→pause. Thus the sounds go on.

Biophysical principle underlying the occurrence of sound in the heart or in the circulation. In general blood flows, under most circumstances, through blood vessels in a streamline or in a lamina. Accordingly streamline flow is **silence** and must not be **noisy.** But under certain condition when this **laminar flow** or **streamline flow** is changed into turbulent flow then a noise may be produced. According to Sir Osborne Reynolds (1890), **turbulent flow** is noisy and this turbulence depends upon

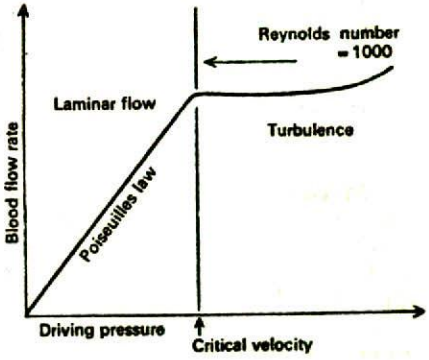


Fig. 183. Graphical tracing of laminar flow and turbulent flow in the tube (diagrammatic).

the **critical velocity.** It is the velocity at which the **turbulence** occurs. Reynolds has shown that the critical velocity depends upon the viscosity of blood, density of blood and also on the radius of the blood vessels, by the relation $V_c=(K\frac{\eta}{\rho r})$, where V_c=critical velocity, K=Reynolds number which is constant about 1,000, η=viscosity of blood, ρ=density of blood and r=radius of the tube (FIG. 183).

Cause of heart sound. The cause of heart sound is due to (*i*) vibration of the leaves of the valves during closure and (*ii*) occurrence of turbulence during rapid rush of blood from the atrium to the ventricle. During gradual closure of valves, the vibrations that occur, are transmitted from the valvular area towards the apices of the ventricles in case of first heart sound and along the arteries (aortic and pulmonary) in case of second heart sound. So the first and second heart sounds are not necessarily due to cause of turbulence but for the cause of closure of the tricuspid and mitral valves in case of first heart sound; and aortic and pulmonary valves for the second heart sound. The third sound occurs during opening of atrioventricular valve and where the rushing of blood through the narrow opening, produces turbulence. The fourth heart sound is due to rapid inrush of blood from the atria to the ventricles due to forceful contraction of the atria.

However in the heart and in blood vessels abnormal sounds which are generally heard are presumably due to abnormally high velocity of blood flow through the valves and blood vessels. These abnormal sounds (**murmurs**) are mostly associated with the occurrence of turbulence. In mitral stenosis or in coarctation of aorta, murmurs are always associated with the occurrence of turbulence. Because during such occurrence the blood flow reaches its critical velocity during flowing of blood through the narrowed lumen of the valves and blood vessels. Besides this, during heavy exercise innocent systolic murmurs are heard in normal individual due to rapid rush of blood from the ventricles to the arteries at mid systole. Experimental shortening of the lumen of blood vessels may produce sound during systole. This procedure is generally used clinically in the measurement of blood pressure indirectly through Sphygmomanometer. The sound that is heard during gradual release of pressure from the cuff is due to production of turbulence for just rushing of blood through narrowed vessels. The sound disappears as soon as the normal blood flow is resumed through the fully released vessels.

Methods of study. (1) *Clinical Stethoscope* is the commonest instrument, used for detecting and demonstrating heart sounds. (2) For more accurate work, a *microphone* is applied to the precordium and is suitably connected to an Oscillograph. It is also connected with a mirror arrangement which reflects a beam of light on a moving photographic plate. Thus the sounds can be graphically recorded (FIG. 184).



FIG. 184. Graphic recording of the heart sounds.

I. Prominent set of vibrations—*first* heart sound. II. Vibrations not so prominent—*second* heart sound. III. Small set of vibrations—*third* heart sound. A. Small set of vibrations—atrial or *fourth* heart sound.

The *first heart sound* is manifested by a prominent set of vibrations. It occurs during the ventricular systole and is noted just before the onset of the *c* wave of the jugular pulse. The *second heart sound* is manifested by a set of vibrations not so prominent as the previous one and occurs during the ventricular diastole and coincides with the notch on the ascending limb of the *v* wave of the jugular pulse. The *third heart sound* is manifested by a small set of vibrations and coincides with the end of the descending limb of the *v* wave of the jugular pulse. The *fourth heart sound* is manifested by another set of vibrations which occurs during the atrial systole and coincides with the *a* wave of the jugular pulse.

The sounds are briefly described below:

I. **First sound.** *It occurs* at the onset of ventricular systole. *Nature*—dull and prolonged, like the word *L-U-B-B* (FIG. 185). *Duration*—**0·1–0·17** sec. (average, half the ejection period). *Clinical identification*—It can be *identified* by the following features: (1) Its nature. (2) It is best heard over the left fifth intercostal space about 1·27 cm (half an inch) inside the midclavicular line. It coincides with the apex beat and with the commencement of the carotid pulse. (3) It comes just after the pause and (4) just before the radial pulse. (5) It coincides with the spike of the R wave of the Electrocardiogram. (6) It precedes the onset of the *c* wave of the jugular pulse.

Cause. First sound is caused due to (*i*) sudden closure of the A. V. valves and the vibrations set up in the valve leaflets due to increase in the intraventricular pressure. (*ii*) Ejection of blood from the ventricles and the vibrations transmitted to the walls of the aorta and pulmonary artery. (*iii*) Contraction of the thick ventricular muscles (muscular element). It is doubtful whether the second factor takes any appreciable part.

In graphic records often two distinct groups of vibrations are seen. The first group corresponds to the isometric contraction period and the second group to the maximum ejection period. The latter suggests that aortic vibrations, due to entry of blood, take part in causing the prolonged character of the first sound. The frequency of vibration varies from 25 to 45 per second.

Significance. (1) First sound indicates the onset of clinical systole of the ventricles. (2) The duration and the intensity of the first sound indicate the condition of the myocardium. In a strong healthy heart these features are prominent and become more so in a hypertrophied heart. If the myocardium is weak, the first sound will be short and low pitched. (3) A clear first sound indicates that the A. V. valves are properly closing, i.e., there is no incompetence.

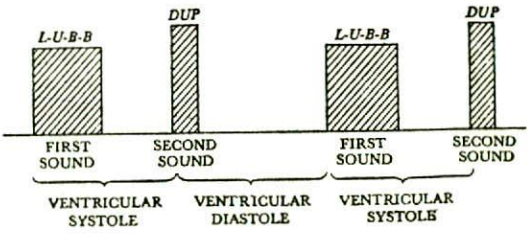


FIG. 185. Schematic representation of heart sounds.

II. **Second sound.** *Nature*—Short and sharp like the word *DUP*, the pitch being higher and duration shorter than the first sound (FIG. 185). *Duration*—**0·1–0·14** sec. *It occurs* at the onset of diastole and is **caused by** the sudden closure of the semilunar valves in the aorta and pulmonary artery and just after the

T wave of the E.C.G. At the end of systole, ventricular pressure falls below the pressure of the aorta and the pulmonary arteries causing a much pressure difference in between the aortic or pulmonary arteries and the ventricles. This increased pressure in the aorta or the pulmonary artery tends to close up the valves through a backflow. The two valves—aortic and pulmonary, do not close simultaneously but the pulmonary pressure precedes the aortic one. During inspiration but not in expiration, the sound is thus split into an aortic component and later a pulmonary component. Its intensity depends on the blood pressure. It consists of three or four chief vibrations with a frequency of about 50 per second.

Clinically, it can be *identified* by (1) its nature; (2) its relation with first sound and the pause; (3) its occurrence just after the apex beat and the carotid pulse; (4) getting the sound; (5) its occurrence at the end of the T wave of the Electrocardiogram; (6) its coincidence with the notch on the ascending limb of the *v* wave of the jugular pulse.

Significance. (1) It indicates the end of systole and beginning of diastole. (2) Its pitch is directly proportional to the blood pressure. (3) A clear second sound indicates that the semilunar valves are closing properly, i.e., there is no regurgitation. (4) The interval between first and second sounds is taken as the clinical systole and that between the second and first as the diastolic period of heart. The diastolic period, generally known as the **pause,** is a little longer than the systolic period. When the heart rate rises, the long pause shortens and the sounds appear to be equidistant.

III. **Third sound.** It takes place just after the second sound and coincides with the opening of the A.V. valves, i.e., with the commencement of the ventricular filling. It is **caused by** the sudden rush of atrial blood into the ventricles when the A. V. valves open. Although it is stated that it can be detected in 60% of normal subjects yet, in actual practice, it is difficult to detect clinically. Its **duration** is about 0·04 second. It can be *identified* by (*i*) its relation with the second sound; (*ii*) its coincidence with the end of the descending limb of the *v* wave of the jugular pulse.

Significance. It indicates the beginning of the ventricular filling.

IV. **Fourth sound.** It is also called the **atrial sound.** It is **caused by** the contraction of the atria and the consequent rush of blood into the ventricles. It is difficult to detect clinically but is found in the graphic records. It coincides with the rise of *a* wave of the venous pulse. It occurs just before the first sound and indicates the end of ventricular filling.

It should be noted that each of the above sounds is really produced at two places—for instance, the first sound is produced at both the A. V. valves, the second sound at both the semilunar valves (aortic and pulmonary) and so on. Yet, only one first sound, one second sound, etc., is heard. This is due to the fact that the two sets of valves move exactly at the same time. If any discrepancy occurs in the pressure and time relations between the different chambers of heart, instead of one sound, two sounds may be heard at each time. Thus reduplication of the sounds occurs in cardiac diseases.

Composite representation of the sequential changes in the pressure and volume events in the heart and blood vessels during the cardiac cycle correlating with phonocardiogram and electrocardiogram (FIG. 186). *I–II* is the *ventricular isometric contraction phase.*

This phase starts with the closure of atrioventricular (A.V.) valve and with the occurrence of the *first sound*. In this phase the ventricle is a closed chamber and with the contraction of the ventricular muscles, the intraventricular pressure rises first slowly but at later stage, rapidly. Notch c_1

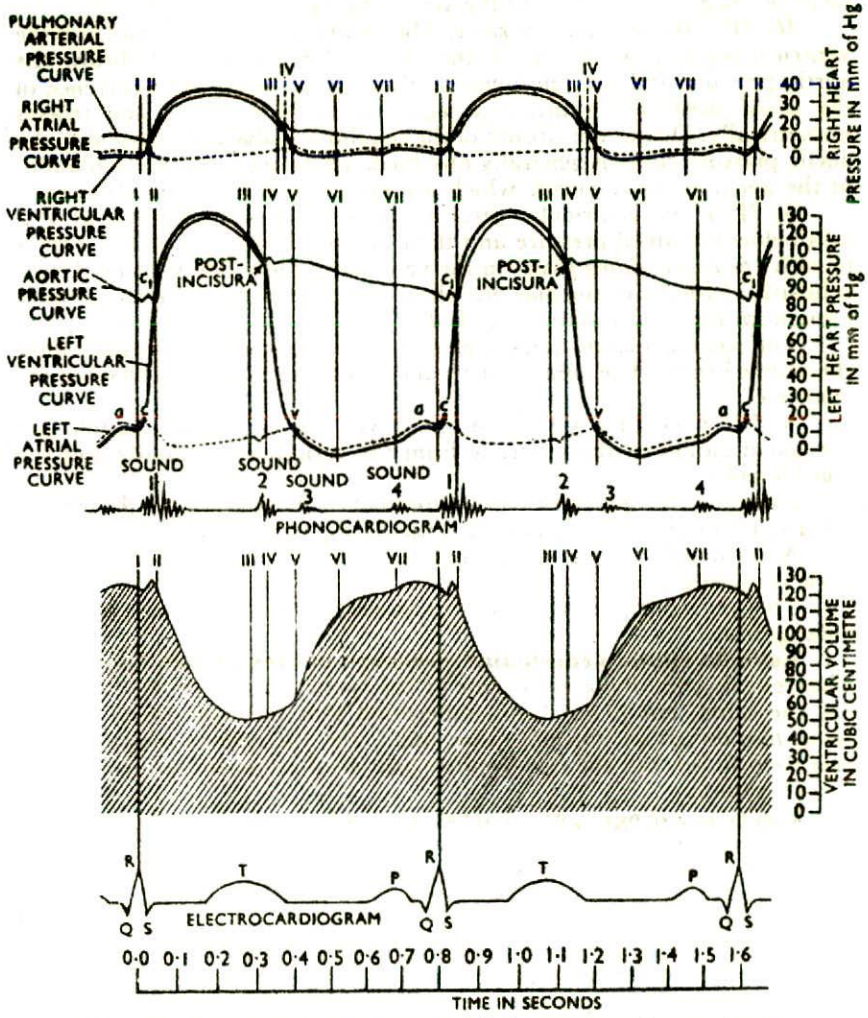


FIG. 186. Diagrammatic representation of the sequence of events in the cardiac cycle.

in the aortic pressure curve and notch *c* in the atrial pressure curve—both are due to the transmission of the intraventricular pressure through the bulging of semilunar (aortic) valve and atrioventricular valve respectively.

II–III is the *ejection phase of the ventricle*. At *II* the ventricular pressure overcomes the aortic pressure and the semilunar valve opens. The blood

begins to flow through the aorta at a higher pressure head. The ventricular pressure remains at a higher level throughout this phase.

The *ventricular volume* begins to decrease with the onset of ventricular systole. The atrial pressure though remains below the ventricular pressure head but begins to rise due to the venous filling.

III–IV is the *protodiastolic phase.* The ventricular systole ceases and the ventricle begins to relax. At *IV* the ventricular pressure falls below the aortic pressure and the semilunar valve is closed with the occurrence of the *second sound.* The ventricle is again a closed chamber and relaxes isometrically. Due to the closure of the semilunar valve a depression in the aortic pressure curve is generally observed. There are multiple oscillations in the aortic pressure curves which are known as *postincisural vibrations.*

At *IV–V* the ventricular pressure curve drops abruptly and at *V* it falls below the atrial pressure and then the blood from the atrium begins to rush (*first rapid filling phase*) in the ventricle rapidly. Here the *third sound* is heard. Throughout the diastolic phase of the ventricle, the atrial pressure remains in higher pressure head (*V–I*).

The *ventricular volume curve* begins to rise and maintains this stage until the systole begins. The *third sound* occurs with the rapid rush of blood in the ventricle.

At *VII–I* the atrial systole coincides with the ventricular diastole and the blood rushes in the ventricle from the atrium very rapidly and the *fourth sound* occurs.

a in the atrial pressure curve represents the cessation of the ventricular diastasis (*slow filling*) and the onset of the atrial contraction.

At *I* the *atrial systole* ceases and the *ventricular systole* starts and the cycle is repeated.

The ventricular volume begins to decrease with the onset of the ventricular systole.

Asynchronous ventricular pressure curves of two ventricles. Theoretically, the dynamic events of the two ventricles or the two atria are the same, but it has been understood that the *right atrium contracts earlier than the left one.* On the other hand, the *left ventricle contracts earlier than the right one,* but the *right ventricle ejects blood earlier* and *ceases later than the left ventricle.*

Electrocardiographic correlation of cardiac cycle. Prior to atrial systole, P wave, the depolarisation wave of atrium occurs. So the interval between the electrical events and the mechanical events of the right and left atria are 0·08 sec. and 0·06 sec. respectively. Similarly the ventricular depolarisation wave QRS starts prior to the onset of ventricular systole. The interval between the electrical events and mechanical events of the left ventricle and right ventricle is approximately 0·05 sec. and 0·04 sec. respectively. T wave which is the repolarisation wave of the ventricle mostly occurs during the systole of the ventricle and thus ends just before the incisura of the aortic pressure curve.

Metabolism and Nutrition of heart muscle

Energy coefficient of the heart is being met in the form of ATP either by glycolysis or by oxidation of carbohydrate (glucose, pyruvate, lactate) and non-carbohydrate (fatty acids, amino acids, ketone bodies). Metabolism of cardiac muscle has got similarities with those of skeletal muscle. Through the glycolytic process (anaerobic) only 2 moles of ATP are derived, but

through the oxidative process (aerobic) 39 moles of ATP are derived. Total ATP thus derived, 65% are transformed into mechanical work and the rest are dissipated as heat. So energy for mechanical work is derived mostly from oxidative process that takes place in presence of oxygen. Cardiac muscle has got high content of myoglobin which can store sufficient quantity of oxygen and this is a great advantage of the cardiac muscle to maintain its O_2 requirement during emergency. The oxidative metabolism of the cardiac muscle is altered greatly by neurohormones liberated during emotional upset or during physical and mental stress. In ischaemic heart disease where the muscle suffers from coronary insufficiency, the metabolism is affected greatly.

Methods of study. Metabolism of cardiac muscle can be studied by determining (1) O_2 consumption and CO_2 production, (2) nature of substrates used up, (3) mechanism of oxidation. O_2 consumption of the muscle can be assessed by determining the arteriovenous O_2 difference in the blood passing through the coronary system per unit time. In isolated mammalian heart preparation the metabolism of different substrates can be studied by detailed analysis of the perfusate. Enzymatic studies of the cardiac muscle homogenate can be made with different substrates in *Warburg's apparatus*. Heart is isolated and perfused through the coronary vessels by inserting a cannula through the aorta. The perfusing fluid is forced under pressure, so that the semilunar valves become closed and the fluid is forced into the coronary vessels.

1. **Respiratory quotient** (R. Q.) of heart varies from 0·7–1·0 showing that heart muscle can utilise not only sugar but also fats and amino acids.

2. **Oxygen requirement.** The oxygen requirement of heart is much higher than that of other muscles. In exercise, it may consume about 250 ml of O_2 per minute—same as that of the whole body at rest per minute. The arteriovenous difference of oxygen is nearly double (12 ml).

3. **Relation between O_2 consumption and work done by heart.** Ordinarily O_2 consumption is directly proportional to the amount of work done by heart, so that it rises if the blood pressure rises. But in the intact animals increased blood pressure causes reflex cardiac slowing. In such conditions the work done by heart increases without increased oxygen consumption. In other words, the mechanical efficiency of heart rises. In presence of O_2, heart poisoned with iodo-acetate can contract for an indefinite period. In the absence of O_2, heart ceases to contract after a few beats. During contraction ATP, and creatine phosphate break down and supply energy. The energy is resynthesised by the oxidation of pyruvic acid or lactic acid. In the absence of O_2, lactic acid is produced by glycolysis which supplies energy. In iodo-acetate poisoned cardiac muscle there is no formation of lactic acid and in the absence of O_2, heart fails to contract after a few beats.

4. The **mechanical efficiency** of heart is higher than that of other muscles and is about 30% (optimum). It rises with the increase of cardiac output and blood pressure up to a level. But if the heart is overworked, the efficiency falls.

5. The **carbohydrate metabolism** of heart muscle shows a number of peculiarities, not shown by other muscles—(*a*) The glycogen content of heart is about 0·6–0·7%. The amount increases in Diabetes

Mellitus and also in starvation—when the glycogen content of other tissues generally falls. (*b*) It can utilise glucose, lactate and pyruvate; but the last two are used in preference to the former. (*c*) Cardiac muscle uses lactic acid completely. Ordinarily, no lactic acid is liberated by cardiac muscle, unless there is oxygen lack. (*d*) Probably, it indicates that heart uses glucose for the synthesis of glycogen while it derives energy by burning lactates and pyruvates.

6. **Measurement of the respiratory quotient (R. Q.) of heart** and the **myocardial extraction of available substrates** have clearly shown the importance of lipid as a fuel for respiration, particularly in a fasting state. The energy requirements are mainly balanced by the utilisation of carbohydrate substrates, but recently it has been suggested that the utilisation of glucose, pyruvate and lactate by the heart is influenced with co-incident availability of the fatty acids and ketone bodies. Nearly all the fatty acids which are utilised by the heart, are derived from the plasma triglycerides and the albumin-bound non-esterified fatty acids (NEFA). Myocardial extractions of fatty acids are influenced by the activity of hydrolytic enzymes located at or near the cell membrane. Fatty acids supplied from circulation in excess of the needs of the heart for aerobic metabolism are deposited as tissue triglycerides and utilised subsequently as fuel for respiration. In fasting and diabetes, energy requirements are mostly met by the heart through the oxidation of fatty acids. An adequate supply of fatty acids from circulation is ensured in these starved or diabetic conditions by the elevated levels of plasma NEFA possibly through the increased activity of lipoprotein *lipase* in cardiac muscle. Lipoprotein lipase activity is reported to be increased in heart muscle and decreased in adipose tissue with starvation, diabetes and exertion. It is known that fatty acids and ketone bodies reduce glucose uptake in isolated heart and divert glucose from oxidation particularly to lactate or glycogen. Glycogen content in the heart muscle is increased in diabetic and starved animals though the myocardial uptake and phosphorylation of glucose are reduced. It has been reported by Pandle and Morgan (1959) and Evans (1964) that fatty acids and ketone bodies inhibit the phosphofructokinase and this might account for the depression of phosphorylation of glucose and the enhancement of glycogen synthesis during starvation, diabetes, etc. During starvation or in diabetes, there is rapid mobilisation of lipid and this state favours the easy availability of fatty acids and ketone bodies to the heart muscle. These fatty acids and ketone bodies are the common factors in inhibiting the phosphofructokinase activity. Myocardial utilisation of pyruvate is also depressed by fatty acids and ketone bodies. It is suggested that pyruvate decarboxylation is inhibited by fatty acids or ketone bodies during starvation or in diabetes. It is postulated that most of the decarboxylase enzymes are confined to the fatty acids for entering into the TCA cycle as acetyl CoA than to the pyruvic acid. These indicate that excess availability of circulating fatty acids diverts the decarboxylase enzymes towards the synthesis of acetyl CoA from fatty acids but not from pyruvate and maintains the TCA. On the other hand, excess pyruvate confines the decarboxylase for the synthesis of acetyl CoA. These however suggest that respiration of fatty acids derived from circulation and also from endogenous triglycerides play an important part in regulating the cardiac metabolism

of carbohydrate through inhibition of phosphofructokinase and pyruvate decarboxylase.

Factors regulating nutrition and action of heart. In addition to above, certain other factors exert considerable influence on the nutrition and activity of heart. They are as follows:

1. **Oxygen supply.** Inadequate oxygen supply causes weakness and irregularity of the heart beat. Sudden anoxia of the heart is the cause of cardiac pain.

2. **Blood pressure.** In perfusion experiments, it is seen that, if an adequate pressure is not maintained, force of contraction is diminished. The coronary circulation is fully dependent upon the blood pressure head. With the decrease of blood pressure, the coronary circulation will be affected greatly and accordingly the nutrition will be affected, leading to death.

3. **Temperature.** Cooling of perfusion fluid causes slowing of the heart rate; warming quickens it. Temperature variation of the fluid directly affects the metabolic rate of the S. A. node.

4. **H-ion concentration.** Slight alkalinity is necessary for optimum cardiac action. Change of pH on either side will disturb cardiac action. Rise of H-ion contraction reduces the strength of contraction and prolongs relaxation. Increased alkalinity causes opposite effects.

5. **Influence of inorganic ions on heart.** Other than factors described above, the presence of certain ions in the surrounding fluid medium is necessary for the maintenance of the normal activity of the heart. From the observation of Ringer in 1880, it is still recognised that cations Na^+, K^+ and Ca^{++} in appropriate proportion in any solutions and with normal pH and temperature can maintain the beat of the heart for a few hours. After Ringer's observation, extensive works have been carried out and the literature on the effects of different ions on the heart are voluminous. Principal actions of Na^+, K^+ and Ca^{++} on the heart have been presented below. Compositions of different perfusion fluids studied by some physiologists are as follows:

Scientists	*Adapted to*	NaCl %	KCl %	$CaCl_2$ %	$NaHCO_3$%	*Other constituents* %
Ringer	Frog	0·6	0·0075	0·01	0·01	—
Howell	Frog	0·7	0·03	0·026	0·003	—
Tyrode	Mammals	0·8	0·02	0·01	0·1	$MgCl_2$ 0·1 Dextrose 0·1 NaH_2PO_4 0·005
Locke	Mammals	0·92	0·042	0·018	0·015	Dextrose 0·1

(*a*) **Effect of K ions on heart.** If the K concentration in the intracellular fluid is increased, then the force of contraction is gradually decreased and ultimately stopped in diastole. According to Hajdu (1953) and Szent Györgyi (1955), excess K^+ in the cell depresses the association of actin and myosin. Tone of the muscle is dependent upon the degree of association of actin and myosin. Hajdu (1953) has stated that in each contraction certain amount of K comes out of the cell and during relaxation certain amount of K goes into the cell. So K-efflux favours the association of actin and myosin. The resting membrane potential depends primarily upon the potassium gradient across the semipermeable membrane. When the cardiac muscle is equilibrated with a solution containing an increased concentration of potassium ions, the resting membrane potential declines.

The resting potential and also the threshold potential are decreased. The excitability of the cell is thus increased. But with fourfold increase of serum K, the conduction velocity is decreased, the efficiency of the action potential as a stimulus to neighbouring cells is diminished. High concentration of K^+ in the extracellular fluid thus depresses the S. A. node as well as A. V. node and slows the rate of diastolic depolarisation phase in between beats. Thus the diminution in contractile strength of the heart muscle due to excess extracellular K^+ is partly due to direct inhibition of contractile processes and partly due to conduction block.

In deficient K concentration in the intracellular fluid, there is a transitory hyperpolarisation followed by a gradual decrease in resting potential. There will be an increased tone of the muscle resembling mostly the Ca^{++} rigor if the heart muscle is perfused with K-free Ringer. Under such state only to make equilibrium of K^+ in between the extracellular and intracellular compartments, certain amount of K^+ will leave the cell presumably favouring association of actin and myosin.

(*b*) **Effect of Ca^{++} ion on heart.** In class experiment with excess calcium it is generally observed that if the Ca concentration in the extracellular fluid is increased then the height of contraction of the heart is increased. But if the concentration is further increased then the heart stops in systole (contracture) which is known as **Ca rigor.** According to Winegrad (1960) if the extracellular Ca concentration is increased then the intracellular calcium concentration is increased during depolarisation. Winegrad (1960) and, Weidmann (1959) have reported that this increased calcium influx during depolarisation phase, has got same relation with **excitation-contraction coupling.** This factor actually determines the strength of twitch. According to Winegrad's further postulation (1960) calcium that enters during excitation (depolarisation), inhibits the relaxing system and thereby initiates contraction. Szent Györgyi has reported more earlier that calcium stimulates the ATP-ase activity and facilitates the breakdown of ATP into ADP and Pi and thus the actin-myosin-ADP complex is formed. The increased tension of cardiac muscle due to excess calcium is presumably the greater association of actin and myosin in presence of ADP. Calcium rigor is possibly due to association of many actin and myosin units through ATP-ase activity.

(*c*) **Effect of Na on cardiac muscles.** Main function of the extracellular fluid is to maintain the osmotic balance in between the blood and the intracellular fluid. In intact animal, loss of intracellular Na has got little effect, but in isolated perfused heart the absence of Na in the perfusion fluid will deteriorate the condition of the heart. The rate of diastolic depolarisation in the pacemaker fibres is showed and the heart rate is slowed. Neidergerke (1963) has suggested a hypothesis for the interrelationship in between the Na and Ca with regard to their effects on the contractile strength of the myocardium. He has postulated that calcium and sodium compete for same anionic groups, R on the cell surface to form either a CaR compound, which activates tension, or a NaR compound, which inactivates tension.

Under normal physiological condition CaR and NaR are present in equilibrium or balanced state at the cell surface. But with the decrease of Na in the extracellular fluid, certain amount of Na is released from the anionic sites of cell membrane and these anionic sites are occupied by Ca—thus increasing CaR concentration on the membrane. This state increases the magnitude of contractile strength. So increased tension in heart muscle following perfusion with Na-free Ringer is partly due to osmotic imbalance and partly due to increased formation of CaR on the membrane site causing the magnitude of contraction.

6. **Neurohormones.** Catecholamines (adrenaline and noradrenaline) and acetylcholine have got some effects on the cardiac metabolism and functions. Adrenaline or noradrenaline augments the cardiac contractility and O_2 utilisation is likewise greatly enhanced. Efficiency is thus greatly affected. On the other hand, the acetylcholine protects the heart muscle from the catecholamines—induced *cardiac hypoxia* and thus the energetic efficiency of cardiac muscle is conserved.

7. **Effect of cardiac active principles of blood plasma.** As early as 1885 Ringer first reported the presence of certain factors in the blood plasma, which could maintain perfused heart for a longer time than with the Ringer fluid only. Afterwards, Hajdu and Leonard (1960) postulated that the amphibian heart is provided normally with certain

substances which maintain the contractility and these substances gradually disappear from the muscle during perfusion with amphibian Ringer. However, if the blood plasma is mixed with the perfusion fluid or the hypodynamic heart is perfused with normal frog plasma then the hypodynamic heart gradually regains its dynamicity.

The substances that have been identified in mammalian tissue are two types of cardiotonic factors: (*a*) **phospholipid** (*β-palmitoyl-lysolecithin*), (*b*) *three plasma globulins* (**cardioglobulin A, B, C**). The β-palmitoyl-lysolecithin has been isolated from the adrenal medulla and is widely distributed within the chromaffin system. It has been observed that in mammalian plasma, these substances are present in a very low concentration and to make the hypodynamic frog heart to dynamic one it requires prolonged exposure to the mammalian plasma. The cardioglobulins A, B, C, present in the mammalian plasma, are also capable of stimulating or maintaining the dynamicity of the hypodynamic heart.

From the above, it is evident that for adequate nutrition and activity of heart, not only foodstuffs and oxygen but an optimum pressure, temperature and pH, as well as a proper balance of the different inorganic ions and neurohormones are essential. *The condition of the coronary vessels is of utmost importance.* Because, it is through them that heart derives everything necessary for its health and activity.

ELECTROCARDIOGRAM

It has been discussed earlier that prior to each contraction an electrical impulse is generated in the S. A. node and thus transmitted to the A. V. node, bundle of His, Purkinje fibre, ventricular muscle fibre and lastly to the surrounding tissue in which the heart is bathed in. Body is a volume conductor and the heart muscle, being the electrical generator with two opposite poles (dipole), is bathed in it (FIG. 187). Under this condition, electrical impulse that is initiated in the cardiac muscle will be transmitted throughout the body. If suitable electrodes (leads) are placed on the body opposite to the heart and connected to a very sensitive galvanometer with a recording device, then the electrical potential can be recorded. The record is known as **Electrocardiogram (E.C.G.).** The machine by which the electrocardiogram is recorded is spoken of as **Electrocardiograph.**

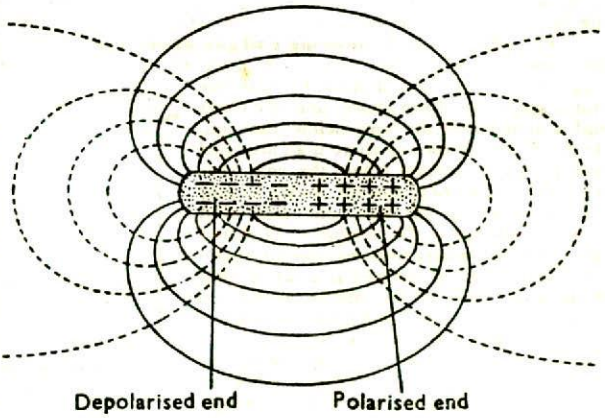


FIG. 187. Diagrammatic representation of electrical generator of a dipole in a volume recorder showing current flow (solid lines) and isopotential lines (dotted lines).

The currents generated from the different chambers of heart are not equally transmitted in all directions. Hence, the record will vary according to parts of the body from which the action current is led off. Consequently, to obtain an accurate information, several records from different parts of the body should be taken.

Methods of recording electrocardiogram. Though Waller (1887) first recorded the electrocardiogram yet Einthoven (1903) was the real father of the electrocardiography. His method of recording E.C.G. through **string galvanometer** was followed until 1930 when it was largely replaced by the amplifier-driven oscillograph provided with direct ink-recording. Principles upon which the string galvanometer was based are as follows: If an electrical current is allowed to pass through a string suspended in a magnetic field, then the string will move. In this string galvanometer there is a thin platinum wire suspended within the magnetic field created by the *south* and *north poles* of the magnets. The string suspended in such a way that it can move freely. There is a thorough passage longitudinally through the two magnetic bars and the rays of light may be collimated through this passage in such a way so that it may fall directly over the photographic screen (Fig. 188). The light source is obstructed by the movement of the galvanometric string and the nature of impression is also changed according to the movement. The two free ends of the string are attached to the body. Electrical impulse that is initiated from the heart is transmitted all throughout the body because the body is a volume conductor. So this impulse will be transmitted through the electrodes to the string galvanometer which will vibrate in the magnetic field.

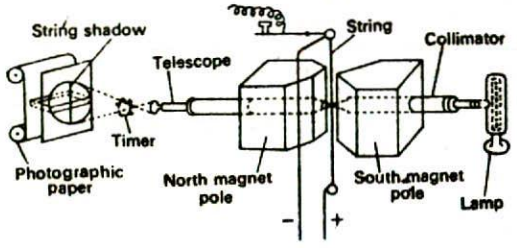


Fig. 188. String galvanometer of the electrocardiograph (diagrammatic) (after Katz, 1946).

Fig. 189 depicts the **moving coil galvanometer** in which a strong magnetic field is developed between south and north poles of an electromagnet or strong permanent magnet. There is a coil of wire whose one end is suspended from above and the other end is joined with the wire below the coil. At the middle of the coil there is an attached mirror which rotates when the coil rotates. When electrical current makes to pass through the coil of wire, one side of it moves backward in the magnetic field and the other side moves forward due to opposite direction of the current. If a ray of light is allowed to fall on the mirror as the coil rotates to left or right, the reflected beam of light can be recorded on a moving photographic paper. This type of galvanometer requires an amplifier to make potential recorded from the surface of body. This type of galvanometer is essentially used for electrocardiographic studies due to rapidity of recording changes (several hundred cycles per second) in electrical potentials.

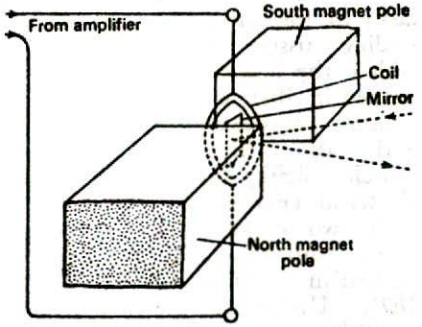


Fig. 189. Moving coil galvanometer of the electrocardiograph (diagrammatic) (after Katz, 1946).

The **direct pen recorder device** is very suitable both clinically and experimentally because the nature of wave is recorded graphically and the wave is visualised on the spot.

Electrocardiographic leads used both clinically and experimentally. When electrocardiographic connections are made between two parts of the body, then this specific arrangement of each pair of connections is designated as **lead.** Fig. 190 represents the arrangement of

different standard limb leads. The different leads that are conventionally used are: (1) **standard limb leads,** (2) **chest leads** and (3) **augmented unipolar limb leads.**

Standard limb leads (Fig. 190). The action current of the heart is recorded by placing two electrodes in two different positions in the body.

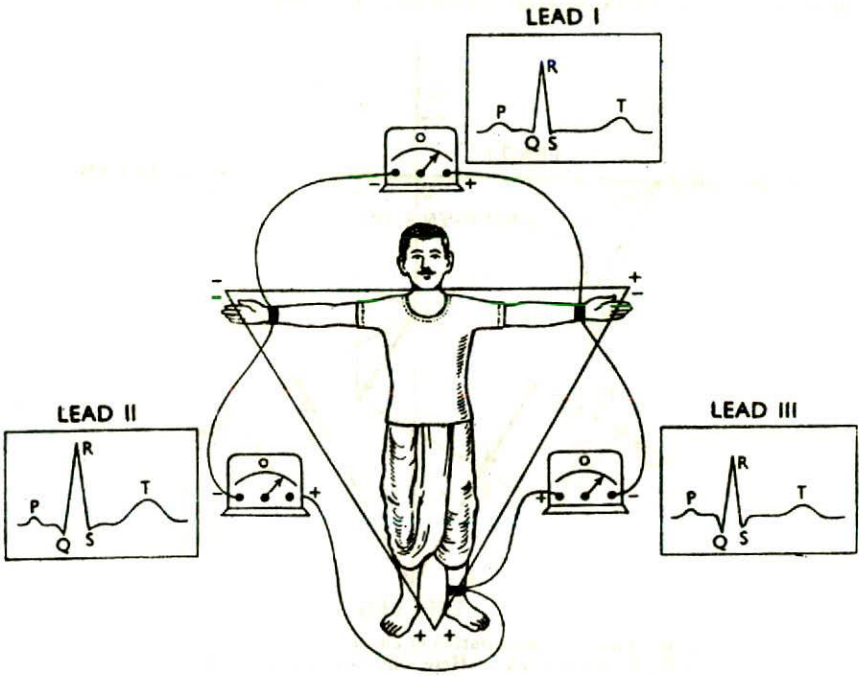


Fig. 190. Schematic representation of bipolar leads—standard limb leads of the Electrocardiogram and general normal recordings from these leads.

Such arrangement of lead is called *bipolar leads*. The following *bipolar leads* (*standard limb leads*) are in common use:

Lead	Negative terminal	Positive terminal
I	Right arm	Left arm
II	Right arm	Left leg
III	Left arm	Left leg

According to convention, the combination of the lead I will be made by connecting the left arm to the positive pole of the galvanometer and the right arm to the negative pole of the galvanometer. The combination of the lead II will be made by connecting the right arm to the negative pole and the left leg to the positive pole of the galvanometer. The combination of the lead III will be by connecting the left arm to the negative pole and the left leg to the positive pole of the galvanometer.

Einthoven's triangle. It is an equilateral triangle drawn arbitrarily around the area of the heart (Figs. 190 & 191).

Einthoven's law. Einthoven's law states that if E.C.G. is recorded through standard limb leads then the sumtotal voltage of the QRS (ventricular complex) in leads I and III is equivalent to lead II. If the voltage of QRS complex in lead III is +2 and in lead I is +3, then the voltage of the same in lead II will be +5. On the other hand, if the voltage of QRS in any two leads is known then the other one will be obtained after deducting the latter from other two (FIG. 191).

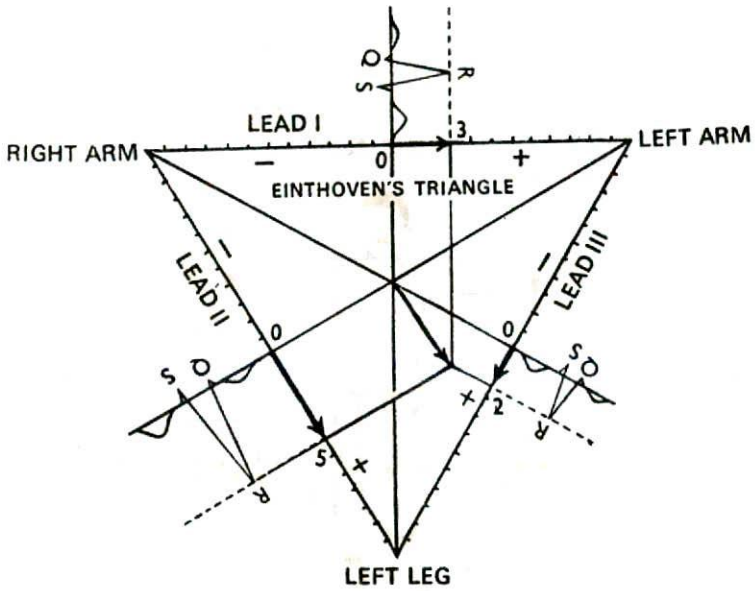


FIG. 191. Diagrammatic representation of electrical axis of QRS complex shown by Einthoven triangle. Here only two leads need be used.

Normal E.C.G. recorded in standard limb leads. E.C.G. recorded simultaneously in three leads shows mostly similar in shape, contour and other feature. P, R, T waves are *positive waves* in all the leads. The voltage of different complexes are different from lead to lead. For clinical purposes in diagnosis of the arrhythmia, it does not matter with which leads, the E. C. G. has been recorded. But for determining the extent of cardiac damage either in the atria or in the ventricles, it does matter with which leads the E. C. G. is taken.

Interpretation of human electrocardiogram (FIG. 192). It shows the following five consecutive waves: **P Q R S T.** There are two *isoelectric periods*—the shorter one, between P and Q; the longer one, between S and T. P, R and T are upward deflections, while Q and S are downward waves. The waves are therefore alternately up and down. P is of atrial origin, hence called the **atrial complex,** while Q R S T being of ventricular origin, are collectively known as the **ventricular complex.** They are briefly described below:

P. This is the first upward deflection. It is a small but constant wave having a rounded or pointed top. It is depolarisation wave of the

atria and takes place when the impulse spreads over the atria and therefore, *caused by the passage of the action current over the atria.* Its **average duration** is about **0·1** sec. (same as atrial systole). Repolarisation wave of the atria is submerged within the ventricular complex.

The impulse arrives at the A. V. node, at about the summit of P. Normal P indicates that: (1) The impulse is originating at the S. A. node. (2) It spreads over the atria in the usual direction. (3) There is no defect of conduction. (4) The strength of contraction, the mass of atrial musculature and its nutrition, are normal. If the P is inverted, it indicates that S. A. node fails to initiate impulse and the atrial muscle depolarises by the *impulse originating in A. V. node.*

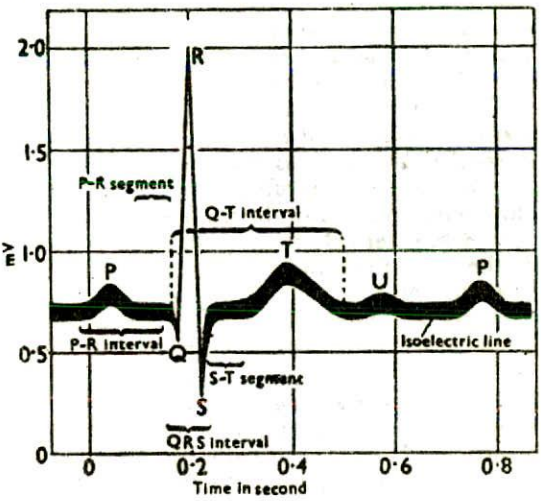


FIG. 192. Conventional terms for electrocardiographic deflections (diagrammatic).

Any abnormality of atrial activity, will be reflected by corresponding changes in the P wave. For instance, in atrial fibrillation it will be absent; in atrial hypertrophy, it will be large and may be, notched; in nodal rhythm, the direction will be reversed.

Q R S T. These four waves are caused by ventricular activity and are collectively known as the **ventricular complex. Q R S** are depolarisation waves of the ventricle; and are the initial group of three waves—one following immediately upon the other. The **average duration of Q R S T** is **0·43** sec.; that of **Q R S** is usually less than **0·08** sec. and should not exceed 0·1 sec.

Q. As soon as the impulse arrives at the muscular part of the septum, the latter contracts producing the first wave Q. Hence, Q *is caused by the activity of the septum.* It is a small, negative wave and often inconspicuous deflection. It is not found in those animals which do not possess an interventricular septum (Reptiles and Amphibia). It is also absent in infants suffering from congenital patency of the septum. Prominent Q wave indicates old infarction.

R & S. R is the most constant and conspicuous wave having the tallest amplitude. It is the first positive deflection during ventricular depolarisation. It follows immediately upon Q. S is the next downward deflection, constant but often inconspicuous. *In lead I,* R *is mainly caused by right ventricle and* S *due to left ventricle. In lead III, it is just the reverse.* In abnormal conditions of ventricles, the shape, size and duration of R S alter. For instance, in bundle-branch heart block their duration is prolonged beyond 0·1 sec. and their relative amplitude varies.

T. R is followed by a long isoelectric period, after which comes the

last upward deflection T. It is a broad, smoothly rounded deflection with an average **duration** of **0·27** sec. *It is caused by the action current due to the contraction of the basal part of the ventricles.* It is repolarisation wave of the ventricle. It is normally positive because the apex of the heart repolarises more earlier than the base of the heart. In young adults, T is very prominent. In old age it is flattened. Exercise increases the amplitude in a healthy heart. It is sometimes inverted in lead III without apparent reason. It is also altered by stimulation of the vagus and sympathetic nerves, by digitalis and other poisons, by anoxia caused by coronary constriction and by the damage of myocardium from any cause.

Abnormalities of T *wave in shape, size, direction, duration and reaction to exercise in leads I and II are of great prognostic significance. It indicates serious myocardial damage and is often associated with* cardiac **hypoxia.**

U. This wave is often seen just after the T wave. It is possibly due to slow repolarisation of the intraventricular conducting system.

R-R interval. It is the interval between the two successive R waves. If the R–R interval in next successive stages are same then they indicate that the ventricle is depolarising rhythmically.

P-P interval. It is the interval between the two successive P waves. Equal intervals in next successive stages indicate rhythmical depolarisation of the atrium.

P-R interval. *This is the interval from the onset of* P *to that of* QRS. It measures the conduction time of the impulse from the S. A. node to the ventricles. Normally, it varies from **0·13** to **0·16** sec. and should not exceed 0·2 sec. A longer interval shows impaired conduction through the bundle. Variable P–R interval in successive stages indicates A. V. dissociation. This indicates ventricle to beat without the influence of S. A. node. [True conduction time, i.e., from the A. V. node to the ventricles, should be measured from the summit of P to the beginning of Q. But since Q is often absent, P–R interval is taken as the conduction time for the sake of convenience.]

Q-R-S interval. It measures the total ventricular depolarisation time. It is measured from the onset of Q wave to the cessation of s wave. It varies from **0·08** to **0·1** sec.

Q-T interval. It measures the ventricular total systolic time. It is generally measured from the onset of Q wave to the end of T wave. It is about **0·36** sec.

RS-T segment. Elevation or sagging of this segment indicates myocardial damage or hypoxia.

T-P interval. Alteration of this interval indicates the alteration of the heart rate. It is measured from the end of T wave to the beginning of P wave. T–P interval *actually measures the diastolic period of the heart.* If the T–P interval in successive stages are variable then it indicates atrioventricular dissociation.

Unipolar limb leads. Electrodes are placed respectively on the left arm, left leg and right arm. They are connected together to form a central terminal which passes through a suitable resistance (5,000 ohm) and is kept almost to zero potential. This is the indifferent electrode. Other electrode is put on different parts of the body surface. This is the exploring electrode. By this arrangement the indifferent electrode is kept at zero degree potential so that the exploring electrode records the local unmodified action current.

The following unipolar leads are in use:
Lead VR—Right arm. Lead VL—Left arm. Lead VF—Left leg (foot).

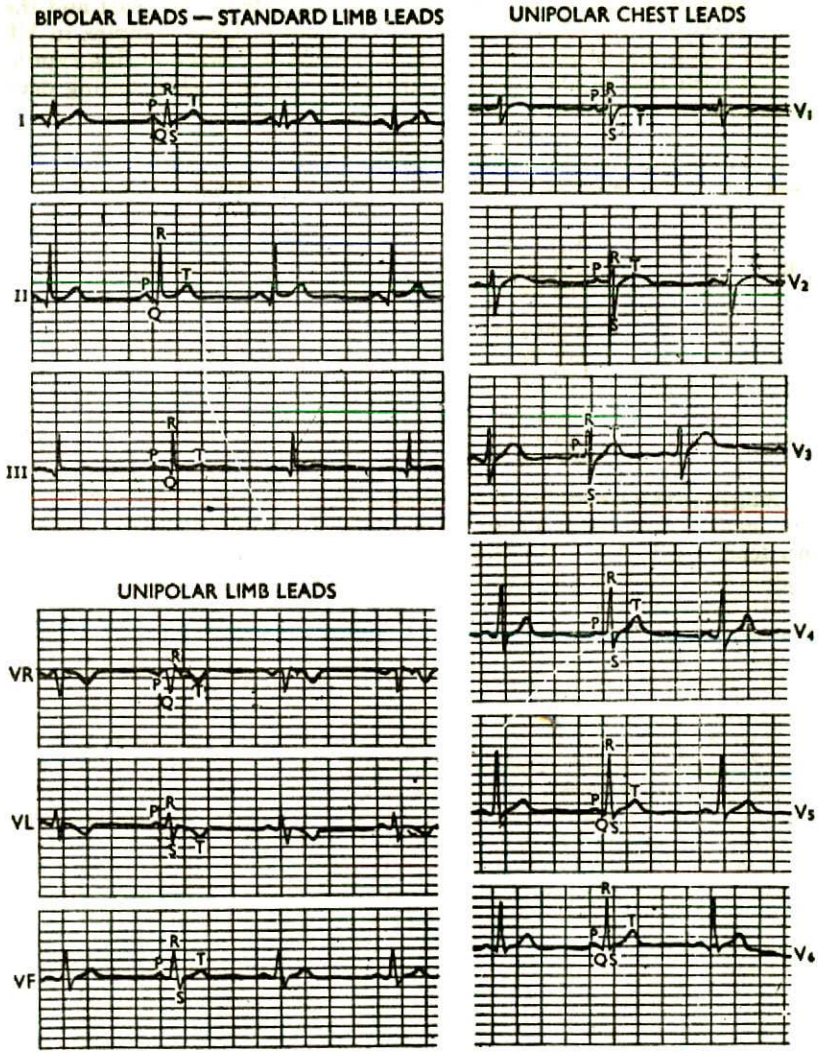


FIG. 193. It represents E.C.G. of bipolar leads, unipolar limb leads and unipolar chest leads (diagrammatic).

By courtesy of Prof. R. N. Chatterjee, M. D. (Cal.).

VR—Q wave is bigger which is followed by small R wave, small S wave and an inverted T wave (FIG. 193).

VL—The waves in VL change with the alteration of the position of the heart. When the heart is vertical, VL resembles with that of VR. R wave is small followed by big S wave. T wave is inverted.

VF—There is a large R wave followed by S wave. T wave is erect.

Through the unipolar limb leads VR, VL, VF, electrical activities of the ventricular cavity, upper part of the left side of the heart and the inferior surface of the heart respectively are known. QRS complex in VF resembles with that of chest lead V_1 if the records are taken during expiration and with that of chest lead V_6 if the records are taken during deep inspiration.

UNIPOLAR LIMB LEADS

Lead	Negative terminal	Positive terminal
VR	Right arm Left arm Left leg	Right arm
VL	Right arm Left leg Left arm	Left arm
VF	Right arm Left arm Left leg	Left leg

Augmented unipolar limb leads. In these types of leads there are three leads widely used. These are aVR, aVL and aVF. In the unipolar limb leads (VR, VL, VF) the amplitudes are small but in augmented unipolar limb leads (aVR, aVL, aVF) the amplitudes are increased by 50%.

In these types of recordings, one limb is connected to the positive terminal and the other two limbs are connected together to the negative terminal. When the right arm is connected to the positive terminal, and the left arm and left leg together to the negative terminals, then the combination will be aVR (denoting block R as *right arm*). Similarly when the left arm is connected to the positive terminal, and the right arm and left leg together to the negative terminals, the combination will be aVL (denoting L as *left arm*). When the left leg is connected to the positive terminal, and the right arm and left arm to the negative terminals, then the combination will be aVF (denoting F as *foot*).

Normal E.C.G. recorded in these leads (FIG. 194) shows more or less similar except that the recording in aVR is inverted. This is because the side of the heart nearest to the right arm is negative in respect to the rest of the heart.

Chest leads (Unipolar). There are six chest leads, viz., V_1, V_2, V_3, V_4, V_5, V_6. In the chest leads (FIG. 194), one electrode is placed on the anterior surface of the chest and connected to the positive pole of the galvanometer and the other electrode—the indifferent electrode placed anywhere in the body is connected to the negative pole of the galvanometer. One such combination actually makes one lead. The conventional **precordial positions** used are as follows:

V_1—Fourth intercostal space at 2·54 cm (1 inch) away from the right sternal border.

V_2—Fourth intercostal space at 2·54 cm (1 inch) away from the left sternal border.

V_3—At the midpoint between V_2 and V_4.

V_4—Fifth intercostal space at left midclavicular line.

V_5—At a point where the anterior axillary line intersects perpendicularly the horizontal line extended from V_4.

V_6—At a point where midaxillary line intersects perpendicularly the same horizontal line extended from V_4.

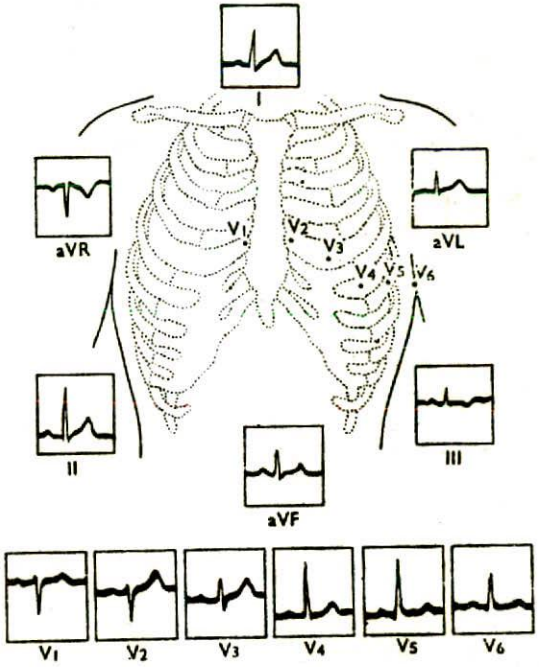


FIG. 194. Diagrammatic representation of normal electrocardiographic patterns and also the different positions of unipolar chest leads (V_1–V_6).

Normal E. C. G. recorded in chest leads (FIG. 194). In leads V_1 and V_2 the QRS complex is normally negative, because the chest electrodes in these leads are nearer to the base of the heart which is the direction of electronegativity during most of the *ventricular depolarisation* phase. On the other hand, in V_4, V_5 and V_6 the QRS complex is positive because these chest leads are nearer to the apex of the heart and are electropositive during *depolarisation*. Localisation and the extent of damage can be determined by using the chest leads.

Normally V_1–V_3 indicates the activity of the right ventricle and is characterised by increasing height of R wave from V_1 and a progressively decreasing S wave. The height of R wave increases from V_1 to V_4 or V_5. V_5–V_6 denotes the activity of the left ventricle and is characterised by a very small Q wave and a tall R wave. T wave is generally upright in all positions except sometimes in V_1.

Significance of various leads and their limitations. In general the **standard limb leads** are most valuable for diagnosis of arrhythmia and also for preliminary studies of the functional abnormalities of the heart.

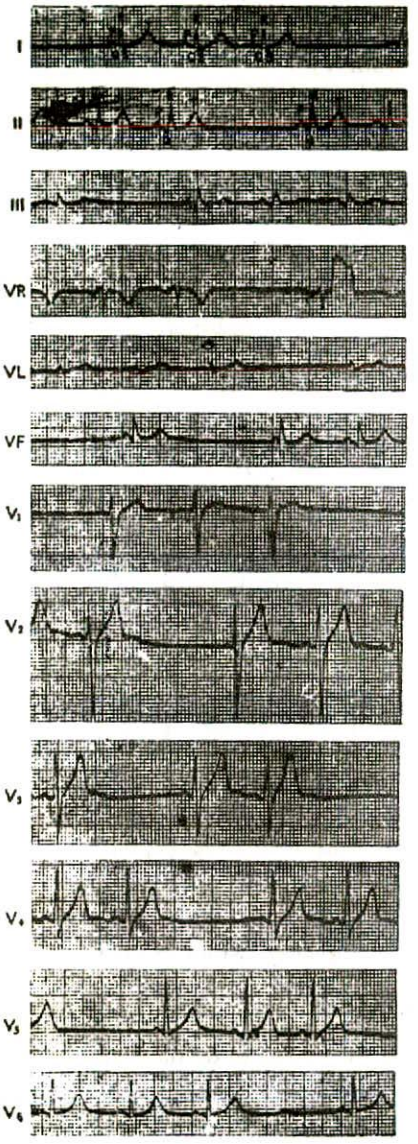


FIG. 195. Sino-atrial heart block.

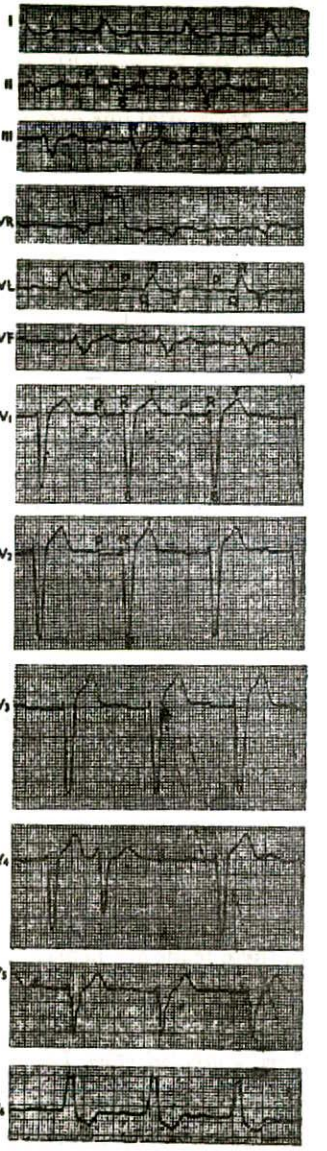


FIG. 196. Prolonged P–R interval.

By courtesy of Dr. Sunil Sen, M.B., M.R.C.P. (Edin.)

The **precordial chest leads** are very important for diagnosis or for (*a*) localisation of the recent or old ventricular damage, (*b*) bundle-branch block and (*c*) detection of ventricular hypertrophy.

The **augmented unipolar limb leads** are most valuable for (*a*) determining the position of the heart, (*b*) confirming the significance of Q and T waves in the standard leads, and (*c*) confirming the evidence of ventricular damage or hypertrophy.

Abnormalities in E. C. G. may not always indicate heart disease, because these abnormalities may be functional, congenital or induced by drugs or by disease.

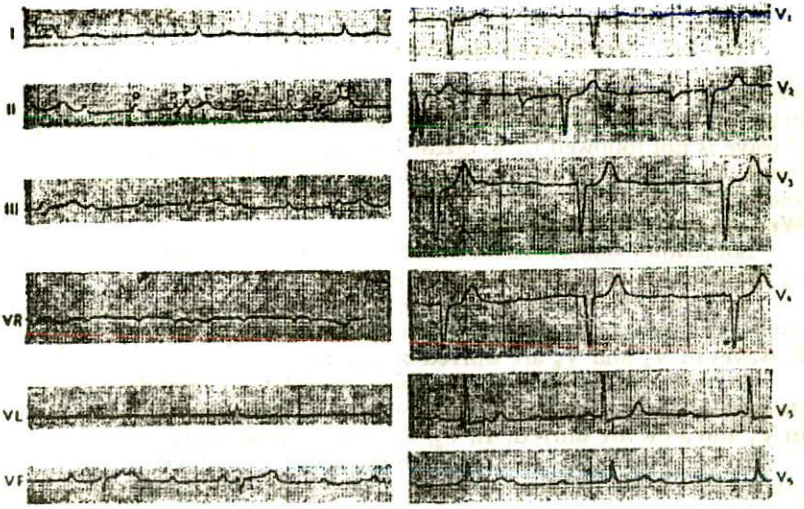


FIG. 197. Complete heart block.
By courtesy of Dr. Sunil Sen, M.B., M.R.C.P. (Edin.)

The **clinical importance** of Electrocardiogram is obviously very great. It gives a fairly accurate information as to the condition of atria and ventricles—almost in all of its functional aspects. In cardiac abnormalities, characteristic variations occur in the Electrocardiogram along with side-by-side clinical findings may act as a dependable guide to the diagnosis, prognosis and treatment.

Electrocardiographic appearances under certain cardiac disorders

1. **Heart block.** *Vide* also page 241. Heart block is the condition when conduction of impulses from pacemaker area through the conducting tissue is interrupted at any degree. Sometimes impulse from S. A. node fails to reach the atrial muscle due to block (sino-atrial block). In E. C. G. (FIG. 195), P is absent due to atrial standstill, but the ventricle beats at the rhythm of the A. V. node and QRS–T complex remains unaltered.

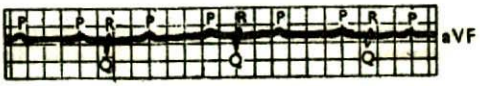


FIG. 198. Second degree heart block (diagrammatic).

Incomplete heart block or **partial heart block** is the condition when the bundle of His is partially blocked. In first degree heart block (Fig. 196), the P–R interval is abnormally increased from 0·16 to 0·38 sec. In the second degree heart block (Fig. 198), QRS–T complex follows each

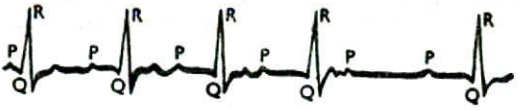


Fig. 199. Second degree heart block of Wenckebach type (diagrammatic).

second or third P wave (2 : 1 or 3 : 1 heart block). In certain partial heart block, P–R interval increases with each successive beat until one P wave is not followed by a QRS–T complex. So in this form of heart block, the P–R interval is gradually increased in successive beats until a ventricular beat fails to occur (Fig. 199). This type of block is known as **Wenckebach phenomenon.**

Sometimes, block occurs in either branch—left or right bundle-branch by injury or by some pathological processes.

In *left boundle-branch block*, there is delay in activation of the left ventricle. Ventricular rate is normal, but duration of QRS complex is greater. R waves in V_5 and V_6 are slurred or notched.

In *right bundle-branch block*, there is delay in impulse conduction through the right ventricle. QRS duration is prolonged and the R waves in V_1 and aVR are slurred. In V_5, V_6, and aVL there is late slurred S wave.

In complete heart block, where the impulse conduction is completely interrupted due to damage of bundle of His, there are complete atrioventricular dissociations. Atrium beats at the rate of sinus rhythm and ventricle at its own. This type of block is known as **complete** or **third**

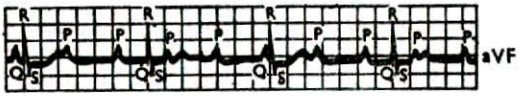


Fig. 200. Complete heart block showing atrioventricular dissociation (diagrammatic).

degree heart block. In the E. C. G., P–P interval and R–R interval will be same all throughout, but P-R interval will be variable because P will not be followed by the QRS–T complex (Figs. 197-& 200). *Resultant cerebral ischaemia* may cause dizziness and fainting **(Stokes-Adams syndrome).**

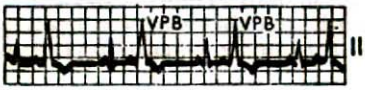


Fig. 201. Ventricular premature beats (diagrammatic).

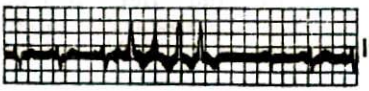


Fig. 202. Ventricular paroxysmal tachycardia (diagrammatic).

2. **Ventricular premature beat or extra-systole,** Fig. 201 illustrates the series of ventricular premature beat or extra-systole. Sometimes, a

portion of the myocardium becomes irritable and ectopic beat occurs before the expected next normal beat. This ectopic beat causes transient interruptions of the cardiac rhythm. This type of ectopic beat is known as **ventricular extra-systole** or **premature beat.**

3. **Ventricular paroxysmal tachycardia.** This is the condition when the ventricular muscle is damaged considerably. The E. C. G. shows the series of ventricular premature beats or extra-systole occurring successively for several beats without any normal beats interspersed (FIG. 202). This is the early stage of *ventricular fibrillation.*

4. **Ventricular fibrillation.** This is the condition of massive damage at multiple areas of the ventricles. In the E. C. G., the complexes are bizarre and the individual component cannot be deciphered (FIG. 203).



FIG. 203. Ventricular fibrillation (diagrammatic)

5. **Ischaemic heart disease.** This is the condition when the circulation of the heart muscle is interfered with. In the E. C. G., there is inversion of T waves. The RS–T segments are sagged.

6. **Myocardial infarction.** It is the condition when an area of the muscle is necrosed due to permanent arrest of blood supply to that area. The cause of arrest of blood supply is due to formation of thrombus in a region narrowed by atherosclerotic plaques (coronary thrombosis). The E. C. G. shows deep Q wave, S–T segment elevation and T wave inversion.

In early stage, the prominent Q wave may not be observed. Only elevation of RS–T segment in lead I, aVL and V_5–V_6 may be observed. Depression in RS-T segment may be observed in leads II, III, and aVF.

In old infarction, there is prominent Q wave which is observed in lead I, aVL, and V_5–V_6.

Mean electrical axis of the heart. It is the resultant electromotive force passing through the heart at a definite direction. The electromotive force having its definite magnitude and direction is known as **vector.** So each *vector is the measure of the instantaneous electromotive force of the heart and its directions* may be regarded as the **instantaneous electrical axis.**

Determination of electrical axis. Electrical axis of the heart is determined on the hypothesis of *Einthoven equilateral triangle.* According to the hypothesis of Einthoven triangle, the heart assumed to be a centre point of electrical generator in the equilateral triangle which is formed by joining the three parts of the limbs and from which the different leads in standard limb leads have been led off. According to the Einthoven principle, the sumtotal voltage of QRS in lead II is equivalent to the sumtotal voltage in leads I and III. According to this method, the centre point of the triangle is drawn by drawing perpendicular line from middle point of each of the sides of the equilateral triangle. From the centre a circle is drawn outside the triangle. Conventionally the *upper half* of the circle is taken as *negative* and the *lower half* of the circle as *positive.* The upper half is divided equally so as to represent $-0°$ to $-180°$ and the lower equally to represent $+0°$ to $+180°$ (FIG. 204). A scale is drawn from the middle point of each side of the triangle. The scale represents the amplitude in mV. Negative and positive representation in the scale is generally made according to the nature of connection in each lead (FIG. 191). For determining the axis, simultaneous E. C. G. at least in two standard limb leads are required. The sumtotal value of the QRS complex of two leads is plotted on the

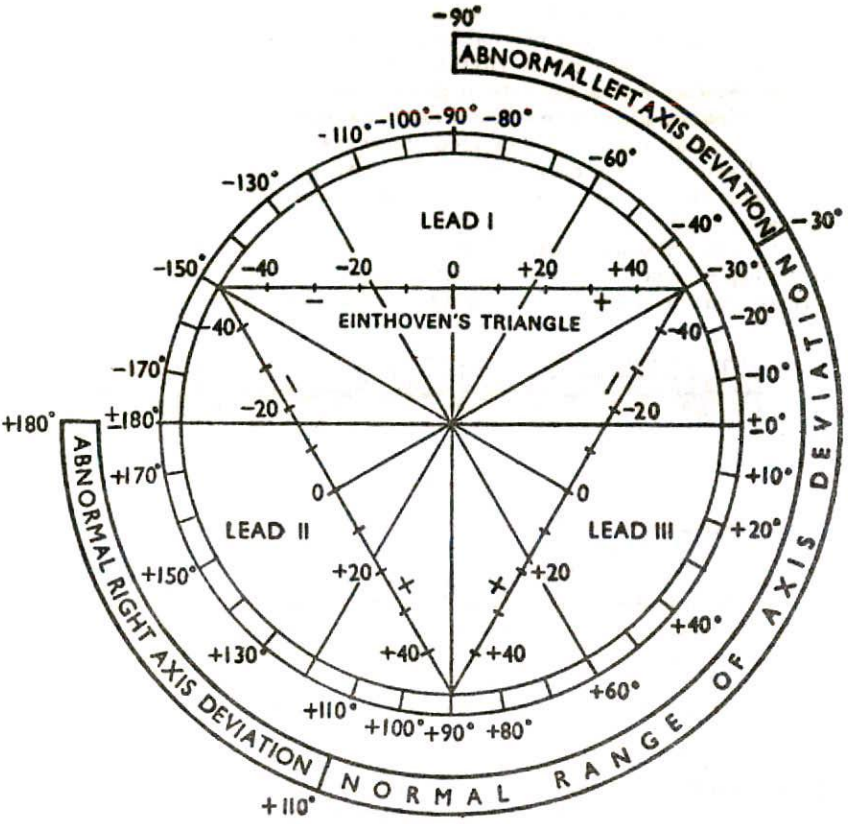


FIG. 204. Diagram showing the normal and abnormal ranges of axis deviation.

sides of the triangle in the positive or negative direction depicting the specific lead and a new point is obtained for each lead (A, B). If the value is positive then it is plotted in the positive direction and if it is negative then it is plotted in the negative direction depicting the specific lead. From each new point a perpendicular is drawn which intersects the other line inside the triangle at point C. The centre O is joined with the point C and is extended outward so as to reach the circle at a point which is the actual axis of the heart (FIG. 205).

The **normal range of axis deviation** lies within −30° to +110°. If the axis is beyond −30° then it is called **abnormal left axis deviation** and if it is beyond +110° then it is called **abnormal right axis deviation** (FIG. 204).

Ventricular conditions that may cause axis deviation. (1) **Change of position of the heart**—Change of position of the heart has got little effect on the axis. The change is only 20° to 30° from the original value. If the heart is shifted to the left then the axis is deviated to the left. During expiration, left axis deviation and during inspiration right axis deviation are often observed. (2) **Hypertrophy of the ventricle**—Hypertrophy of the ventricle alters the axis greatly. It is generally due to increase of muscle mass. Axis is generally deviated towards the hypertrophied side. This is due to increase of muscle mass in the hypertrophied side, the depolarisation wave takes much longer time to cover the hypertrophied side than the normal one. Accordingly the normal

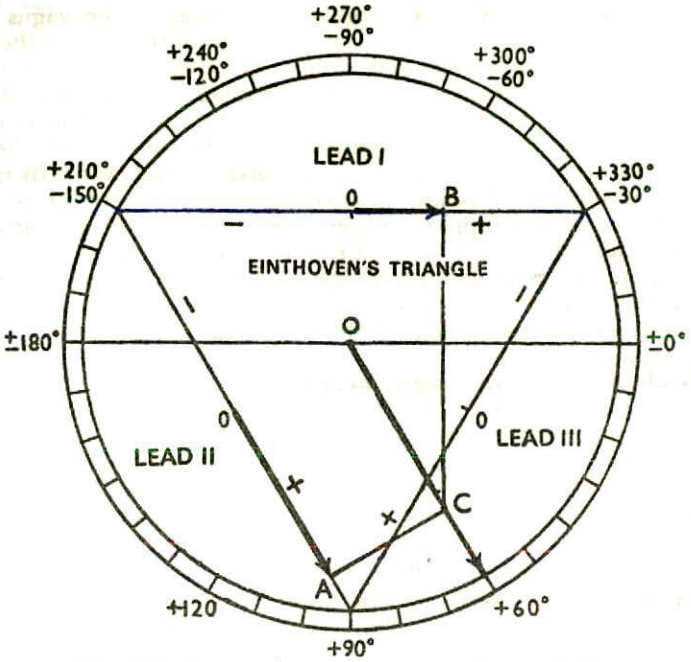


FIG. 205. Calculation of the electrical axis. The net deflection of QRS complex plotted on equilateral triangle.

ventricle becomes depolarised more earlier than the hypertrophied one and strong vector is shifted towards the hypertrophied side. For this reason, the right axis deviation is observed in hypertrophy of the right ventricle and left axis deviation in case of the hypertrophy of the left ventricle. (3) **Bundle-branch block**—In bundle-branch block the axis is deviated towards the side of the block. Because in normal condition the impulse is transmitted to the lateral walls of two ventricles through the two branches almost at the same instant and two ventricles depolarises almost at the same time. If one branch is blocked then the impulse will be transmitted more earlier by the normal one. The affected side will be depolarised more earlier and the affected side will remain still in polarised state. So the axis will be deviated towards the side of injury or a block. In left bundle-branch block the deviation will be towards the left and in the right bundle-branch block the axis will be deviated towards the right. (4) **Muscular destruction**—If any muscular damage occurs then the deviation will be opposite the side of damage of the ventricle. In such case depolarisation wave will fail to transmit through the injured side as this side will remain in refractory state due to development of local injury potential. This injury potential will depolarise this side of the ventricular muscle more earlier than the normal healthy one. So the axis will be deviated opposite the side of injury.

NERVES OF HEART AND THEIR ACTION

The regulation of the heart is effected through the afferent (*centripetal*) and efferent (*centrifugal*) nerves of the heart (FIG. 207). The **afferent nerves** are: (*a*) from the heart through the vagus nerve and from the aortic arch, the aortic nerve, (*b*) from the heart through the inferior cervical and first four thoracic ganglia and first four thoracic nerve roots into the spinal cord, (*c*) from the carotid sinus through the sinus nerve, a branch of glossopharyngeal nerve. The **efferent nerves** are: (I) vagus and (II) sympathetic (FIG. 206).

I. Vagus nerves. The preganglionic fibres of the vagus nerves arise from the dorsal nuclei of the vagus situated in the floor of the fourth ventricle in the medulla (FIG. 206). After their origin they descend downwards. The cardiac fibres separate from the main nerve trunk in the neck and proceed towards the heart and form deep and superficial cardiac plexuses with the fibres of the sympathetic. The fibres reach the atrial muscle and make synaptic connections with **intraganglionic cells** situated near the sinoatrial and atrioventricular nodes. From here the postganglionic fibres arise and supply the specialised tissues of the sino-atrial and atrioventricular nodes and also extend between the muscle fibres. The postganglionic fibres do not extend beyond the upper part of the bundle of His and the base of the ventricles. Ventricular myocardium of the apex is said not to receive any vagal fibres. The vagus nerves also supply fibres to the coronary vessels.

Tonic action of the vagus nerves. The vagus exerts a tonic inhibitory control over all parts of heart. Acetylcholine is released by the postganglionic fibres on stimulation. *Atropine* prevents action of acetylcholine on the cardiac muscle and the heart rate is increased even up to 150 per minute in human beings. This proves that a constant inhibitory influence is exerted by the vagus on heart. The *vagal tone* is of reflex in origin being, produced by the sino-aortic nerves. Section of these nerves reduces the vagal tone and increases the heart rate.

Stimulation of the vagus nerves causes the following effects:

1. *The heart rate is slowed down*—even it may stop. This is caused by reducing the rhythmicity of the S. A. node. This is known as the negative **chronotropic** effect of the vagus.
2. *The conductivity of the bundle is reduced*—thus producing various degrees of heart block. This effect is known as negative **dromotropic** effect. This may be an additional cause for slowing.
3. *The force of contraction is diminished*—In the frog the vagus directly depresses the ventricular muscle. This is known as the negative **inotropic** effect of the vagus.
4. *The duration of systole is diminished*, but the duration of diastole is increased.
5. *The length of refractory period* (which depends upon the systolic length) *is diminished.*
6. *Excitability of the heart is also reduced* and this condition is known as negative **bathmotropic** effect.

On the whole, the vagus acts as the inhibitor of heart.

Vagus escape. *In animals* (*frogs*, etc.), stimulation of the vagus by a tetanising current causes slowing or stoppage of heart rate. But after a little while, heart starts beating again even if the stimulation is continued. This phenomenon is called *vagus escape*—meaning by that the heart escapes from inhibitory influence of the vagus. Four explanations have been advanced:

(*a*) *Bainbridge reflex* (page 290). Due to slowing or stoppage of the heart rate, engorgement of the great veins and right atrium takes place. This may mobilise this reflex, hence the heart starts beating. This reflex takes place only in normal animal but not in pithed animal or in animals whose brain has been damaged. However this effect has been contradicted by many.

(*b*) *Sino-aortic reflex* (page 289). The fall of blood pressure in the aorta reflexly increases the heart rate through sino-aortic mechanism in animal with intact central nervous system. The chemoreceptors which are present in carotid bodies and aortic bodies are stimulated and reflexly stimulate the heart by depressing the vagi but exciting the sympathetic.

(*c*) *Idioventricular rhythm.* Due to complete heart block, ventricle originates its own rhythm. In the mammalian heart, the vagal fibres are not extended beyond the upper part of the bundle. So the vagus nerves exert their effect upon the heart through their action on atrial muscle and the slowing or stoppage of heart rate following vagal stimulation is due to the depression of conduction in the atrioventricular connections. So the ventricular stoppage is due to an indirect effect of atrial slowing. If this effect

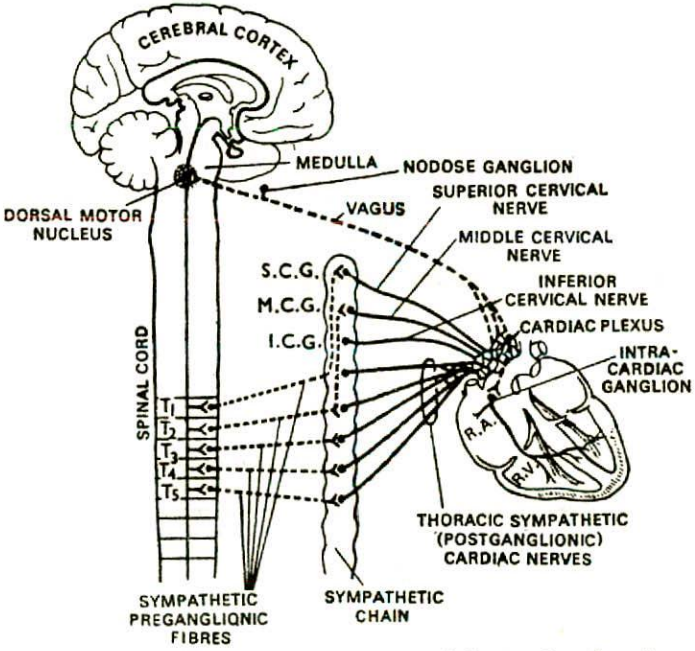


FIG. 206. Diagrammatic representation of autonomic innervation of cardiac nerves.

is prolonged then atrioventricular dissociation may take place and ventricles escape from the sino-atrial control and beat at its own rhythm (*idioventricular rhythm*). Sometimes shifting of pacemaker is taken place if the normal pacemaker function is totally depressed and subsequently impulse formation is totally suppressed due to vagal stimulation. In such case pacemaker regions, next to the S. A. node or A. V. node, become developed and maintained the heart beat.

(*d*) *Differential effect of the vagus and sympathetic. In frogs* or *other animals*, sympathetic fibres pass through the vagus (vagosympathetic). Stimulation of the trunk produces vagal effect first, but if the stimulation is continued further, the vagal effect is possibly ineffective and when the sympathetic

becomes effective. This ineffectiveness of the vagus is either due to exhaustion of acetylcholine for continued stimulation or the heart muscle becomes refractory to the effect of acetylcholine.

II. Sympathetic nerves (FIG. 206). **Connector cells** of the sympathetic nerves are situated in the lateral horn cells of the upper thoracic segments of the spinal cord (T. 1-5 or 6). **Excitor cells** are situated in the superior, middle and inferior cervical ganglia from where the postganglionic or excitor fibres take origin and pass directly to the heart. Cardiac branches from the sympathetic chain also runs from the upper thoracic ganglia, to the heart (FIG. 206). The fibres supply the specialised tissues of the sinoatrial and atrioventricular nodes, atrial and ventricular muscles. Nonidez has described that middle cardiac nerves supply efferent fibres to the heart; and superior cardiac nerves supply nerves to large arteries at the base of the heart, while the inferior cardiac nerves supply only afferent fibres to the heart. The sympathetic fibres carry vasodilator fibres to the coronary vessels. The sympathetic exerts a slight tonic accelerating action on the human heart. *Noradrenaline* is released by the postganglionic fibres of the sympathetic on stimulation. Slowing of the heart rate occurs after bilateral excision of the first to sixth thoracic ganglia. Action potential, recorded in the sympathetic nerves of the heart of cat, has demonstrated the existence of accelerator tone. [Of the two nerves—vagus and sympathetic—the former exerts a much stronger influence on the heart than the latter.]

Stimulation of the sympathetic nerves causes the following:

1. *Increases the frequency of heart rate* (*Accelerator*). It is due to its effect on sino-atrial node. This is known as (positive) *chronotropic* effect of the sympathetic.
2. *Increases the force of contraction* (*Augmentor*). It is due to its effect on atrial and ventricular muscles. This is known as (positive) *inotropic* effect of the sympathetic.
3. *Increases the excitability* (positive bathmotropic) and *irritability of heart* and thereby may cause extra-systoles (*ectopic beats*).
4. *Increases the conductivity* (positive dromotropic) *of the myocardium and the bundle of His.*

On the whole the sympathetic is taken as the accelerator and augmentor of heart.

Cardiac centres (FIG. 207). Though the existence of separate centres (areas) for each vagus and sympathetic has been described by many, yet their anatomical positions particularly of the latter one has been a point of much dispute and it requires further study. The **dorsal motor nucleus of vagus in the medulla** is the cardio-inhibitory centre and it transmits continuous tonic inhibitory vagal impulses to the heart. This centre has got direct connection with the afferent nerves coming from the baroreceptors or chemoreceptors. *Reflex bradycardia* during the rise of systemic blood pressure is due to stimulation of the cardio-inhibitory centre. On the other hand, *tachycardia* is observed during the fall of blood pressure—which is due to inhibition or depression of the cardio-inhibitory centre along with the withdrawal of vagal tone from the heart. Under such state sympathetic cardiac centres get the upper hand.

The **sympathetic cardiac centres** or **cardio-accelerator centres** are situated in the lateral horn cells of the upper thoracic segments of the spinal cord (T. 1–5 or 6). The preganglionic fibres enter the sympathetic

ganglia to connect with the cells of thoracic ganglia and inferior, middle and superior cervical ganglia. In animals and even in human beings the

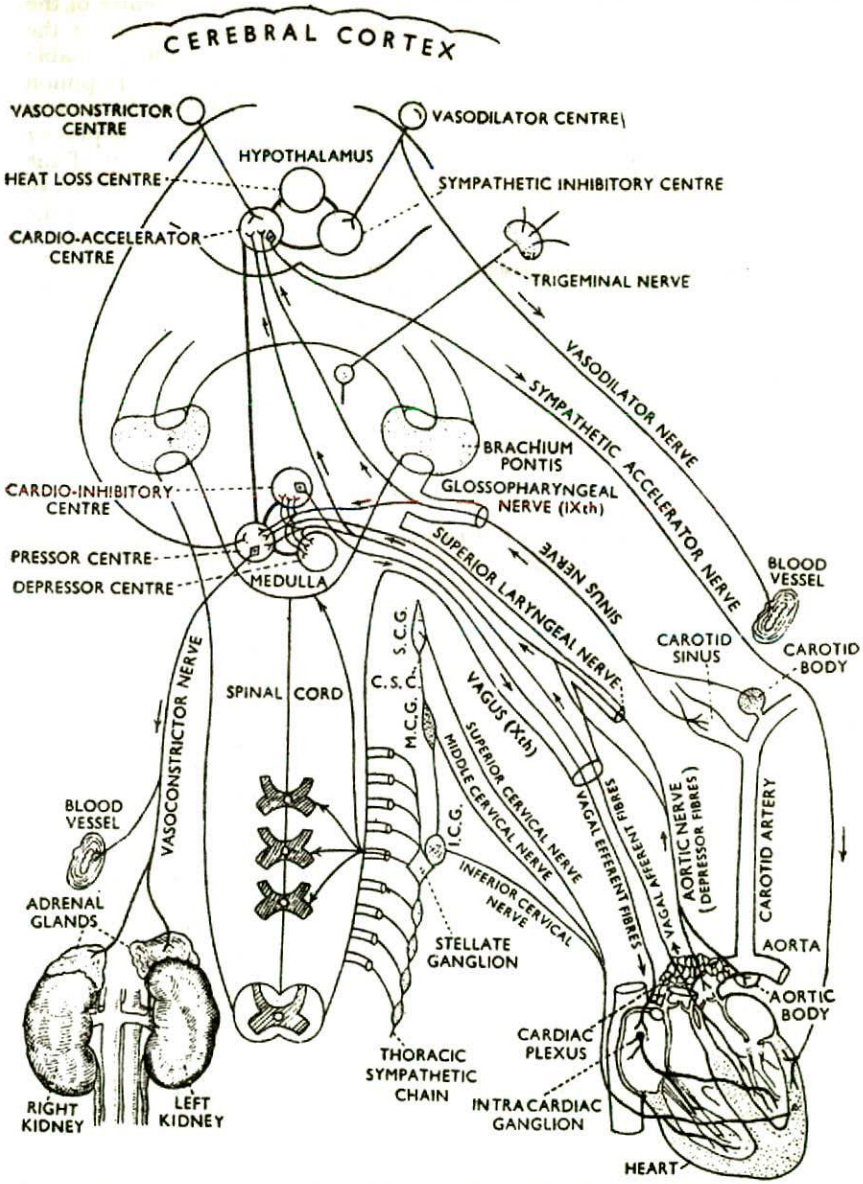


FIG. 207. Schematic representation of the connections of different cardiac and vasomotor centres as located in the different areas of the central nervous system.
C. S. G.—Cervical sympathetic chain, S. C. G.—Superior cervical ganglion,
M. C. G.—Middle cervical ganglion, I. C. G.—Inferior cervical ganglion.

first thoracic ganglion and inferior cervical ganglion are fused to form the stellate ganglion from which postganglionic fibres (accelerator fibres) run directly to the heart. The function of the cardio-accelerator centre of the spinal cord is modified by the higher centres. The exact location of the higher cardio-accelerator centre is not yet fully known and the probable existence of the same in the medulla cannot be denied. Some are of opinion that there is no separate cardio-accelerator centre in the medulla and in addition to the cardio-inhibitory centre, there are pressor and depressor centres (areas) in the medulla. With the increase in the activity of the pressor centre along with the rise of blood pressure, heart rate and stroke volume are also increased. This pressor centre possibly functions with the superior control of the same in the hypothalamus and cerebral cortex.

The **posterior hypothalamic nuclei** have been indicated to be the cardio-accelerator centres by Beattie, Brow and Long. Sympathetic activities on the heart are increased following stimulation of these centres. These centres have got connections with *motor* and *premotor areas* (centres) of the cerebral cortex. If these cortical areas are stimulated, the increase of heart rate is encountered. The middle groups of nuclei of the hypothalamus are related with the parasympathetic—whose stimulation causes the slowing of heart rate.

HEART RATE

Normal values. In adult males—72 *per minute*, the range is from 70–80 per minute. **In adult females**—the rate is slightly higher than in males. Cause may be due to (*a*) lower blood pressure, (*b*) more sympathetic tone. Apart from sex, heart rate depends on the following factors:

1. **Age.** Roughly the heart rate is inversely proportional to age. For instance, in the foetus—140–150 per minute; new-born—130–140 per minute; 1st year—115–130 per minute; 2nd year—100–115 per minute; 3rd year—95–100 per minute; 7th–14th year—80–90 per minute; over 15th year—70–80 per minute; but in old age it is slightly higher—75–80 per minute. At younger ages the cause may lie in the higher basal metabolic rate (B.M.R.). In old age the rate is slightly higher—probably due to compensatory circulatory adjustment against gradual circulatory failure with the aging process.

2. **Metabolic rate.** Heart rate is directly proportional to the metabolic rate. They always run parallel. Anything that increases the basal metabolic rate, viz., exercise, excitement, etc., will also increase the heart rate. Similarly, factors which reduce basal metabolic rate diminish the heart rate.

3. **Respiration.** Heart and respiration run parallel. Stimulation or depression of one will always cause parallel changes in the other under normal conditions.

4. **Size of the animals.** It is seen that under normal conditions heart rate has an inverse relation with the size of the animal. Smaller the size, greater the heart rate. For instance, heart rate of canary is about 1,000 per minute, that of an elephant, only 25 per minute.

Regulation of heart rate. Heart rate can be adjusted according to the metabolic needs. In exercise the rate increases; during sleep it falls. The purpose of this regulation is to maintain an optimum blood pressure and an optimum rate of blood supply to the tissues.

Mechanism of regulation. The mechanism involves two factors: (1) The **local mechanism**—This includes the S. A. node and the junctional tissues. Any factor, which by its local action on the S. A. node, can alter its rhythmicity will also alter the heart rate. (2) The **nervous mechanism**—It includes—(*a*) *Cardio-inhibitory centre*—connected with the vagus. (*b*) *Cardio-accelerator centre*—connected with the sympathetic. Stimulation of the vagus depresses and that of the sympathetic increases the heart rate. Of the two nerves, the vagus exerts a stronger action. Atropine prevents action of acetylcholine to the cardiac muscle and increases the heart rate even up to 150 per minute. This proves that the *vagus exerts a tonic inhibitory control over heart rate.* This vagal tone is reflexly produced through the sino-aortic nerves. The sympathetic also exerts a tonic accelerating effect but to a much lesser extent.

The variations of heart rate, under normal physiological conditions, are mainly brought about by alteration of vagal tone. It is only in extreme cases that sympathetic stimulation comes into play.

Thus alterations of heart rate may be brought about in two ways: (*a*) **by affecting the local mechanism,** i.e., the S. A. node and the junctional tissues or (*b*) **by acting through the nervous mechanism.** The cardiac centres, again, may be influenced in two ways—*directly* or *reflexly.* There is evidence to show that the two cardiac centres are in reciprocal relation. Stimulation of one will depress the other and *vice versa.*

The following **factors affect heart rate** through one or both the above mechanisms:

1. **Impulses from the higher centres.** Excitement generally quickens the heart rate but sudden shock may slow or even stop the heart rate. These changes are due to the influence of frontal lobes (area 13) of the cerebral cortex and the hypothalamus.

2. **Respiration.** During inspiration heart rate increases; during expiration it falls. This phenomenon is known as **sinus arrhythmia.** It is very often found in healthy children. In adults, it becomes prominent after deep voluntary respiration. It is abolished by atropine, showing that the vagus is involved. Three explanations are advanced: (*a*) Afferent impulses arise from the lungs during inspiration and reflexly inhibit the vagal tone. (*b*) During inspiration venous return increases, causing congestion of the right atrium and great veins, and thus mobilising Bainbridge reflex (page 290). (*c*) Central irradiation—During inspiration, motor impulses irradiate from the respiratory centre to the neighbouring cardiac centre and inhibit the vagal tone. Experimental evidence shows that this is likely to be the chief cause.

3. **Reflexes.** Factors influencing the cardiac centre have been presented in FIG. 208. Heart rate can be altered by various reflexes. For instance, (*a*) *cardio-inhibitory reflexes,* (*b*) *cardio-accelerator reflexes,* (*c*) *reflexes from other parts of the body.*

(*a*) **Cardio-inhibitory reflexes (Sino-aortic or Marey's reflex).** There are stretch receptors in the carotid sinus and aortic arch. When blood pressure rises, these nerve endings become stimulated due to stretching, sensory impulses pass up through the sino-aortic nerves and increase the vagal tone, so that heart rate falls. When blood pressure falls, no inhibitory impulse passes up and heart rate rises. *Thus heart rate and blood pressure have an inverse relation.* This is known as **Marey's law.**

This sino-aortic effect is best seen when the initial blood pressure remains near about the normal range. A fall of pressure from 125 to 100 mm of Hg or a rise from 125 to 150 mm of Hg causes more quickening or slowing respectively, than changes of same magnitude that alter the heart rate in subjects whose initial blood pressures are already higher or lower. Since the sino-aortic nerves help to maintain blood pressure variations through a limited range by regulating the heart rate, these nerves are called the **buffer nerves of heart.** [The inverse relation between heart rate and blood pressure does not hold good in all conditions. For instance, exercise, emotion, anoxia, etc., increase both heart rate and blood pressure.]

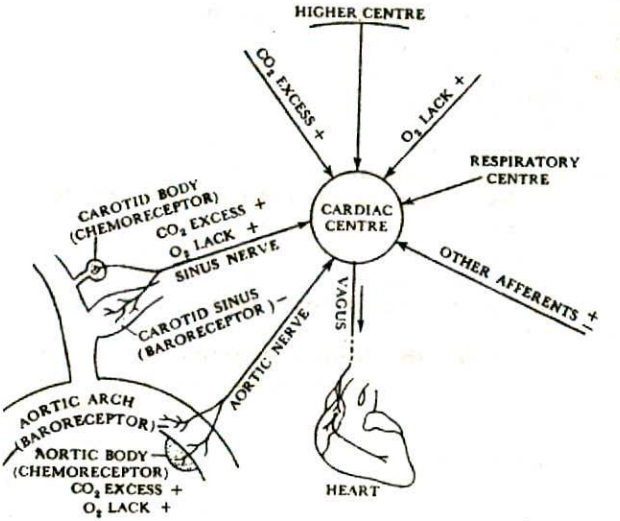


FIG. 208. Factors influencing the cardiac centre.

(*b*) **Cardio-accelerator reflexes.** Venous engorgement of the right atrium and the great veins reflexly increases the heart rate. The afferent fibres, arising from the roots of the great veins and right atria, pass along the trunk of the vagus to the cardiac centre. Engorgement of these parts stimulates the nerve endings, reflexly inhibit the vagal tone and also stimulates the sympathetic to some extent. Thus heart rate rises. This reflex is called **Bainbridge reflex** (more appropriately **venous reflex**). This happens in muscular exercise and in deep inspiration when venous return increases. This is also a cause of increased heart rate during congestive cardiac failure.

(*c*) **Reflexes from other parts of the body.** Sensory stimuli from other parts of the body may alter the heart rate in either direction. Moderately painful stimuli generally quicken the heart rate. Stimulation of the central end of the fifth nerve or of the splanchnic nerve slows the heart rate. A sudden blow on the abdomen may stop the heart rate.

4. **Anoxia.** It increases the heart rate which is directly proportional to the degree of anoxia. The effect is due partly to its action on the cardiac centre and partly to reflex stimulation through the chemoreceptors in the

carotid and aortic bodies. This is one cause of rapid pulse in heart failure, anaemia, haemorrhage, high altitude, CO poisoning, etc.

5. **CO_2 excess.** In moderate amounts it increases the heart rate, partly by its direct action and partly reflex. But in larger amounts it produces heart block and reduces heart rate. [It should be noted that *circulation* is more sensitive to O_2 lack but *respiration* is more sensitive to CO_2 excess.]

6. **Body temperature.** Rise of body temperature (muscular exercise, fever, hyperthyroidism, etc.) increases the heart rate (*a*) by acting on the S. A. node, and (*b*) by stimulating the cardio-accelerator centre.

7. **Increased intracranial pressure.** It slows the heart rate by directly stimulating the vagus.

8. **Adrenaline.** Since it acts like the sympathetic, it should accelerate the heart rate, but in intact animals the rate is often reflexly reduced. Because, by causing vasoconstriction, adrenaline raises blood pressure and thus mobilises the sino-aortic reflex, so that heart rate may be reduced. But the force of contraction invariably rises.

9. **Thyroxine.** It quickens the heart rate (*a*) by directly stimulating the metabolic rate of the sino-atrial node, (*b*) by increasing the basal metabolic rate of the body, and (*c*) by a probable stimulating effect on the sympathetic.

10. **Muscular exercise.** It increases the heart rate. Because most of the factors, concerned with acceleration, are operating during exercise. For instance, increased venous return initially mobilises Bainbridge reflex. Increased respiration, excitement, anoxia, CO_2 excess, adrenaline secretion, etc., all come in and increase the heart rate.

CARDIAC OUTPUT

At each beat, certain amount of blood is pumped out by each ventricle into the circulation. This is called *cardiac output*. Two terms are used: (1) **stroke volume** or **systolic discharge** (*output*), and (2) **minute volume** (*minute output*). *Stroke volume means the output per ventricle per beat. Minute volume means the output per ventricle per minute.* Hence, minute volume = stroke volume × heart rate.

As the volume of blood put out by both sides of the heart is same, cardiac output is to be multiplied by 2 so as to calculate the quantity of blood pumped by the heart as a whole.

Normal values. In adults the average stroke volume is **70** ml and the minute volume about **5–6** litres. In other words, the amount of blood expelled per ventricle per minute, is approximately the same as the total blood volume of the body.

The output is directly proportional to the *metabolic rate*, and as such, to the **surface area** and **body weight.** The cardiac output per minute per square metre of body surface is known as **cardiac index.** The average value is **3·3** litres. The surface area of an average-sized adult is about 1·7 m^2. Accordingly, the average cardiac index is about 3·3 litres/min/m^2 (5·6/1·7). The stroke volume per square metre of body surface is known as **stroke volume index.** The average value is 47 ml. Anything that increases or diminishes basal metabolic rate, body weight or surface area, also alters the minute volume proportionally.

Distribution of cardiac output. Since venous return per minute should be the same as the minute output, it follows that blood flow through the tissue per minute must also be the same. In other words, 5 litres of blood passes out per ventricle per minute, 5 litres of blood flows through the tissues per minute and the same 5 litres come back to heart per minute. It is really astonishing, how accurately these constant relations—of time and quantity—are maintained.

Although full data are not known, yet the **minute volume of heart** is mainly distributed as follows:

(1) Kidneys—1,300 ml per minute. (2) Brain—700–800 ml per minute. (3) Coronary—200 ml per minute. (4) Muscle—600–900 ml per minute. (5) Liver—about 1,500 ml per minute. Total quantity of blood distributed in these organs does not exceed 4,500 ml per minute. So the remaining amount is distributed to the skin, bones and gastro-intestinal tract.

Translocation of blood. For a short period of time, left and right ventricles may pump different amount of blood. When the cardiac output of left ventricle is greater than that of the right, there is *translocation of blood* from pulmonary circulation to systemic circulation. If the cardiac output of right ventricle is greater than that of the left, there may be *translocation of blood* to the pulmonary vessels.

Cardiac reserve. It is the capacity of heart to generate sufficient energy for expelling a large quantity of blood and for raising blood pressure above the basal level during emergency. Generally, the normal heart expels about 5 to 6 litres of blood per minute per ventricle and during exercise this amount may be about 30 to 40 litres per minute. According to *Starling's law*, it is nothing but *physiological capacity of the heart.*

Control of cardiac output. Cardiac output depends upon the following four factors: (1) **venous return,** (2) **force of heart beat,** (3) **frequency of heart beat,** (4) **peripheral resistance.** Their roles are summarised below:

1. **Venous return.** Anything that increases or diminishes the venous return, will alter the cardiac output accordingly. Venous return depends upon the following: (*a*) *Muscular exercise*—When muscles contract, they squeeze the capillaries and venules and help in venous return. This is aided by the valves of veins, which prevent the passage of blood back towards the capillary bed. (*b*) *Respiration*—During inspiration intrathoracic pressure falls and intra-abdominal pressure rises. Hence, with each inspiration venous blood is sucked up by the thorax and is pumped out by the abdomen. (*c*) *Pressure difference between capillaries and venules*—Normally, there is a slight positive pressure (32–12 mm of Hg) in the capillary area (*capillary tone*), while in the great veins it may be even negative. Vascular dilatation without fall of general blood pressure will increase the capillary pressure and thereby raise the venous return (viz., muscular exercise). But if it causes a general fall of blood pressure—as in shock,—venous return will fall. (*d*) The *vasomotor system* adjusts the lumen of the arterioles and venules and thereby alters the venous return.

2. **Force of heart beat.** The strength of contraction depends mainly on three factors: (*a*) *The initial length* of the cardiac muscle—Within physiological limits, *greater the initial length, stronger will be the force of contraction* **(Starling's law** (Fig. 209)—which is an inherent, self-regulating mechanism that permits heart to adjust to changing end-diastolic volumes). It is

obvious that the initial length is proportional to the degree of filling, which again, depends on the venous return. (*b*) *The length of diastolic pause*—Filling, rest and recovery take place during diastole. Hence, with a shorter diastolic period which is inadequate for these, the force of contraction will diminish unless the rate of venous return is raised. (*c*) *Nutrition and oxygen supply*—An adequate supply of nutrition and oxygen is essential for efficient cardiac activity.

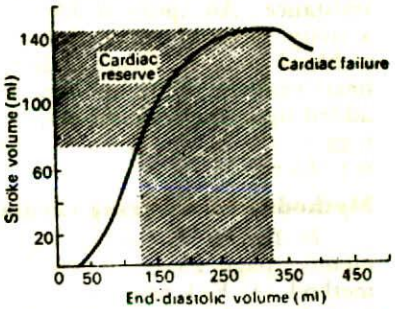


FIG. 209. Graphical representation of Starling's law of heart. Showing when the end-diastolic volume increases, ventricles contract more vigorously and thereby stroke volume increases. But when normal functioning (*shaded portion*) is beyond the range, the stroke volume decreases and the relationship is reversed (diagrammatic).

In addition to this, an optimum H-ion concentration, a proper balance of inorganic ions and an appropriate temperature and pressure, are also required for strong heart beat.

3. **Frequency of heart beat.** Heart rate affects both stroke volume and minute volume by altering the length of diastole and thereby the degree of filling and force of contraction. It should be noted that blood pressure depends upon the minute volume and not on the stroke volume. The following consideration will clarify. Venous return remaining constant, the rise of heart rate will reduce the diastolic pause and therefore the stroke volume. But the product—stroke volume × heart rate—may not fall, even it may rise above the resting value. Thus minute volume and therefore blood pressure (B. P.) may rise even if the stroke volume falls. This happens with a moderate rise of the heart rate. But if the heart rate be too high, the stroke volume becomes so low that the minute output falls far below the normal (FIG. 210). Blood pressure drops and the subject may be unconscious. This happens in *paroxysmal tachycardia* when the frequency suddenly becomes 150–200 per minute. [Muscular exercise is an exception. Here, both the frequency of heart beat and the rate of venous return increase. Cardiac filling becomes more than normal even during the short diastolic period. Hence, both stroke volume and minute output increase.] On the other hand, when the heart rate becomes very slow (as in *Heart Block*)—although the stroke volume is much bigger than normal, yet, the minute volume may fall, because the product may be less than normal. But with a moderate slowing the minute volume may not fall at all. In some instances it may rise (recovery from heart failure). Thus alteration of heart rate on either side will generally raise the minute volume up to a certain extent. Beyond that, the minute output will fall.

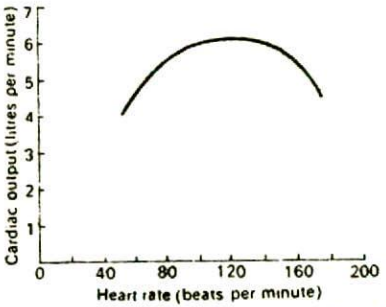


FIG. 210. Graphical representation of the relationship of cardiac output and heart rate assuming constant venous pressure and ventricular residue (diagrammatic).

4. **Relation with peripheral resistance.** Heart maintains a constant cardiac output and blood flow even against increased peripheral resistance. An optimum blood pressure is essential for adequate cardiac activity. General vasoconstriction of the arterioles will cause an increase in blood pressure. Heart at first fails to expel all its blood but in the next heart beat the filling becomes more, because the normal venous return is added upon the residual blood. Consequently, the initial length becomes bigger, the heart contracts with greater force and the normal output is restored.

Methods of measuring cardiac output

In Animals. The output can be measured with the help of (1) Cardiometers (page 255), (2) Heart-Lung preparation (Fig. 211), (3) Dye method, (4) Fick principle using O_2 or CO_2, (5) Physical method (Ballistocardiography).

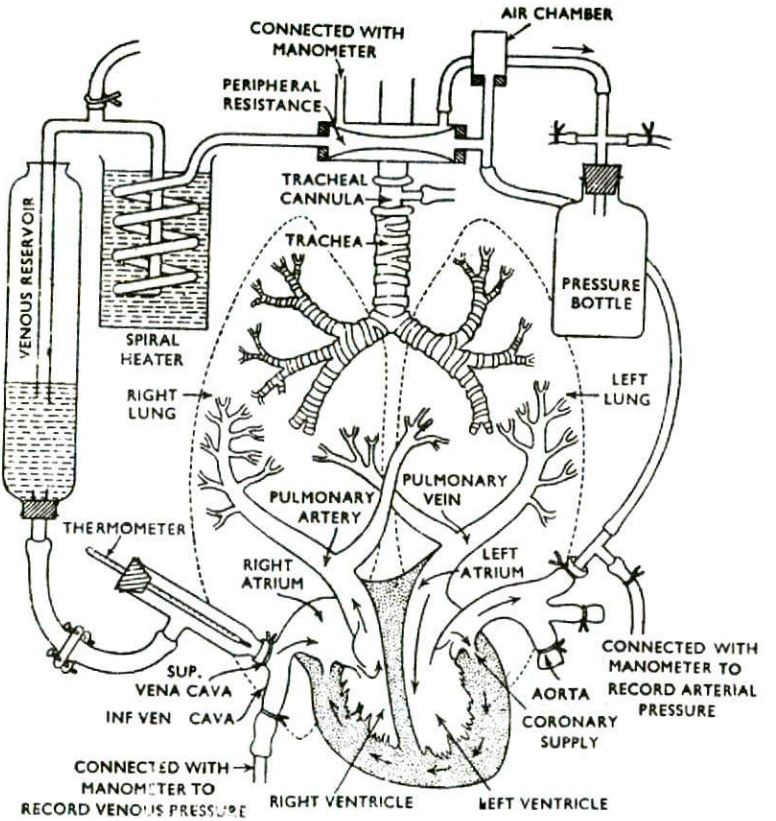


Fig. 211. Heart-Lung preparation.

Knowlton-Starling heart-lung preparation. This is a very useful method for studying cardiac output under different experimental

conditions, viz., variation of pressure, temperature, H-ion concentration, inorganic ions, etc. The procedure is as follows:

Thorax of an animal is opened, heart is exposed under anaesthesia. Artificial respiration is maintained. Both vagi are severed to prevent the variation of heart rate. The branches arising from the arch of the aorta, viz., the brachiocephalic and left subclavian arteries (in the dog) are ligated. A three-way cannula is inserted in the brachiocephalic artery. The cannula is connected with a mercury manometer to record the mean arterial pressure and through another three-way tube with a bottle containing air. The air of the bottle due to its compressing capacity serves the purpose of elasticity of the arterial wall. The other limb of the three-way tube is connected with a glass tube lined with a thin-walled rubber tube. The pressure inside this tube can be varied at will. This is an artificial resistance. The glass tube has got two side tubes—one of which is connected with a manometer for recording the pressure inside it and the other is connected with the pressure bottle from where air may be pumped inside it. This rubber-lined glass tube is connected with a spiral heater which opens in the venous reservoir filled with heparinised blood. The reservoir is connected through a rubber tube with a three-way cannula one limb of which inserted into the superior vena cava. A thermometer is kept in the cannula to record the temperature. The inferior vena cava is connected with a water manometer to record the pressure of the right atrium. There is a screw clamp on the rubber tube connecting the venous reservoir with the three-way cannula which adjusts the rate of flow from the venous reservoir into the right atrium. From the venous reservoir blood enters the right atrium, right ventricle and then through the lungs, left atrium, into the left ventricle. From the left ventricle through the brachiocephalic artery, resistance tube, spiral heater, blood comes again into the venous reservoir and the cycle is repeated. The output of the left ventricle can be determined by opening the clamp on the tube in between the spiral heater and venous reservoir and collecting blood for a specified period in a measuring cylinder. The blood flow through the coronary arteries must be added to give a correct figure of the output of the left ventricle. This experiment does not give any indication regarding the output in the human beings or in the intact animal.

Stewart and Hamilton's dye dilution method. There are certain difficulties invariably in introducing cardiac catheterisation. So the dye method is often the method of choice. A known quantity of Evans blue (non-diffusible dye, known as T–1824) is injected into the basilic vein. The dye will circulate through the heart, lungs and appear in the carotid artery. The concentration of the dye when it first appears in the artery is determined with the help of colorimeter from the samples of arterial blood taken every few seconds interval. The concentration of each sample of blood is determined by Photocolorimeter and plotted on a semilogarithmic paper. The dye concentration rapidly rises to a peak, then falls and rises again due to recirculation of dye. The mean concentration of the dye is calculated from the curves. The volume flow in litres per second is determined with the help of the following formula: $F=D/ct$, where F=volume flow in litres per second, D is the quantity of dye (Evans blue) injected, c is the mean concentration of the dye and t is the duration in seconds of the first passage of dye through the artery.

Fick principle. It was shown by Fick that cardiac output can be calculated by noting certain data about O_2 or CO_2 exchange. When applied to oxygen it will be as follows:

O_2% of mixed venous blood is determined, say 15 ml.
O_2% of arterial blood is determined, ,, 19 ml.
Arteriovenous O_2 difference per 100 ml of blood is therefore— 4 ml.
Total O_2 consumption per minute (Douglas bag), ,, 200 ml.

Hence, each 100 ml of venous blood, while passing through lungs, takes away 4 ml of O_2. Therefore, 200 ml of O_2 will be carried away by $\frac{100}{4} \times 200$ ml $= 5$ litres of blood. Obviously, this is the minute output of right ventricle, which is same as that of left ventricle. Similar figures will be obtained by applying the principle to CO_2. So the cardiac output can be determined with the help of the following formula:

$$\text{Cardiac output (ml/min)} = \frac{\text{consumption of } O_2 \text{ (ml per minute)}}{\text{difference of } O_2 \text{ content in arterial and venous blood (ml/min)}}$$

In man there is difficulty in applying direct *Fick method* during heavy exercise. So the other method, viz., Dye method is preferred.

1. **Fick principle using O_2.** (*a*) Total O_2 consumption per minute is determined with Douglas bag. (*b*) O_2 content of arterial blood is calculated from Hb%, assuming 95% saturation. (*c*) A sample of mixed venous blood is collected from the right atrium by introducing a fine rubber catheter into the cubital vein and pushing it gradually into the right atrium (Cournand's method) and its O_2% is determined.

From these data minute volume can be calculated as shown above.

2. **Fick principle using CO_2.** *This method can be readily adopted at the bedside.* The steps are as follows: (*a*) CO_2 output per minute is determined with Douglas bag. (*b*) Alveolar air is collected and its CO_2 tension —which is identical with that of arterial blood—is determined. (*c*) Alveolar air is again collected after holding the breath for 5 seconds. The CO_2 tension of this air is same as that of venous blood.

CO_2% of arterial and venous blood is then determined from the CO_2 dissociation curves. From these data minute volume can be calculated.

Physical method. Another method of determining cardiac output in human beings is the Ballistocardiography which was originally devised by Henderson and later on modified, by Starr and his associates. The method is based on the principle of Newton's third law of motion—"every reaction has an equal and opposite reaction." **Ballistocardiogram** is a record of the recoil of the body caused by the movement of heart and blood within it in opposite direction. It can be recorded by allowing subject to lie on a suitably suspended table. The more convenient method is the recording of the movement of a steel rod kept on the stretched legs while lying supine on a fixed table. The movement of the rod can be recorded by suitable sensitive electronic instrument. The normal Ballistocardiogram shows following distinct waves : H I J K L M N, of which H I J are the systolic waves. H wave is the small positive wave and occurs due to headward movement of the body in response to footward movement of the heart and blood within it during isometric phase of systole. I wave is the negative wave and is inscribed due to footward

movement of the body in response to ejection of blood into the aorta during ejection phase. J wave is a large positive wave occurring during headward movement of the body due to rapid flow of blood through descending aorta (Fig. 212). The stroke volume can be calculated by applying the formula:

Stroke volume =

$$=7\sqrt{\tfrac{1}{3}(I+J)AC}$$

where I and J are areas of the waves, A is the diameter of the aorta and C is the duration of cardiac cycle. Stroke volume multiplied by the heart rate gives the minute output. This method is not accurate.

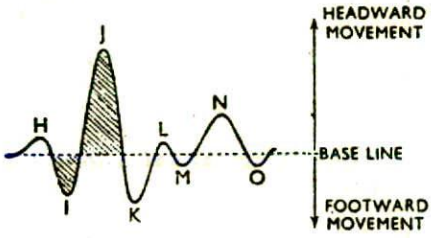


Fig. 212. Ballistocardiogram.

Factors influencing cardiac output

1. **Muscular exercise.** In heavy exercise the output may be 30–40 litres, i.e., 6–10 times the normal minute volume (stroke volume 170–200 ml; heart rate 150–180 per minute).
2. **Posture.** The minute volume is greater in the recumbent posture than in standing, because gravity retards venous return in the latter.
3. **Fever, hyperthyroidism, excitement** (10–25%), adrenaline, ingestion and digestion of food (10–20%), anoxia, CO_2 excess, intravenous (I.V.) saline, pregnancy (45–85% at full term), etc.,—increase cardiac output.
4. **Hypothyroidism, haemorrhage, shock, heart-failure,** etc., reduce cardiac output.
5. **Sleep.** May reduce slightly but usually not much.

BLOOD PRESSURE

Blood pressure is the lateral pressure exerted by blood on the vessel walls while flowing through it.* Four terms are in common use: (*a*) **Systolic pressure** (S. P.)—the maximum pressure during systole. (*b*) **Diastolic pressure** (D. P.)—the minimum pressure during diastole. (*c*) **Pulse pressure** (P. P.)—the difference between systolic and accepted diastolic pressure. (*d*) **Mean pressure** (M. P.)—It is roughly the arithmetic mean of the diastolic and the systolic pressures. But a close approximation to the mean pressure may be obtained by adding the diastolic pressure with *one-third* of the pulse pressure**. In true sense it is the level of the line halving area between the pulse wave contour and the diastolic pressure level.

In adults the relation between the three pressures is as follows: S.P./D.P./P.P.=3/2/1, viz., if systolic pressure be 120, diastolic pressure should be 80 and pulse pressure 40 mm of Hg.

Basal blood pressure. As blood pressure differs from an individual to another one and under different circumstances it varies in the same individual, it is permissible to use the term **normal range of blood pressure.** When an individual is with the least possible amount of strain or stress, **basal blood pressure** is generally considered. It may also be

* *Lateral pressure* is that pressure when force is exerted at right angles to the direction of flow at any point within a tube filled with a circulating fluid. *Resistance* is opposition to force.

** Sometimes, the M.P. is stated as the D.P. *plus* one-half of the P.P.

regarded as the lowest pressure necessary in maintaining blood flow sufficient for needs of the body. When a subject is in reclining state, 5–6 hours after last meal, in a comfortably warm room, after resting for at least 30–40 minutes and with a mind at possible ease, the basal pressure is obtained. In adult males, the average systolic pressure is 125–130 mm of Hg ± 15 (viz., from 110–145 mm of Hg) and average diastolic pressure, 70–90 mm of Hg. Although it is constant in a given individual, yet basal pressure varies in different ones with the following factors:

Physiological variations. (1) *Age*—Blood pressure rises with age. During infancy, the systolic pressure is from 70–90 mm of Hg; childhood, 90–110 mm of Hg; puberty, 110–120 mm of Hg; old age, 140–150 mm of Hg.* At any age, a systolic pressure persistently above 150 mm of Hg and a diastolic pressure above 100 mm of Hg should be accepted as high. On the other hand, systolic pressure below 100 mm of Hg and diastolic below 50 should be taken as low in the adults. Recent observations indicate that the pressure which is reached in adolescence does not normally rise with age any more.

The average systolic pressure is 110–120 mm of Hg and diastolic pressure 70–80 mm of Hg. The normal upper limits of systolic and diastolic pressures are placed at 140 and 90 mm of Hg respectively.

AVERAGE BLOOD PRESSURE AND STANDARD DEVIATIONS IN APPARENTLY HEALTHY PERSONS (assuming *diastolic end point is disappearance of sound*)

Age group	MALES		FEMALES	
	Systolic	*Diastolic*	*Systolic*	*Diastolic*
20–29	124·0 ± 13·2	77·0 ± 9·5	116·5 ± 11·6	73·0 ± 9·4
30–39	126·5 ± 13·9	79·5 ± 10·0	122·0 ± 14·0	76·5 ± 10·4
40–49	129·5 ± 16·0	81·5 ± 10·2	129·0 ± 18·3	81·0 ± 11·1
50–59	136·5 ± 19·0	83·5 ± 11·4	138·0 ± 21·4	84·0 ± 12·0
60–69	142·5 ± 23·5	84·0 ± 11·2	149·0 ± 25·7	85·0 ± 13·4
70–79	145·5 ± 24·0	81·5 ± 14·1	158·5 ± 26·0	84·5 ± 14·2
80–89	145·0 ± 25·0	80·5 ± 12·4	155·5 ± 28·0	82·5 ± 15·2

(2) *Sex*—In females both systolic and diastolic pressures are slightly lower than in males up to the age of 45–50 years.

(3) *Build*—The systolic pressure is usually high in obese person. In most of the overweight persons the blood pressure is found to be high.

(4) *Exercise*—In strenuous exercise the systolic pressure rises and may reach even up to 180 mm of Hg. In moderate exercise there is slight rise of systolic blood pressure.

(5) *Posture*—The diastolic pressure is slightly higher in the standing position. In the recumbent position the diastolic pressure is lower than in the standing or in the sitting position.

(6) *Sleep*—The systolic pressure falls by about 15 to 20 mm of Hg during sleep.

(7) *After ingestion of meals*—There is a slight rise of systolic pressure.

(8) *Emotion* or *Excitement*—It causes increase of systolic pressure.

* To obtain a rough estimate of the systolic pressure of a particular subject, several formulae are often used by clinicians. They are as follows: (1) 100 + age; (2) 100 + 2/3rds the age; (3) 90 + age, etc.

Significance of blood pressure. Systolic pressure undergoes considerable fluctuations. Excitements, exercise, meals, etc., increase it, while sleep, rest, etc., diminish it. The height of systolic pressure indicates: (1) The extent of work done by heart. (2) The force with which the heart is working. (3) The degree of pressure which the arterial walls have to withstand.

Diastolic pressure undergoes much less fluctuations in health and remains within a limited range. Increase of diastolic pressure indicates that the heart is approaching towards its failure. Consequently, variations of diastolic pressure are of greater prognostic importance than those of systolic. *Diastolic pressure is the measure of peripheral resistance.* It indicates the constant load against which heart has to work.

Pulse pressure generally varies directly as the stroke volume. But this quantitative relation may not be true in all cases.

The **normal function** of blood pressure is (1) to maintain a sufficient pressure head to keep the blood flowing; (2) to provide for the motive force of filtration at the capillary bed—thus assuring nutrition to the tissue cells, formation of urine, lymph and so on.

From the above considerations, it is seen that, the height of blood pressure gives correct informations about the state of the circulatory system as a whole and also about the functional condition of the tissue cells and organs.

Measurement and recording of blood pressure

Arterial blood pressure can be measured by two methods: (1) direct and (2) indirect. In **direct method,** the artery is exposed and an arterial cannula of which one tapering end is inserted directly into the lumen of the exposed vessel and the other end is connected to the U-shaped mercury manometer that shows the actual blood pressure in mm of Hg. As the mercury column in one limb (that has direct contact with the blood vessel) descends and the other limb of the U-tube ascends, the value in the scale will be doubled so as to get the actual blood pressure. For convenience it is generally considered to be 1 mm in the scale equivalent to 2 mm of Hg of pressure. Before recording the blood pressure, the mercury levels in both limbs of the U-tube must be adjusted to the 0 mark of the scale. For recording pressure a floating stylus with a writing pointer that marks on the smoked paper may be used (FIG. 213). This method is only suitable in animals and gives the idea about mean pressure. Due to high inertia of the mercury, the blood pressure changes associated with cardiac cycle are damped. Respiratory undulation of mean pressure waves are clearly seen in this direct method.

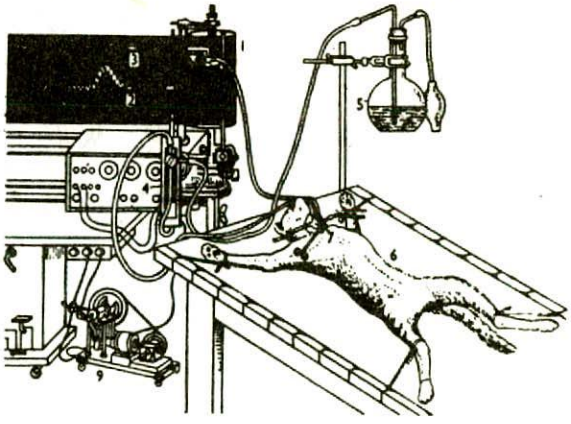


FIG. 213. Direct method for measurement of arterial blood pressure. 1=Kymograph. 2=floating stylus for blood pressure recording. 3=stylus for respiration recording. 4=mercury manometer. 5=reservoir. 6=animal (cat). 7=artery cannula. 8=operation table. 9=respiratory pump.

In **indirect method,** the pressure may be measured without any surgical procedure

and thus it is very convenient clinically in human being. Riva-Roci (1896) first introduced this indirect method and afterwards **Korotkoff** (1905) introduced a convenient method by which the systolic and diastolic pressures could be ascertained only through listening to a sound. This is the standard method of recording blood pressure all throughout the world.

In this method commonly the pressure of the brachial artery is measured. The instrument used is known as *Sphygmomanometer.* Three methods: (*a*) **oscillatory,** (*b*) **palpatory,** (*c*) **auscultatory.**

Oscillatory method. Inspection of oscillation in spring gauge or mercury manometer is the basis of this method. In this method a pressure cuff is wrapped over the brachial artery and the oscillations that are produced by the pulsations, are observed. The instrumeut is always kept at the heart level. When the cuff pressure is increased and raised above the systolic pressure, the oscillations disappear, but on releasing the pressure gradually, the oscillations become larger and prominent. The pressure head at which the larger oscillations are seen, is considered as systolic pressure. But on further release of pressure, the oscillations become smaller and disappeared. The pressure at which the oscillation just becomes smaller or disappears is known as diastolic pressure.

Palpatory method. The instrument is kept at the level of the heart and the cuff is tied round the upper arm. Pressure is raised to 200 mm of Hg and then gradually released. When the pulse just appears at the wrist, the pressure is noted. This is the systolic pressure. This method is not accurate. By this method the diastolic pressure cannot be determined.

Auscultatory method. The instrument is kept at the level of the heart and the cuff is tied round the upper arm. Pressure is raised to 200 mm of Hg and then gradually released. Variations of sounds are heard with a Stethoscope placing its chest piece on the brachial artery, a little below the cuff. *The sounds are heard due to occurrence of turbulence in the flow of blood through the narrowed blood vessels when the manometric pressure just coincides with the systolic blood pressure.* Due to giving air pressure in the cuff, the vessel is pressed and blood flow is obliterated. But while releasing the air pressure gradually, blood just begins to flow through the narrowed blood vessels and the pattern of flow is changed from streamline flow (silent) to turbulent flow (noisy). When the pressure is further released, normal streamline flow sets in and the sound is no longer heard. At this point manometric pressure coincides with the diastolic blood pressure. So, as the pressure is released the following variations of sounds are heard: *First phase*—sudden appearance of a clear *tapping sound. This indicates systolic pressure.* It persists while the pressure falls through 15 mm of Hg. *Second phase*—the tap sound is replaced by a *murmur* persisting for another 15 mm of Hg. *Third phase*—

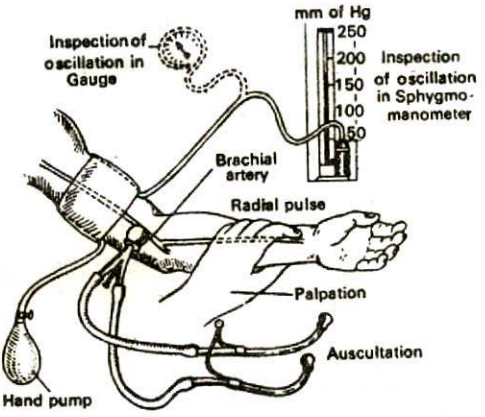


FIG. 214. Measurement of arterial blood pressure in human beings (after Harris).

the murmur is replaced by a clear loud *gong sound* lasting for the next 20 mm of Hg. *Fourth phase*—the loud sound suddenly becomes *muffled* and rapidly begins to fade. *This point indicates diastolic pressure. Fifth phase*—absence of all sounds.

Venous pressure. It is the pressure which is exerted by the blood within the veins. Average venous pressure of human being in recumbent position is about 60–120 cm of H_2O. The venous pressure can be measured by inserting a needle directly into the anticubital vein and by connecting the needle to a water manometer (FIG. 215). Venous pressure is a valuable index in determining the efficiency of the heart.

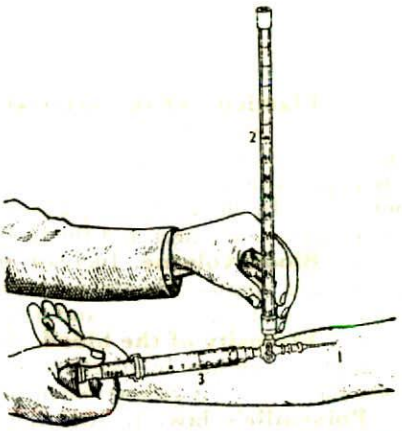


FIG. 215. Use of water manometer for measurement of venous pressure. 1=anticubital vein. 2=manometer. 3=syringe.

Factors controlling arterial blood pressure

1. **Pumping action of the heart.** Effectual contraction of the heart is the main factor for controlling the cardiac output, blood pressure and flow within the blood vessel. Because in each effectual contraction of the ventricle certain amount of blood is ejected out into the aorta. The driving force of blood is mainly created by the pumping action of the heart. The efficiency of the heart is considered upon how much amount of blood is driven out by the heart into the aorta in each beat.

2. **Cardiac output.** Alterations of cardiac output will alter blood pressure. Cardiac output depends upon venous return, force and frequency of heart beat. Blood volume affects blood pressure directly, by mainly modifying the cardiac output.

3. **Peripheral resistance.** *It is the resistance which blood has to overcome while passing through the periphery. The chief seat of peripheral resistance is the arterioles* and to a smaller extent the capillaries (*vide* below). Peripheral resistance depends on the following: (1) Velocity of blood, (2) Viscosity of blood, (3) Elasticity of arterial walls, (4) Lumen of the blood vessels. Resistance is directly proportional to the first two and inversely to the last two factors.

(1) *Velocity*—A rapidly flowing stream will have more frictional effect than a slower one. Hence, pressure is high in the aorta but low in the capillaries. (2) *Viscosity*—Other factors remaining constant, a more viscid blood will have a higher friction than a lesser one. For this reason, plasma transfusion is sometimes more effective to maintain blood pressure than ordinary saline. (3) *Elasticity*—Due to elastic properties, the arteries can dilate and accommodate considerable amount of blood with relatively less rise of blood pressure. In old age, the arterial walls become stiff. Hence, blood pressure rises. (4) *Lumen of the vessel*—Peripheral resistance is inversely proportional to the lumen of the vessels. In other words, smaller the vessel, higher will be the resistance. One should expect therefore that the capillaries, having the smallest lumen, should have the highest pressure.

But this is not the case. Because the velocity of blood being lowest in the capillaries, the frictional effect is very low. Hence, the pressure is also low. The seat of peripheral resistance is found to be chiefly in the arterioles, where the velocity is fairly high and the lumen is narrow.

$$\text{Peripheral resistance} \propto \frac{\text{Mean arterial pressure}}{\text{Cardiac output}}.$$

Mean arterial pressure can be expressed in *dynes* per square centimetre by multiplying the pressure in mm of Hg by 1,332.

4. **Elasticity of the arterial walls.** In normal diastolic pressure arterial walls are stretched but due to the presence of elastic tissues in their walls, they tend to recoil. Due to elasticity of the arterial walls the blood flow is pulsatile in the arteries. In the capillaries and venules the flow is continuous. In old age the expansion of the arterial walls becomes limited due to sclerotic changes and the blood pressure rises.

5. **Blood volume.** Increase in blood volume will raise both the systolic and diastolic blood pressures due to the increased quantity of blood in the arterial system and greater stretching of the arterial walls.

6. **Viscosity of the blood.** Alteration in blood viscosity will affect the diastolic pressure by its effect on the peripheral resistance. The intramolecular friction is greater when the viscosity is high.

Poiseuille's law. In 1841 the French Physician J. L. M. Poiseuille studied the factors regulating the flow of viscous fluids through the capillary tubes. He showed that **resistance to blood flow** in any blood vessel proportionally varies directly with the viscosity of the blood and also with the length of the blood vessel, and inversely with the *fourth power* of the radius of the blood vessel. It can be represented by the following formula:

$R=\frac{\eta l}{r^4} \times \frac{8}{\pi}$, where R stands for resistance to blood flow, η for viscosity of blood, l for length of blood vessels, r for radius of the blood vessel, 8 for Hagen's integration and π factor for a cylindrical tube.

Taking this value for resistance in the formula it is found that blood flow proportionally varies directly with the blood pressure and the fourth power of the radius of the blood vessel, and inversely with the viscosity of the blood and the length of the blood vessel. The following formula, known as *Poiseuille's law*, expresses the above relations.

$BF=K\frac{BP}{R}$ or $BF=BP \times \left(\frac{\pi}{8}\right) \times \left(\frac{1}{\eta}\right) \times \left(\frac{r^4}{l}\right)$, where BF stands for blood flow, BP for blood pressure, r for radius of the blood vessel, η for viscosity of blood, l for length of the blood vessel and π for 3·14. This law is not applicable when the arterial pressure falls below 20 mm of Hg.

Adjustment of blood pressure

In the normal individual the constancy of the internal environment is being adjusted by the well-organised controlling system—which is called *Milieu intérieur* after Claude Bernard and *Homoeostasis* after Cannon. Adjustment of blood pressure, according to the needs of the body, may be carried out by the several complex reflexes whose centres are lying in the *cerebral cortex, formatio reticularis, hypothalamus, medullary and spinal vasomotor centres*. The (A) efferent and (B) afferent pathways constituting the above reflexes are lying within the *sympathetic and parasympathetic nervous systems* whose activities are modified by the hypothalamus and other centres.

A. **Efferent pathways of this self-adjustment or homoeostasis of blood pressure** are the vagi and the sympathetic nerves which control the blood pressure by (*a*) *modifying the cardiac activity*, (*b*) *altering the cardiac output*, and (*c*) *altering the lumen of the blood vessels*. The relative activities of the vagi and the sympathetic of the efferent pathways are under the control of *vasomotor systems*, which are described below:

Vasomotor system. This system consists of (1) **vasomotor centre,** (2) **vasoconstrictor nerves,** (3) **vasodilator nerves.** They supply vasomotor nerves—mainly to the arterioles but to some extent to the capillaries and venules. This vasomotor centre is highly developed in higher animals and human beings. In infants and children it is imperfect. By regulating the radius of the blood vessels this system takes part in adjusting blood pressure and blood supply to a particular part. It also plays an immense role in heat regulation.

Vasomotor centre (V.M.C.). Vasomotor centre is situated on the floor of the fourth ventricle in the reticular formation at the level of the **calamus scriptorius.** It extends from the lower part of the pons to the obex and forms a diffuse network of neurones. After section of the brain stem at the level of the calamus scriptorius there is fall of blood pressure. There are practically two areas in the reticular formation of the medulla:

(*a*) *Pressor centre*—which causes rise of blood pressure.

(*b*) *Depressor centre*—which causes fall of blood pressure.

The depressor centre is not the *vasodilator* centre. This centre causes inhibition of the vasoconstrictor tone. The depressor centre relays the inhibitory impulses to the pressor centre. Pressor and depressor centres form one functional unit and it is defined as the vasomotor centre. The vasomotor centre discharges impulses which pass down the lateral white column of the spinal cord in the cervical, thoracic and lumbar segments of the spinal cord and form synaptic connections with the lateral horn cells of the spinal cord.

Vasomotor reflexes. (1) Depressor reflex. (2) Pressor reflex.

Depressor reflex. Blood pressure falls due to diffuse dilatation of the arterioles. Rise of blood pressure stimulates the **baroreceptors** of the carotid sinuses and aortic arch, and causes slowing of the heart and arteriolar dilatation. The vasodilatation is due to inhibition of vasoconstrictor effect of the sympathetic.

Pressor reflex. Blood pressure rises due to diffuse constriction of the arterioles. Diminution of blood pressure fails to stimulate the baroreceptors of the carotid sinuses and aortic arch, and the parasympathetic inhibitory tone over the heart and blood vessels is withdrawn. Blood pressure is raised reflexly through overactivity of the sympathetic. Vasoconstriction of the arterioles is due to activity of the vasoconstrictor centre. Reflex vasoconstriction also occurs due to stimulation of **chemoreceptors** during the fall of blood pressure.

Control of V.M.C. Vasomotor centre is under the superior control of cerebral cortex and hypothalamus (FIG. 216). Factors influencing V.M.C. have been described as follows:

1. **Higher centre** (including Hypothalamus). *Emotion* generally stimulates, causing vasoconstriction. But *shock* may depress the centre—leading to a sudden fall of blood pressure and fainting (vasovagal attacks).

2. **Respiration.** During inspiration systemic blood pressure is generally decreased but increased during expiration. This is due to the decrease of left ventricular cardiac output during inspiration. Reverse is the effect during expiration. There is no evidence of direct respiratory centre—effect on vasomotor centre.

3. **CO_2 excess.** Excess stimulates. The action is mainly on the centre but partly reflexly through the sino-aortic nerves.

4. **O_2 lack.** Generally stimulates V.M.C. The effect is mainly reflex through the sino-aortic nerves and slightly direct on the centre.

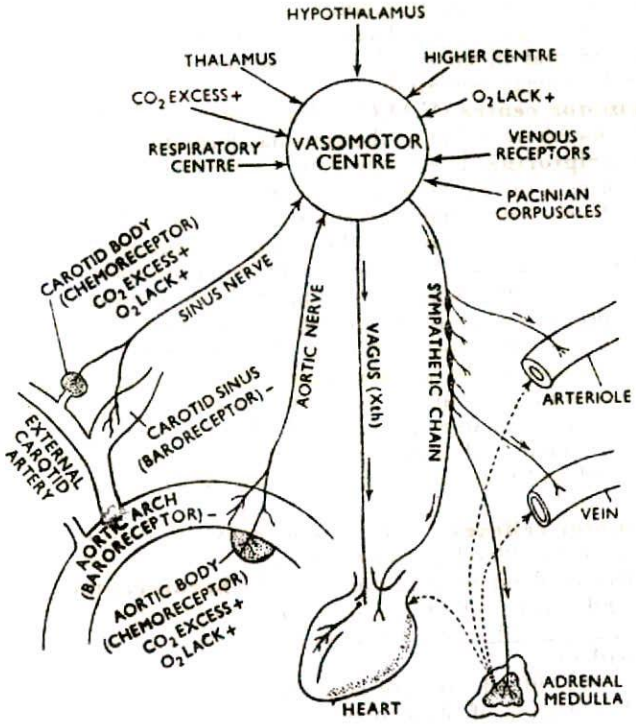


FIG. 216. Diagrammatic representation of different factors that influence the vasomotor centre.

5. **Sino-aortic nerves.** Variations of blood pressure, CO_2 tension, O_2 tension, etc., reflexly regulate the activity of the vasomotor centre through the sino-aortic nerves. Normally, a stream of inhibitory impulses is carried up by these nerves depressing the vasomotor centre. When blood pressure rises, V.M.C. is depressed, vasodilatation occurs and further rise of blood pressure is checked. When blood pressure falls, the centre is released causing vasoconstriction and raising blood pressure. [Sino-aortic nerves also control cardiac centre, respiratory centre and adrenaline secretion.] [*Vide* pages 306–07.]

6. **Other afferents.** Local vasomotor tone is altered by afferent nerves originating from different baroreceptor and chemoreceptor areas, distributed all throughout the body. The baroreceptors are located in the *right atrium*, in the *left atrium and left ventricle*, in the *pulmonary arch of aorta*, in the *junction of the superior thyroid artery and common carotid artery, junction of the subclavian artery and common carotid artery*, and *all throughout common carotid artery in between the superior thyroid artery and subclavian artery, mesenteric blood vessels* (Pacinian corpuscles), *thoracic arch of the aorta* and in the *central vein* (venous receptor). The chemoreceptors are located in the ventricular cavity and all throughout the blood vessel wall. *Reactive hyperaemia* is the consequence of local chemoreceptor activity on the blood vessel wall by the accumulated metabolites. Heat dilates and cold constricts the skin vessels reflexly.

Vasoconstrictor nerves. The fibres pass along the sympathetic outflow from the first thoracic to the second lumbar segments. Brief details are as follows:

1. *To the skin and muscles*—pass out through the grey rami communicantes—to the mixed spinal nerves—and finally distributed through ordinary motor and sensory nerves. The distribution is strictly unilateral, stopping sharply at the midline.
2. *To the head and neck*—come from the first to the fourth thoracic segments—enter the superior cervical ganglion from which postganglionic fibres arise and pass along the carotid artery and its branches.
3. *To the fore limbs*—arise from the fourth to tenth thoracic segments —enter the stellate ganglion from which the postganglionic fibres arise and pass along the spinal nerves and supply the blood vessels.
4. *To the hind limbs*—arise from the eleventh thoracic to the second lumbar segments—relay in the lower lumbar and upper sacral ganglia, the postganglionic fibres accompany the nerves of the sacral plexus.
5. *To the abdominal viscera*—from the lower thoracic and upper two lumbar segments—pass through the splanchnic nerves to coeliac ganglion —the postganglionic fibres pass along the blood vessels.
6. *To the thoracic viscera—Heart* receives constrictor fibres through the vagus; *lungs* from the sympathetic.

Vasodilator nerves. There are three types of vasodilator nerves: (1) **parasympathetic** (craniosacral), (2) **sympathetic,** (3) **antidromic fibres** of the posterior spinal root.

1. **Parasympathetic vasodilators**

(*a*) Cranial: (*i*) Chorda tympani—to the submaxillary or submandibular gland. (*ii*) Lesser superficial petrosal—to the parotid gland. (*iii*) Lingual—to the vessels of tongue.

(*b*) Sacral: Nervi erigentes—to the vessels of genitalia.

2. **Sympathetic vasodilators**

Sympathetic fibres are mostly vasoconstrictor in nature. But some vasodilators are also present. For instance, (*a*) the dilator fibres of the coronary vessels come through the sympathetic. (*b*) Sympathetic dilator fibres have been demonstrated in the peripheral nerves in human beings. (*c*) Stimulation of the last anterior thoracic root produces dilatation of the kidney vessels. (*d*) Stimulation of the right splanchnic nerve sometimes causes vasodilatation and fall of blood pressure.

3. **Antidromic vasodilators** in the posterior spinal root (FIG. 217). When posterior spinal root is cut, distal to the ganglion and the peripheral end is stimulated--although the nerve is afferent, yet the vessels in the periphery—both skin and muscles—dilate **(axon reflex).** In the

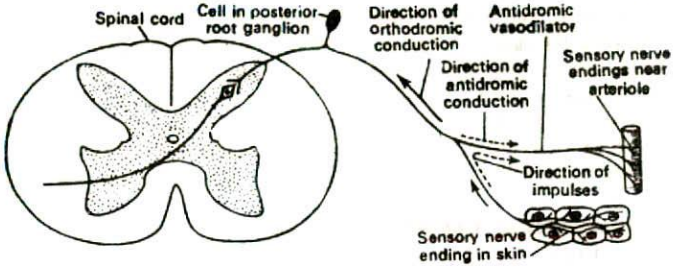


FIG. 217. Antidromic nerve fibres in the posterior nerve root.

skin, it is due to liberation of histamine and as such produces the typical triple response: dilatation, flare and wheal. In the muscle it liberates acetylcholine and thereby causes vasodilatation.

B. **Afferent pathways** are lying in two sets of receptors that carry the information of the instantaneous circulatory status to the centre. These sensory receptors are (*i*) **chemoreceptors** and (*ii*) **baroreceptors** distributed all throughout the cardiovascular system. The relative roles of the different afferent pathways have been described under separate headings, viz., (1) **sino-aortic mechanisms** controlling systemic blood pressure and flow, and (2) **vascular receptors** other than sino-aortic—controlling mostly the local blood pressure and flow.

I. ROLE OF SINO-AORTIC MECHANISM IN THE REGULATION OF NORMAL BLOOD PRESSURE. From the above, it is evident that blood pressure can be adjusted according to the needs of the body in various ways. Of all the factors, the sino-aortic mechanism plays the chief role. The sino-aortic mechanism is carried on by *baroreceptors* and *chemoreceptors*. This mechanism regulates blood pressure by adjusting the heart rate, vasomotor centre, and secretion of adrenaline and noradrenaline. It also adjusts respiratory centre in such a way that the functions of heart and respiration may run parallel.

SINO-AORTIC MECHANISM

(*a*) **BARORECEPTORS.** This includes *carotid sinus* and *aortic arch* (FIG. 218).

Carotid sinus. It is a dilatation at the root of internal carotid artery, often involving the common carotid. The exact location varies in different species. The wall of the sinus is thinner due to less muscle fibres in the media. In the deeper parts of adventitia, an extensive network of afferent nerve fibres is present. The fibres end in free nerve terminals and characteristic minisci. These pressor receptors are sensitive to stretch (*distortion effect*) being stimulated by rise of blood pressure.

The **sinus nerve** (afferent) arises from the carotid sinus and carotid body, passes along the glossopharyngeal nerve and ends in the medulla in close relation with respiratory, cardiac and vasomotor centres.

Aortic arch. Afferent nerves and stretch receptors—similar to those

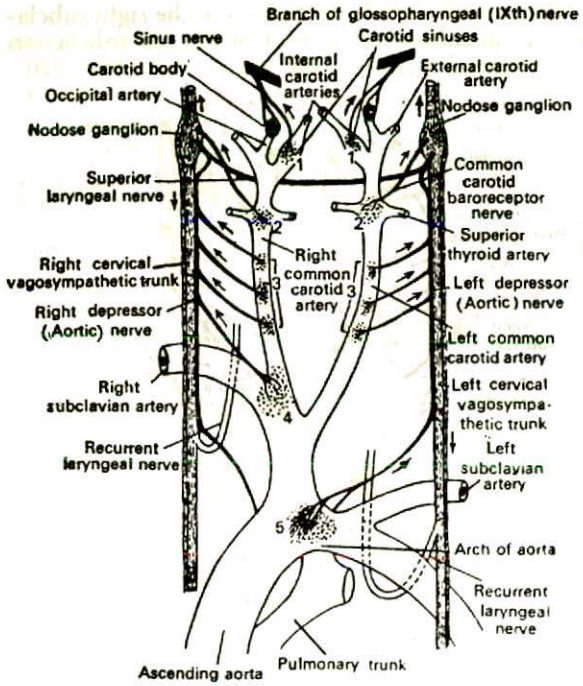


FIG. 218. Diagram represents the distribution of different baroreceptors on the walls of the blood vessels. 1 = carotid sinus. 2 = baroreceptors at the junction of the superior thyroid artery and common carotid artery. 3 = baroreceptor areas on the wall of the common carotid arteries. 4 = baroreceptors at the junction of the subclavian artery and common carotid artery. 5 = aortic arch baroreceptors.

in the carotid sinus—are also present in the adventitia of aortic arch, the roots of great vessels and even the adjoining parts of left ventricle. They serve the same function as the carotid sinus.

Aortic nerve. This nerve arises from the aortic body, the aortic arch and the basal part of left ventricle. It is a purely afferent nerve. Its course varies in different species but in human being it mostly passes in the vagus. Like the sinus nerve it ends in medulla being closely related to cardiac, vasomotor and respiratory centres.

(*b*) **CHEMORECEPTORS.** This includes *carotid* (G. *Karos* = sleep) *body* and *aortic bodies* (FIG. 220).

Carotid body (FIG. 219). It is a small nodule situated on the occipital artery, a branch of the external carotid artery very close to the carotid sinus. It consists of clumps of large polyhedral cells (*Glomus cells*), richly supplied with blood vessels and nerves. The vessels arise from the carotid artery. Some of the cells stain with chromic acid and belong to the chromaffin system but do not contain adrenaline. Numerous afferent nerve fibres surround the cell clumps and even the individual cells, and terminate in special *chemoreceptors*. They are sensitive to chemical changes in blood.

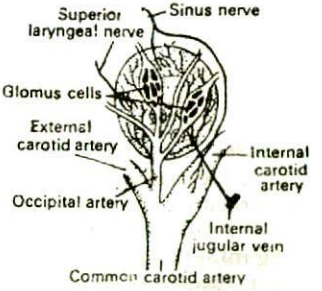


FIG. 219. Carotid body (Glomus caroticum) showing blood vessels and nerve supply.

Aortic bodies. Four groups of aortic bodies have been shown in cat (Howe, 1956). These are small nodular structures, supplied by a special blood vessel and situated (*i*) on the thorax between the pulmonary trunk and

ascending aorta, (*ii*) on the ventral surface of the root of the right subclavian artery, (*iii*) on the ventral surface of the root of the left subclavian artery, and also (*iv*) on the ventral surface of the aortic arch (FIG. 220). Afferent pathways from these chemoreceptor areas are lying in the aortic nerves and vagi. Their structures, nerve endings and functions are similar to those of carotid body.

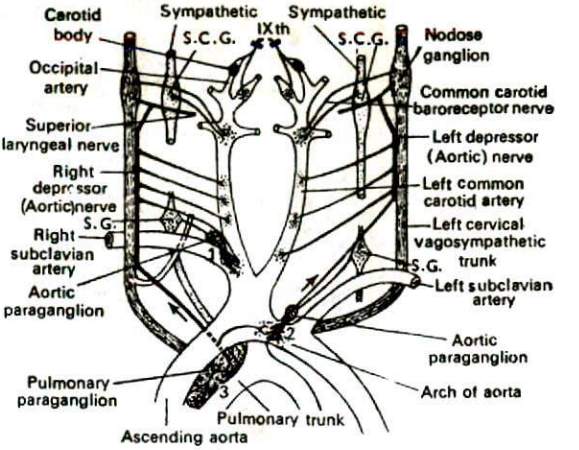


FIG. 220. Diagram represents the distribution of chemoreceptors at areas of the blood vessels. 1, 2, 3 are the chemoreceptor areas.

By perfusion experiments, the effects of chemical changes in blood, as brought about through the sino-aortic chemoreceptors, have also been studied in detail. It is seen that CO_2 excess, O_2 lack and increased H-ion concentration stimulate respiration (mainly), increase heart rate, produce vasoconstriction and raise blood pressure. After haemorrhage or in enfeebled circulation a rhythmic blood pressure wave (**vasomotor wave**) is often encountered. These vasomotor waves are due to chemoreceptor activities under such state. These waves were observed by Mayer (1876) and known as **Mayer's wave.** Following inactivation of chemoreceptors, these waves disappear completely.

Mechanisms of stimulation of chemoreceptors. It has been laimed that for the stimulation of chemoreceptor nerve endings, the beration of acetylcholine plays as the chemical intermediary (*vide* Chemial regulation of respiration).

Experimental observations. To study the functions of the sinoortic nerves various experiments have been performed. For instance, 1) *Section and stimulation* of the sinus and carotid nerves. (2) *Perfusion periments* in which the carotid sinus region is isolated and perfused with lood or other fluids whose pressure and composition can be varied at will. 3) *Electrophysiological study* shows that in normal arterial pressure the sinus erves discharge impulses, the frequency of which rises with systolic pressre and diminishes with diastolic pressure. Rise in systolic pressure creases the frequency of impulse discharge. (4) *Cross-circulation experints*—Heymans and his associates have studied the functions of the rotid sinus and sinus nerve by cross-circulation experiments (FIG. 221). ıe carotid sinus of the second dog B was isolated (the nerve supply remang intact) and perfused with the blood of the first dog A. When the arte-l pressure of the dog A was raised the arterial pressure of the dog B s diminished. Again when the arterial pressure of the dog A was lowered, arterial pressure of the dog B was increased by secretion of adrenaline videnced from splenic contraction in dog C which got adrenaline from

dog B through anastomoses of the suprarenal vein and the jugular vein. The followings are the complete observations:

On raising the pressure in the carotid sinus, the following reflex effects are produced: (1) Slowing of the heart rate. (2) Peripheral vasodilatation preferably in the splanchnic bed so as to increase the total vascular capacity. (3) Fall of blood pressure. (4) Diminished adrenaline secretion. (5) Slowing or stoppage of respiration. (6) Diminished tone in voluntary muscles. (7) Various changes in the viscera, viz., increased volume and movement of the stomach, decreased tone of urinary bladder, etc., caused by disturbed activity of the autonomic system. Fall of sinus pressure or section of the sinus nerve produces opposite effects. Stimulation of the central cut end of the sinus nerve also produces similar effects.

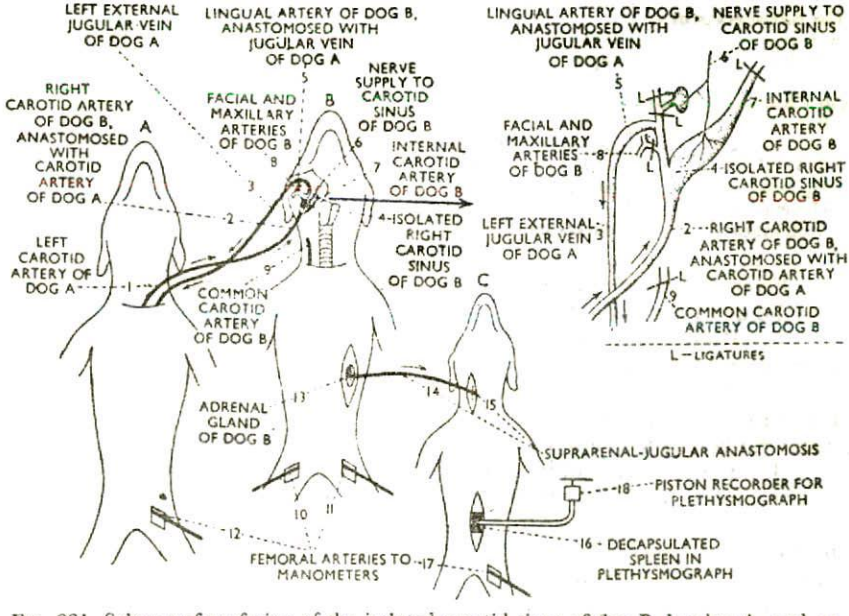


FIG. 221. Scheme of perfusion of the isolated carotid sinus of dog B, by dog A, and an anastomosis between the suprarenal vein of dog B and the jugular vein of dog C. The blood from dog A flows through the carotid sinus of dog B and back to dog A *via* anastomosis between the lingual artery of dog B and the external jugular vein of dog A (after *Heymans*).

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Raising the aortic pressure causes the following effects: (1) Slowing of the heart rate—mainly due to the stimulation of cardio-inhibitory centre and partly to the inhibition of accelerator centre. (2) Inhibition of the vasomotor centre causing vasodilatation. (3) Depressed adrenaline secretion. (4) Fall of blood pressure. (5) Depressed respiration. Fall of aortic pressure or section of the aortic nerve—produces reverse effects. Stimulation of the central cut end of the aortic nerve produces similar effects. Sometimes stimulation of the central cut end of vagus or aortic nerve may raise blood pressure by reflex cardiac acceleration and vasoconstriction. This proves that these nerves also carry some pressor fibres.

For the last few years there is considerable progress regarding the studies in connection with changes in the circulation and arteriolar resistance in blood pressure. In hypertension of the sino-aortic origin there occurs vasoconstriction and stimulation of the sympathetic nerves of the heart. After occlusion of the common carotid arteries, hypertension occurs with decrease in the volume of spleen, kidney, limbs, etc.

Thus, it is evident that the functions of the sinus and aortic nerves (*Buffer nerves*) are very similar. The effects of the various factors are summarised as follows:

Factors	Respiration	Heart rate	Vasomotor	Adrenaline secretion	Blood pressure
On Baroreceptors					
B.P. rise	slow	slow	dilatation	depressed	rise checked
B.P. fall	rapid	rapid	constriction	stimulated	fall checked
On Chemoreceptors					
B.P. fall	rapid	rapid	constriction	stimulated	raised
CO_2 excess	rapid	rapid	constriction	stimulated	raised
CO_2 fall	slow	slow	dilatation	depressed	lowered
O_2 lack	rapid	rapid	constriction	stimulated	raised
H-ion concentration changes	effects same as CO_2 changes.				

From the above observations, the **functions of sino-aortic nerves** may be described as follows:

1. Reflexly maintain the vagal tone and thus exert tonic inhibitory control on the heart.
2. Reflexly maintain the inverse relation between blood pressure and heart rate and thus keep the variations of blood pressure within an optimum range (hence called *Buffer nerves*).
3. Exert tonic inhibitory action on respiratory centre and vasomotor centre (vasoconstrictor).
4. Reflexly regulate the activity of the respiratory, cardiac, vasomotor centres and adrenaline secretion and thus bring about a perfect coordination among them.
5. Changes in viscera, viz., variations of movement, tone, etc., may be reflexly produced through autonomic nerves.

II. **VASCULAR RECEPTORS OTHER THAN SINO-AORTIC FOR THE CONTROL OF BLOOD PRESSURE AND FLOW.** The sino-aortic mechanisms are meant for the maintenance of systemic blood pressure and flow. But the vascular receptors other than sino-aortic are responsible mostly for control of local blood pressure and blood flow. These are as follows:

(*a*) As Baroreceptors

(*i*) **At the junction of superior thyroid artery and common carotid artery.** These baroreceptors mainly control the pressure and flow of the thyroid gland. When the systemic pressure is raised, these baroreceptors may be stimulated and impulse is carried through the common carotid nerve (C. C. N.) and is reflexly produced dilatation of the thyroid blood vessels. The presence of these baroreceptors has been demonstrated by Green (1956) in cats.

(*ii*) **Several baroreceptor areas in the wall of right and left common carotid arteries** between the level of the superior thyroid artery and subclavian bifurcation—have been demonstrated by Green (1956). Afferent impulses from these areas are carried through the branches of the aortic nerves.

(*iii*) **Baroreceptor areas at the junction of the right subclavian artery and common carotid artery.** These baroreceptor areas have been demonstrated by Heymans (1956) in cats and also in other mammals. Rise of pressure in these areas produces reflex *systemic hypotension* and *hypopnoea*. Afferent impulses are carried from these area *via* the branch of the aortic nerves.

(*iv*) **Baroreceptors of the pulmonary arch of aorta.** These baroreceptors are present in the pulmonary conus of bifurcation. It has been claimed by Aviado and Schmidt (1955) that *reflex bradycardia* and *hypotension* are produced if these receptors are stimulated due to rise of pressure.

(*v*) **Receptors in thoracic aorta.** The presence of baroreceptors has been claimed by Gruhzit and Moe (1953) and also others. Rise of blood pressure may produce reflex vasodilatation in the innervated limb through the stimulation of these baroreceptors (Tournade and Malmejac, 1933).

(*vi*) **Mesenteric baroreceptors.** Gammon and Bronk (1935) first demonstrated the presence of mesenteric baroreceptors. The *Pacinian corpuscles* are the actual baroreceptors of the mesenteric blood vessels. These receptors are not directly related to the level of systemic blood pressure, but to a degree of distention of the mesenteric blood vessels. It has been observed by Heymans and his colleagues (1937) under isolated cross-circulation technique that increases pressure in mesenteric blood vessels produces reflex vasodilatation of the spleen. But the specific function of these baroreceptors are not yet clear. These receptors do not play any important role in the regulation of systemic blood pressure but they may play in the regulation of blood flow in the abdominal viscera.

(*vii*) **Peripheral vascular receptors.** Presence of other peripheral vascular receptors have been observed by many. Yamado and Burton (1954) have observed decrease of flow in the finger if negative pressure is exerted on it. It is claimed that this reflex decrease of blood flow is through **venous-arteriolar reflex**—causing constriction of the arterioles due to (*a*) *distention* and (*b*) increase of transmural pressure of the veins. In congestive heart failure there is general occurrence of peripheral vasoconstriction (in the fingers and nose) is mostly due to reflex effect of increased central venous pressure (Heymans et al, 1958). Ganglionic blocking agents and sympatholytic drugs relieve these conditions. The *venous-arteriolar reflexes* may play an important role in relieving the venous congestion because with the increase of venous congestion, the arterioles are constricted so that the outflow from the veins will exceed inflow from the constricted arterioles. The presence of **veni-venimotor reflexes** have also been described by Wallis and others (1963). They have observed vasoconstriction in the haemodynamically isolated venous segment due to venous congestion produced by blowing up a cuff on the arm. Local anaesthesia abolishes this response.

(*viii*) **Löven reflex.** This is nothing but **axon reflex.** If any portion of the vessel is dilated then the neighbouring vessel is constricted. This was first observed by Löven.

(*ix*) **Bainbridge reflex.** Bainbridge (1915) showed that intravenous administration of saline or blood produced reflex acceleration of the heart. He claimed this to be reflex arising from the stretch receptors present in the venous side of the heart (great vein and also right atrium) and bilateral sectioning of the vagi abolished the response. His observation has been criticised by many but Jones (1962) has observed that reflex acceleration of the heart rate due to venous engorgement following infusion of saline or blood is dependent upon pre-existing heart rate of the animal. He claimed that if the heart rate is initially high (above 130 per min) then the reflex effect will be *bradycardia* instead of *tachycardia*.

(*x*) **Right atrial receptors (A and B).** Aviado and Schmidt have claimed that increasing the perfusion pressure in the right atrium produces bradycardia. This reflex effect is abolished by atropine or vagotomy. They suggest that the Bainbridge effect is the cause of stimulation of 'chemoreceptors supplied by the vagodepressor trunk which might well be activated by the changes in gas content, acidity, tonic balance and viscosity of the blood associated with the massive intravenous infusion'.

(*xi*) **Pulmonary deflation receptors.** Paintal (1955a) has claimed that these receptors are stimulated by congestion of lungs during rapid venous return and produce reflex bradycardia. These receptors are also a part of pulmonary depressor chemoreflex.

(*xii*) **Reflexes from the inflation of the lungs.** The physiology of these reflexes has been studied by Irving (1939) and Scholander (1963). They have described these reflexes to be an important line of defense against death due to asphyxia of the divers. They observed bradycardia and selective vasoconstrictions in non-vital organs (limbs, kidneys and mesenteries) after diving. They claimed that these reflex effects are due to stimulation of stretch receptors in the lungs.

(*xiii*) **Left atrial and left ventricular receptors.** Paintal (1955b) has shown that these receptors are excited by the increased pressure in the left side of the heart and produce bradycardia.

(*b*) As Chemoreceptors

(*i*) **Bezold and Jarisch reflex.** Bezold and Hirt (1868) and Jarisch (1938) observed profound bradycardia, hypotension and apnoea following intravenous injection of veratrine alkaloid. They considered to be the direct effect of the drug on this cardiac receptors in left ventricle (mostly) that causes reflex cardiac and respiratory effects. Jarisch has claimed that these are proprioceptive receptors and are normally responsive to stretch of the ventricular wall. Paintal (1955b) has shown that veratrine and related substances may stimulate the ventricular receptors and also some of atrial receptors ('A' and 'B'). He also claimed that these drugs do not act directly on these receptors but act through changing the ionic status of the receptor areas.

(*ii*) **Pulmonary depressor chemoreflex and pulmonary respiratory chemoreflex.** Brodie (1900) observed bradycardia and hypotension following intravenous administration of egg-white and serum into cats. He claimed that these effects are due to stimulation of receptors of the pulmonary vascular bed. These have been investigated by many. Dawes and Mott (1950) also observed bradycardia and hypotension after administration of phenyl diguamide. They claimed that these effects were due to direct stimulation of the pulmonary vascular receptors. Paintal (1955a) has claimed these pulmonary depressor chemoreflex, pulmonary respiratory chemoreflex to be responsible for the stimulation of the pulmonary deflation receptors.

(*iii*) **Reactive hyperaemia.** Chemoreceptors are present all throughout the vascular wall and are stimulated by the local accumulation of metabolites. Hyperaemia caused by locally accumulated metabolites acting on the blood vessels are called reactive hyperaemia. It is a kind of autoregulation of blood circulation of the organ itself.

(*iv*) **Abdominal chemoreceptors.** It has been described by a group of workers that certain peripheral (abdominal) vascular chemoreceptors are present which, when stimulated by strongly irritant chemicals, may produce reflex respiratory effects. But the presence of these receptors has not yet been substantiated and Heymans and his colleagues have shown that these effects are not observed if the drugs are administered in the isolated organs.

Summarily, it can be argued that nature's mission is to protect the vital organs like heart and brain from any unphysiological conditions. Whenever there is any rise of blood pressure or fall of pressure, the normal range of blood pressure and blood flow of the vital organs are maintained by redistribution of blood. This redistribution of blood is made by withdrawing or heightening the vasomotor tone. In condition of increased blood pressure, there is depression of sympathetic tone along with activation of parasympathetic tone—causing peripheral vasodilatation so as to shift the blood to the splanchnic bed (peripheral bed); but in condition of decreased blood pressure, there is increase of sympathetic tone along with decrease of parasympathetic tone—causing profound vasoconstriction in the splanchnic bed (other peripheral bed) so as to shift the blood to the vital organs.

Chemical control of blood pressure influenced by vasomotor mechanism

Many substances produced in the body are known to increase or decrease blood pressure by influencing the vasomotor mechanism. Some of these are:

CO_2 Tonic activity of the vasoconstrictor area may be due to stimulating action of CO_2 in blood. During early stage of asphyxiation this may bring about a great increase in blood pressure. It is observed that overventilation of lungs, as by voluntary deep inspiration and expiration for 3 or 4 minutes, causes a feeling of giddiness. As a large amount of CO_2 are expelled from blood by overventilation, the vasoconstrictor

area is deprived from proper stimulation by CO_2. As a result, a fall in blood pressure and vasodilatation in splanchnic area occur.

Epinephrine. If it is injected into blood, epinephrine constricts the cutaneous and abdominal arterioles, and this results in a very sharp rise of blood pressure, but the elevated pressure does not stand for a long time. By application locally, it is used in minor operation on the eye, nose, etc. In contrast, there is a dilatation of the coronary and skeletal muscle arterioles.

Ephedrine. It is much weaker in action than in that of epinephrine. It is much used in bad colds and hay fever because of its constricting action. When inhaled or applied locally by drops or a spray, it brings about an immediate shrinkage of the congested blood vessels of the nasal mucosa. After 3 or 4 hours, the opening of nasal passages by vasoconstriction becomes freer and more comfortable for breathing.

Histamine. It causes a marked dilatation of capillaries and arterioles in lowering of blood pressure.

Alcohol. It causes a marked dilatation of blood vessels as a depressant on the vasomotor centre. On a cold day after consuming alcohol the cutaneous vessels are especially affected.

Tobacco. Smoking increases both systolic and diastolic blood pressure. There are an increase of pulse rate materially and a decrease of temperature of extremities. So the use of tobacco may be injurious in arteriosclerosis and also in cardiac diseases associated with arteriosclerosis or even high blood pressure.

Vasopressin. Though it is an internal secretion of the posterior pituitary, it causes an increase of blood pressure. But this rise in pressure is not so great as that of epinephrine, yet this pressure continues for a long time.

Acetylcholine. Direct action of acetylcholine on coronary blood vessels is dilatation.

WORK DONE BY THE HEART

Work done by the heart is spent for two purposes: (1) for ejecting a certain amount of blood against the mean aortic pressure and (2) for imparting a definite velocity to it. Work done at each beat may be calculated from the following formula: $W = QR + (wV^2/2g)$, where W stands for work in gram metres, w for the weight of blood in gram ejected, Q for the quantity of blood expelled, R for average arterial B.P. in Hg, V for the mean velocity of blood and g for acceleration due to gravity. The work of heart can be adjusted to the body needs. Cardiac work divided by the surface area of the body is known as **cardiac work index.** Stroke work divided by the surface area is known as **stroke work index.**

The broad facts about work of the heart are as follows:

1. At rest, work done by left ventricle per beat, is about **100 gram metres** per beat (right ventricle—16 gram metres per beat). In 24 hours it comes to about 10,000 kilogram metres.
2. During heavy exercise, work increases from 5 to 10 times, hence, the *functional reserve* of heart is believed to be about 10 times its resting value.
3. Mechanical efficiency of heart is about 30% (page 265).

Cardiac efficiency test (Exercise tolerance test). By increasing the work of heart its efficiency can be tested. The principle is to allow the

subject to undergo a definite piece of exercise and then note the variations of heart rate. It may be done in two ways: (1) **Light exercise**—The resting pulse rate is noted. The subject is made to hop twenty times, the hop height being 15–23 cm (6"–9"). Heart rate should not rise more than 10 to 30 per minute and should return to normal by 30 seconds to 2 minutes. This test is often modified in various ways, e.g., rising a flight of 10 stairs, alternate sitting and standing, or sitting and lying for about 10 times and so on. (2) **Heavy exercise**—Two five-Kg weights are raised with two hands from the ground—up over head, once every two seconds for 30–60 times. In a sedentary healthy young man the heart rate may go up to 150–170 per minute along with respiratory distress. The heart rate comes to normal in 3–5 minutes.

CIRCULATION TIME

Definition. *It is the time taken by a particle of blood to flow from one point in the circulation to the other.* It measures the average linear velocity of blood.

Methods of determination. The principle is to inject some substance intravenously and then to note the arrival of the substance at the point in question. Generally, the cubital vein is selected but other veins can also be used. Many substances are used, such as histamine, fluorescin, potassium ferrocyanide, calcium chloride, calcium gluconate, magnesium sulphate, saccharin, ether, sodium dehydrocholate (decholin), radioactive substances, sodium cyanide, etc.

Other factors remaining constant, circulation time will depend upon the length of the circuit and the method employed. Single estimations are not of much value. Repeated estimations, using the same method, give a more correct information. The time is measured with a stop-watch—from the beginning of the injection to the signal of its arrival. Each substance produces a characteristic effect by which the arrival can be detected. For instance, decholin—by bitter taste; ether—by smell; magnesium sulphate —by a feeling of heat; sodium cyanide—by respiratory stimulation; histamine—by flushing of face and so on.

Normal values of circulation time

1. **Arm to tongue. Decholin**—5 ml of a 2% decholin is injected quickly into the cubital vein. As soon as the drug reaches the tongue, the patient feels a bitter taste. This is the end point—13 sec. (8–16 sec.).
2. **Arm to lungs. Ether**—5 minims of ether mixed with 5 minims of normal saline is given intravenously (I.V.). Smell of ether in the expired air indicates the end point—6 sec. (4–8 sec.).
3. **Arm to face. Histamine**—0·001 mgm of histamine phosphate per Kg body weight is given I.V. Onset of flushing of the face indicates end point—[The time should be more or less same as decholin time. But it is nearly double. Probably vasodilatation involves longer time.] 24 sec.
4. **Arm to heart.** (Radioactive method)—6·6 sec. (2–14 sec.).
5. **Arm to carotid body.** (Sodium cyanide)—12–15 sec.
6. **Total circulation time.** 25 sec. (12–26 sec.).

Dye injection and radioactive methods are of much wider use. In the radioactive method, radioactive isotopes can be easily detected by isotope counters.

Factors affecting circulation time. (1) Increased cardiac output, (2) exercise, (3) excitement, (4) adrenaline, (5) rise of basal metabolic rate

(B.M.R.), etc., will increase the velocity of blood and reduce circulation time. It is not affected by height, weight, pulse rate or blood pressure provided other factors remain constant. In animals, it is seen that smaller the animal, higher is the heart rate and shorter is the total circulation time.

On the whole, the number of total heart beats for one complete circulation time is same in all species.

The significance of alteration in circulation time is still a debatable matter. It is a poor indicator of vasomotor change, or blood flow or blood volume.

Clinical importance of circulation time

I. **Circulation time is reduced** (i.e., blood flow rapid) in the following conditions: (1) Increased B.M.R., such as (*a*) hyperthyroidism, (*b*) fever. (2) Anaemia (due to increased cardiac output, low viscosity, etc.).

II. **Circulation time is increased** in the following conditions: (1) Heart failure: (*a*) In right-sided failure—Ether time is lengthened. (*b*) In left-sided failure—Decholin *minus* Ether time is lengthened. In bronchial asthma arm to tongue time is normal. But in cardiac asthma it is lengthened. Hence, circulation time is a good guide in differentiating between right and left heart failure, also between cardiac and bronchial asthma. (2) Hypertension. (3) Myxoedema. (4) Polycythaemia vera. (5) Postoperative conditions. (6) Shock. (7) Peripheral failure, etc.

III. Conditions of the peripheral vessels affect circulation time as follows: (1) Circulation time is lengthened—(*a*) if the limb is immersed in cold water, (*b*) by sympathetic stimulation leading to vasoconstriction. (2) It is shortened in: (*a*) elevation of the limb above the heart, (*b*) sympathectomy, (*c*) application of the heat, (*d*) exercise of the limb, etc.

VELOCITY OF BLOOD

Definition. *It is the rate of blood flow through a given vessel.* Blood flow is the volume of blood flowing through a particular vessel in given interval of time. Difference between the velocity and blood flow is that, the flow remaining constant, the velocity is inversely proportional to the cross-sectional area of the blood vessel. But blood flow is directly proportional to the cross-sectional area of the vessel. But velocity in local blood vessel, if constricted, is increased and sometimes it reaches the critical velocity producing sound **(turbulent flow).** Velocity of blood depends upon the following factors:

1. **Lateral pressure and kinetic energy for flow.** In a tube of varying diameter, the lateral pressure varies directly and velocity inversely with the cross-sectional area of the tube. That is where there is any increase of velocity, the lateral pressure will be decreased at that unit area due to conversion of certain amount of potential energy into kinetic energy for flow.

2. **Total cross-sectional area of the vascular bed.** It is inversely proportional to the total cross-sectional area of the vascular bed. As one proceeds to the periphery the total vascular bed enlarges and velocity falls. Hence, **in the aorta** and larger arteries, it is about **0·5–1 metre** per sec., whereas **in the capillaries,** about **0·5–1 mm** per sec. As the capillaries join up to form bigger and bigger veins, the vascular bed shortens and the velocity increases. Near the heart, the total cross-sectional

area of the great veins is nearly double that of the aorta. Hence, velocity is about half.

3. **Pumping action of the heart.** It is directly proportional to the force with which blood is propelled. Other factors remaining constant the velocity will, therefore, depend upon the minute output of the heart. Velocity thus increases during systole and diminishes during diastole.

4. **Peripheral resistance.** Blood flow is inversely proportional to the peripheral resistance. Vascular dilatation will reduce the resistance and increase blood flow. While vasoconstriction will increase the resistance and reduce the blood flow. But the velocity of blood flow is just the reverse. If blood vessel is locally dilated or constricted then the velocity of blood flow is decreased or increased respectively. This principle is very helpful in maintenance of blood flow in the locally constricted blood vessels due to atherosclerotic invasion **(Bernouilli's principle).** Because due to constriction at that area the kinetic energy for blood flow is increased but the lateral pressure is decreased. If the peripheral resistance is increased in general then there is possibility of decreasing the both (velocity and blood flow).

Methods of measurement of velocity of blood

I. **In the capillaries.** The velocity can be measured by noting the rate of progress of a red blood corpuscles under the microscope.

II. **In the larger vessels.** (In animals):

1. *Ludwig's stromuhr* (FIG. 222). With this instrument the amount of blood passing through a vessel per unit time is measured. The velocity is then calculated by dividing the total volume flow (V) with the cross-sectional area of the vessel (πr^2=area of circle).

2. *Differential stromuhr* (Fleischl). This is a more accurate instrument by which the change of velocity during each heart beat can be recorded.

3. *Thermostromuhr* (Rein). The principle is to heat a particular spot on the vessel by high frequency current at a known rate and then the rise of temperature of blood is noted a little down the stream by a thermo-couple. The rise of temperature is inversely proportional to the velocity.

4. *Electromagnetic method.* A more advanced method based on electromagnetic principle has also been devised.

Mean volume flow. Instrument used—*Plethysmograph* (FIG. 223). The total volume of blood passing through an organ or any other part, does not depend upon the velocity of blood flow through the corresponding artery. It depends upon three factors: (1) The total

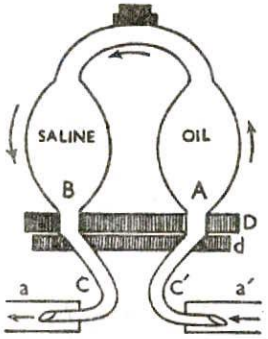


FIG. 222. Ludwig's stromuhr. Two intercommunicating glass bulbs—A & B—fitted to a disc D which can be rotated over another disc, d. To d are fixed two cannulae C and C. C' is inserted into the proximal cut end of the artery and C to the distal end. A contains oil and B contains saline. Blood enters through C', fills up A, pushing out the oil into B. The saline of B in the mean time enters circulation. When B is just filled up with oil (or A is just filled up with blood) the bulbs with the disc D is quickly rotated through 180°, so that B now comes over C' and A over C. Thus the process is repeated and calculation is made from the number of times the bulb, whose capacity is known, was filled with blood in a given period.

cross-sectional area of the vascular bed in the organ. (2) The rate of metabolism in the organ. (3) The degree of vasodilatation or vasoconstriction in the locality. The following figures give the mean volume flow per minute for each 100 gm :

Thyroid—560 ml.
Kidney—150 ml. **Brain**—130 ml.
Liver—150 ml (1/3rd arterial, 2/3rds portal). **Intestine**—70 ml.
Heart (Coronary)—100 ml.

Alteration of volume of a limb is recorded by means of an instrument called *Plethysmograph* (Fig. 223). The cuff of the Sphygmomanometer is applied to the arm and inflated up to a certain pressure which is less than the arterial pressure. The veins are occluded but the arterial blood flow in the limb remains unchanged. The volume of the limb gradually increases as no blood can leave due to occlusion of the veins. The limb is kept in a water-tight glass vessel which is connected with the volume recorder. Changes in the volume of the limb will displace water from the glass vessel and this displacement of water will be recorded in a sensitive electronic apparatus through transducer system.

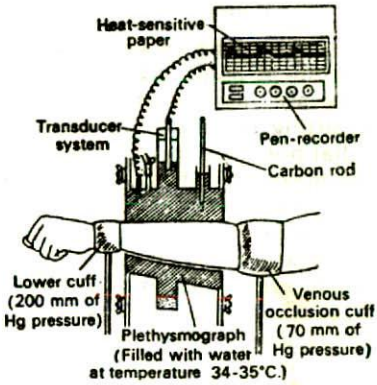


Fig. 223. Use of Plethysmograph for recording of blood flow in the forearm.

RADIAL PULSE

By the term **pulse** is meant *the expansion and elongation of the arterial walls passively produced by the pressure changes* during systole and diastole of ventricles.

Pressure pulse. It is the pressure wave created by the ventricle while ejection of blood into the fully distended aorta and then propagated as a wave through the blood column towards the periphery.

The sudden dilatation of the aorta, to accommodate the output, is transmitted in the form of a wave throughout the arterial system and this wave constitutes the so-called pulse. [In the capillary area no pulsation is normally found. Due to enlargement of the vascular bed pulsatile circulation in the arteries becomes a smooth continuous flow in the capillary bed.]

Velocity of pulse wave. *The velocity of pulse wave is much more rapid* (about 6 times) *than the velocity of blood flow.* Because, the former is conducted through the solid vessel walls, whereas the latter by propelling a liquid. Pulse velocity depends on the degree of elasticity of vessels. By the term *elasticity* of a vessel is meant by the percentage increase in the volume of the artery with each mm of Hg rise in blood pressure. Its relation with pulse velocity is as follows:

$$\text{Elasticity} = \frac{1{\cdot}7}{\text{velocity of pulse wave}}.$$

The elasticity at different ages as found from this formula is as follows: Between the ages of five and six—0·47; between eighteen and twenty—

—0·33; between forty and forty-five—0·24; between seventy and seventy-five—0·18. *Thus elasticity decreases with age, so that in older people the same cardiac output will cause a higher systolic pressure.*

With age, the arteries become less elastic, hence the velocity increases. Blood velocity is inversely proportional to the total cross-sectional area of the vascular bed at any part. In the aorta it is about 1 metre per second, whereas in the capillaries it is about 0·5 to 1 mm per second. The average velocity in metres per second at different ages are as follows: Between the ages of five and six—5·2 metres; between eighteen and twenty—6·2 metres; between forty and forty-five—7·2 metres; between seventy and seventy-five—8·3 metres.

Recording of radial pulse. For clinical purposes, the commonest instrument used, is Dudgeon's Sphygmograph. For more accurate work, elaborate apparatus for optical recording is used. The record of radial pulse is shown in FIG. 224. The upstroke is abrupt and without any secondary wave on it. Near the middle of the downstroke there is a sharp depression called the *dicrotic notch*. This is immediately followed by a small wave, the *dicrotic wave*. These two features are constantly present in a normal pulse tracing. The wave from the beginning of the tracing up to the dicrotic notch is called the *primary wave* or *percussion wave*. This whole wave corresponds to ventricular systole. The rise and fall of pressure in this wave follow the similar pressure changes in the aorta and ventricles (pages 299–301). *The dicrotic notch is due to the sharp fall of pressure caused by the rolling back of aortic blood towards the left ventricle at the beginning of diastole. The dicrotic wave is caused by the return of the same blood column being reflected back by the closed semilunar valves.* Sometimes secondary oscillations are found on the downstroke both above and below the dicrotic wave, being known as the *predicrotic wave* and *postdicrotic wave* respectively. These are due to elastic oscillations of the aorta. The normal pulse is called **catacrotic pulse.** When a secondary wave is found on the upstroke the wave is called *anacrotic wave* and the pulse is called **anacrotic pulse.** When the dicrotic wave becomes so prominent that it can be easily felt with the fingers the pulse is known as **dicrotic pulse.**

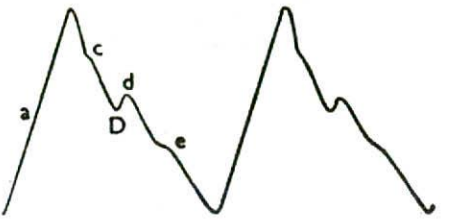


FIG. 224. Tracing of radial pulse. a=primary wave; c=predicrotic wave; d=dicrotic wave; D=dicrotic notch; e=postdicrotic wave.

Significance. A large primary wave is generally due to—(1) a large stroke volume, (2) slow heart rate, (3) low peripheral resistance. A small primary wave is due to—(1) small output, (2) rapid heart rate, (3) high peripheral resistance (i.e., high blood pressure), (4) stiffness of the vessel walls. The downstroke becomes more abrupt in subjects with low diastolic pressure. It becomes more sloping in cases with high blood pressure.

Clinical features of radial pulse. While examining pulse the following features are to be noted: (1) **Rate** means the frequency of pulse per minute. Normally, it corresponds to heart rate. Increased pulse rate is called **tachycardia** and diminished pulse rate is called **bradycardia.**

(2) **Rhythm** indicates whether the beats are equidistant or not. (3) **Volume** means the rise of the pulse wave above the diastolic level. Other factors remaining constant it varies as the stroke volume. (4) **Tension** is the approximate measure of the systolic pressure. It is determined by noting the amount of pressure required to obliterate the pulse wave. *It is examined with three fingers* placed side by side on the radial artery. The proximal finger adjusts the pressure, the middle finger remains stationary and only feels the appearance and disappearance of the pulse wave; while the distal finger applies a constant maximum pressure to stop retrograde pulsation.

Special varieties of pulse. Depending on the variations of the above features, various types of pulse waves are clinically described. The following types are of special interest: (1) **Sinus arrhythmia**—The frequency of the pulse increases during inspiration and falls during expiration. Sometimes it is found in children. It is due to alteration of the vagal tone during respiration. (2) **Water-hammer pulse**—The rise and fall are steep and abrupt without any dicrotic notch or wave. This is typically found in aortic incompetence. (3) **Pulsus alternans**—Here, the pulse is alternately large and small. It is found in serious myocardial damage. (4) **Pulsus paradoxus**—The volume and frequency is more during expiration than during inspiration, i.e., reverse of sinus arrhythmia. (5) **Weak pulse**—A weak pulse at the radial artery generally indicates that the quantity of blood ejected by the left ventricle to the arteries with each beat is less than normal.

From the above discussion, it will be noted that examination of pulse is of great clinical importance. From it, the condition of the heart, of the arteries, the extent of blood pressure, etc., may be known.

ATRIAL FIBRILLATION AND ATRIAL FLUTTER. **Atrial fibrillation.** It is a clinical condition in which normal co-ordinate contraction of the atrium is replaced by inco-ordinate contraction of the individual fibres characterised by irregularly irregular pulse. The incomplete contraction of the atrial muscle is at the rate of 400 to 600 per minute. Only a part of the atrial impulses pass through the A. V. bundle to the ventricle due to long refractory period of the conducting tissue. So the ventricular rate is not so fast. Again, some of the ventricular beats are so weak that they are not transmitted to the radial pulse. The apex beat therefore does not correspond with the pulse rate. This is called the **pulse deficit.** Atrial fibrillation is frequently seen in mitral stenosis, thyrotoxicosis, myocardial disease, etc. The underlying process in the production of atrial fibrillation was explained by 'circus movement' theory but the recent evidence goes against this theory.

Atrial flutter. It is a clinical condition in which there is marked acceleration of the co-ordinate contraction of the atria. The atria contract at the rate of 180 to 360 per minute. The usual rate is about 300 per minute. The ventricular rate is not so fast as all the impulses from the atria are not transmitted to the ventricles due to longer refractory period of the junctional tissues. Atrial flutter is also seen in mitral stenosis, myocardial disease, etc. The underlying process in the production of atrial flutter was explained by the 'circus movement' theory but the recent evidence goes against this theory.

REGIONAL CIRCULATION

Circulation in a particular region or organ is directly proportional to the degree of local activity. It is adjusted on two lines: (1) by regulating the general circulation and (2) by adjusting the local blood vessels. Generally, vasodilatation of an active part is accompanied with vasoconstriction of other inactive parts. In this way, blood is shifted from the inactive to the active regions without any fall of general blood pressure.

Methods of study

1. **Plethysmography.** A *Plethysmograph* or an *Oncometer* is an airtight or watertight vessel, connected with a suitable recording instrument. An organ (heart, spleen, liver, kidney, etc., in animals) or a limb (in human beings) is introduced into the vessel. The volume changes of the part cause corresponding pressure changes in the instrument which are recorded. Increased volume is caused by increased blood flow due to vasodilatation. Decreased volume is due to vasoconstriction. The size and shape of the oncometer differ according to the part or the organ whose volume changes are to be measured. Cardiometer (page 255) is a special type of oncometer.

2. **Venous occlusion plethysmography** (*vide* FIG. 223). The principle is same as above, with the difference that, the venous outflow is stopped by occluding the veins (by raising the pressure on veins to about 50–70 mm of Hg, viz., a little below the diastolic pressure of the subject) for short periods. Rise of volume is due to accumulation of arterial blood. From these data the minute flow can be roughly estimated.

3. **By noting skin temperature.** Done by a thermo-couple connected to a galvanometer. Fall of temperature shows less blood flow (vasoconstriction). Rise of temperature shows more blood flow (vasodilatation).

Through the above methods, a rough idea about the circulatory status of a particular organ can be studied. But for quantitative evaluation of different regional flows, the following methods are generally followed: (1) Electromagnetic flowmeter. (2) Rotameter. (3) Bubble flowmeter. (4) Thermostromuhr. (5) Orificemeter. (6) Nitrous oxide method. (7) Isotope clearance methods.

The following regional circulations are of special physiological importance: (1) **Coronary circulation.** (2) **Cerebral circulation.** (3) **Pulmonary circulation.** (4) **Hepatic circulation.** (5) **Splenic circulation.** (6) **Renal circulation.** (7) **Capillary circulation.** (8) **Cutaneous circulation.** (9) **Skeletal muscle circulation.** They are briefly described below:

1. CORONARY CIRCULATION

Anatomical considerations. Blood supply to the heart is mainly carried out by the two coronary vessels, e.g., right and left coronary arteries arising from the sinuses behind the cusps of the aortic valve at the root of the aorta. Both the arteries are patent throughout the cardiac cycle as the eddy currents keep the cusps of the valve away from the orifices of the arteries. The left coronary artery gives off the anterior descending and the left circumflex branch. The latter runs along the atrioventricular groove to the left and proceeds downwards as the posterior descending branch. The anterior descending branch runs downwards up to the apex. The right coronary artery gives off several descending branches on both ventricles (FIGS. 225 & 226). Predominance of the coronary artery supply is seen in about 50% of human heart by the right coronary artery; and in about 20% of human heart by the left coronary artery and in about 30% of cases by both coronary arteries. According to Schlesinger the last group

in which the nature of supply is not made predominantly by either right or left coronary artery is least vulnerable to the cardiovascular disorder. The right and left coronary arteries break up into a large number of capillaries.

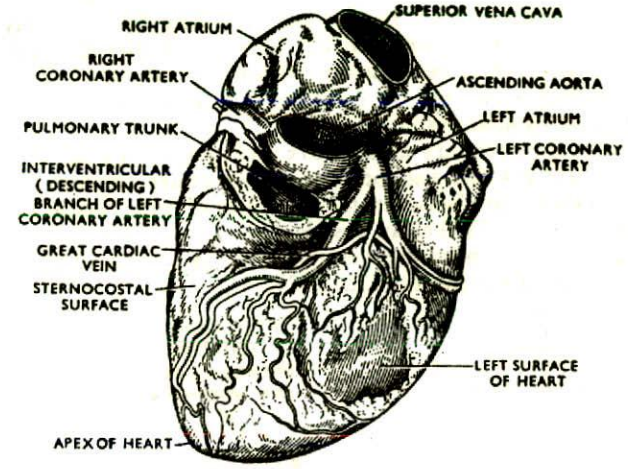


FIG. 225. The heart showing the disposition of the left coronary artery and its branches (left surface).

The venous blood from the myocardium is chiefly returned through two systems: **superficial venous system** and **deep venous system.**

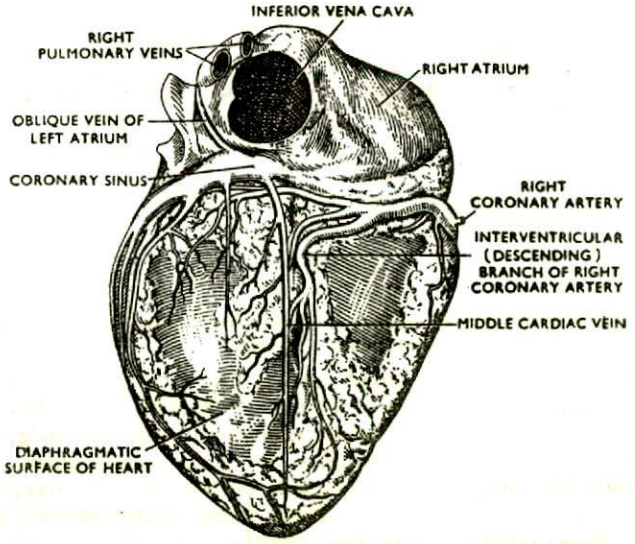


FIG. 226. The heart showing the disposition of the right coronary artery, its branches and coronary sinus (diaphragmatic surface).

The *superficial venous system* lies beneath the epicardium and consists of (1) the *coronary sinus*, draining mostly the blood from the left coronary artery, partly from the right coronary artery, and ends ultimately in the posterior part of the right atrium; (2) the *great cardiac vein*, draining blood from the left heart, ends in the coronary sinus; (3) the *anterior cardiac veins* which are generally 2 to 3 in number, draining blood mostly from the right heart and partly from the left heart, end directly into the right atrium. The *deep venous system* arises within the substance of the myocardium and ends directly into the cavity of the right heart by the Thebesian, luminal and sinusoidal vessels.

Normally, the coronary arteries are end arteries though the functional anastomoses are present and become active under unphysiological state. These anastomoses are between (*a*) branches of one coronary artery with that of the other, (*b*) Thebesian vessels and cavity of the heart, (*c*) arterioluminal and arteriosinusoidal vessels with the cavity of the heart and (*d*) extracardiac anastomoses (FIG. 227).

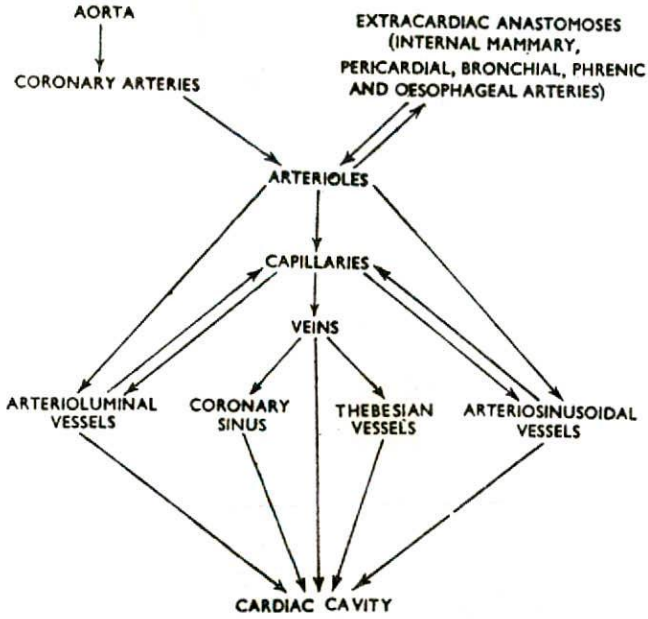


FIG. 227. Schematic representation of coronary circulation along with anastomotic channels.

Heart muscle has a rich blood supply. The total capillary length per cu. mm of cardiac tissue, is about 11 metres (Rabbit). It is known that each fibre in the adult human heart receives one capillary twig, whereas in foetal life one capillary twig supplies four to six muscle fibres.

Methods of study. The coronary blood flow and the oxygen usage of the heart can be studied by the **Pitot tube, orificemeter, electromagnetic flowmeter, thermostromuhr** and also by the use of nitrous oxide gas. **Nitrous oxide method** (Fick principle) gives almost accurate values. The subject inhales a mixture of 15% of nitrous oxide and

air for 10 minutes. The amount of nitrous oxide taken up per minute is determined. Several samples of blood are taken from an artery and from a catheter introduced into the mouth of the coronary sinus at intervals during inhalation of nitrous oxide by the subject and their nitrous oxide content is determined. The arteriovenous difference of nitrous oxide is then calculated. Coronary inflow is then determined with the help of Fick principle:

$$\frac{\text{Quantity of nitrous oxide inhaled per minute}}{\text{Difference of nitrous oxide content of arterial and venous blood}}$$

Normal values. (1) During rest for each 100 gm of the left ventricle, the left coronary inflow varies from 65 to 85 ml per minute. The arteriovenous O_2 difference is very high and is about 10 to 15 ml per 100 ml. So the extraction of O_2 by the cardiac muscle is very high. (2) During heavy exercise minute volume increases about ten times, and coronary inflow also rises tenfolds, i.e., about 2 litres. The O_2 usage of the heart is very high. The blood in the anterior cardiac veins or in the coronary sinus shows 20% saturation with O_2. During exercise, heart consumes about 250 ml of O_2 per minute (same as the resting O_2 consumption of the whole body). The arteriovenous O_2 difference of heart is about 10–15% (skeletal muscle—5–6%). This is equivalent to a minute flow of about 2 litres of blood through the coronary vessels.

Variations of coronary inflow during different phases of cardiac cycle. Ventricular action affects coronary circulation in two ways: (*a*) by altering the aortic pressure, (*b*) by exerting a variable degree of compression on the coronary vessels. The following phases are seen (Fig. 228).

Coronary Inflow

1. **Left coronary artery.** *During isometric contraction phase*, coronary inflow sharply falls and reaches minimum and even falls below the zero level due to backflow. Because, the aortic pressure is at minimum and the compression on the coronary vessels is maximum.

During maximum ejection phase, coronary inflow rises rapidly due to sudden rise of aortic pressure and reaches its maximum when the aortic pressure is maximum.

During reduced ejection phase, the coronary inflow again falls, because, the aortic pressure is falling and the compression is continued.

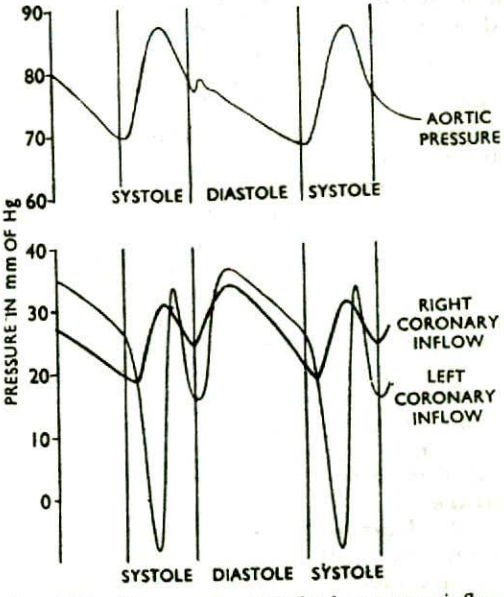


Fig. 228. Diagram showing phasic coronary inflow.

During isometric relaxation phase, the coronary inflow sharply rises, because, the aortic pressure is fairly high and the compression is minimum.

Maximum coronary filling takes place during this phase due to fall of coronary vascular resistance.

During rapid ventricular filling phase, the coronary inflow continues to rise but slowly, because, the relaxation of the cardiac musculature continues and the vessels open up further.

In the later part of diastole, the coronary inflow slowly diminishes, because, the aortic pressure is falling and the coronary vessels are stretched due to filling of heart and the consequent elongation of cardiac muscles.

2. **Right coronary artery.** *During isometric contraction phase,* the coronary inflow sharply falls and rapidly rises again during the maximum ejection phase and falls during the reduced ejection phase. In the isometric relaxation phase the coronary inflow rises but not so steeply like the left coronary inflow.

So greater coronary inflow takes place in diastole than systole due to less compression of the coronary vessels during relaxation of the cardiac muscle and diminution of intramural tension. The left coronary inflow during systole is affected much as the pressure differential between aorta and left ventricle becomes −1 mm of Hg. But the right coronary inflow during systole is not so affected as such pressure differential is 95 mm of Hg.

In the coronary sinus the **outflow of blood** gradually rises from the isometric contraction phase and reaches its peak during protodiastolic phase and then gradually falls.

Factors influencing coronary circulation. The amount of blood passing through the coronary vessels is directly proportional to the work done by the heart. Blood flow can be adjusted on two principles: (1) By adjusting the lumen of the coronary vessels. (2) By adjusting the mean aortic pressure. The aortic pressure acts as the driving force. The lumen of the vessels may be altered in two ways: (*a*) through the vasomotor centre (directly or reflexly) and (*b*) by directly acting on the vessels. The following factors modify coronary circulation, through one or both the above principles:

1. **Mean aortic pressure.** It is the chief motive force for driving blood into the coronary vessels. Any alteration of aortic pressure will, therefore, cause parallel changes in coronary circulation. In a denervated heart-lung preparation of dog, it is observed that a rise of blood pressure from 50 to 130 mm of Hg increases the coronary inflow from 20 to 250 ml per minute. In partial clamping of the aorta or in coarctation of the aorta, the central aortic pressure is increased and the coronary flow is also increased. But if this state is kept for some time then the blood flow is not maintained at the same degree. It has been observed that if the aorta remains in a state of partial occlusion, then the work load of the left heart is increased as the peripheral resistance is increased. This increased work load of the heart ultimately becomes the cause of the **congestive heart failure.**

2. **Role of cardiac output.** Obviously, the coronary inflow is directly proportional to the cardiac output. Increased output raises coronary inflow in two ways: (*a*) By raising the aortic pressure. (*b*) By reflex inhibition of the vagal vasoconstrictor tone (Anrep).

3. **Metabolic factors.** With the increased metabolism of heart, the O_2 requirement is increased and the circulation is greatly increased. There is a causal relationship between the myocardial metabolic activity,

oxygen consumption and coronary blood flow. In the normal heart blood oxygen content of coronary sinus is low under a variety of physiological conditions which supports the view of metabolic regulation of coronary blood flow (CBF) by **reactive hyperaemia. Adenine nucleotide** may be responsible for this reactive hyperaemia.

4. **CO_2 and O_2.** It has been observed by Katz and also by others that if O_2 requirement of the heart is increased then the coronary circulation is increased. Furthermore if the O_2 supply to the heart muscle is decreased then the coronary flow is increased. But if the O_2 is supplied more than it is required, then the coronary circulation is decreased. Similarly, CO_2 stimulates the coronary flow. During **asphyxia** or inhalation of CO_2, when CO_2 concentration in the blood is increased, coronary flow is also increased at the first stage in order to maintain the total O_2 requirement of the cardiac muscle. If this state prevails further, the coronary blood flow is decreased abruptly and heart stops in diastole. Similarly in **hypoxia** when the O_2 saturation in the arterial blood of normal haematocrit is gradually decreased then the coronary flow is also gradually increased only to meet the adequate requirement of O_2 of the cardiac muscle.

5. **Effect of ions.** It has been observed by Katz that K^+ in low concentration dilates the coronary vessel, whereas K^+ in higher concentration constricts. Calcium in therapeutic doses increases the flow and O_2 consumption of the cardiac muscle.

6. **Polypeptides. Bradykinin** has been claimed to have vasodilating effect on coronary vessels but its normal physiological role is not yet fully known. **Angiotensin II** is an active octapeptide which causes arteriolar constriction in the skin, kidney, brain and also in coronary vessels.

7. **Adenine nucleotides.** Adenine nucleotides have been known to be potent coronary vasodilators. ATP and ADP are equally potent vasodilators. AMP is a bit weaker vasodilator than those of ATP and ADP. ATP is not permeable to cell membrane, but adenosine can easily pass through the cell membrane (Berne, 1963). Berne has described that adenosine, the breakdown product of ATP during **hypoxia,** permeates through the cell membrane to dilate the coronary vessels. Possible metabolic regulation of coronary blood flow by adenosine has been presented schematically by Berne (1963) (Fig. 229).

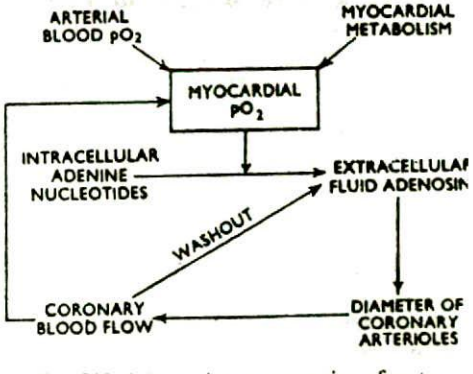


Fig. 229. Schematic representation of metabolic regulation of the coronary blood flow (*after Berne*, 1963).

8. **Cardiac sympathetic and parasympathetic nerves.** Stimulation of cardiac sympathetic fibres from the stellate ganglion or the ganglion itself, produces increased coronary inflow. This is mainly due to the influence of the cardiac sympathetic on coronary blood vessels resulting from the release of norepinephrine which cause vasodilatation of the coronary vessels and increases the coronary inflow

It has been observed under different experimental conditions that stimulation of sympathetic cardiac nerves causes increase of coronary flow. But the mechanism by which the coronary flow is increased is not yet settled. From the observations of increased flow following intracoronary administration of adrenaline or noradrenaline it is claimed that liberation of noradrenaline from the postganglionic sympathetic nerve ending following stimulation is the probable cause. Gregg (1963) has described that *acute metabolic changes* of the cardiac muscle due to increase of cardiac work following sympathetic stimulation is possibly the cause of increased coronary flow. Furthermore, the mediator released at sympathetic postganglionic endings of the cardiac muscle following stimulation increases the O_2 consumption and this state causes the cardiac muscle hypoxia, a condition favourable for increasing blood flow through reactive hyperaemia.

Regarding the role of vagus on coronary flow there was conflicting opinion. But recent studies claim that the vagal stimulation produces vasodilatation of the coronary vessels through liberation of acetylcholine. It is quite unlikely that the vagus will be coronary vasoconstrictor since its chemical mediator acetylcholine is a coronary vasodilator.

9. **Heart rate.** When the heart rate is increased, minute cardiac output, aortic blood pressure may increase but the **stroke volume** decreases. The phasic coronary inflow and O_2 consumption per beat decrease, but minute coronary flow and O_2 consumption per minute are increased. With the increase of heart rate, O_2 requirement of the heart muscle is increased and is maintained normally through increase of minute flow. It has been observed that with the increase of heart rate the extravascular resistance is increased, but the intravascular resistance is actually decreased causing a decrease of resistance, hence increase of minute flow.

10. **Hormones.** (*a*) **Thyroid**—In thyrotoxicosis metabolism is increased along with increased coronary inflow and O_2 consumption per minute. In hypothyroidism the flow is decreased which is possibly related with the altered metabolism of the cardiac muscle.

(*b*) **Adrenaline and noradrenaline**—These cause increased coronary inflow along with increased O_2 consumption per minute. These produce the relaxation of the coronary vessels by acting on the β-receptor of the vessel. **Nicotine** also increases the coronary flow through the liberation of noradrenaline. Relaxation of coronary blood vessels is prohibited by β-adrenergic blockers.

(*c*) **Pitressin**—It causes increased coronary resistance and diminution of coronary inflow. In the open chest or closed chest dog, pitressin causes decrease of coronary flow all throughout the cardiac cycle in the presence of an increased central coronary pressure. This decreased flow is presumably due to direct vasoconstrictor effect on the coronary vascular bed. This vasoconstrictor effect is not due to metabolic effect or due to increase of intracellular and extracellular K^+ values. It possibly constricts the vessels at arteriolar level.

(*d*) **Acetylcholine**—It increases coronary inflow due to dilatation of the coronary vessels. This increased flow response is completely abolished by atropine. It increases the mean diameter of the coronary vessels.

11. **Temperature.** With the rise of body temperature, the metabolism is increased and for the maintenance of normal O_2 need the coronary circulation is increased. But with the fall of body temperature, as in

the case of **hypothermia,** the coronary circulation is greatly decreased along with the decreased metabolic need of the cardiac muscle. The coronary vessels are dilated greatly at that state. With the increase of body temperature by fever or by external application of heat (hyperthermia), though the heart rate, cardiac output and work of the heart are increased, yet coronary flow possibly remains unchanged. In heart-lung preparation if the myocardial temperature is increased, coronary flow is also increased but if the temperature of blood is increased, then the flow remains unaltered.

12. **Muscular exercise and excitement.** As mentioned above, coronary inflow is adjusted according to the work done by heart. During *heavy exercise* the inflow rises about ten times. This is due to the fact that almost all the factors which increase coronary inflow come into action during muscular exercise, viz., O_2 lack, CO_2 excess, increased H-ion concentration, metabolites, increased temperature, adrenaline secretion, raised blood pressure, etc. During *excitement*, as the heart rate is increased, the coronary blood flow is also increased greatly, although the diastolic phase is decreased.

13. **Anaemia.** In anaemia, the coronary flow is increased sharply in order to maintain the normal O_2 need of the cardiac muscle, because the O_2 carrying capacity of the blood is decreased under such state. The increase in the coronary flow is related partly to the decreased viscosity of blood and mostly to the active vasodilatation (*Reactive hyperaemia*) resulting from (*i*) **anaemic hypoxia** and (*ii*) **metabolic hypoxia** due to compensatory increased heart rate.

14. **Intraventricular pressure.** The increase of intraventricular pressure also alters the coronary flow. The increase of the right ventricular pressure (due to *mitral stenosis*, *emphysema*, *atelectasis*, etc.) affects coronary flow greatly as this pressure is reflected in the *coronary venous bed* of the right ventricle. In case of the left ventricle, the coronary flow through this side is initially increased with the rise of intraventricular pressure (due to *coarctation of the aorta* or *increase of peripheral resistance* by any means). Under such state the left ventricular work load is increased greatly and ultimately the heart muscle is hypertrophied and coronary flow is gradually decreased. Ultimate fate of the heart is the degeneration of cardiac muscle fibres leading to **congestive heart failure.**

15. **Transfusion.** During transfusion, ventricular load is increased due to rapid venous return; and the systolic- and diastolic-heart size, ventricular stroke volume and work and also arterial blood pressure are all increased. Under such state the heart rate is decreased causing greater increase of stroke volume, diastolic pause and thus the coronary flow per beat and per minute is increased.

16. **Extravascular pressure.** This is an important determinant of the coronary flow as the coronary vascular resistance is increased due to rhythmical compression of the myocardial vessels during contraction.

17. **Viscerocardiac reflex.** The coronary flow is markedly altered during visceral distention and it is often encountered in a patient with *ischaemic heart disease*. Anginal pain, following a meal in such cardiac patient, is the consequence of decreased coronary flow. The reflex pathways for the manifestation of this pain following visceral distention are possibly lying in the vagi and the sympathetic. Thorough works in this line are required.

Circulatory status of the cardiac muscle under certain diseased conditions

1. **Aortic stenosis.** In aortic stenosis, there is initially increase of coronary flow along with increase of coronary perfusion. With the stenosis of the aorta, the intraventricular pressure of the left ventricle is increased and the left heart has to work against increased resistance. Consequently there is hypertrophy of the left ventricle with decrease of coronary flow if the stenosis is maintained for some time.

2. **Pulmonary hypertension.** Pulmonary hypertension may be the cause of mitral stenosis, emphysema, atelectasis, pneumonia, etc. Under such state the right ventricular pressure is greatly increased and this increase of intraventricular pressure causes decrease of coronary flow of the right heart because the arteriovenous pressure difference is greatly decreased. Pulmonary hypertension may be associated with right ventricular hypertrophy and ultimately leading to *right heart failure*.

3. **Aortic insufficiency.** Patients suffering with aortic insufficiency are always associated with *anginal pain*. This anginal pain is due to coronary insufficiency. This coronary insufficiency is mostly due to decrease of aortic pressure and also of central coronary diastolic pressure.

4. **Mitral stenosis.** In mitral stenosis, an obstruction is exerted during flow of blood from left atrium to left ventricle. If this state is prolonged then pulmonary hypertension may happen and coronary flow of the right heart is greatly affected.

5. **Aortic coarctation.** It is the condition when a vessel remains constricted or narrowed and thereby the blood flow through the vessel is decreased. In coarctation of the thoracic aorta, work load of the heart is increased as the heart has to work against the resistance. The venous return by way of the inferior vena cava may be decreased but the total venous return may be unaffected only by opening up of other branches of the aorta. Thus in case of mild form of coarctation, the cardiac output and at the same time coronary flow may be maintained but if the constriction is in severe form and the blood flow through the aorta is severely affected then the venous return, cardiac output and the coronary flow are greatly decreased. As the heart has to work against increased resistance, there is possibility of left ventricular hypertrophy along with decreased coronary flow. Ultimate fate of it is the *congestive heart failure*.

6. **Hypertensive cardiovascular disease.** In essential hypertension having no organic changes in the heart and blood vessels, the mean coronary flow remains unaltered although the systemic pressure remains elevated. But in hypertension having coronary *atherosclerosis* or arteriosclerosis, the elastic behaviour of the coronary vessels are altered, the flow may be affected greatly, although the systemic pressure remains at higher level.

7. **Ischaemic heart disease.** Ischaemic heart disease is the condition, when cardiac muscle suffers from coronary insufficiency. This coronary insufficiency is due to major cause of (*i*) *sclerosis of the coronary vessels* or (*ii*) *coronary occlusion by thrombosis*. In both the cases if these are not so severe then the mean coronary flow is maintained through the development of anastomosing channels in between the affected vessels and the unaffected vessels. In such case the affected area (*ischaemic area*) gets blood supply through backflow. If the subject maintains a normal well-adjusted life and the heart is not given any unusual work load then the management or rehabilitation of this patient is possible through the newly adjusted circulatory machineries. But further cardiac attack or any increased work load of the heart becomes an unmanageable episode of such patient because readjustment becomes impossible.

Coronary spasms and intercoronary reflexes. Coronary spasms have been described to be the major cause of acute myocardial infarction. It is of general opinion that occlusion of one branch of coronary vessels by thrombus or an *embolus* may cause widespread spasm in the other arteries causing massive damage of the cardiac muscle and fatal ventricular fibrillation may occur. Le Roy and Snider (1941) have claimed that the sudden death of a patient following myocardial infarction is due to widespread reflex vasoconstriction of the other coronary vessels, whose primary stimulus is the infarct; the afferent pathway is the cardiosensory nerves and the efferent pathway is the vagus. Hall, Manning and others favour these concepts of intercoronary reflex because ventricular fibrillation and death due to acute coronary occlusion may be averted if the subjects are under deep anaesthesia or cholinergic blockade particularly of atropine. But the role of vagus in precipitating this reflex vasoconstriction is still under doubt because intercoronary administration of acetylcholine, the neurohumour of vagus, always causes vasodilatation. So this part should require further elucidation.

Pathological physiology of angina pectoris and acute myocardial infarction. Ischaemia is the cause of pain of angina pectoris and of acute myocardial infarction. Angina pectoris is thus a symptom of cardiac ischaemia but not a disease. The anginal pain is often associated with disproportionate blood supply according to myocardial

requirement. In ischaemic heart disease the patient often complains this pain following a heavy meal or a physical exertion or an excitement. The pain is due to accumulation of metabolites produced during coronary ischaemia. The metabolites stimulate the nerve endings. But the actual stimulus at the nerve endings that may cause the pain is not yet known. Sir Thomas Lewis has described it the **P factor** which has some characteristics with lactic acid.

Predisposing cause of myocardial infarction is the coronary obstruction due to atherosclerosis. The obstruction may be due to gradual shortening of the vessels itself by the deposition of lipid in the intima or by the locally formed thrombus. If the ischaemia is prolonged then it may lead to irreversible changes of necrosis.

2. CEREBRAL CIRCULATION

Anatomical considerations. Blood enters the cranium through four vessels: two internal carotid and two vertebral arteries. The last two combine to form the basilar artery which divides into two posterior cerebral arteries. Each internal carotid artery divides into two branches: the middle and anterior cerebral arteries. Intercommunicating branches unite the six arteries on two sides forming the **circle of Willis** (FIG. 230). These vessels supply the different parts of brain.

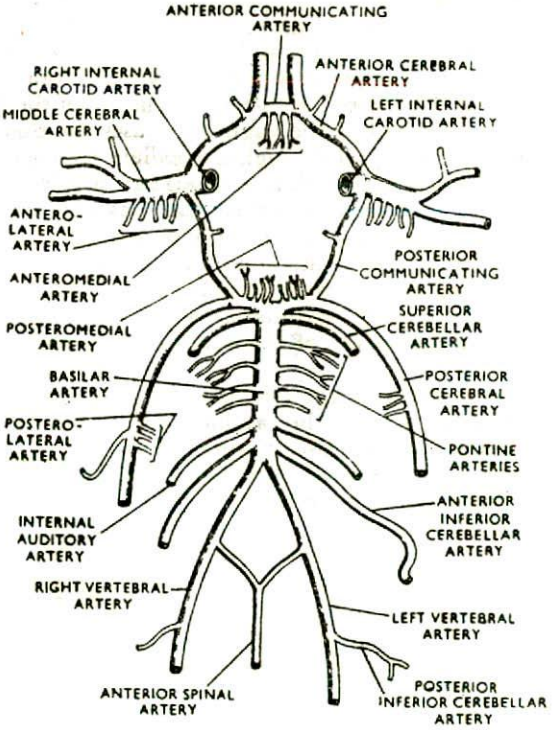


FIG. 230. Arrangement of cerebral blood vessels and formation of the circle of Willis (diagrammatic).

Brain has a rich blood supply. The grey matter is more vascular than the white matter. The total capillary length per cu. mm of the grey and white matter is about 1 metre and 200 mm respectively. The cerebral

vessels are not strictly end arteries. They freely anastomose. The free anastomosis in the circle of Willis makes an adequate distribution of blood to the different parts of the brain tissue and this is the only contributory help during emergency. A red cell from one lobe can easily pass to another lobe.

Venous blood drains into large cerebral sinuses, e.g., the superior sagittal, inferior sagittal, cavernous, straight, etc., all of which ultimately unite to form the two transverse sinuses—which become continuous with the two internal jugular veins.

Method of study: Nitrous oxide method—Fick principle. The subject inhales a mixture of air and 15% of N_2O. Blood samples are collected from a peripheral artery and from the jugular vein at frequent intervals during the period when the subject inhales the mixture. N_2O content of the arterial and venous blood is determined. Cerebral blood flow per minute is determined from the arteriovenous difference of N_2O and the partition coefficient for N_2O between blood and brain. Results are recorded in millilitre per 100 gm of brain tissue per minute.

Vasomotor supply. The sympathetic carries vasoconstrictor fibres. Their stimulation causes an average reduction in diameter between 7–8%. The dilator fibres pass in the vagus and the VIIth nerve. The vagus carries the afferent fibres and the great superficial petrosal branch of the facial nerve carries the efferent fibres. Hence, stimulation of the VIIth nerve or that of the central cut end of the vagus increases the diameter to about 22%. Since, the flow of liquid through a capillary tube is directly proportional to the *fourth power* of its radius, a dilatation of 22% will increase the flow by about 150%. There is evidence that vascularity of a particular part of brain increases during the activity of that part and may be associated with vasoconstriction of the other parts of brain.

Normal values of cerebral circulation. (1) The *average blood flow* of normal subjects in resting condition is 54 ml per 100 gm of brain tissue per minute. Taking the weight of brain as 1,400 gm total cerebral blood flow is 750 ml.

(2) *Blood pressure* in the large cerebral arteries is 100 mm of Hg systolic and 65 mm of Hg diastolic. In the capillaries, it is about 13 mm of Hg. It rises during inspiration and falls during expiration. But forced expiratory efforts, specially with closed glottis, raise the pressure by 30–50 mm of Hg.

(3) The *total oxygen consumption* of the brain is 50 ml per minute. Hence, the rate of oxygen consumption is fairly high. Arteriovenous O_2 difference is 6·2 ml % (arterial—19 ml %, jugular—12·8 ml %).

(4) Respiratory quotient (R. Q.) is unity, showing that carbohydrates are mainly used (*probably only as galactose*).

(5) *Cranial circulation time* (carotid to jugular) is 3 seconds (Radioactive method).

The capillaries of the cerebral vessels, choroid plexus, etc., are less permeable. As a result of this less permeable crystalloid

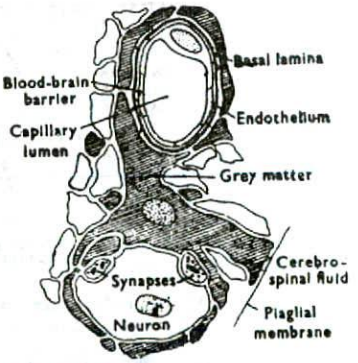


FIG. 231. Diagrammatic representation of protoplasmic astrocyte showing blood-brain barrier.

elements of the blood cannot pass into the cerebral tissue spaces. This is called **blood-brain barrier** (FIG. 231).

Regulation of cerebral circulation. Cranium being a rigid box, the amount of blood in it, at any moment, cannot rise to any considerable degree. Only slight rise may take place by compressing the veins and displacing a little cerebrospinal fluid (CSF). Hence, blood supply to the brain can only be increased by raising the velocity of blood flow through it. Broadly speaking, cerebral blood vessels have got no well-organised vasomotor control and the circulation can be maintained (*i*) by adjusting the general blood pressure through the sino-aortic mechanism, (*ii*) by regulating the lumen of the cerebral vessels.

Existence of autoregulation of cerebral blood flow. Autoregulation in cerebral blood flow was first described by Fog in 1934. However, Sagawa and Guyton (1961) on the basis of their pressure/flow studies of cerebral circulation in dogs described the absence of such autoregulation. But Harper (1963) has observed autoregulation in normocapnoic dogs. He described that in dogs having arterial CO_2 tension of about 40 mm of Hg, the pressure/flow relationship is absent after pressure head of 80 mm of Hg. But in hypercapnoic animal this autoregulation is absent and cortical blood flow is increased with increase of pressure, i.e., the pressure/flow relationship is linear. Thus it seems that in normal individual the autoregulation of cerebral blood flow as if subserves a homeostatic function. As the increased CO_2 tension of the blood abolishes the autoregulatory mechanism, it is quite likely that two factors may play. One is the myogenic response of smooth muscle which is effective with the increase of pressure and the other, the metabolic factors involving the tissue tensions of the respiratory gases, to which the cerebral arterioles are highly sensitive.

There is phenomenon which has interested physiologists for a long time is the cause of **sleep.** This has been discussed by many as the *ischaemia of the brain.* But Mangold and Sokoloff (1955) have been able to show no changes in the cerebral O_2 consumption along with circulation during sleep. Sometimes they have observed the increase of cerebral blood flow instead.

The cerebral circulation is higher in the youngest group particularly in the *first decade* but falls rapidly with the advent of puberty. This fall is possibly due to sex hormones (liberated during this age) which have got some constrictor effects on the cerebral blood vessels (Gordon, 1956).

Factors controlling cerebral circulation

There are so many factors that may control the cerebral circulation. The main factors that generally operate are the **driving force,** i.e., the difference between the mean arterial blood pressure (MABP) and the internal jugular pressure ((IJP), and the cerebrovascular resistance (CVR). So the cerebral blood flow (CBF) is directly proportional to driving force (the difference between the mean arterial blood pressure and the internal jugular pressure) and inversely proportional to the cerebrovascular resistance, i.e.,

$$\text{CBF} = \text{K} \frac{\text{driving force}}{\text{cerebrovascular resistance}},$$

Driving force or arterial pressure head. This factor depends upon the cardiac output and peripheral resistance. The arterial blood

pressure is the sole determinant of driving force and internal jugular pressure has little role under normal condition. But in case of positive *g*, this internal jugular pressure plays an immense role. In human beings with centrifugal accelerative stress, the cerebral circulation is still maintained for several seconds though the arterial blood pressure at head level is practically nil. This maintenance of pressure under such state is due to simultaneous fall of pressure in the internal jugular vein.

In normal individual having well-organised homeostatic control, any alteration of the systemic pressure will have practically no effect on the cerebral blood flow but if the homeostatic control fails, then hazard may occur. Sometimes cerebral haemorrhage or senselessness occurs possibly due to absence of this homeostatic control. Kety (1958) has described that there is a correlation between the cerebral blood flow and arterial blood pressure only at a very low pressure head, where the pressure level may be considered to be the limiting factor. So long the pressure head remains above a certain minimal value, i.e., about 70 mm of Hg, the pressure no longer exerts a control on the circulation and the correlation disappears. Intrinsic factors play only when pressure drops further and the flow is maintained by lowering the cerebrovascular resistance.

Cerebrovascular resistance. The cerebrovascular resistance depends upon the following factors:

1. **Intracranial pressure.** Rise of intracranial pressure (brain tumour, meningitis, etc.) reduces the blood flow, by mechanically compressing the cerebral capillaries and veins. Cerebrovascular resistance has got mostly a linear relationship with intracranial pressure. The cerebral blood flow has got negative correlation with increased intracranial pressure, however this correlation only comes into play until pressure exceeds 500 mm of H_2O.
2. **Viscosity of blood.** In *Anaemia* the viscosity of blood is decreased due to fall of *haematocrit value* and hence the increase of flow. But in case of *polycythaemia vera* the flow is decreased as the viscosity is higher due to raised haematocrit value.
3. **Diameter of the cerebral blood vessels.** Cerebral vascular resistance has got inverse relationship with the diameter of the blood vessels. The diameter of the cerebral blood vessels are altered under the following factors, viz., neurogenic factors, CO_2 and O_2 level in blood, neurohormones, etc.

There is intrinsic nerve supply that possibly control the state of constriction and dilatation of the cerebral blood vessels. These nerves originate from the plexus of nerves which surround the carotid and vertebral plexus as they enter the brain. Fibres originating from the cervical sympathetic chains are constrictor, whereas the greater superficial petrosal nerve originated in the medulla is vasodilator. But the relative roles of these two nerves are not clear. Because bilateral blocking of the stellate ganglia has got little effect on CBF and CVR. Similarly the role of vasodilator fibres on the cerebral blood flow is not known.

4. **Carbon dioxide tension.** Increased CO_2 tension raises the flow. It causes cerebral vasodilatation by local action but general vasoconstriction through vasomotor centre (V.M.C.) and sino-aortic reflexes. Cerebral blood flow increases by 75% after inhalation of 5–6% of CO_2.
5. **O_2 lack.** It increases cerebral circulation by local vasodilatation

as well as by general vasoconstriction (V.M.C., sino-aortic reflex, etc.) and thus raises blood pressure.

6. **Excess O_2.** It causes reduction of cerebral blood flow provided the concomitant hypocapnia is prevented.

7. **Adrenaline and Noradrenaline.** The *adrenaline* increases the cerebral blood flow through vasodilatation but the *noradrenaline* decreases the cerebral blood flow through profound vasoconstriction.

8. There are other drugs which may modify the cerebral circulation. **Ethyl alcohol** in therapeutic doses has got no significant effect but in severe alcoholic intoxication it may increase the cerebral blood flow. This effect is possibly due to effect of accumulated CO_2 in the blood.

Papaverine is a good cerebral vasodilator.

Xanthine group of drugs have got some vasoconstrictor effects. **Aminophylline** in therapeutic dosage produces vasoconstriction. **Caffeine** has got similar effects. **Nicotinic acid** injected intravenously, though produces facial vasodilatation but does not produce any cerebral vasodilatation.

Though **histamine** produces cerebral vasodilatation yet it is not so effective as it simultaneously produces systemic vasodilatation causing fall of systemic blood pressure.

Clinical conditions. In essential *hypertension*, the cerebral circulation remains unaltered though the vascular resistance is greatly increased. But in case of **cerebral arteriosclerosis,** the cerebral blood flow is diminished due to increased cerebrovascular resistance and loss of elasticity of the blood vessel wall.

3. PULMONARY CIRCULATION

Anatomy of circulation. Blood enters lungs through two sources: pulmonary artery and bronchial arteries. The cross-sectional area of the pulmonary artery is same as that of the aorta, but it is more elastic and distensible. Through the pulmonary artery venous blood of the right ventricle goes to the lungs for oxygenation. It also carries nutrition to the pulmonary tissues. Bronchial arteries, originating from the aorta, carry oxygenated blood for the nutrition of bronchi and bronchioles (Fig. 232). The pulmonary artery breaks up into wide arterioles and capillaries which form a rich network surrounding the alveoli where gaseous exchange takes place. The bronchial artery also breaks up into capillaries which partly join the alveolar network but is mostly returned through bronchial veins and partly through azygos vein. The branches of the bronchial artery are also distributed to the bronchial glands and walls of the bronchioles as well as respiratory bronchioles and thus form capillary plexuses which drain blood into the pulmonary venules (Fig. 233). The oxygen supply to the pulmonary tissues comes from the deoxygenated blood as well as from the oxygenated blood.

Method of recording pulmonary arterial pressure. *With the help of the cardiac catheter*—It is inserted through the systemic vein into the right atrium and then into the right ventricle and then into the pulmonary artery from where the pulmonary arterial pressure can be recorded.

Vasomotor supply. The sympathetic supply is from upper thoracic segments and the parasympathetic supply from the vagus. Results of stimulation of nerves are variable. Stimulation of the chemoreceptors of the

carotid body causes diminution of the pulmonary vascular resistance which disappears after section of the vagus and the sympathetic. So pulmonary circulation is under *reflex control.*

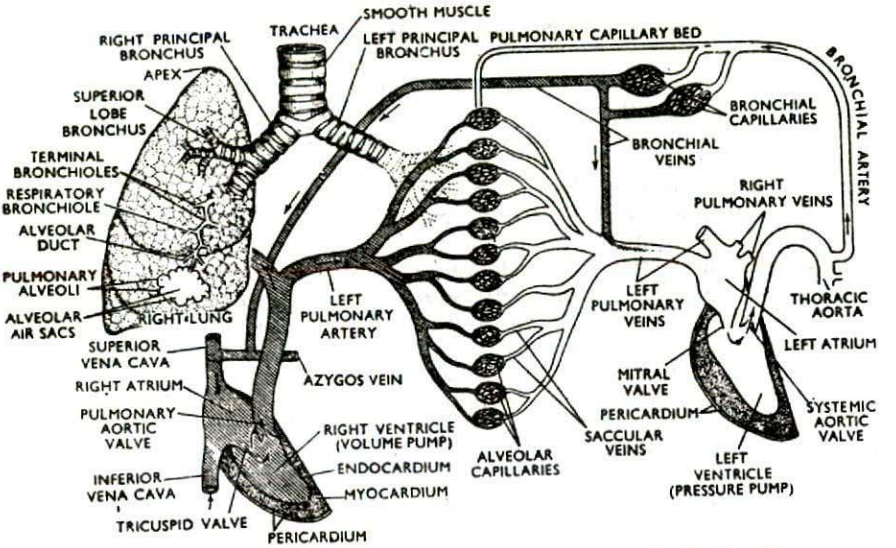


FIG. 232. Diagrammatic representation of the vascular supply showing the pulmonary circuit, and the bronchial arteries and veins.

Normal values of pulmonary circulation

1. **Minute blood flow.** It is the sum total of right ventricular output and blood flow through the bronchial arteries. Hence, a little over 4–5 litres.
2. **Blood pressure.** The systolic pressure in the human pulmonary artery is about 22 mm of Hg (right ventricle—about 22 mm of Hg). The diastolic pressure is about 10 mm of Hg (right ventricle 0 to 1 mm of Hg). With each heart beat the pressure rises in the pulmonary artery and thus causes pulsation in these vessels. The pulmonary capillary pressure is about 8 mm of Hg. The pulmonary venous pressure is about 5 mm of Hg (left atrium—approximately 4 mm of Hg).
3. **Circulation time.** 3–9 seconds (Ether).

Functions of pulmonary circulation

1. **Gas exchange.** It is the main function of the pulmonary circulation. Through circulation the mixed deoxygenated blood is passed through alveolar capillaries and thus gaseous exchange in between the alveolar air and alveolar capillaries takes place. Due to gaseous exchange, blood that passes through alveolar capillaries gets proper amount of O_2 and gets rid off proper amount of CO_2.
2. **Filter.** The fine pulmonary blood vessels act as a filter. It traps the emboli that pass through the pulmonary capillaries. Thus filter prevents from reaching and blocking the vessels in the brain and heart.
3. **Nutrition.** Pulmonary circulation maintains the nutrition of the lung tissue.
4. **Fluid exchange.** Pulmonary capillary pressure is very low which

tends to pull fluid from the alveoli and thus any fluid accumulation in the alveoli is speedily absorbed into the blood. This phenomenon has been observed by Colin (1873). He introduced 25 litres of water through the trachea slowly and observed no discomfort in the animals. Of course, rapid absorption of water in the blood may cause haemolysis and at the same time may increase the work load of the heart due to increase of plasma volume.

5. **Reservoir for left ventricle.** Left ventricular output is fully dependent upon the return of blood from the pulmonary bed to the left atrium. So any alteration of the pulmonary haemodynamics will alter the left ventricular function.

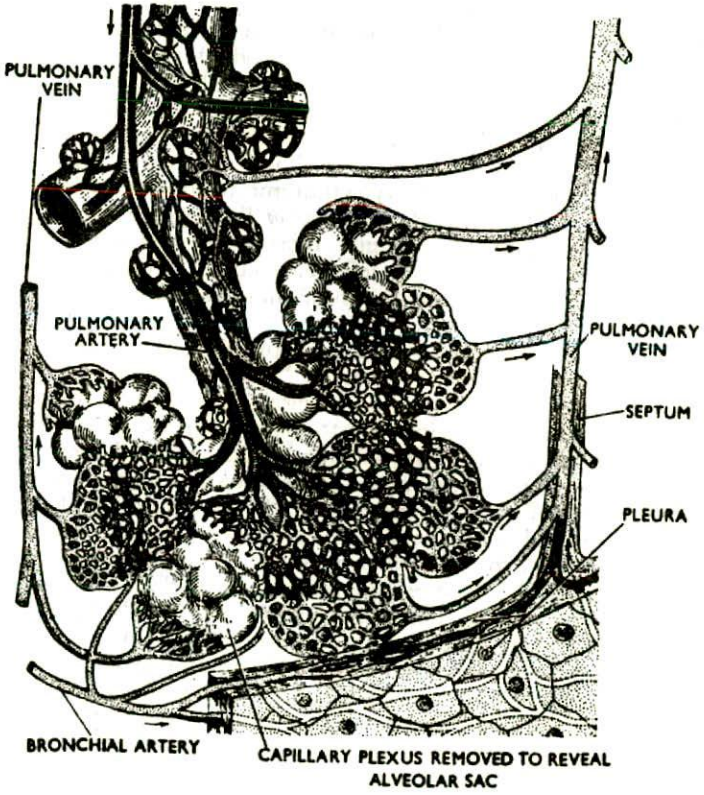


FIG. 233. Intrapulmonary anastomoses in between the pulmonary artery and bronchial artery.

Control of pulmonary circulation. The amount of blood passing through lungs follows the same general principles as elsewhere. It depends upon the following factors:

1. **Output of the right ventricle (Mechanical factor).** It depends upon the force and frequency of contraction and the degree of

venous return. Cardiac output may increase 3 or 4 times but the pulmonary arterial pressure does not rise appreciably.

2. **Resistance of the pulmonary bed.** It depends upon the following factors: (*a*) *Lumen of the pulmonary vessels*—Hypoxia produces pulmonary vasoconstriction. Increased CO_2 tension in the blood constricts the pulmonary blood vessels. It has been observed that if one lung is ventilated with a mixture of CO_2 and O_2, and the other lung with air then most of the blood is shifted to the normally ventilated lung so as to protect the body from hypercapnoic effect. This is **autoregulation of pulmonary blood flow.**

Adrenaline and noradrenaline also produce vasoconstriction. Acetylicholine also dilates the pulmonary blood vessels but the degree of vasodilatation is mostly dependent upon pre-existing tone of the smooth muscle of the pulmonary blood vessel. **Serotonin,** a humoral substance originating from disintegrating platelets or by secretory products of chromaffin tissues also constricts the pulmonary blood vessels. Recently it has been observed that the emboli in the pulmonary capillaries produce reflex vasoconstriction of the pulmonary arterioles. This, according to some physiologist, is due to stimulation of the vagal receptors lying near these small vessels. The receptors respond to 5-hydroxytryptamine (serotonin) released from the platelets near the emboli. (*b*) *Condition of the lungs*—Fibrosis, emphysema (overstretching), pneumonia, etc., increase the resistance. (*c*) *Condition of the heart*—Mitral stenosis or left heart failure retards venous outflow from the lungs and increases the pulmonary resistance. (*d*) *Respiration* (*vide* below).

3. **Role of respiration.** During inspiration, the pulmonary bed enlarges, capillary pressure falls to about −2 mm of Hg and therefore more blood enters the lungs. This is caused by elongation of the capillaries due to stretching and their dilatation due to negative pressure and probably vasomotor effect. Thus during inspiration, lungs can hold about 10% of total blood volume. During expiration, reverse changes take place, pressure rises to about 4 mm of Hg and lungs can hold only about 6% of the blood volume. But total pulmonary vascular resistance increases during both maximal inflation and forced deflation of the lungs. *Measurement of vital capacity acts as a guide.* A fall shows pulmonary congestion.

4. **Nervous control.** The pulmonary blood vessels have got both parasympathetic and sympathetic nerve supply. But there is still doubt that these nerve supplies have got any major physiological role in maintenance of normal circulation. Gracia Ramos and Rudomin (1957) have claimed the presence of active nervous control of the pulmonary blood vessels as they have observed reduction in O_2 saturation of arterial blood following stimulation of the sympathetic nerve. Electrical stimulation of caudal end of cut cervical vagosympathetic nerve also causes vasodilatation which is observed following administration of atropine.

5. **Reflex control.** The pulmonary circulation is also modified through reflexes originated due to stimulation of baroreceptors and chemoreceptors present in the sino-aortic areas. Stimulation of baroreceptors in the carotid sinus and aortic arch produces reflex vasodilatation in the pulmonary vascular bed, whereas stimulation of chemoreceptors in the aortic bodies or carotid bodies produces pulmonary vasoconstriction.

Peculiarities of pulmonary circulation

1. Pulmonary artery carries deoxygenated blood and pulmonary veins carry oxygenated blood.

2. **Filtration of fluid.** In systemic capillaries filtration of fluid takes place into the tissue spaces, but, nothing such happens in the lungs. The purpose is obvious. Filtration would cause collection of liquid in the alveoli and retard oxygenation of blood. The mechanism is also obvious. In the pulmonary capillaries the colloidal osmotic pressure (25 mm of Hg) is much higher than the blood pressure. In the systemic capillaries it is just the reverse. Hence, no filtration in the lungs. Pulmonary congestion, from any cause, will increase the local blood pressure leading to filtration and causing **oedema of lungs.**

3. **Filtration of emboli.** The fine pulmonary capillary acts as a filter that traps emboli from reaching and blocking the blood vessels of heart, brain or other organs.

4. Blood enters lungs through pulmonary and bronchial arteries. Blood is returned from the lungs through similar two channels: the pulmonary veins (oxygenated blood) and bronchial veins (reduced blood). One may think that the reduced blood instead of being returned through the bronchial veins could have easily joined the alveolar capillaries, become oxygenated and be returned through the pulmonary veins to the left heart. But in that case the venous return to the left heart would be more than the output of the right heart. This discrepancy may lead to **heart failure.** Only that amount of blood which was expelled by the right heart will return to the left heart, so that the output of the two ventricles may remain same. Thus blood flow through the two systems—pulmonary and systemic, are equal*

5. The pulmonary vascular bed is a low resistance circuit, whereas the systemic one is a high resistance circuit.

6. Pulmonary vascular bed has to supply blood to one type of tissue, whereas the systemic one has to supply blood to different types of tissues.

7. Pulmonary vascular bed is relatively short distensible with large calibre and can accommodate a large volume of blood (blood reservoir).

8. As the pulmonary vascular bed is exposed to subatmospheric pressure, the pulmonary pressure and flow are altered during inspiration and expiration.

9. As the pulmonary vascular bed is short and distensible, blood flow is not fully dependent upon neurogenic control; and mechanical factor of the right heart plays an important role in maintenance of normal blood flow.

10. Local actions of CO_2 and low O_2 on the pulmonary vascular bed are of vasoconstrictions which are just the reverse in case of the systemic one.

11. Though the pulmonary vascular bed has got both sympathetic and parasympathetic innervations, yet its role in the maintenance of circulation is less importance than the systemic one.

Effect of respiration on the systemic blood pressure. Generally systemic blood pressure falls during inspiration and rises during

* This is not actually true. Because, a certain amount of systemic blood, flowing through the bronchial arteries, do not drain into bronchial veins and right atrium, but drain into pulmonary veins and left atrium. Some amount of systemic blood, flowing through the coronary arteries, return directly to the cavity of the heart through the Thebesian vessels.

expiration. This is due to increased capacity of the pulmonary vascular bed during inspiration holding a larger volume of blood and thus momentarily reducing the return of blood to the left heart. Because during inspiration, pulmonary vascular resistance is greatly reduced as the intrathoracic pressure is below the atmospheric pressure. So at the first phase of inspiration, aortic pressure is decreased and at the last phase of inspiration as well as with the onset of expiration the systemic pressure is increased. Because venous returns to the left heart is gradually increased at the later phase of inspiration and towards the early phase of expiration.

Pulmonary vascular reflex. There are baroreceptor areas in the pulmonary arch of aorta and when these receptors are stimulated, reflexly alter the systemic blood pressure, heart rate and capacity of the peripheral blood vessels. An increase in the pulmonary arterial pressure produces *reflex bradycardia, hypotension* and increase of blood flow in the splanchnic bed. These responses are abolished following divisions of the vagus nerves:

(*a*) Reflexes from the pulmonary vascular bed may participate in the regulation of blood volume. Increased blood volume in the thoracic cavity reflexly produces **diuresis** through the inhibition of the antidiuretic hormone (ADH) secretion.

(*b*) Intravenous injection of starch grain, multiple emboli may produce rapid shallow breathing. This reflex respiratory response is due to the stimulation of receptors in the pulmonary vascular bed and can be abolished following section of the vagi.

Pulmonary depressor chemoreflex (Paintal, 1955). Intravenous injection of phenyl diguanide induces bradycardia and hypotension. It has been claimed that these reflex effects are initiated through the stimulation of **pulmonary deflation receptors.** Likewise serotonin, starch grain, multiple emboli stimulate these deflation receptors and induce pulmonary depressor chemoreflex.

Circulatory status in different cardiopulmonary diseases

1. **Mitral stenosis.** It is the condition when the orifice of the valve is narrowed by fusion of the cusp margins. The cusps become rigid and thickened. The chordae tendineae hold the valve in a fixed position and the opening becomes narrowed. The whole ring looks like a narrow rigid funnel. Due to narrowing of the opening, a resistance is offered for blood flow from the left atrium to the left ventricle. The left atrium is dilated and thickened due to accumulation of blood within itself. Furthermore the great problem that arises due to this, is the occurrence of pulmonary hypertension. With the obstruction of blood flow from the left atrium to the left ventricle, the left atrial pressure is tremendously increased causing decrease in pulmonary driving force. So the consequence is the decrease in pulmonary flow, right ventricular hypertrophy or cor pulmonale ultimately leading to right heart failure.

2. **Emphysema.** It is the condition in which there is enlargement of the air spaces distal to the terminal bronchiole. Obstruction to expiration due to oedema, inflammatory changes or mucus in the bronchi may cause emphysema. In emphysema, pulmonary vascular resistance is greatly enhanced causing obstruction to blood flow. Ultimately, the pulmonary hypertension and then right heart failure may occur. The increase of pulmonary vascular resistance is the consequence of destruction of pulmonary blood vessels. Poor exchange of air in the emphysematous alveoli may also cause increase of vascular resistance by accumulated CO_2 in the blood.

3. **Pulmonary embolism.** In pulmonary embolism either massive or diffuse, the blood flow is greatly affected due to blockade of pulmonary blood vessels by free-moving clot **(embolus).**

4. **Atelectasis.** It is the condition when a lung or a part of a lung remains in a collapsed state. In pneumothorax that is when the chest cavity is opened to atmospheric pressure. In such condition, the pulmonary vascular resistance is greatly increased causing the decrease of pulmonary blood flow. In natural atelectasis, the alveoli not only constrict,

blood vessels lining the alveoli are also constricted causing vascular detachment with the rest of the lung. This is an safety mechanism of the lung so that the ill-ventilated lung is prevented from supplying major quantities of blood.

5. **Removal of lung.** In case of pneumectomy or lobectomy, pulmonary haemodynamics remain unaltered so long the subject maintains a sedentary life. But if the subject performs heavy work then due to increase of cardiac output, the pulmonary pressure may be increased drastically because in such subject the pulmonary reserve is very low.

6. **Diffuse sclerosis of lung vessels.** In sclerosis of the pulmonary blood vessels, the elasticity as well as the distensibility of the lung vessels are decreased. Pulmonary vascular capacity is also affected greatly. In such case if subjects do not have such heavy or even mild work so that the cardiac output is increased, then there should have no trouble. In late or extreme stages of sclerosis, the pulmonary blood flow is greatly decreased and pulmonary hypertension along with the right heart hypertrophy may be happened.

7. **Pulmonary fibrosis.** It is the cause of formation of fibrous tissue during healing of the wound. The generalised fibrosis happens in lung tissue following recovery from tuberculosis, bronchopneumonia, pneumoconiosis, gas poisoning, etc.

Under such condition the pulmonary vascular resistance is increased. Thus obstruction to blood flow may be offered causing pulmonary hypertension in late stage.

4. HEPATIC CIRCULATION

Vascular arrangement. Blood enters the liver through two sources: (*i*) portal vein, and (*ii*) hepatic artery (Fig. 234). The hepatic artery is

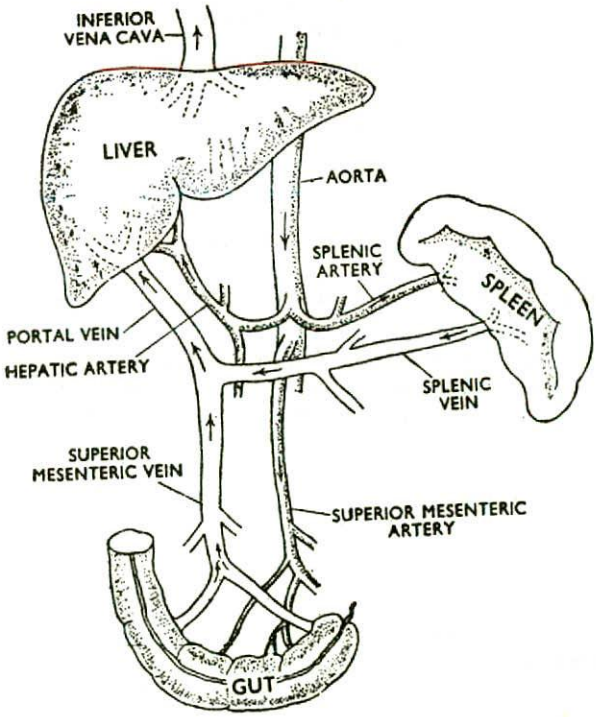


Fig. 234. Macro-anatomy of the hepatic circulation.

not an end artery and has got anastomotic channels with the portal vein at several levels of the interlobular regions (Fig. 235). The hepatic artery transfuses the portal vein as well as the sinusoid at a higher pressure

head. The portal vein is originated from two vessels: (*i*) the *superior mesenteric vein* draining blood from the mesenteric bed and (*ii*) the *splenic vein* draining blood from the spleen. The left lobe of the liver gets blood from the spleen and the right lobe of the liver gets it from the superior mesenteric vein. Though the major blood supply is made by the portal vein, yet the hepatic artery ligation may or may not be compatible with survival but it is depending mostly on the level of the ligation and species. The portal

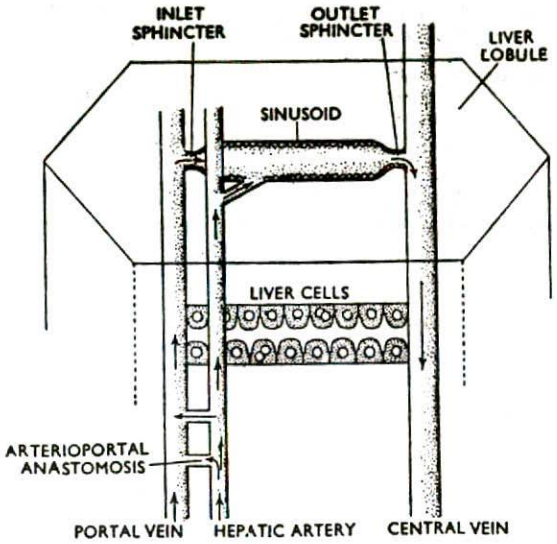


FIG. 235. Micro-anatomy of the hepatic circulation in the liver lobule (*after Block*, 1956).

vein and the hepatic artery have anastomotic connections with the sinusoid. The sinusoid is a smooth-walled cylindrical tube and is lined by *phagocytic cells* (Kupffer). It is guarded by inlet and outlet sphincters at their terminals and these sphincters play an important role in the regulation of flow and storage of blood.

Vasomotor supply. Constrictor fibres are carried in the splanchnic (sympathetic) fibres and stimulations of the splanchnic nerves cause vasoconstriction in the sinusoids, arterioles and other intrahepatic vessels. The vagus has got no role on the hepatic circulation and there is still doubt about the existence of any vasodilator fibres in the liver.

Normal values of hepatic circulation

1. **Hepatic blood flow.** The portal area can hold about a quarter of the total blood volume. The average minute flow is about 100 ml per 100 gm of the liver tissue. The hepatic artery supplies about one-third to one-fourth of the total blood flow and 40% of O_2 requirement. The portal vein supplies two-thirds to three-fourths of the total blood flow, 60% of O_2 requirement and major part of nutrition.

2. **Hepatic blood pressure.** Pressure in the portal vein is about 10 mm of Hg. Measured directly at operation in man, it comes to

about 14–22 mm of H_2O. This indicates that in the hepatic capillaries the pressure must be much lower (about 2 mm of Hg). Otherwise such a large amount of blood could not pass through it.

Factors modifying hepatic circulation. The principles are same as elsewhere. Hepatic circulation can be adjusted either by altering the lumen of the local vessels or by adjusting the rate of blood flow through them. The following factors regulate hepatic circulation:

1. **CO_2 and H-ion concentration changes, metabolites, O_2 lack,** etc., alter the lumen of the vessels and adjust the flow as elsewhere.
2. **Respiration** helps in two ways. During inspiration (*a*) intrathoracic pressure falls and intra-abdominal pressure rises, so that blood is sucked in by the thorax and pumped out by abdomen, and thus portal flow rises. (*b*) Diaphragm descends and exerts a massaging action on the liver—thus pushing out more portal blood towards the heart.
3. **Contraction of the spleen and movements of the intestine** also help in driving blood through the liver.
4. **Systemic blood pressure.** Effects of systemic pressure on hepatic circulation are as follows: (*a*) When pressure falls, O_2 supply to the liver decreases (*i*) due to less blood flow through the hepatic artery, and (*ii*) due to less oxygen being carried by portal blood which is more reduced owing to slow circulation. (*b*) Rise of systemic pressure will cause opposite effects. The principle is that a rise of systemic pressure, without constriction of the splanchnic vessels, will raise the hepatic flow. Opposite changes will reduce. [O_2 tension in the centre of the liver lobule is much lower than in the tissues elsewhere. These cells are therefore easily injured by poisons, congestion, etc.]
5. **Neurogenic factors.** It has been discussed earlier that the sympathetic stimulation changes the hepatic blood flow by increasing resistance of the hepatic blood vessels. But the role of vagi on the hepatic blood flow is uncertain.
6. **Vasomotor reflex control.** Heymans and others (1930, 1931) have shown that the volume of liver is increased following increase of pressure in the carotid sinus and the aortic arch. They have also described the importance of liver as blood depot for the maintenance of blood supply to the vital organ like the heart and brain during haemorrhage.
7. **Adrenaline and Noradrenaline.** Adrenaline has got both constrictor and dilator effects but the nature of effect is depending upon the concentration of adrenaline given. In higher concentration it has got constrictor effect whereas in lower concentration has got dilator effect. Noradrenaline has got constrictor effect.
8. **Effect of posture.** Due to changes of posture from the supine to the upright positions, the hydrostatic factor (ρgh) may decrease the blood pressure of the upper part of the body but the splanchnic bed compensates it reflexly through the redistribution of blood from its own area to the upper part of the body (mainly the heart and brain) by increasing vascular resistance. If the splanchnic nerves are sectioned then this autotransfusion process does not take place.
9. **Effect of exercise.** Muscular exercise decreases the splanchnic blood flow by redistributing blood to the active muscle and brain. The reduction of sympathetic blood flow is caused by increased vascular resistance.
10. **Haemorrhage.** Following haemorrhage the blood flow to the

liver is decreased but the vascular resistance in the splanchnic bed remains unaltered and normal flow is resumed within an hour. Increased arteriovenous oxygen difference across the splanchnic bed actually maintains the constant oxygen supply of the liver during haemorrhage. In *severe massive haemorrhage*, the liver blood flow is curtailed so greatly that the compensation becomes inadequate resulting **hepatic hypoxia.** This hypoxic state of the liver actually determines the irreversibility of the **fatal haemorrhagic shock.**

11. **Visceral distention.** Distention of the stomach due to intake of food reduces the hepatic blood flow probably by increasing the blood volume in the spleen and mesenteric blood vessels.

12. **Clinical conditions.** In cirrhosis of liver, the hepatic vascular resistance is increased and in order to maintain the normal blood flow the portal venous pressure is also increased (also due to decrease of blood flow). But the ultimate fate is the accumulation of fluid in the peritoneal cavity—causing **dropsy.** In congestive heart failure, the hepatic blood flow is also decreased greatly.

Peculiarities of hepatic circulation

1. Hepatic circulation is a portal system. Blood has to pass through two capillary networks—at first, the splanchnic and then the hepatic.

2. Although blood enters liver through two vessels (portal vein and hepatic artery), yet the outflow from the liver is only through the hepatic vein. There is no vein corresponding to the hepatic artery (contrast with pulmonary circulation).

3. The pressure difference between portal vein and portal capillaries are not very high, yet a large amount of blood passes through the liver. Mechanical factors, mentioned above, help. Union between the radicles of the hepatic artery and portal vein possibly adds motive force to the latter.

4. Filtration in the capillary area elsewhere takes place, because capillary pressure (32 mm of Hg) is more than colloidal osmotic pressure (25–30 mm of Hg). But in the liver, the osmotic pressure is same, while the capillary pressure is almost zero.

5. In the liver, blood comes into direct contact with the hepatic cells to some extent. This may partly explain (4).

5. SPLENIC CIRCULATION

The anatomical organisation of the splenic circulation has already been considered in detail (*vide* page 199). The peculiarities that have been encountered in the splenic circulation are the presence of both 'open' and 'closed' circulation (*vide* page 201). The pulp acts as filter for separating R.B.C. from plasma. Phagocytes of the pulp removes the foreign particles from the blood. Pulp also acts as blood reservoir yet its function as such in human beings is not clear but in dogs and cats, it is fully settled. During emergency, such as exercise, shock, haemorrhage, asphyxia, etc., there is profound contraction of the spleen causing discharge of a large amount of blood rich in R.B.C. in the general circulation. However, its role in human being is not fully known because splenectomy has got no effect.

The circulation of spleen has a capacity of about 500 ml. When sympathetic stimulation occurs, this capacity is lowered quickly and about 300 ml are added to general circulation. This added blood possesses a very high concentration of erythrocytes. During splenic relaxation, R.B.C. are

filtered out of the circulation and stored in the pulp. On the other hand, the splenic contraction causes return of R.B.C. to the circulation.

Rate of blood flow. Blood flow pattern of the spleen has not been studied in detail. Most of the investigators have concentrated in studying the volume change rather than its rate of blood flow. Accordingly, flow pattern of the spleen has been mostly considered by the volume change of the spleen. Increase of volume as dilatation of splenic blood vessels causing increase of flow. Reverse is the case when the volume is decreased. However Grim (1963) has described the rate of blood flow in dogs of 15 Kg body weight and 130 mm of Hg arterial blood pressure to be 70 ml/min/100 gm tissue.

Control of blood flow. Pressure/flow relationship of the spleen indicates that the resistance is greatly decreased during increase of perfusion pressure. This decrease in resistance has considered to be the cause of opening of the vascular sinuses. Factors that alter the splenic blood flow are described below:

(*a*) **Neurogenic factor.** Neurogenic factors seem to have an important role in the regulation of blood flow in the spleen. Stimulation of the splanchnic nerve causes rapid and intensive rhythmical contraction of the spleen along with decrease of flow. During contraction it gives into the general circulation a considerable amount of blood. Green and his associates (1960) have considered the splenic-emptying mechanisms being under the sympathetic control. Splenic nerve stimulation causes decrease of arteriolar inflow, decrease of splenic volume and weight and increase of venous outflow.

(*b*) **Reflex control.** Stimulation of baroreceptors in the carotid sinus and aortic arch baroreceptors causes reflex modification of the splenic volume, splenic weight and splenic circulation. Profound increase of the splenic volume following increased pressure in the isolated carotid sinus of dogs has been observed by Heymans (1929). Reflex dilatation of the splenic vessels is possibly the cause of this response. On the contrary during increase of pressure in the sinus causes reflex decrease of splenic volume through the activation of the sympathetic nerve.

(*c*) **Humoral control.** *Adrenaline* and *noradrenaline* both decrease the splenic volume. Splenic rhythmical contraction is increased following administration of adrenaline or noradrenaline. It is claimed that these hormones play an important role in emptying mechanisms of spleen. The noradrenaline helps by arteriolar constriction whereas the adrenaline helps by increasing the venous outflow through venular dilatation or through contraction of the splenic smooth muscle.

Acetylcholine and *methacholine* generally increase the arterial and venous outflow. The volume of the spleen is also slightly decreased. But topical application of acetylcholine, adrenaline, noradrenaline and histamine cause arteriolar constriction.

(*d*) **Haemorrhage.** During haemorrhage, when the systemic blood pressure falls, the contractions of the spleen along with arteriolar constriction, decrease of splenic weight and increase of venous outflow are observed due to reflex sympathetic activity through the stimulation of chemoreceptors.

(*e*) **Exercise.** During exercise, the contraction of the spleen is increased (Barcroft, 1929). This is due to redistribution of blood from the

inactive area to the active area. Increased sympathetic activity during exercise is the possible cause.

(*f*) **Distention of viscera.** The splenic vein and the superior mesenteric veins provide the major blood supply to the liver through the portal vein. Thus the splenic venous drainage is through the portal vein. So if there is any distention of liver vascular bed due to increase of sinusoidal resistance or due to pathological conditions then splenic drainage may be affected. Besides this, recently it has been observed that if the hollow viscera like stomach is distended then redistribution of blood occurs there. Under such state the hepatic blood flow is decreased whereas splenic and mesenteric blood flow are increased.

6. RENAL CIRCULATION

The kidneys are not only an essential secretory organs, but they also play an important role in circulatory dynamics. The renal circulation will be discussed when kidney function is considered in chapter XII. About 1,300 ml of blood flows through the kidneys per minute due to relatively low resistance in the renal circulation although a large fraction of cardiac output flows through them. The kidneys can markedly influence the general circulation by the secretion of *renin*. The renal vessels act under the control of sympathetics and participate in general circulatory adjustments. Due to haemorrhage or diminished cardiac output or during exercise, renal vasoconstriction elevates the resistance and diminishes renal blood flow.

7. CAPILLARY CIRCULATION

Histology. The average length of a capillary is 0·5–1 mm, average diameter, 8 μ or often less than a red cell, average velocity of flow, 0·5–1 mm per second. Capillaries are lined by a layer of the flat endothelial cells bound together by an intracellular cement substance. A basement membrane surrounds capillary endothelial cells. A *pericapillary sheath* forms the outer wall of the capillary. In the pericapillary sheath there are branched *Rouget cells* or *pericytes* representing modified muscle cells. Zweifach has shown various types of arrangements of the capillaries in the muscle and nail bed (Figs. 138 & 236). The arterioles are connected with metarterioles. Metarterioles leads into *thoroughfare (preferential) channels* which resemble a large capillary and are connected with venules. The *true* capillaries are shorter in length and led from the metarterioles and arterioles into venules. At the root of each capillary there is a *precapillary sphincter* which adjusts the flow of blood whereas in the thoroughfare (preferential) channel there is no such sphincter and the blood flow cannot be adjusted through it.

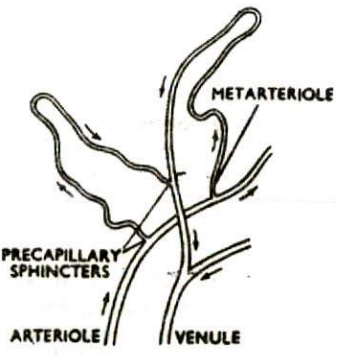


Fig. 236. Diagrammatic representation of the terminal vascular beds showing the unique hairpin capillary loop of the nail bed. (*Redrawn & modified after* Zweifach)

Methods of study of capillary circulation. Capillary circulation can be studied as follows: It may be watched in the web of frog's foot or

omentum, etc., under a microscope with suitable light arrangement. Projection of the some on a screen with the help of an Epidiascope is very helpful for demonstration.

Vasomotor supply. Sympathetic constrictor fibres pass to the Rouget cells. Antidromic dilator fibres are also present.

Peculiarities of capillary circulation—1. **Direction of flow.** There is no fixed direction of capillary flow. Blood may be found to pass in opposite directions through two capillaries running side by side.

2. **Nature of the stream.** In the arterioles, the blood stream can be divided into two parts: (*a*) *axial stream* consisting of red cells mainly and (*b*) *peripheral stream* consisting of plasma and stray leucocytes. But in the capillaries, due to narrow lumen, only a single file of cells can pass through. Often a red cell may be found to be folded upon itself and squeezing somehow through the capillaries.

3. **Capillary tone.** In the resting condition the majority of the capillaries remain collapsed. During activity they open up and increase the vascularity of the part. In the muscles, the blood supply may increase by 750 times during activity.

4. **Independent contractility of the capillaries.** The capillaries can adjust their diameters independent of arterioles and venules. Raised venular and arteriolar pressure cannot distend the capillaries if the tone is high. Ordinarily, however, the capillary lumen changes in the same direction as the arterioles and venules.

5. **Capillary pressure—Method of recording intracapillary pressure.** Landis method of recording intracapillary pressure is the most satisfactory one. A fine micropipette is introduced into the capillary loops of the skin of the nail bed and observed through a binocular microscope. It is connected by fine tubes containing citrate solution to a mercury manometer by which the pressure may be recorded.

In man, the average pressure at the arterial end is about 32 mm of Hg, at the venous end 12 mm of Hg, and at the summit 20 mm of Hg. There is a difference of 5–10 mm of Hg between systolic and diastolic pressure, at the arterial end. Hence, the flow is pulsatile there. But at the venous end it is continuous. Capillary pressure is affected by the following factors:

(*a*) *Heart level.* When lowered below the heart level, the capillary pressure rises proportionately. But if the part is raised above the level of heart, there is a slight fall in the arterial side of capillary pressure but none on the venous side.

(*b*) *Venous pressure.* Venous obstruction raises capillary pressure.

(*c*) *Condition of arterioles.* Dilatation of arterioles (without fall of general blood pressure) increases both arterial and venous capillary pressure (from 40–60 and 10–40 mm of Hg respectively). Under such conditions, capillary pulsation is seen. This is due to the fact that, systemic blood pressure is more directly transmitted to the capillary area. General vasodilatation, with marked fall of blood pressure, will have opposite effects. Constriction of the arterioles beyond the optimum limit may raise systemic blood pressure but reduces capillary pressure and flow.

(*d*) *Visceral characteristics.* In the viscera, capillary pressure differ according to the nature of local mechanism. For instance, in the renal glomeruli, it is about 75 mm of Hg, in the intestinal capillaries about 10–20 mm of Hg, in the liver about 2 mm of Hg, etc.

Control of capillary circulation. The extent of capillary flow is directly proportional to the activity of the locality. This adjustment of vascular supply to local needs can be carried out by adjusting the general blood pressure and arteriolar tone on the one hand and by regulating the number of the patent capillaries and their diameters on the other. Apart from their independent contractility, the capillaries respond to chemical, hormonal, physical and nervous stimuli. They are as follows:

1. **Chemical stimuli.** CO_2 excess, increased H-ion concentration, O_2 lack, non-acid dilators (metabolites), histamine, adenylic acid and certain other products of tissue activity dilate the capillaries.

2. **Hormonal stimuli.** Adrenaline, noradrenaline and pituitrin not only constrict the arterioles but also the capillaries.

3. **Physical stimuli.** Application of heat or strong light (including ultraviolet and infrared rays) dilates the vessels and increases the vascularity of the part due to direct action of the rise of temperature on the capillaries and probably also due to histamine liberation. Cooling constricts the arterioles and capillaries. Freezing produces damage of the tissues and liberation of H-substances which causes redness, flare and wheal.

4. **Nervous stimuli.** Nervous control of capillaries are carried out in two ways: (*i*) *Through the vasoconstrictor nerves* which reduce the capillary lumen by causing contraction of the Rouget cells. Their inhibition will naturally produce dilatation. (*ii*) **Axon reflex** (*Antidromic vasodilators*)—Irritation of the skin produces vasodilatation in the locality. This response persists even when the posterior root is severed either proximal or distal to the posterior root ganglion, but not when the peripheral nerves are allowed to degenerate. This shows that, the dilatation is not due to the direct action of any substance on the blood vessels but through the intact peripheral sensory nerves (probably *nocifensor* system). Since no nerve cell is involved in the process, the reflex arc is completed by the two branches of the same sensory fibre. Through one branch, the impulse is received and through the other, it is transmitted back to the peripheral vessels, causing vasodilatation. The impulse is called *antidromic impulse* and the reflex is known as the *axon reflex* (*vide* page 306, Fig. 217).

Interchange in the capillary area (Fig. 237). At the arterial end of the capillary loop, blood pressure is about 32 mm of Hg and colloidal osmotic pressure about 25 mm of Hg. Hence, filtration takes place and water, nutrition, salts, etc., pass out into the tissue fluid. At the venous end, blood pressure is only 12 mm of Hg and colloidal osmotic pressure is raised due to concentration of proteins. Hence, water and crystalloids are again reabsorbed. In this way capillary circulation and interchange go on.

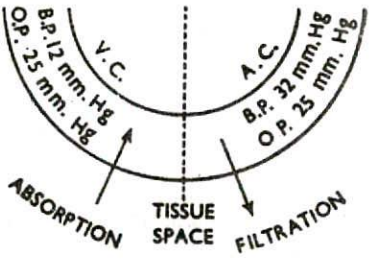


Fig. 237. Illustrates the mechanism of exchange in the capillary bed.
A.C. = arterial side of capillary loop. V.C. = venous side of capillary loop. B.P. = blood pressure. O.P. = osmotic pressure. On the arterial side B.P. > O.P., hence filtration. On the venous side O.P. > B.P., hence absorption.

8. CUTANEOUS CIRCULATION

Anatomy of cutaneous circulation. Vascular architecture of the skin has the general pattern of the capillary circulation. For the most part, papillae contain capillary blood vessels and nerve endings. The arteries that supply the skin, originate from the richly anastomosing irregular plexus (first plexus) of the deepest part of the corium (dermis). From this cutaneous arterial plexus, the single arteriole arises and ascends through the corium and forms the second plexus just below the dermis. Capillaries arising from this plexus supply the hair follicles and papillae of the dermis. The arterioles also ascend towards the superficial layer and form the third plexus in the subpapillary region of the dermis. Every papilla gets capillary network from this plexus.

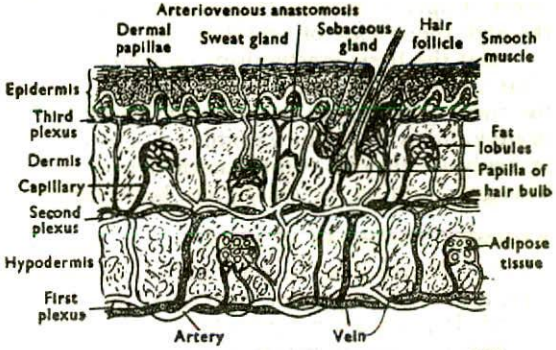


FIG. 238. Diagram represents three plexuses at different levels of the skin and by means of arteriovenous anastomoses and precapillary spincters, blood can be routed into or away from the capillary beds.

The arterial limb of the capillary loop ascends in the papillae and turns back to form the venous limb. The venous limb then reaches the base of the papillae and joins with the venous limb of the neighbouring loops to form the **collecting venule.** The collecting venules then anastomose with one another and form the so-called **subpapillary venous plexus.** This subpapillary venous plexus runs horizontally at the base of the papillae and drains in the deeper veins (FIG. 238).

Rate of blood flow. Rate of blood flow alters under different conditions like haemorrhage, temperature of the surroundings, metabolic activities of the body, emotional and physical stress of the body. Under ordinary cooled atmosphere, the blood flow is about 0·30 litre/sq. metre of the body surface or total about 400–450 ml per minute. This value is increased during exercise or decreased during fall of surrounding temperature.

Regulation of blood flow—Nervous control. Considering the temperature control as the main function of the skin, the blood flow through the skin is mainly maintained through the nervous mechanism rather than through autoregulatory mechanism.

(1) **Role of hypothalamus.** Hypothalamus, being the autonomic centres for the sympathetic and the parasympathetic, plays an important role in controlling blood supply of the skin. Besides this, the temperature-regulatory centre is situated at the pre-optic region of the anterior hypothalamus which modifies the skin blood flow in altered body temperature, through the activation of either the sympathetic vasoconstrictor or sympathetic vasodilator pathway. If the above temperature-regulatory centre is heated, then vasodilatation along with sweating occurs and on the contrary if the same centre is cooled, then vasoconstriction along with cessation of sweating occurs.

(2) **Sympathetic adrenergic vasoconstrictor pathways.** These fibres secrete noradrenaline at their nerve endings and when excited, on exposure to cold, profound vasoconstriction occurs. These vasoconstrictor effects are most powerful in the hands, lips, nose, ears, etc.

(3) **Sympathetic cholinergic vasodilator pathways.** These fibres produce vasodilatation by liberating acetylcholine at their endings. When the body temperature is increased, these fibres are activated causing vasodilatation and sweating. It has been claimed that the sympathetic nerve supply to human fingers exerts a tonic dilator influence on vessels through the release of acetylcholine.

But the basic mechanisms by which the vasodilatation occurs are not clearly known. Recently it has been claimed that the factors which excite the sweat glands may cause formation of a substance **bradykinins.** This bradykinin is a potent vasodilator. On excitation, sweat glands release a proteolytic enzyme—**kallikrein** which acts on the *decapeptide*, **bradykinogen** forming the *nonapeptide*, **bradykinin.**

Vascular response of skin

1. **White line.** In a normal subject, if a light stroke is applied on the skin, a *white line* appears exactly on the area stroked, after a brief latent period. It persists for a minute or two and then gradually fades away. It occurs even when nerves are cut and allowed to degenerate. Hence, it is due to local constriction of capillaries as a response to the mechanical stimulus.

2. **Triple response.** In subjects with hypersensitive skin, a moderate stroke elicits the following triple response:

(*a*) **Red line.** A red line appears on the line of stroke after a short latent period, caused by vasodilatation independent of nerves, because it occurs even after section and degeneration of nerves.

(*b*) **Flare.** After 15–30 seconds a red flush or *flare* appears and spreads beyond the area. It is not obtained when peripheral nerves degenerate. It is caused by arteriolar dilatation through antidromic axon reflex.

(*c*) **Wheal.** A local oedema develops in the area of stroke and spreads a little beyond, reaching its maximum in about 5 minutes. It is caused by escape of fluid from blood vessels resulting from increased permeability of the latter.

All evidences suggest that triple response is due to the action of *histamine*, which is liberated in the area as a result of stroke. The red line is due to dilatation of capillaries and venules caused by the direct action of histamine on them. The flare is due to vasodilatation brought about by the action of histamine on the nerves, thus eliciting axon reflex. The wheal is due to increased permeability caused (1) by stagnation of blood flow, and (2) by the action of histamine on the capillaries.

3. **Direct effect of cold on the skin.** If cold is directly applied on the skin then vasoconstriction occurs. If a finger is immersed in cold water then vasoconstriction occurs very promptly but fluctuation in blood flow occurs in most cases due to alternate vasoconstriction and vasodilatation. This vasodilatation is presumably the cause of *local axon reflex* and occurs as a protection against cold injury.

Autoregulation of skin blood flow. Regarding the autoregulation of skin blood flow, evidence for the presence of autoregulation in skin blood flow is lacking. Barcroft (1968) did not observe any such autoregulation

in the skin of cats and dogs. But the vessels that supply the nutrition to the skin may have some basal tone and autoregulation (Folkow, 1962). Thus local autoregulation mechanisms in the skin like other tissues are linked with the nutritional aspects during emergency.

Normal colour of the skin. Colour of the skin is mostly dependent upon the blood flow through the capillary loops and subpapillary plexus. Diameter and degree of engorgement of superficial blood vessels actually determine the depth or intensity of the skin colour. *Light and pale colour* of the skin is due to the constriction of blood vessels. *Intense scarlet colour* is due to increased blood flow and dilated vessels. *Deep blue colour* is due to decreased blood flow and dilated vessels.

9. SKELETAL MUSCLE CIRCULATION

Vascular arrangement in skeletal muscle. Blood vessels and also nerves (*vide* p. 59) enter the muscle at neuromuscular hilus, which is often located, at the half length of the muscle. Arteries, after entering the substance of the muscle, branch freely along the perimysium and forms numerous anastomoses, the **primary network.** Small arteries are given off at regular interval from this network and again finer arteries come out and cause free anastomosis of **secondary cubical network.** From the threads of the secondary network, smallest arteries or terminal arterioles generally branch off transversely to the long axis of the muscle fibre and at fairly regular intervals of 1 mm. Finally these arterioles open up into capillary network that runs parallel to the long axis of the muscle fibre and with frequent transverse linkages forming a delicate oblong mesh. The venules are intercalated regularly between arterioles and follow almost exactly the course of arterioles and arteries. The veins have got valves which direct the blood to flow towards the heart.

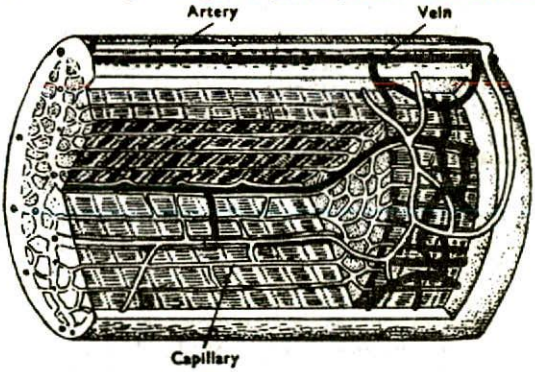


FIG. 239. Diagrammatic representation of vascular supply of skeletal muscle showing capillaries run parallel to the fibrils which ultimetely make up fibres.

The muscles usually possess a rich capillary blood supply. A large man having a muscle mass of 50 Kg, possesses about 2,000 capillaries/mm^2. Total length of the capillary of such muscle will be 100,000 Km (62,000 miles). Krogh (1929) has described that during *rest* approximately 100 capillaries/mm^2 remain open but during *exercise* as great as 3,000 capillaries/mm^2 are open up (Fig. 241).

Muscle blood vessels are comprised of large elastic vessels which may convert the pulsatile flow into smooth steady flow. Gollenhofen (1968) has described a spontaneous fluctuation in muscle blood flow even in resting state.

There are two sets of **resistance vessels:** one is the precapillary, mostly the arterioles and other is the postcapillary which are mainly small veins. These vessels actually offer the major resistance to blood flow. There are

capacitance vessels which are the veins and have little effect on resistance but have got influence on cardiac output.

Arteriovenous anastomosis is present in skeletal muscle. Microscopic studies on the circulation of rat skeletal muscle show many arteriovenous communications. In resting state most of the flow is through these anastomoses and to the muscle fibres proper. Functional importance of arteriovenous anastomosis is not clear.

Rate of blood flow through muscle. Resting muscle blood flow is about 7–9 ml/100 gm tissue. During *exercise*, the blood flow is tremendously increased. It may be increased more than 100 ml/100 gm tissue. During exercise nearly all the capillaries are open up and for this reason the blood flow is increased. During *rest*, only 3–4% capillaries remain open.

During rhythmic muscle contraction, the steady blood flow to the muscle is greatly affected and flow becomes intermittent, i.e., flow increases during relaxation and decreases during contraction. The cause of decreased blood flow during contraction is due to compression of blood vessels.

Basal tone of arterioles. In resting state, muscle blood vessels, particularly the arterioles, exhibit a tremendous basal vasomotor tone as indicated by 80–90% decrease of vascular resistance following intra-arterial administration of acetylcholine. This basal tone is considered to be due to sympathetic supply to muscle. Because blocking of the sympathetic nerves may reduce the vascular resistance.

Control of skeletal muscle blood flow

Autoregulation of blood flow. In isolated and denervated muscle preparation, blood vessels exhibit good autoregulation when perfused at controlled arterial pressure. Jones and Berne (1965) have described that equilibrium value of blood flow following a change in arterial pressure, venous pressure or ambient pressure appears to result from a response of the resistance vessels, based on metabolic rather than myogenic mechanism. The tremendous increase of blood flow that occurs following onset of exercise is presumably due to local vasodilatation of arterioles. It has been described that during exercise, skeletal muscle exhibits local autoregulation which is probably due to local increased need of O_2. Berne (1963, 1968) has described a metabolic regulation of blood flow (*vide* p. 325) in relation to O_2 need of the cardiac muscle. He has described that blood flow in the muscle is metabolically controlled when the O_2 content of the venous blood is decreased. This increased blood flow takes place during such condition through *reactive hyperaemia*. However Berne in 1968 did not consider the adenosine to be the chemical agent responsible for active hyperaemia in skeletal muscle. Whether any related substances are involved, is not clear.

Nervous control. In skeletal muscle, the sympathetic nerve has got dual functions. It has got vasoconstrictor and vasodilator function. The blood vessels receive both sympathetic **adrenergic vasoconstrictor** fibre and sympathetic **cholinergic vasodilator** fibre. The vasoconstrictor fibres when stimulated, cause profound decrease of blood flow through the liberation of noradrenaline. This vasoconstrictor effect has got some physiological importance because during shock or in other conditions of stress, when blood pressure falls greatly, peripheral vasoconstriction may improve the blood flow of the vital organs (brain and heart) by curtailing the blood flow of the muscle bed.

In certain condition, epinephrine may indirectly cause vasodilatation through the activation of metabolic regulation of blood flow as in case of exercise.

Sympathetic cholinergic vasodilator fibres often cause vasodilatation by the liberation of acetylcholine at their nerve endings when stimulated. These fibres are possibly activated under emotional stress or in fainting reaction. Forearm blood flow is increased greatly when a subject is frightened.

Evidence of functional existence of parasympathetic nerve supply to the muscle is lacking.

Reflex control of blood flow. The skeletal muscle blood flow is reflexly controlled under certain conditions of the body.

(*i*) **Sino-aortic baroreceptor reflexes.** During systemic rise of blood pressure, the baroreceptors of carotid sinus and aortic arch are stimulated causing withdrawal of vasoconstrictor activities of the sympathetic vasoconstrictor fibres. On the contrary on withdrawal of baroreceptor activity by **bilateral carotid occlusion** (BCO), the vasoconstriction occurs in the muscle. This vasoconstriction may be abolished by α-receptor blockades or by sympathetic nerve denervation. But this effect is unaffected by atropine.

(*ii*) **Carotid and aortic chemoreceptor reflexes.** During hypotension or in haemorrhage the carotid and aortic bodies are stimulated causing systemic rise of pressure by the decrease of blood flow to the muscle and splanchnic bed. If the sympathetic nerves to the muscle are cut, then this decrease of blood flow no longer occurs.

(*iii*) **Thoracic aorta baroreceptor reflexes.** Gruhzit and others (1953) have observed the reflex vasodilatation of the limb muscle following stimulation of the mechanoreceptors of the wall of the thoracic aorta.

(*iv*) **Cardiopulmonary receptor reflexes.** In human beings, vasodilatation may occur only in the forearm if the lower limbs in a recumbent subject are elevated. It is the result of shifting of blood from limbs to the thorax by stimulation of the receptors in the cardiopulmonary low-pressor area, so that the sympathetic vasoconstrictor tone is altered.

Role of sympathetic vasodilator fibres on the above reflexes is not known.

Neurohormones. Acetylcholine has got dilator effects on the skeletal muscle blood vessels. Intra-arterial administration of acetylcholine has got no effect if atropine is administered previously. **Adrenaline** has got both vasodilator and vasoconstrictor effects as because it activates both α- and β-receptors of the skeletal muscle blood vessels. **Noradrenaline,** on the other hand, has got only vasoconstrictor effect and activates only the α-receptors of the blood vessels.

Blood gases. If the pCO_2 in the systemic blood is increased, then the muscle circulation is decreased due to reflex vasoconstriction by the activation of carotid and aortic chemoreceptors, whereas local accumulation of CO_2 causes vasodilatation by reactive hyperaemia.

Local hypoxia may also produce vasodilatation by same mechanism.

But the role of blood gases on the skeletal muscle blood flow is inconclusive and requires further study.

Blood pH. A decrease or an increase of pH has practically no effect in innervated muscle in the forearm blood flow. If the sympathetic nerves are blocked then an increased or decreased pH may alter the blood flow.

Nucleotides. Studies on adenosine, AMP, ADP and ATP show arteriolar vasodilatation but relative role of these substances in the skeletal muscle blood flow during reactive hyperaemia is not yet fully known.

Polypeptides. (*i*) **Bradykinin** is a potent vasodilator of skeletal muscle as evidenced from plethysmographic studies. However, the relative role of bradykinin on skeletal muscle vasodilatation is not known. (*ii*) **Angiotensin** administered intravenously produces renal vasoconstriction and to some extent the splanchnic bed resistance is increased but the muscle vascular bed remains unaffected. This effect causes marked shift of blood from the viscera to the muscle bed (Brod et al, 1968).

Ions. Increased blood levels of potassium and magnesium elicit arteriolar dilatation. These ions produce their effects by acting directly on the vascular smooth muscle.

Other metabolites. Citrate, acetate, pyruvate also produce arteriolar dilatation. Lactic acid also has got similar effect.

Hypoxia, increased CO_2 tension, lactic acid, bradykinin, histamine, acetylcholine, adenosine triphosphate, adenylic acid and potassium ions have been considered to be the determinant of muscle circulation during exercise hyperaemia.

Exercise. Muscle blood flow during exercise has also been considered (*vide* Muscle Physiology). With the onset of muscular work, the metabolic need of O_2 is increased tremendously and such need is made adequately through activation of cardiovascular, respiratory and neuroendocrine processes along with local modification of muscle blood circulation. If these mechanisms fail then the anaerobic processes prevail, causing accumulation of lactic acid in the muscle and blood and ultimately leading to exhaustion or fatigue.

The blood circulation that increases during exercise is possibly due to reactive hyperaemia caused through metabolites acting directly on the vascular smooth muscle or indirectly through **axon reflex.** It has been considered that the hyperaemia which is produced by metabolites, is mostly dependent upon combinations of several factors instead of one single factor.

In the working muscles, local changes of pH and composition of interstitial fluid cause opening up capillaries and arterioles that are not already dilated by the sympathetic vasodilator activities. Extracellular K^+ concentration is so much increased during muscular exercise, that this can account for a major part of the vascular dilatation accompanying muscular activity.

FOETAL CIRCULATION

Circulation in the body before birth differs from circulation after birth. Because foetal blood secures oxygen and metabolites from maternal blood instead of its own lungs and digestive organs. The details of this will be discussed when reproduction is considered in chapter XV on endocrinology.

HAEMORRHAGE

Definition. *Escape of blood from ruptured blood vessels is called haemorrhage.*

Effects of haemorrhage. The effects of haemorrhage depends on the amount and rapidity of blood loss, and the efficiency of the compensatory power of the subject. If the haemorrhage be severe it may lead to

circulatory collapse and death. If it is moderate (5-15 ml per kg body weight) and the subject is healthy, compensatory changes take place and normal condition is restored. From a professional healthy donor about, 500-1,000 ml of blood may be taken at a time, at three to four months' intervals.

Haemorrhage produces the following disturbances: (1) *Blood volume* is diminished. (2) *Blood pressure*— Due to decreased blood volume cardiac output is diminished and there is reflex vasoconstriction. Vasoconstriction leads to increased peripheral resistance. There is also venous constriction and more blood is propelled towards the heart. Less blood goes to the skin, splanchnic area, muscle, etc. due to constriction of arterioles. There is fall of pressure in the arterioles. The pressure in the capillaries also falls and less amount of fluid is transuded from the blood to the tissue spaces. Although the capillary pressure falls, but there is no change in the osmotic pressure and so fluid from the tissue spaces enters the blood and keeps the blood volume almost constant. If the haemorrhage occurs slowly the blood pressure level may be maintained for a considerable time. In case of severe haemorrhage, there is fall of cardiac output and diminution of peripheral resistance, dilatation of the vessels of the skeletal muscles. All these lead to profound fall of blood pressure. The heart rate is markedly diminished. There is diminution of cerebral blood flow which results in sudden loss of consciousness or fainting. (3) Heart rate is increased to maintain cardiac output. (4) Respiration increases both in rate and depth. Anoxia develops due to less haemoglobin. (5) *Pallor of the skin* occurs due to diminution of blood flow in the skin. (6) *Cold sweat*— The skin is cold and there is less evaporation of sweat. (7) *Excitement* is caused by anoxia. (8) Diminution in urine flow occurs due to impaired renal circulation.

Role of atrial and ventricular receptors and the sino-aortic baroreceptors. The discharge of impulses from the receptors in the atria and ventricles is not dependent upon the mean systemic pressure, but upon the venous return to the heart. In haemorrhage there is diminution of venous return, stroke volume and pulse pressure. Due to the reduction of venous return the inhibitory effect of these afferents on arteriolar constriction is reduced. The resultant effect is the increase of peripheral resistance and consequently there is some improvement of the venous return. Again, stimulation of the sino-aortic baroreceptors is dependent on pulse pressure. In haemorrhage due to the fall of pulse pressure the stimulation of the baroreceptors is diminished. So there are vasoconstriction and tachycardia due to reflex chemoreceptor's influence following haemorrhage. Tachycardia further reduces the stroke volume and pulse pressure.

Compensatory changes after haemorrage

I. **Changes in the cardiovascular system.** *The immediate need*

is to maintain the blood pressure. To attain this need the following changes take place:

(*a*) *Heart rate rises*—to maintain cardiac output—caused by low blood pressure, O_2 lack, CO_2 excess, etc. through central and sino-aortic mechanism.

(*b*) *General vasoconstriction*—caused by the effects of (*i*) O_2 lack, (*ii*) CO_2 excess, etc directly on the vasomotor centre as well as reflexly through the chemoreceptors of the sino-aortic nerves. (*iii*) In the experimental animal it has been observed that after severe bleeding the blood pressure falls much below normal. The chemoreceptors of the sino-aortic nerves bring about reflex vasoconstriction and exert their influence to maintain the mean systemic pressure in the bled animal. But after section of the vagi reflex vasoconstriction disappears and the blood pressure falls still further

(*c*) *Adrenalin and Noradrenaline secretion*—caused by reflex chemoreceptor's activity and excitement leading to further vasoconstriction and increase of heart rate.

(*d*) *Contraction of spleen and mesenteric bood vesseles*—expelling stored corpuscles into circulation.

(*e*) *Liver blood valume*—The volume of liver blood is also decreased so as to compensate the blood loss following haemorrhage.

II Changes in respiration. Respiration increases both in rate and depth and thus total pulmonary ventilation rises, caused by low blood pressure, anoxia, CO_2 excess, etc. by central as well as sino-aortic process. Its purpose is to supply more oxygen.

III. Renal changes. Volume of urine decreases due to fall of blood pressure, renal vasoconstriction and consequent less renal circulation But the *filtration fraction* is found to be more than normal, showing that the efferent glomerular vessels undergo a selective constriction. Besides these, angiotensin II that is formed due to interaction of plasma globulin substrate (α_2-fraction), and renin (secreted from the juxtaglomerular region of ischaemic kidney) has got the effect. This renin-angiotensin system also stimulates the secretion of *aldosterone* and also *glucocorticoids* from the adrenal cortex. Aldosterone by maintaining electrolyte balance (Na^+ retention and K^+ excretion through the kidneys) restores blood volume Under such state vasopression (antidiuretic hormone) is also secreted from the posterior pituitary and this helps further in restoration of blood volume through excretion of *less* urine. Due to less urine formation, nitrogen retention takes place in the blood and may lead to azotemia or uraemia. In case of prolonged hypotension there may occur severe renal tubular damage (*lower nephron nephrosis*).

IV. Restoration of blood. The lost blood is regained. At first the fluid, then the plasma proteins and lastly the red cells and haemoglobin are restored. The brief details are as follows:

Fluid. The first change in the indrawing of water from the tissue spaces even before the haemorrhage is over. Due to low blood

pressure, the capillary pressure falls much below the colloidal osmotic pressure of plasma. Hence, instead of normal filtration, water from the tissue spaces is drawn in and thus blood volume starts rising. A definite increase of plasma volume takes place after one hour, as shown by dilution of plasma proteins and haemoglobin. In *24 hours plasma volume is fully restored* and even may rise above normal to compensate for the low red cell count. During this period the subject feels thirsty and takes a lot of water. This is a great help for restoring blood volume.

Proteins Plasma proteins are replenished in two stages: (*a*) The stored proteins (labile protein) are mobilised within a few hours from the tissues and organs, chiefly liver. (*b*) They are also actively manufactured by the liver. During this regeneration, a sequence is seen—at first the fibrinogen, then the globulin and lastly the albumin is regenerated. Provided the blood is adequate, *the lost plasma proteins are fully restored in a few days.*

Red cells Red cells are rapidly manufactured by the red marrow after a few days. Anoxia stimulates the marrow. *Full restoration of the red cells and haemoglobin requires* 3 to 5 *weeks' time*, if the diet is adequate. [Effect of Splenic Contraction—*vide* page 354]

Clinical aids The best remedy lies in whole blood transfusion, because, it fully supplies all the materials lost. Plasma transfusion comes next. Dried plasma can be preserved and may be used after suitable dilution.

Compensatory reactions in haemorrhage may be summarised thus: (*i*) venoconstriction, (*ii*) vasoconstriction, (*iii*) increased secretion of epinephrine, norepinephrine, vasopressin, aldosterone and glucocorticoids, (*iv*) rapid rate of thoracic pumping and of skeletal muscular pumping (occasionally), (*v*) increased flow of interstitial fluid in the capillaries, (*vi*) secretion of erythropoietin, (*vii*) increased plasma protein synthesis and (*viii*) tachycardia.

MUSUCLAR EXERCISE

Work physiology is a branch of science which deals with the physiology of man at work. Volitional muscular movement or exercise is a cortical phenomenon and is under the 'feedback' control of cerebellum (*vide* Functions of the cerebellum in Nervous System). During muscular exercise, the energy needs of the muscle are increased tremendously and these energies are met with through increased metabolism of the *active* muscle. With the increase of metabolism, the oxygen needs of the muscle are increased and these requirements are met with by causing oxygen-rich RBC more available to the active site. This is happened by (*i*) *increasing heart rate*, (*ii*) *increasing cardiac output*, (*iii*) *increasing venous return*, (*iv*) *decreasing rate of blood flow in the inactive muscle*, (*v*) *increasing vascular resistance in the inactive muscle*, (*vi*) *redistribution of blood from non-vital organs* (splanchnic bed) *to vital organs* (brain and heart) *and active site*, (*vii*) *increasing blood*

pressure, (*viii*) *increasing pulmonary ventilation*. Other bodily functions that are altered during exercise are the (*i*) *blood cell changes*, (*ii*) *kidney functions*, (*iii*) *body temperature regulation*, (*iv*) *digestive function*, (*v*) *water and salt balance*, (*vi*) *endocrine function*.

These show that during exercise cerebral cortex mobilises several functions only to cope with the high degree of metabolism that is brought about by the active muscles. These changes are described below under the following headings :

1. **Changes in cardiovascular system.** (*a*) **Heart and exercise.** Prolonged and systematic exercise causes enlargement of the heart and this is happened only to cope with the excessive work load imposed upon the heart during work. There is a lot of misunderstanding that prolonged exercise may cause dilatation of the heart similar to that it is happened in heart disease. But the hypertrophy of the heart in athletes is caused by physiological processes. The nature of processes is similar to the hypertrophy of skeletal muscle resulting from systematic exercise. Thus hypertrophied athletic heart is more powerful, efficient and capable of greater increase in stroke volume but the dilated diseased heart is less efficient and has a limited capacity for work.

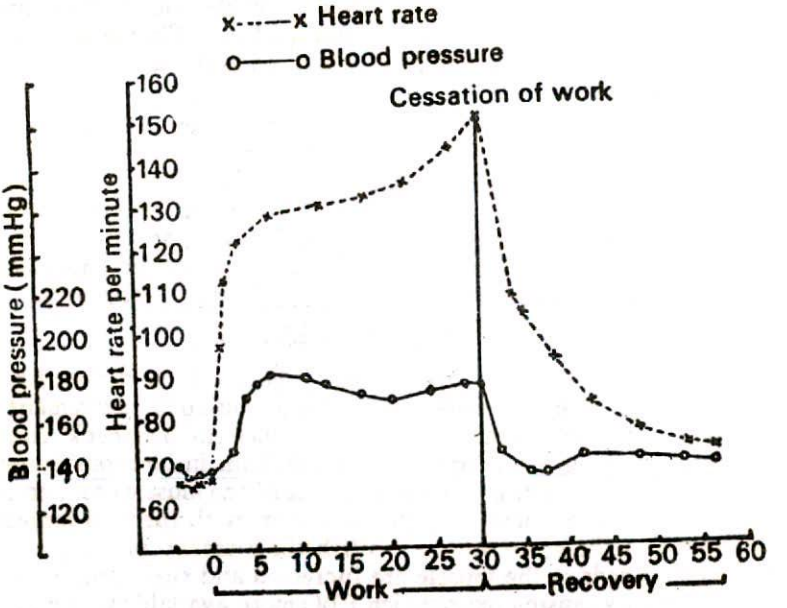


Fig. 240. Diagrammatic tracing of cardiovascular response during work and recovery.

(*b*) Heart rate changes during exercise Fig. 240). The acceleration of the heart is observed immediately following exercise. It has been observed that the heart is increased slightly even before onset of

exercise and it is presumably due to influence of the cerebral cortex on the medullary cardiac centre. A short rise of heart rate is observed at first minute of exercise but after that this rate of rise is slightly decreased Within 4 to 5 minutes of exercise the maximal rise is more or less achieved A 'plateau' is observed if the exercise is further continued. But the time is variable from individual to individual and even with different degrees of work load. In athletes, the rate of rise of the heart will be slower. Besides these, the maximal heart rate that is reached during exercise and the rapidity with which the maximal value is attained depends upon several factors which are (*a*) *emotional*, (*b*) *environmental temperature and humidity*, (*c*) *physical conditions of the subjects.*

There is no satisfactory explanation of the increase of heart rate in man during exercise. The explanation is mostly based on the animal experimentation. It is claimed that both nervous and chemical factors are playing in such process. Initial rise of heart rate (anticipatory heart rate) just before exercise is due to the influence of cerebral cortex and other higher brain centres. With the onset of exercise the rise of heart rate may be due to (*a*) *reflexes originating in the receptors of moving joints or cotracting muscles*, (*b*) *stimulation of chemoreceptors in muscles by the acid metabolites*, (*c*) *sympathetico-adrenal activation causing secretion of much larger amounts of epinephrine in the blood*, (*d*) *rise of body temperature and* (*e*) *stimulation of stretch receptors in atrium by the rapid venous return in heart thus causing Bainbridge reflex* There is controversial opinion regarding the Bainbridge reflex. None does believe. that the increase of heart rate during exercise is due to the effect of such reflex, because during exercise the right atrial pressure does not rise and if it is so then instead of rise there is possibility of decrease of heart rate. [*Vide* Receptor of right heart, page 361.]

Regarding the return of heart rate to initial resting level depends upon the intensity of work load and also on the physical condition of the individual. The rapidity with which the heart rate returns to the resting level following cessation of exercise is considered as a test for physical fitness. In trained individual or in physically fit person the recovery period is very short.

(*c*) Cardiac output. During exercise the cardiac output is greatly increased. In trained athletes, it may achieve a maximal output of 30 litres per minute, at an O_2 uptake of 4 litres per minute but in non-athletes, the output may be average 22 litres at an O_2 uptake of 3·3 litres per minute. The exercise in cardiac output during exercise is the result of the increase in stroke volume and heart rate.

It has been claimed for a long time that the increased stroke volume during exercise is due to functioning of Starling law of heart, But Starling law of heart cannot hold good because modern technique claims that the diastolic size of the heart is not increased during exercise. Instead, the diastolic size of the heart is decreased during exercise so that the increased stroke volume cannot be caused by greater stretching. Besides this, Rushmer (1959) has claimed that the increased cardiac output during exercise does not necessarily involve increase in stroke volume and heart rate. He claimed that the stroke volume during exercise is increased no doubt, but by about the same amount on changing from standing to the supine position. He claimed that increase in cardiac output is mostly due to increase of heart rate.

(*d*) Venous return. Venous return is greatly increased during exercise for the following reason : (*i*) milking or massaging action of skeletal muscles—During exercise, the alternate contraction and relaxation of the muscle act as a booster pump for flowing blood towards the heart. Due to presence of valves in the veins, the blood is squee-

sed out from the vein towards the heart during contraction and allowed to fill blood during relaxation of the muscle. This pumping mechanism depends upon intensity and type of exercise. (*ii*) **Respiratory movements**—Respiratory movements exert a sucking effect over the right heart and great veins so that greater venous return may occur. Vis a fronte is the consequence of the above effect during respiratory effort. During inspiration the thoracic cavity is enlarged causing fall of intrathoracic pressure. This fall of intrathoracic pressure as well as increase of pressure on the anterior abdominal wall due to descent of diaphragm causes rapid return of blood into the heart. Expiration has got the opposite effect. (*iii*) **Contraction of limb veins**—It is claimed that limb veins undergo reflex vasoconstriction during exercise thus facilitating rapid venous return to the heart.

(*e*) **Blood pressure.** Blood pressure is raised with the onset of exercise. There may be an anticipatory blood pressure due to nerve impulses originating from the cerebral cortex to the medullary cardiac and vasoconstrictor centres. Other factors that may participate in the rise of blood pressure during exercise are due to activation of sympathetico-adrenal systems causing shifting of blood from the splanchnic beds to the other parts of the body.

So the rise of arterial blood pressure during exercise is due to (*i*) increase of cardiac output, causing greater distention of aorta and large arteries, (*ii*) increase of heart rate and (*iii*) compensatory vasoconstriction in the non-active organs (splanchnic beds and skin) and vasodilatation in the active organs so as to perfuse the active organs with a greater pressure.

The nature of blood pressure rise cannot be generalised because the pressure changes mostly depend upon the type, speed and duration of the activity and also of the physical condition of the subject.

(*f*) **Circulatory status during exercise.** During exercise, the circulation is adjusted in such a way that the active muscles as well as the vital organs get blood supply to a greater proportion than that of the inactive organs and the non-vital organs. It has been observed that the active muscle gets more blood supply during exercise and the circulation is increased more than about 30 times (Fig. 241). It is claimed that this greater supply is due to decrease of vascular resistance caused by locally accumulated metabolites. During exercise sudden lack of O_2 caused the increased accumulation of CO_2, lactic acid, adenosine, intracellular K^+ and histamine. These substances may cause hyperaemia (reactive hyperaemia) and thus the resistance to blood flow is decreased. As the work load of the heart is increased tremendously during exercise, the coronary flow is increased accordingly to its own nourishment, otherwise hypoxia may prevail. So in moderate exercise, coronary flow is increased according to the O_2 requirement of the cardiac muscle. But in severe exercise, the coronary flow may be increased no doubt but the cardiac muscle due to tremendous increase of heart rate, will fail to maintain

its O_2 according to its need and the subject may feel ar ginal pain. Pulmonary circulation dur ng exercise is increased in proportion to

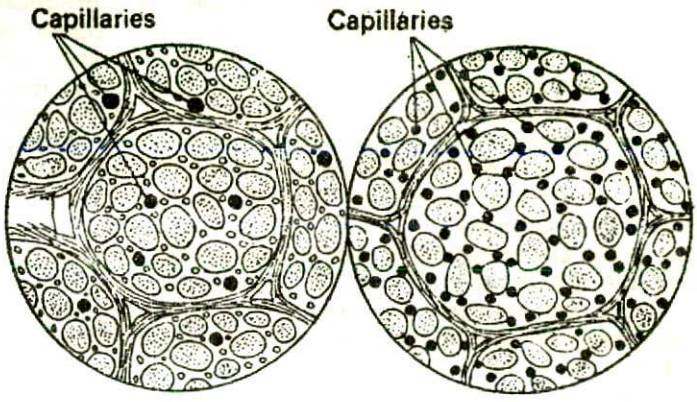


Fig.241. Represents the circulatory status of the muscle during rest and exercise.
A = smaller number of capillaries in respect to a muscle bulk present at rest.
B = greater number of capillaries opened up in the same muscle during exercise.

the increase in venous return to the heart. But with the increase of pulmonary circulation, the pulmonary arterial pressure is insignificantly increased possibly due to distensibility of its blood vessels. Blood flow to the brain is relatively under normal state and remains mostly unaltered during exercise.

During exercise the blood flow in the active muscle, lung, heart is increased, but the same in the abdominal organ, kidneys and in the skin (initially) is greatly decreased due to compensatory vasc constriction. This is happened possibly through the chemoreceptor reflex initiated by the accumulated metabolities during exercise so as to cause redistribution of blood from abdominal organs tothe exercising muscle, heart, lung and skin (later stage). Skin blood flow is initially decreased but as the work is continued and the body temperature is increased the skin blood flow is also increased only to eliminate excess heat produced by the contracting muscle.

2. Changes in respiration

(*a*) Pulmonary ventilation. *Pulmonary ventilation* in moderate exercise is always linear with the amount of O_2 absorbed. It has been observed that a linear relationship between the work load and the pulmonary ventilation is maintained until the work load is so increased that the steady state is not achieved. It has been so observed that the pulmonary ventilation is increased without appreciable increase in O_2 consumption with graded increase of work load. This shows that pulmonary ventilations do not limit the work load but the O_2 consumption limits work load because the cardiac output is not increased accordingly. It then indicates that with the increase of work load, pulmonary ventilation is still capable of further adjustment when the cardiovascular system has reached to its limit.

(*b*) **Breathing** With the increase of O_2 demand during exercise, the rate and depth of respiration are increased. These effects may be due to (*i*) direct effect (*centrogenic*) of increased CO_2, produced by the working muscle, on the respiratory centre, (*ii*) indirect effect (*reflexogenic*) of metabolites on respiratory centre through chemoreceptors (carotid body and aortic body), (*iii*) proprioceptive impulses from the joints of the extremities, (*iv*) stimulation of chemoreceptors present in pulmonary aorta, (*v*) increase of temperature causing rise of breathing by (*a*) direct stimulation of respiratory centre, (*b*) stimulation of cortical centre or carotid and aortic bodies, and (*c*) other reflex pathways

None of the above factors is solely responsible for increase in breathing during exercise and possibly multifactors are responsible for it. Other factors that may take part in increasing the respiration during exercise are the impulses from the cortex and adrenaline liberated into the blood.

Nature of second wind. During violent exercise initially there is developed a frequent feeling of distress but if the exercise is further continued then this sense of distress is replaced by a sense of great relief, which is called second wind. The distresses that precede the *second wind* are the (*a*) breathlessness, (*b*) throbbing of the head, (*c*) fluttering and irregular pulse, (*d*) muscle pains and (*e*) feeling of sensation of constriction around the chest.

With the onset of second wind, the facial distress disappears and breathlessness other than discomforts disappear. The subject feels a sense of comfort. The second wind should not be confused with the *steady state* which is the condition in which oxygen need and oxygen supply are balanced in such a way that the *lactic acid* and *oxygen debt* do not take place

The physiological basis of second wind is not clear and it is a complex phenomenon in which different types of physiological adjustments take place.

Oxygen exchange during exercise. It has been described by Morehouse and Miller (1967) that in light and moderate exercises 400 and 700 kg-m/minute respectively, both the alveolar and the arterial O_2 tension rise. The differences between the alveolar and the arterial O_2 tension fall from 14·7 mm Hg to 11·0 mm Hg during exercise. With the increase of cardiac output during exercise, the velocity of blood flow is not increased but the volume flow of blood in each minute is increased and this permits oxygen exchange in the lungs quite adequately so as to bring about normal saturation of blood with O_2 so long as the oxygen uptake does not exceed 4 litres per minute. In moderate exercise the amount of lactic acid formed, can be fully disposed of the muscle buffers and the greater amount of oxygen, supplied by increased blood flow. But in severe exercise the rate of oxygen supply lags behind and lactic acid rapidly accumulates. It enters the blood stream and

causes acidosis. Thus in severe exercise the lactate content of blood may go up to 100—200 mg% (10—20 mg% resting). In order to dispose of these excess metabolites and lactic acid, extra amount of O_2 is needed. This is called oxygen debt (energy debt). During the first few minutes of recovery period, the lactate content of plasma or muscle does not diminish –showing that O_2 is used or the resynthesis of creatine phosphate and ATP during recovery period. The oxygen used for this purpose is called alactic acid debt. Alactic acid debt is paid at a much faster rate than the lactacid debt (Karpovich, 1959).

(*c*) R.Q. It varies according to the degree of exercise. In *moderate exercise* R.Q varies from 0·85 to 0·89, i.e. more or less same as in rest. If exercise be prolonged with a high fat diet, R.Q. falls to 0·7. But in *severe exercise* (*i*) the R.Q. of excess metabolism (i.e, gaseous exchange over and above the resting) during the period of exercise rises above unity and may go up to 1·5 to 2· This is due to the fact that, the H-ion concentration is much greater in this case than in moderate exercise—being partly due to excess CO_2 and partly to the entry of lactic acid from the muscles. Lactic acid combines with bicarbonates liberating more carbonic acid. Hence, respiration is much more stimulated in this case and more CO_2 is liberated without any corresponding oxygen utilisation. Thus R.Q rises above unity. The extent to which it rises above unity is a measure of the severity of the exercise and extent of lactic acid formation. (*b*) Late in the recovery period, R.Q falls to 0·5, because respiration is depressed and CO_2 is retained to form the lost bicarbonates. This CO_2 comes from the burning of the lactic acid part of Na^+-lactate in the tissues and combines with the Na^+ of the lactate, now left free.

3. Blood cell changes during exercise. RBC count is increased in the early part of the exercise and it is probably due to haemoconcentration. This haemoconcentration is the cause of transfer of fluid from the blood to the tissues. But with more prolonged exercise the fluid passes back to the blood causing haemodilatation and RBC count is thus lowered. In strenuous exercise there may happen haemolysis.

WBC count is increased significantly at any type of exercise. It has been claimed that the greater rise of the WBC count is related with the degree of stress produced with the exercise. In less fit person the rise is more than in athletes under the same work load. Specific gravity of blood in a muscular activity is increased and it varies directly with the RBC.

4. Body temperature. Normally the body temperature is balanced by the rate of the heat production and heat loss. During exercise the heat production is greatly increased and when simultaneous heat loss is not happened then body temperature is raised. In exercise, the body temperature is raised and it is possibly

due to the failure of temperature-regulating centre to maintain the normal body temperature.

5. **Body fluid changes during exercise.** During exercise acute dehydration is a great problem because there is rapid loss of water through sweating and expired air. In *acute exercise* there is haemoconcentration due to (*i*) shifting of fluid from the blood to the tissue spaces, (*ii*) sweating and (*iii*) rapid expiration. But if the exercise is continued then water loss is partly checked and dehydration may be minimum presumably by the return of fluid from the tissue spaces to the blood. In *chronic exercise* as in the case of athletes or in subjects undergoing systematic exercise there appears no permanent shifts of body fluid. Along with water loss there is excessive loss of salt which deteriorates work performace. If the fluid and salt losses are adjusted by taking water along with salt during the period of exercise then the work performance may be increased. But it is not generally taken as there is a general belief of the coaches and of the trainers that drinking is harmful during exercise.

6. **Kidney function in exercise.** Alteration in kidney functions that are generally observed during exercise is presumably due to shupting of blood from the kidneys and other abdominal organs to the vital organs and the active muscle. The renal blood flow is considerably decreased during exercise and this decrease of flow is maintained as long as an hour following cessations of exercise :

Rate of urine formation is greatly diminished due to (*i*) excessive reabsorption of fluid from the renal tubles with the help of antidiuretic hormone (ADH) secreted by the posterior pitutary and (*ii*) decreased renal blood flow. Furthermore, the kidneys excrete excessive acid metabolites that are accumulated in the blood during exercise. Besides these, there is often transient *proteinuria* with exercise. After strenuous exercise there is accumulation of albumin in the urine and has been considered to be the cause of increased permeability of these substances in the glomerular capillaries. Some are of opinions that the increased activity of the kidney tissues may alter the kidney functions during exercise. Often **Masch Haemoglobinuria** a condition in which physical exertion causing formation of ***red urine*** containing haemoglobin is observed. This condition is

mostly due to intravascular breakdown of RBC during strenuous exercise. Haemoglobin generally appears 1-3 hours after severe exercise. Exercise myoglobinuria is often encountered after severe exercise. Stahl (1957) has observed *black urine* formation 24-48 hours after exercise. He has described that breakdown of muscle fibres during exhaustive exercise is the cause of *myoglobinuria*.

7. **Digestive system.** Strenuous exercise inhibits both the motor and secretory functions of the stomach. Campbell and others (1928) have described that moderate exercise inhibits gastric secretion as well as motility of the stomach but the lighter exercise (walking helps in gastric juice secretion and also in emptying of the stomach. But after exercise the motility of the stomach and secretion of gastic juice are increased considerably. This shows that the depressed motility and gastic juice secretion during strenuous exercise are balance by the increased motility of the stomach and gastric juice secrtion after the cessation of activity.

8. **Endocrine status.** Endocrine functions under physical exertion have not yet been studied in detail. Adrenal hypertrophy has been observed in animals under prolonged continuous exertion or training programme. Increased utilisation of cortical hormones during exercise has been observed by many. Besides this, improvement of work performance after administration of corticoids in adrenalectomised animals has also been observed.

Growth hormone utilisation during exercise is increased. It has been observed that during exercise, mobilisation of depot fat is increased by the growth hormone secreted in larger quantity. It is claimed that the liberation of growth hormone or STH appears mostly responsible for mobilisation of depot fat when the exogenous carbohydrate is not made available during exercise.

It has already been discussed that the ADH secretion is increased during physical exercise. This secretion of ADH actually combats against dehydration during exercise.

Function of thyroid hormone during exercise is not yet fully worked out. Lashof and others (1954) found no alterations in thyroid hormone functions in modrate exercise.

DISTINCTION BETWEEN MODERATE AND SEVERE EXERCISES

Changes	Moderate exercise	Severe exercise
Cardiovascular		
1. General	Heart rate, venous return, cardiac output—increase. VMC stimulated—vasoconstriction. Blood pressure raised.	Same but more.
2. Local	Closed vessels open up. Vasodilatation. Increased vascularity. Slow blood flow. Blood more extensively reduced.	Same but more.
espiration		
1. Pulmonary ventilation	Increases proportionaliy bub comes to normal quickly after stopping exercise.	Remains high for a long time after exercise, to supply oxygen debt.
2. R.Q.	Almost normal 0·85-0·20.	High—1·5-2·0. Later on falls—0·5.
ood		
. Cell count	Rises.	Rises.
Acidosis	Present—only for H_2CO_3	More—for H_2CO_3 and latic acid.
Alkali reserve	Reduced	More reduced.
Lactate	Normal (10-20 mg%).	Raised (100-200 mg%)
O_2 content	Less than normal.	Further reduced.
Cori cycle	Nil	Mobilised.
ine		
Volume	Less.	Less.
Reaction	Acid.	Acid, later alkaline.
n		
Volume	Constriction, later dilatation to help heat loss.	Same.
. Sweat	Reduced, later increases.	Same.
xygen debt	Nil.	Present.
econd wind	Possible.	Not possible.
eady state	Possible.	Not possible.
atigue	Delayed.	Early.
uration	Can be continued for a long time.	For short periods only.
ecovery	Quick.	Delayed.