Cardiovascular System

Cardiovascular system comprises heart and blood vessels. Heart is the central pump and the blood vessels are the series of distributing and collecting tubes. The function of cardiovascular system is to supply oxygen, nutrients and other essential substances to the tissues of the body and to remove metabolic end products from the tissue.

Heart

The heart is a muscular organ situated in between the two lungs in the mediastinum. It is made up of two atria and two ventricles. The ventricles are ticker and more muscular than the atria.

The right atrium has the pace maker known as sino-atria node that produces cardiac impulses and atrioventricular node that conducts these impulses to the ventricles. It also has two large veins namely (i) superior vena cava that returns the deoxygenated blood from the head, neck and upper limbs and (ii) inferior vena cava that returns the deoxygenated blood from lower parts of the body.

Right atrium communicates with the right ventricle through the tricuspid valve. Deoxygenated blood from the right atrium enters the right ventricle through this valve.

From the right ventricle, pulmonary artery arises through which deoxygenated blood is pumped into the lungs. In the lungs, the deoxygenated blood gets oxygenated and is returned to left atrium as arterial blood through pulmonary veins.

The left atrium communicates with the left ventricle through the mitral valve (bicuspid valve). Left atrium empties the oxygenated blood into the left ventricle through this valve. From the left ventricle, the systemic aorta arises through which the oxygenated blood is pumped throughout the body.

Two types of tissues are found in the heart. (i) The Predominantly myocardial or contractile cell. (ii) The cell of the conducting system of the heart.

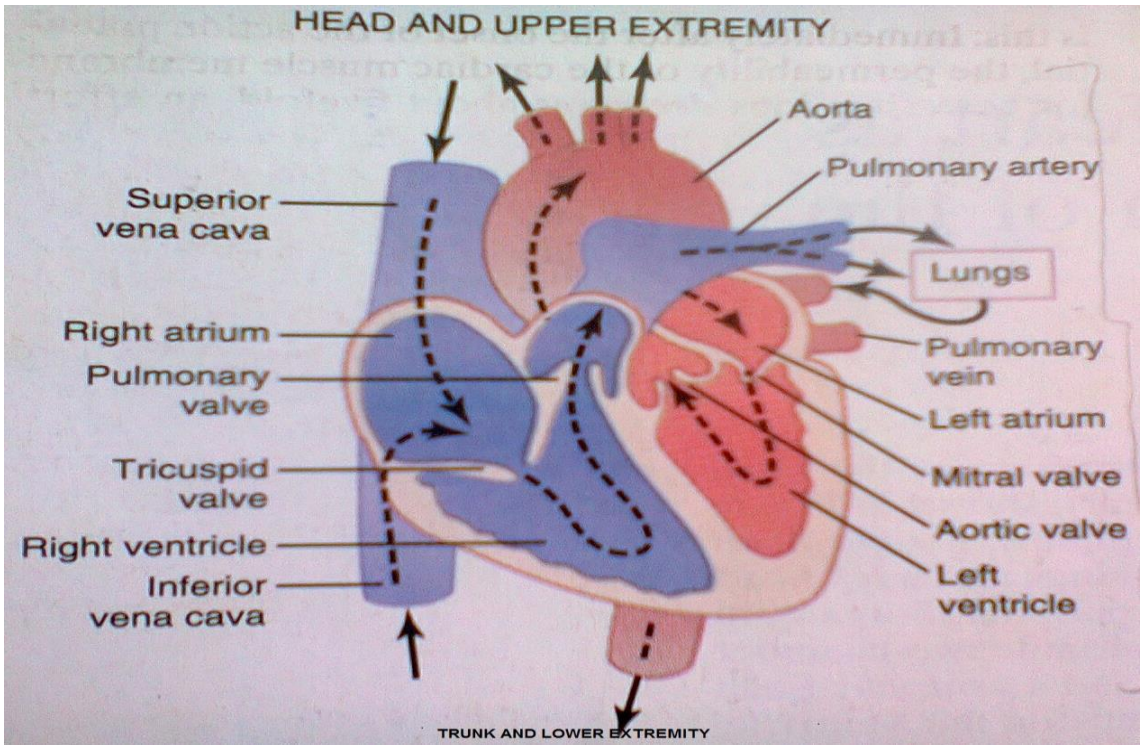


Figure 1. Structure of the heart, and course of blood flow through the heart chambers and heart valves.

Blood Vessels

Vessels of circulatory system are the aorta, arteries, arterioles, capillaries, venules, veins and venae cavae.

Divisions Of Circulation

Blood flows through two divisions of circulatory system:

1. Systemic circulation
2. Pulmonary circulation.

Systemic Circulation

Systemic circulation is otherwise known as **greater circulation** (Fig. 2). Blood pumped from left ventricle passes through a series of blood vessels, arterial system and reaches the tissues. Exchange of various substances between blood and the tissues occurs at the capillaries.

After exchange of materials, blood enters the venous system and returns to right atrium of the heart. From right atrium, blood enters the right ventricle.
Thus, through systemic circulation, oxygenated blood is supplied from heart to the tissues and venous blood returns to the heart from tissues.

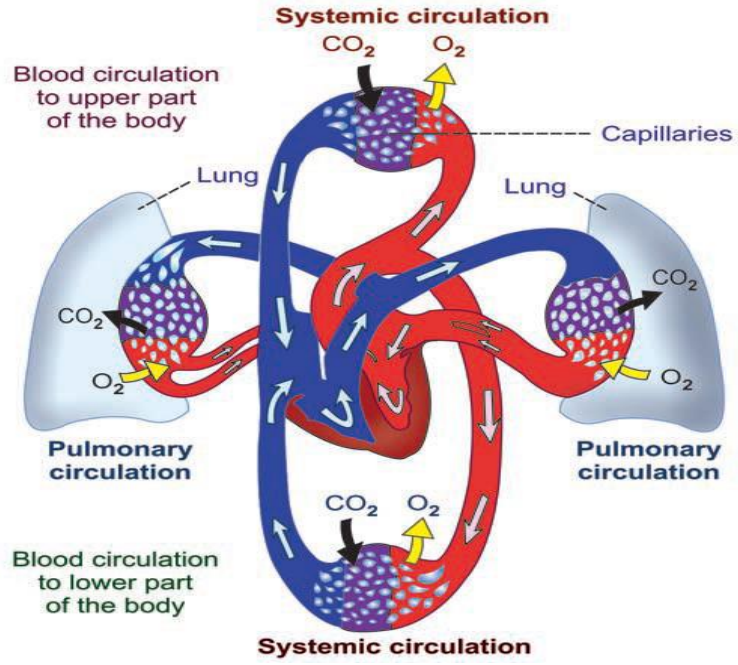


FIGURE 2: Systemic and pulmonary circulation

Pulmonary Circulation

Pulmonary circulation is otherwise called **lesser circulation.** Blood is pumped from right ventricle to lungs through pulmonary artery. Exchange of gases occurs between blood and alveoli of the lungs at pulmonary capillaries. Oxygenated blood returns to left atrium through the pulmonary veins.
Thus, left side of the heart contains oxygenated or arterial blood and the right side of the heart contains deoxygenated or venous blood.

Physiologic Properties of The Heart

1. **Lenght-tension relation.** If the length of the cardiac muscle is increased, the force of contraction increases. This is described by Starling's law which states that "The force of contraction of the heart is proportional to the initial length length of cardiac muscle fibre.
2. **Spontaneous rhythm.** This is inherent, by which the heart initiates its own beating without the influence of an external sources. The ability to do this is due to the cells of the conducting system which have an

unstable membrane potential which results in spontaneous depolarization. This occurs in the SA node, AV node, and the His-Purkinje fibres. The rate of depolarization is fastest in the SA node and hence is known as the *pacemaker*. Pacemaker potential are partly due to fast inward sodium current and mostly due to inward calcium currents which is also responsible for the upstroke (Fig.3).

3. **Prolong repolarization.** The action potential in the myocardial or contractile cell lasts about 250milliseconds (0.25sec), compare with about 2milliseconds in skeletal muscle. This is due to the fact that the repolarization phase of the potential is prolonged in cardiac muscle. The prolongation of the action potential is due to "slow inward calcium current" which allows Ca^{2+} to move inside the cell, causing the plateau, and thus resulting in the "persistent depolarisation".
4. **Cardiac muscle as a syncytium.** The dark areas crossing the cardiac muscle fibers are called *intercalated discs;* they are actually cell membranes that separate individual cardiac muscle cells from one another. That is, cardiac muscle fibers are made up of many individual cells connected in series and in parallel with one another (Fig.2)
   At each intercalated disc the cell membranes fuse with one another in such a way that they form permeable "communicating" junctions (gap junctions) that allow almost totally free diffusion of ions. Therefore, from a functional point of view, ions move with ease in the intracellular fluid along the longitudinal axes of the cardiac muscle fibers, so that action potentials travel easily from one cardiac muscle cell to the next, past the intercalated discs. Thus, cardiac muscle is a *syncytium* of many heart muscle cells in which the cardiac cells are so interconnected that when one of these cells becomes excited, the action potential spreads to all of them, spreading from cell to cell throughout the latticework interconnections.

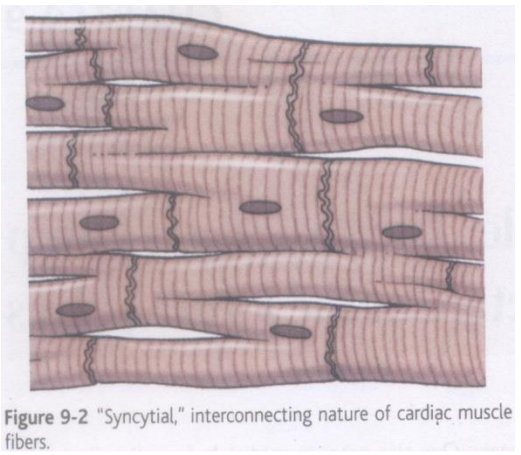


Figure 2
"Syncytial," interconnecting nature of cardiac muscle fiber.

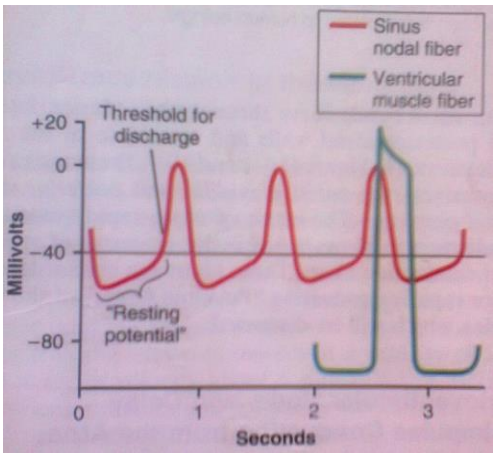


Figure3
Rhythmical discharge of Sinus nodal fibre & action potential of ventricular muscle fibre.

Action Potentials in Cardiac Muscle

In *cardiac muscle*, *the action potential* is caused by opening of two types of channels: (1) *fast sodium channels* and (2) *slow calcium channels,* which are also called *calcium-sodium channels.* The slow calcium channels are slower to open and, even after opened, remain open for several tenths of a second. During this time, a large quantity of both calcium and sodium ions flows through these channels to the interior of the cardiac muscle fiber, and this maintains a prolonged period of depolarization, *causing the plateau* in the action potential. Further, the calcium ions that enter during this plateau phase activate the muscle contractile process. Immediately after the onset of the action potential, the permeability of the cardiac muscle membrane for potassium ions *decreases.* When the slow calcium-sodium channels do close and the influx of calcium and sodium ions ceases, the membrane permeability for potassium ions increases rapidly; this rapid loss of potassium from the fiber immediately returns the membrane potential to its resting level, thus ending the action potential (fig.4).

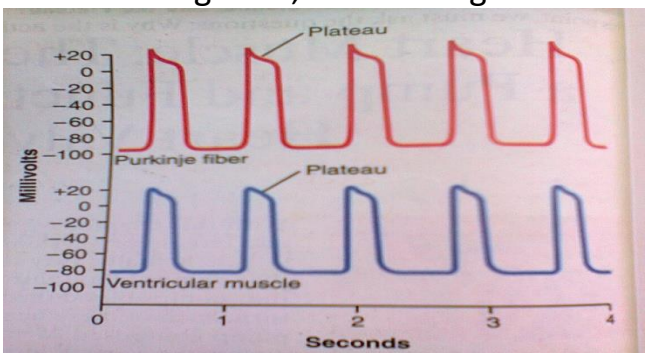


Figure 4 Rhythmical action potentials (in millivolts) from a Purkinje fiber and from a ventricular muscle fiber, recorded by means of microelectrodes.

The Cardiac Cycle

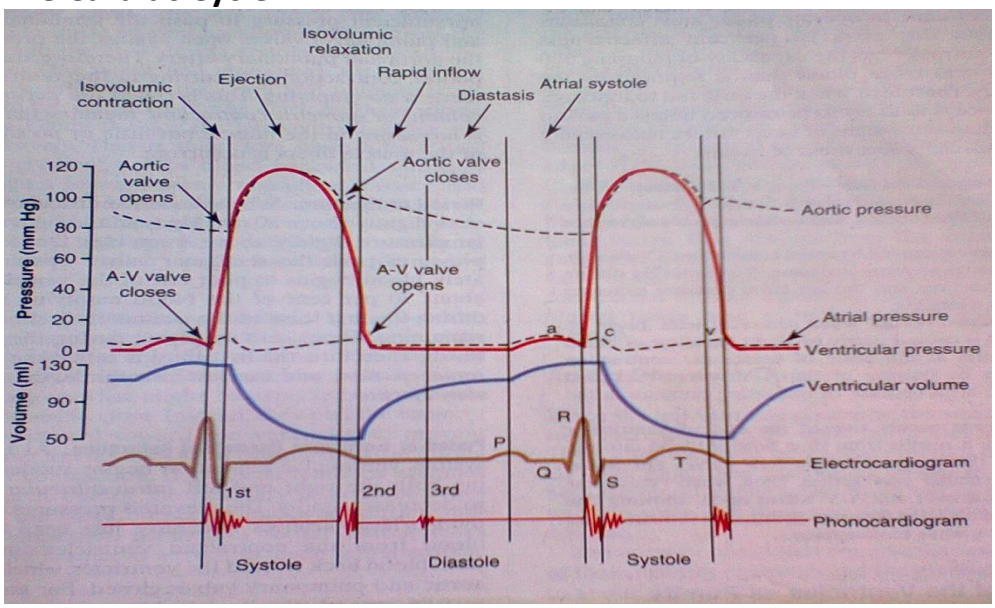


Figure 5: Events of the cardiac cycle for the left ventricular function.

The cardiac events that occur from the beginning of one heartbeat to the beginning of the next are called the *cardiac cycle.* Each cycle is initiated by spontaneous generation of an action potential in the *sinus node*. The action potential travels from *sinus node* rapidly through both atria and then through the A-V bundle into the ventricles. Because of this special arrangement of the conducting system from the atria into the ventricles, there is a delay of more than 0.1 second during passage of the cardiac impulse from the atria into the ventricles. This allows the atria to contract ahead of ventricular contraction, thereby pumping blood into the ventricles before the strong ventricular contraction begins. Thus, the atria act as *primer pumps* for the ventricles, and the ventricles in turn provide the major source of power for moving blood through the body's vascular system.

The cardiac cycle consists of a period of relaxation called *diastole,* during which the heart fills with blood, followed by a period of contraction called *systole.*The figure below shows the different events during the cardiac cycle for the left side of the heart.The top three curves show the pressure changes in the aorta, left ventricle, and left atrium, respectively. The fourth curve depicts the changes in left ventricular volume, the fifth the electrocardiogram, and the sixth a phonocardiogram, which is a recording of the sounds produced by the heart—mainly by the heart valves—as it pumps.

The electrocardiogram shows the *P, Q, R, S,* and *T waves*. They are electrical voltages generated by the heart and recorded by the electrocardiograph from the surface of the body. The *P wave* is caused by *spread of depolarization* through the atria, and this is followed by atrial contraction, which causes a slight rise in the atrial pressure curve immediately after the electrocardiographic P wave.

About 0.16 second after the onset of the P wave, the *QRS waves* appear as a result of electrical depolarization of the ventricles, which initiates contraction of the ventricles and causes the ventricular pressure to begin rising, as also shown in the figure. Therefore, the QRS complex begins slightly before the onset of ventricular systole.

Finally, the *ventricular T wave* in the electrocardiogram represents the stage of repolarization of the ventricles when the ventricular muscle fibers begin to relax. Therefore, the T wave occurs slightly before the end of ventricular contraction.

Blood normally flows continually from the great veins into the atria; about 80 per cent of the blood flows directly through the atria into the ventricles even before the atria contract. Then, atrial contraction usually causes an additional 20 per cent filling of the ventricles. Therefore, the atria simply function as primer pumps that increase the ventricular pumping effectiveness as much as 20 per cent.

In the atrial pressure curve, there are three minor pressure elevations, called the *a, c,* and *v atrial pressure waves*. The *a wave* is caused by atrial contraction. Ordinarily, the *right* atrial pressure increases 4 to 6 mm Hg during atrial contraction, and the *left* atrial pressure increases about 7 to 8 mm Hg. The *c wave* occurs when the ventricles begin to contract; it is caused partly by slight backflow of blood into the atria at the onset of ventricular contraction but mainly by bulging of the A-V valves backward toward the atria because of increasing pressure in the ventricles. The *v wave* occurs toward the end of ventricular contraction; it results from slow flow of blood into the atria from the veins while the A-V valves are closed during ventricular contraction.

During ventricular systole, large amounts of blood accumulate in the right and left atria because of the closed A-V valves. Therefore, as soon as systole is over and the ventricular pressures fall again to their low diastolic values, the moderately

increased pressures that have developed in the atria during ventricular systole immediately push the A-V valves open and allow blood to flow rapidly into the ventricles, as shown by the rise of the left *ventricular volume curve*. This is called the *period of rapid filling of the ventricles.*

The period of rapid filling lasts for about the first third of diastole. During the middle third of diastole, only a small amount of blood normally flows into the ventricles; this is blood that continues to empty into the atria from the veins and passes through the atria directly into the ventricles.

During the last third of diastole, the atria contract and give an additional thrust to the inflow of blood into the ventricles; this accounts for about 20 per cent of the filling of the ventricles during each heart cycle.

Immediately after ventricular contraction begins, the ventricular pressure rises abruptly, causing the A-V valves to close. Then an additional 0.02 to 0.03 second is required for the ventricle to build up sufficient pressure to push the semilunar (aortic and pulmonary) valves open against the pressures in the aorta and pulmonary artery. Therefore, during this period, contraction is occurring in the ventricles, but there is no emptying. This is called the period of *isovolumic* or *isometric contraction,* meaning that tension is increasing in the muscle but little or no shortening of the muscle fibers is occurring.

When the left ventricular pressure rises slightly above 80 mm Hg (and the right ventricular pressure slightly above 8 mm Hg), the ventricular pressures push the semilunar valves open. Immediately, blood begins to pour out of the ventricles, with about 70 per cent of the blood emptying occurring during the first third of the period of ejection and the remaining 30 per cent emptying during the next two thirds. Therefore, the first third is called the *period of rapid ejection,* and the last two thirds, the *period of slow ejection.*

At the end of systole, ventricular relaxation begins suddenly, allowing both the right and left *intraventricular pressures* to decrease rapidly. The elevated pressures in the distended large arteries that have just been filled with blood from the contracted ventricles immediately push blood back toward the ventricles, which snaps the aortic and pulmonary valves closed. For another 0.03 to 0.06 second, the ventricular muscle continues to relax, even though the ventricular volume does not change, giving rise to the period of *isovolumic* or *isometric relaxation.* During this period, the intraventricular pressures decrease rapidly back to their low diastolic levels. Then the A-V valves open to begin a

new cycle of ventricular pumping.

During diastole, normal filling of the ventricles increases the volume of each ventricle to about 110 to 120 milliliters. This volume is called the *end-diastolic volume.* Then, as the ventricles empty during systole, the volume decreases about 70 milliliters, which is called the *stroke volume output.*The remaining volume in each ventricle, about 40 to 50 milliliters, is called the *end-systolic volume.* The fraction of the end-diastolic volume that is ejected is called the *ejection fraction*—usually equal to about 60 per cent. When the heart contracts strongly, the end-systolic volume can be decreased to as little as 10 to 20 milliliters.

Function of the Valves

The *A-V valves* (the *tricuspid* and *mitral* valves) prevent backflow of blood from the ventricles to the atria during systole, and the *semilunarvalves* (the *aortic* and *pulmonary artery* valves) prevent backflow from the aorta and pulmonary arteries into the ventricles during diastole.

The Normal Electrocardiogram

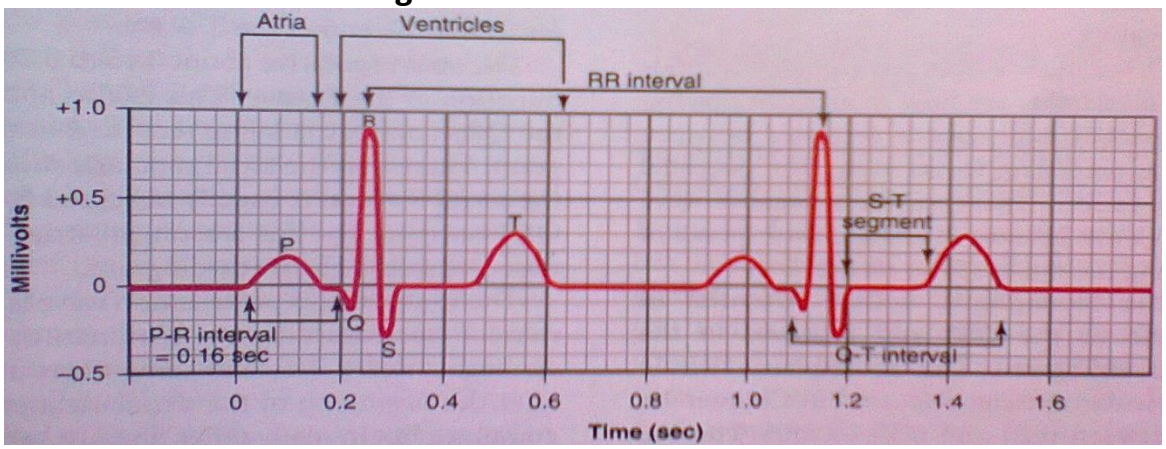


Figure 6. Normal electrocardiogram

When the cardiac impulse passes through the heart, electrical current also spreads from the heart into the adjacent tissues surrounding the heart. A small portion of the current spreads all the way to the surface of the body. If electrodes are placed on the skin on opposite sides of the heart, electrical potentials generated by the current can be recorded (Fig.6); the recording is known as an *electrocardiogram.*

Characteristics of the Normal Electrocardiogram

The normal electrocardiogram (Fig.5) is composed of a P wave, a QRS complex, and a T wave. The P wave is caused by electrical potentials generated when the atria depolarize before atrial contraction begins. The QRS complex is caused by potentials generated when the ventricles depolarize before contraction. The T wave is caused by potentials generated as the ventricles recover from the state of depolarization.

P-Q or P-R Interval.

The time between the beginning of the P wave and the beginning of the QRS complex is the interval between the beginning of electrical excitation of the atria and the beginning of excitation of the ventricles. This period is called the P-Q interval. The normal P-Q interval is about 0.16 second.

Q-T Interval.

Contraction of the ventricle lasts almost from the beginning of the Q wave (or R wave, if the Q wave is absent) to the end of the T wave.

Rate of Heartbeat as Determined from the Electrocardiogram.

The rate of heartbeat can be determined easily from an electrocardiogram because the heart rate is the reciprocal of the time interval between two successive heartbeats. The normal interval between two successive QRS complexes in the adult person is about 0.83 second. That is heart rate = 1/RR = 1/0.83 times per sec or 1/0.83 × 60 times per minute, or 72 beats per minute.

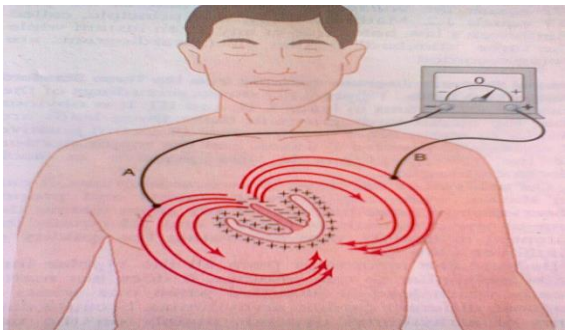


Figure 6
Flow of current in the chest around partially depolarized Ventricles

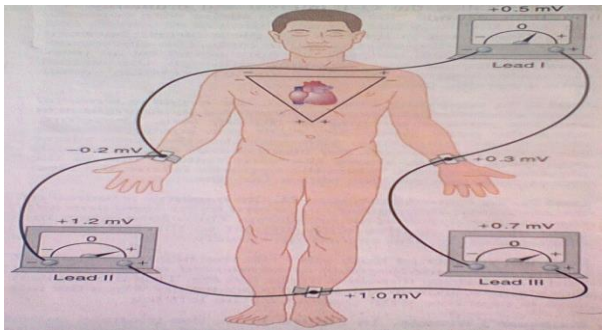


Figure 7
Conventional arrangement of electrodes for recording the standard electrocardiographic leads. Einthoven's triangle is superimposed on the chest.

Electrocardiographic Leads

Three Bipolar Limb Leads

The term "bipolar" means that the electrocardiogram is recorded from *two* electrodes located on different sides of the heart, in this case, on the limbs. Thus, a "lead" is not a single wire connecting from the body but a combination of two wires and their electrodes to make a complete circuit between the body and the electrocardiograph (Fig.7).

Lead I. In recording limb lead I, the *negative terminal of the electrocardiograph is connected to the right arm* and the *positive terminal to the left arm.* Therefore, when the right arm is negative with respect to the left arm; the electrocardiograph records positively.

Lead II. To record limb lead II, the *negative terminal of the electrocardiograph is connected to the right arm* and the *positive terminal to the left leg.* Therefore, when the right arm is negative with respect to the left leg; the electrocardiograph records positively.

Lead III. To record limb lead III, the *negative terminal of the electrocardiograph is connected to the left arm* and the *positive terminal to the left leg.* This means that the electrocardiograph records positively when the left arm is negative with respect to the left leg.

Einthoven's Triangle.

The triangle, called *Einthoven's triangle,*(fig 7.) is drawn around the area of the heart.This illustrates that the two arms and the left leg form apices of a triangle surrounding the heart. The two apices at the upper part of the triangle represent the points at which the two arms connect electrically with the fluids around the heart, and the lower apex is the point at which the left leg connects with the fluids.

Einthoven's Law. Einthoven's law states that if the electrical potentials of any two of the three bipolar limb electrocardiographic leads are known at any given instant, the third one can be determined mathematically by simply summing the first two (but note that the positive and negative signs of the different leads must be observed when making this summation). For instance, let us assume that momentarily, as noted in Figure 7, the right arm is -0.2 millivolt

(negative) with respect to the average potential in the body, the left arm is + 0.3 millivolt *(positive),* and the left leg is +1.0 millivolt *(positive).*
Observing the meters in the figure, it can be seen that lead I records a positive potential of +0.5 millivolt, because this is the difference between the -0.2 millivolt on the right arm and the +0.3 millivolt on the left arm. Similarly, lead III records a positive potential of +0.7 millivolt, and lead II records a positive potential of +1.2 millivolts because these are the instantaneous potential differences between the respective pairs of limbs.

Now, note that *the sum of the voltages in leads I and III equals the voltage in lead II;* that is, 0.5 plus 0.7 equals 1.2.

Normal Electrocardiograms Recorded from the Three Standard Bipolar Limb Leads. Figure 8 shows recordings of the electrocardiograms in leads I, II, and III. The electrocardiograms in these three leads are similar to one another because they all record positive P waves and positive T waves, and the major portion of the QRS complex is also positive in each electrocardiogram.

Because the recordings from all the bipolar limb leads are similar to one another, it does not matter greatly which lead is recorded when one wants to diagnose different cardiac arrhythmias, because diagnosis of arrhythmias depends mainly on the time relations between the different waves of the cardiac cycle. But when one wants to diagnose damage in the ventricular or atrial muscle or in the Purkinje conducting system, it does matter greatly which leads are recorded, because *abnormalities of cardiac muscle contraction* or *cardiac impulse conduction* do change the pattern of electrocardiograms markedly in some leads yet may not affect other leads.

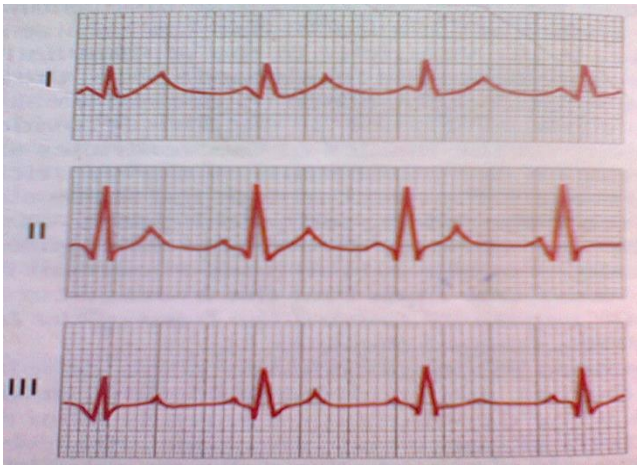


Figure 8: Normal electrocardiograms recorded from the three *standard* electrocardiographic leads.

Chest Leads (Precordial Leads)

Often electrocardiograms are recorded with one electrode placed on the anterior surface of the chest directly over the heart at one of the points shown in Figure 9.This electrode is connected to the positive terminal of the electrocardiograph, and the negative electrode, called the *indifferent electrode,* is connected through equal electrical resistances to the right arm, left arm, and left leg all at the same time, as also shown in the figure. Usually six standard chest leads are recorded, one at a time, from the anterior chest wall, the chest electrode being placed sequentially at the six points shown in the diagram. The different recordings are known as leads V1, V2, V3, V4, V5, and V6.

In leads V1 and V2, the QRS recordings of the normal heart are mainly negative because, as shown in Figure 9, the chest electrode in these leads is nearer to the base of the heart than to the apex, and the base of the heart is the direction of electronegativity during most of the ventricular depolarization process. Conversely, the QRS complexes in leads V4,V5, and V6 are mainly positive because the chest electrode in these leads is nearer the heart apex, which is the direction of electropositivity during most of depolarization.

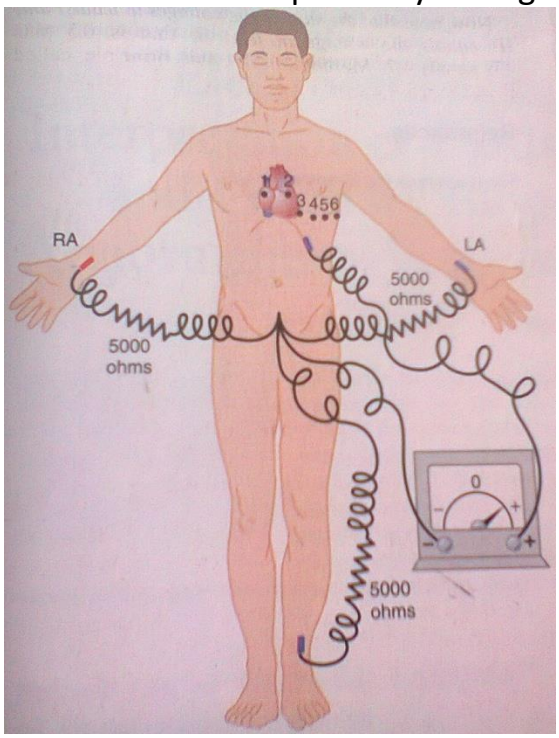


Figure 9

Connections of the body with the electrocardiograph for recording *chest leads*. LA, left arm; RA, right arm.

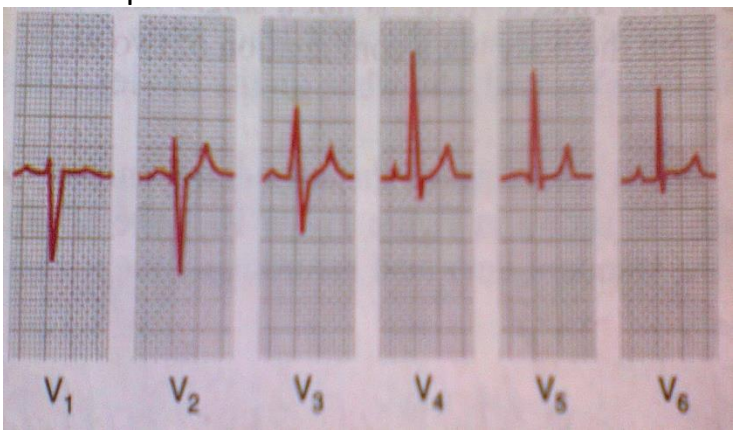


Figure 10

Normal electrocardiograms recorded from the six standard chest leads.

Augmented Unipolar Limb Leads

Another system of leads in wide use is the *augmented unipolar limb lead.* In this type of recording, two of the limbs are connected through electrical resistances to the negative terminal of the electrocardiograph, and the third limb is connected to the positive terminal. When the positive terminal is on the right arm, the lead is known as the aVR lead; when on the left arm, the aVL lead; and when on the left leg, the aVF lead.

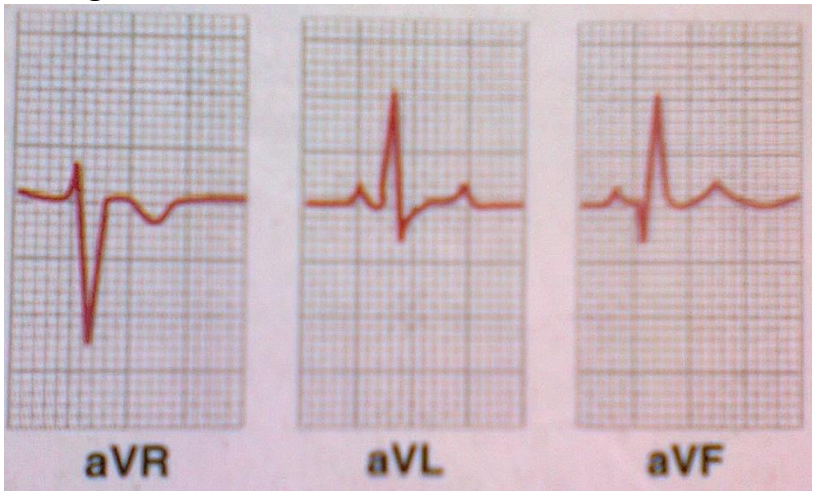


Figure 11

Normal electrocardiograms recorded from the three *augmented unipolar limb leads.*

HEART SOUND

Heart sounds are the sounds produced by mechanical activities of the heart during each cardiac cycle.

Types of Heart Sound

1. *First heart sound* - Sound produced due to closure of atrioventricular valves.
2. *Sound heart sound* – Sound produced due to sudden closure of semilunar valves.
3. *Third heart sound* – Sound produced as a result of vibration set up in the ventricles during rapid ventricular filling.
4. *Fourth heart sound* – Sound produced as a result of vibration set-up in the ventricles during atrial contraction to fill the ventricles.

CARDIAC MURMUR

Cardiac murmur is the abnormal or unusual heart sound heard by stethoscope along with normal heart sound. It is also called abnormal heart sound or cardiac bruit. The abnormal sound is produced because of the change in the pattern of blood flow. Normally blood flow in streamline through the heart and blood vessels. However, during the abnormal conditions like valvular diseases, the blood flow is turbulent. It produces the cardiac murmur.

The murmur is produced because of valvular diseases, septal defects and vascular defects.

Valvular diseases are of two types-

1. Stenosis – refers to narrowing of the heart valves.
2. Incompetence- refers to weakening of the valves in the heart.

Classification of Murmur

i. Systolic murmur
ii. Diastolic murmur
iii. Continuous murmur

Systolic Murmur

1. Incompetence of atrioventricular valves:- These cause regurgitation of blood from ventricles to atria.
2. Stenosis of semilunar valves:-These cause blood to rush through the narrow orifice between the valves.
3. Murmur due to anemia:- Anemia reduces blood viscosity leading to rapid blood flow through the vascular system and murmur is heard.
4. Septal defect:- This causes blood to flow from left ventricle to right ventricle.
5. Coarctation of aorta:- This is the narrowing of a part of systemic aorta.

Diastolic Murmur

1. Stenosis of atrioventricular valves
2. Incompetence of semilunar valves.

Continous Murmur

Continous Murmur is the murmur

CARDIAC OUTPUT

Cardiac output is the amount of blood pumped out of the left ventricle in one minute. The normal value of cardiac output is 5litres/minute, it is the product of stroke volume and the heart rate.

Cardiac output = Stroke volume X Heart rate

The normal stroke volume is between 60-70m, while the normal heart rate is 72 beat/minute

Factors Maintaining Cardiac Output

Cardiac output is maintained by four factors.

1. Venous return
2. Force of contraction
3. Heart rate
4. Peripheral resistance

Venous Return

Venous return is the amount of blood which is returned to the heart from different parts of the body. When it increases the ventricular filling and cardiac output are increased. Thus, cardiac output is directly proportional to venous return provided other factors remain constant. Venous return in turn depends upon five factors;

i. Respiratory pump
ii. Muscle pump
iii. Venous pressure
iv. Sympathetic tone
v. Gravity

i. *Respiratory Pump:-* Respiratory pump is the respiratory activity that helps return of the blood back to heart during inspiration. It is also called abdomino thoracic pump. During inspiration thoracic cavity expands and makes the intrathoracic pressure more negative. It increases the diameter of inferior vena cava resulting in increased venous return. At the same time, descent of diaphragm increases the intra-abdominal pressure which compresses abdominal veins and pushes the blood upward towards the heart and thereby the venous return is increased.

ii. *Muscle Pump:-* This is the muscular activity that helps return of blood back to the heart. During muscular activities, the veins are compressed or squeezed. Due to the presence of valves in veins, during compression the blood is moved towards the heart. When muscular activity increases the venous return is more.

When the skeletal muscles contracts the vein located in between the muscles is compressed. The valve of the vein proximal to the contracting muscles is opened and the blood is propelled towards the heart. The valve of the vein distal to the muscles is closed by the back flow of blood.

During relaxation of the muscles, the valve proximal to the muscles closes and prevents the back flow of the blood. And the valve distal to the muscles opens and allows the blood to flow upwards.

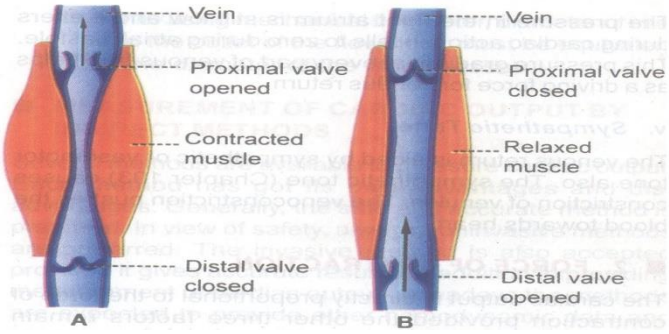


Figure: showing muscular pump

iii. *Gravity:-* Gravitational force reduces venous return. When a person stands for a long period gravity causes pooling of blood in the legs, which is called venous pooling. Because of venous pooling, the amount of blood returning to the heart decreases.

iv. *Venous Pressure:-* Venous pressure also affects the venous return. The pressure in the venules is 12-18mmHg. In the smaller and larger veins, the pressure gradually decreases. In the great vein, i.e. inferior vena cava and superior vena cava, the pressure falls to about 5.5mmHg. At the junction of vena cava and right atrium, it is about 4.6mmHg. The pressure in the right atrium is still low and it alters during cardiac action. It falls to zero during atrial diastole. This pressure gradient at every part of venous free helps as a driving force for venous return.

v. *Sympathetic Tone:-* Venous return is aided by sympathetic or vasomotor tone also. The sympathetic tone causes constriction of venules. The venoconstriction pushes the blood towards heart.

Force of Contraction

The cardiac output is directly proportional to the force of contraction provided the other three factors remain constant.

According to Frank-Sterling law, the force of contraction of heart is directly proportional to the initial length of muscle fibers before the onset of contraction. The force of contraction depends upon preload and after load.

i. *Preload*:- Preload is the stretching of the cardiac muscle fibres at the end of diastole just before contraction. Preload depends upon venous return and ventricular filling.

ii. *Afterload*:- Afterload is the force against which the ventricles must contract and eject the blood. The force is determined by aterial pressure. Thus, the afterload for left ventricle is determined by aortic pressure and afterload for right ventricular pressure is determined by pressure in pulmonary artery.

Heart Rate

Cardiac output is directly proportional to heart rate provided the other three factors remain constant. If there is an increase in heart rate, cardiac output increases, and a decrease in heart rate result in decrease in cardiac output provided other factors remains the same.

Peripheral Resistance

Peripheral resistance is the resistance offered to blood flow at the peripheral blood vessels. So the cardiac output is inversely proportional to peripheral resistance.

The resistance is offered at arterioles. So the arterioles are called resistance vessels. In the body, the maximum peripheral resistance is offered at the splanchnic region.

Blood Flow

Blood flow means simply the quantity of blood that passes a given point in the circulation in a given period of time. Ordinarily, blood flow is expressed in *millilitres per minute* or *liters per minute*. The overall blood flow in the total circulation of an adult person at rest is about 5000 ml/min.This is called the *cardiac output* because it is the amount of blood pumped into the aorta by the heart each minute.

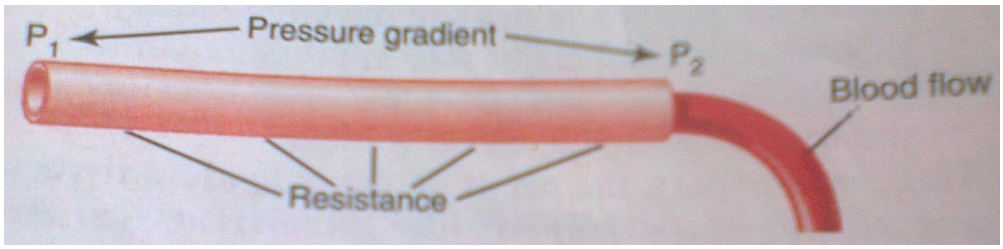


Figure 12
Interrelationships among pressure, resistance, and blood flow.

The flow through the vessel can be calculated by the following formula, which is called Ohm's law:

$$F = \triangle P/R$$

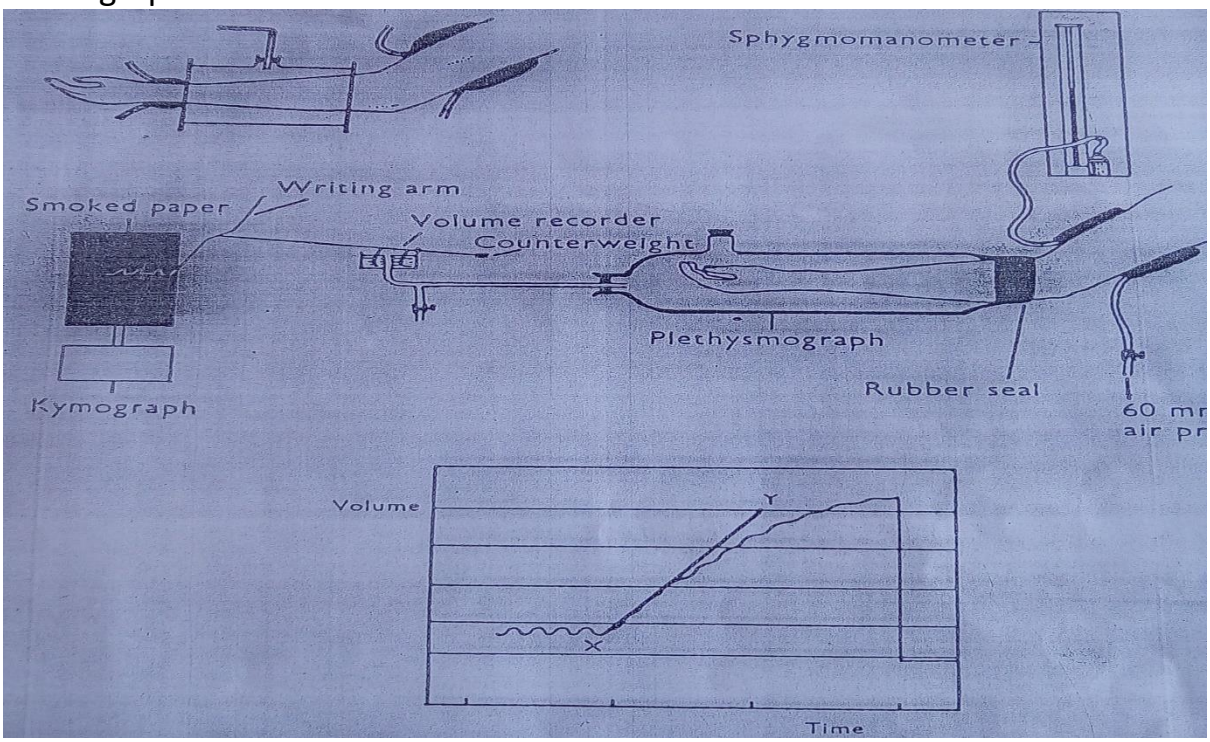
Importance of Blood Flow

1. Transport of food stuff to the tissues.
2. Transport of oxygen to the tissues.
3. Removal of waste product away from the tissues.

Methods of Measuring Blood Flow

1. **By using flowmeter**: Many mechanical and mechanoelectrical devices can be inserted in series within a blood vessel or, in some instances, applied to the outside of the vessel to measure flow. They are called *flowmeters.* These include:
   (i)Electromagnetic Flowmeter,
   (ii)Ultrasonic Doppler Flowmeter.
2. **By Fick's principle:** Adolph Fick described Fick principle in 1870. According to this principle, the amount of a substance taken up by an organ (or by the whole body) or given out in a unit of time is the product of amount of blood flowing through the organ and the arteriovenous difference of the substance across the organ. Amount of substance taken or given = Amount of blood flow per minute × Arteriovenous difference
3. **By using plethysmograph:** is an instrument used for an instrument used for measuring the volume of an enclosed organ.
4. **By venous occlusion plethysmography:** Here, the venous outflow is stopped while the artery supplying the organ or region is not affected. The blood flowing into organ or region will cause a corresponding increase in volume for the first few seconds. This increase in volume is recorded

graphically. The amount of flow is determined by proper calibration of the graph.



Recording blood flow in the hand and forearm using the plethysmograph. The cuff is inflated rapidly to 60mmHg, thus occluding the veins. The rate of blood flow into the arm is measured by the rate of air or fluid displacement from the plethysmograph to the volume recorder at the beginning of the occlusion. This is given by the X Y. The hand blood flow (mainly skin flow) may be recorded by having only the hand in the plethysmograph. When recording forearm blood flow only (mainly muscle), a wrist curve may be inflated to 200mmHg to cut off blood flow to the hand (top left).

TYPES OF BLOOD FLOW

Blood flow through a blood vessel is of two types: 1. Streamline or laminar flow 2. Turbulent flow.

1. **Streamline Flow**

Streamline flow is a silent flow. Within the blood vessel, a very thin layer of blood is in contact with the vessel wall. It does not move or moves very slowly. Next layer within the vessel has a low momentum. Next layer of blood has a slightly higher momentum. Gradually, the momentum increases in the inner layers, so that the momentum is greatest in the center of the stream. This type of flow is

known as streamline flow and it does not produce any sound within the vessel (Fig. 102.1). Streamline flow occurs only at velocities up to a critical level.

2. Turbulent Flow

Turbulent flow is the noisy flow. When the velocity of blood flow increases above critical level, the flow becomes turbulent. Turbulent flow creates sounds. Critical velocity at which the flow becomes turbulent is known as Reynolds number.
Formula to determine Reynolds number:

$N_R = PVD/\eta$

N_R = Reynolds number

P = Density of the blood

D = Diameter of the vessel

V = Velocity of the flow

η = Viscosity of the blood

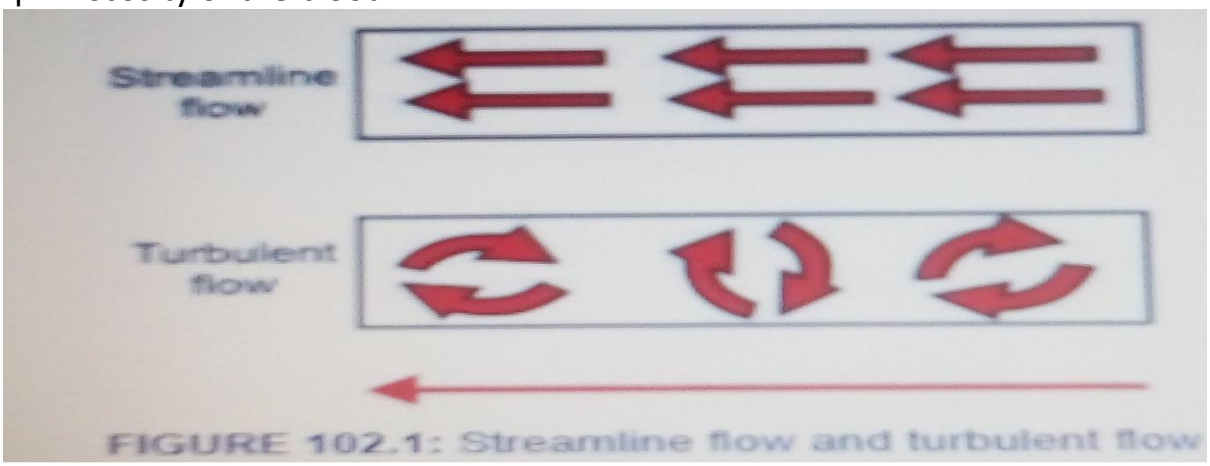


FIGURE 102.1: Streamline flow and turbulent flow

FACTORS DETERMINING VOLUME OF BLOOD FLOW

Volume of blood flow is determined by five factors:

1. Pressure gradient
2. Resistance to blood flow
3. Viscosity of blood
4. Diameter of blood vessels
5. Velocity of blood flow.

The Renin-Angiotensin System: Its Role in Pressure Control *Renin* is a protein enzyme released by the kidneys when the arterial pressure falls too low. In turn, it raises the arterial pressure in several ways, thus helping to correct the initial fall in pressure.

Renin is synthesized and stored in an inactive form called *prorenin* in the *juxtaglomerular cells* (*JG cells*) of the kidneys. The JG cells are modified smooth muscle cells located *in the walls of the afferent arterioles immediately proximal to the glomeruli*.When the arterial pressure falls, intrinsic reactions in the kidneys themselves cause many of the prorenin molecules in the JG cells to split and release *renin*.Most of the renin enters the renal blood and then passes out of the kidneys to circulate throughout the entire body.

Renin acts enzymatically on another plasma protein known as *angiotensinogen*, to release, *angiotensin I*. Angiotensin I has mild vasoconstrictor properties but not enough to cause significant changes in circulatory function. The angiotensin I is later converted to *angiotensin II*. This conversion occurs almost entirely in the lungs while the blood flows through the
small vessels of the lungs, catalyzed by an enzyme called *converting enzyme* that is present in the endothelium of the lung vessels.

Angiotensin II is an extremely powerful vasoconstrictor, It has two principal effects that can elevate arterial pressure. First, it causes *vasoconstriction in many areas of the body*. Constriction of the arterioles increases the total peripheral resistance, thereby raising the arterial pressure.
Also, the mild constriction of the veins promotes increased venous return of blood to the heart, thereby helping the heart pump against the increasing pressure.

The second principal means by which angiotensin increases the arterial pressure is to *decrease excretion of both salt and water* by the kidneys and this is achieved in two ways.
I. Angiotensin acts directly on the kidneys to cause salt and water retention.
II. Angiotensin causes the adrenal glands to secrete aldosterone, and the aldosterone in turn increases salt and water reabsorption by the kidney tubules. This slowlyincreases the extracellular fluid volume, which then increases the arterial pressure during subsequent hours and days.

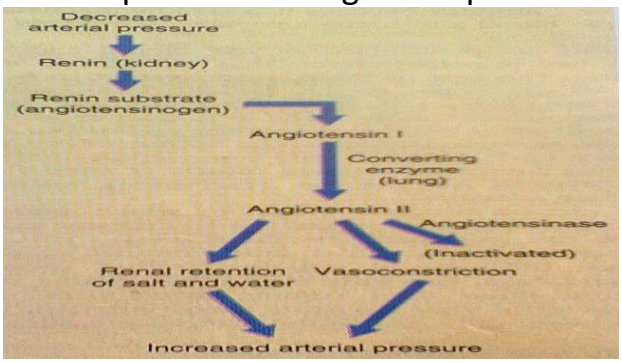


Figure 13

Renin-angiotensin vasoconstrictor mechanism for arterial pressure control.

Neural Control of Arterial Pressure

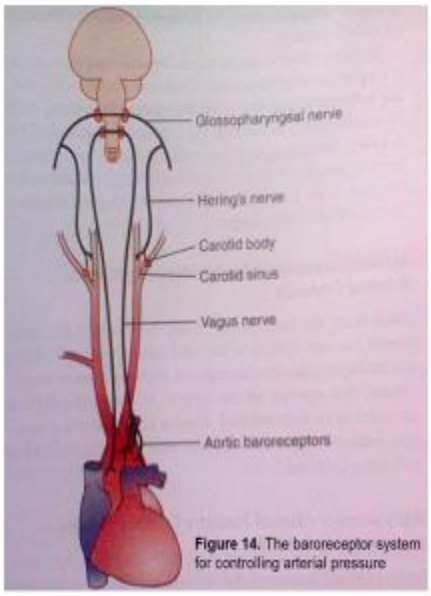


Figure 14. The baroreceptor system for controlling arterial pressure

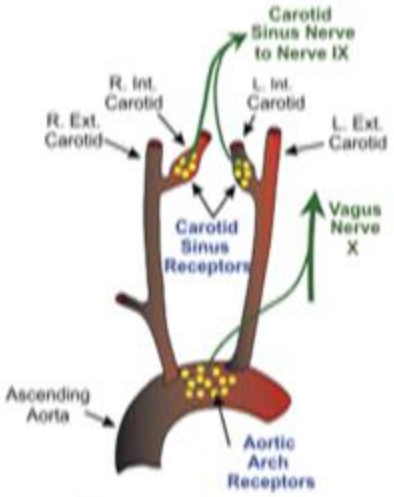


Figure 14 , Location and innervation of arterial baroreceptors.

The carotid sinus is a small dilation of the internal carotid artery just above the bivocation of the common carotid artery into external and internal carotid branches. Baroreceptors are located in this dilation. They are also found in the wall of the arch of the aorta. The receptors are located in the adventitial of the vessels. They are extensively branched,knobby, coiled,and interwined ends of myelinated nerve fibres that resemble Golgi tendon organs. The afferent nerve fibres from carotid sinus (carotid sinus nerve i.e, a branch of glossopharyngeal nerve) and aortic arch (vagus nerve) are commonly called the buffer nerves.

The normal operating range of arterial pressure is around 100 mm Hg, a slight change in pressure causes a strong change in the baroreflex signal to readjust arterial pressure back toward normal. An increase in arterial blood pressure beyond this range causes distension of *carotd* and *aortic sinus* and then brings about stimulation of the *baroreceptors* in them. Afferent signals from carotid and aortic sinus are sent via *glossopharyngeal* and *vagus nerves* respectively to the *tractus solitaries* in the medulla.

After the baroreceptor signals have entered the tractus solitarius of the medulla, secondary signals *inhibit the vasoconstrictor center* of the medulla and *excite the vagal parasympathetic center.* The net effects are (1) *vasodilation* of the veins and arterioles throughout the peripheral circulatory system and (2) *decreased heart rate* and *strength of heart contraction.* Therefore, excitation of the baroreceptors by high pressure in the arteries reflexly *causes the arterial pressure to decrease* because of both a decrease in peripheral resistance and a decrease in cardiac output. Conversely, low pressure has opposite effects, reflexly causing the pressure to rise back toward normal.

Measurement of Arterial Blood Pressure

In human patients, systolic and diastolic pressures are determined by indirect means, usually by the *auscultatory method*.

Auscultatory Method. A stethoscope is placed over the antecubital artery and a blood pressure cuff is inflated around the upper arm. As long as the cuff continues to compress the arm with too little pressure to close the brachial artery, no sounds are heard from the antecubital artery with the stethoscope. However, when the cuff pressure is great enough to close the artery during part of the arterial pressure cycle, a sound then is heard with each pulsation. These sounds are called *Korotkoff sounds*.

In determining blood pressure by the auscultatory method, the pressure in the cuff is first elevated well above arterial systolic pressure. As long as this cuff pressure is higher than systolic pressure, the brachial artery remains collapsed so that no blood jets into the lower artery during any part of the pressure cycle. Therefore, no Korotkoff sounds are heard in the lower artery. But then the cuff pressure gradually is reduced. Just as soon as the pressure in the cuff falls below systolic pressure, blood begins to slip through the artery beneath the cuff during the peak of systolic pressure, and one begins to hear *tapping* sounds from the antecubital artery in synchrony with the heartbeat. As soon as these sounds begin to be heard, the pressure level indicated by the manometer connected to the cuff

is about equal to the systolic pressure.

As the pressure in the cuff is lowered still more, the Korotkoff sounds change in quality, having less of the tapping quality and more of a rhythmical and harsher quality. Then, finally, when the pressure in the cuff falls to equal diastolic pressure, the artery no longer closes during diastole, which means that the basic factor causing the sounds (the jetting of blood through a squeezed artery) is no longer present. Therefore, the sounds suddenly change to a muffled quality, then disappear entirely after another 5- to 10-millimeter drop in cuff pressure. The manometer pressure when the Korotkoff sounds change to the muffled quality is about equal to the diastolic pressure.

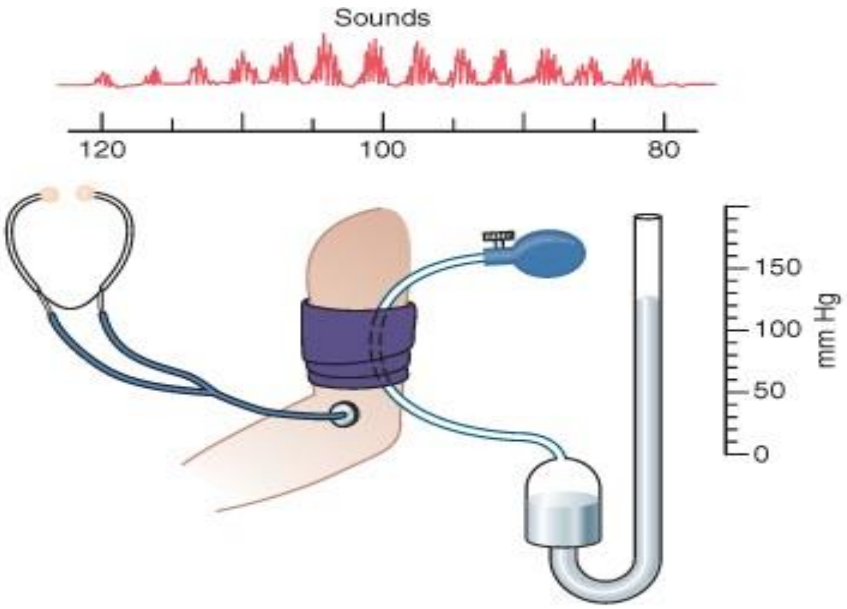


Figure 15. Auscultatory method for measuring systolic and diastolic arterial pressures

Pulse pressure: Systolic pressure – Diastolic pressure

Mean arterial pressure (MAP) = Diastolic pressure – 1/3 Pulse pressure

MECHANISMS OF BLOOD FLOW CONTROL

Some tissues of the body require more blood supply to function effectively than others, for example the liver receives 1,350ml/min of blood, kiney receives 1100ml/min of blood, whereas only a total of 750ml/min of blood, flows to all

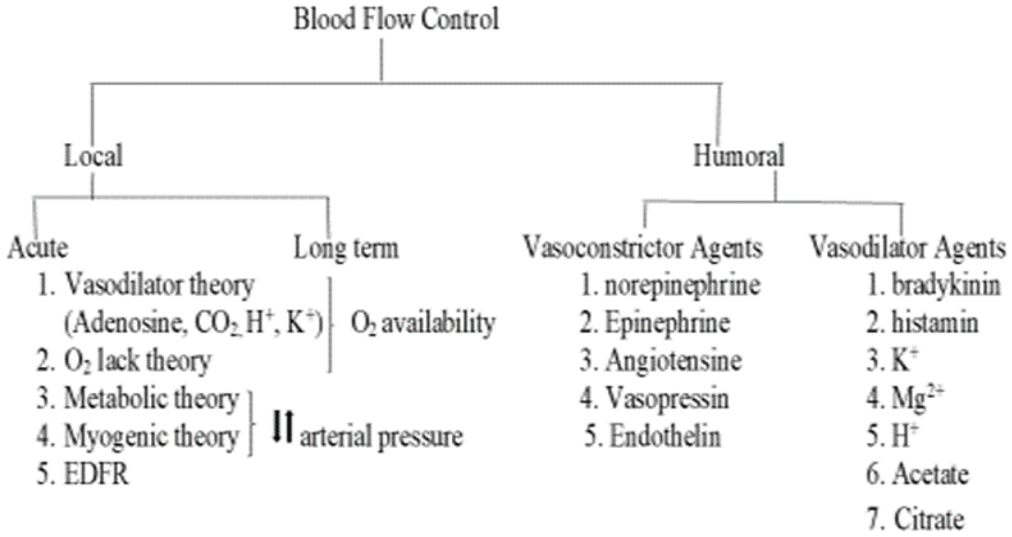
inactive muscles of the body. The heart can only pump 5000ml of blood per min., and hence the need for circulatory control.

Table 1

Blood Flow to Different Organs and Tissues Under Basal Conditions

	Percent	ml/min	ml/min/100g
Brain	14	700	50
Heart	4	200	70
Bronchi	2	100	25
Kidney	22	100	360
Liver	27	1350	95
Portal	(21)	1050	
Arterial	(6)	300	
Muscle (inactive state)	15	750	4
Bone	5	250	3
Skin(cool weather)	6	300	3
Thyroid gland	1	50	160
Adrenal glands	0.5	25	300
Other tissues	3.5	175	1.3
Total	100.0	5000	

Circulatory control can broadly be divided into *local and humoral conrol.*



Local Blood Flow Control

This can be divided into two phases; (1) acute control and (2) long-term control

Acute control

Is achieved by rapid changes in local vasodilation or vasoconstriction of the arterioles, metarterioles and precapillary sphincter, occurring within seconds minute to provide very rapid maintenance of appropriate local tissue blood flow. An increase in tissue metabolic rate, or decrease in oxygen availability to tissue increases blood flow to the tissue.

Acute Local Blood Flow Control When Oxygen Availability Changes There are two basic theories for the regulation of local blood flow when either the rate of tissue metabolism changes or the availability of oxygen changes. They are (1) the vasodilator theory and (2) the oxygen lack theory.

Vasodilator Theory -Possible Special Role of Adenosine According to this theory, the greater the rate of metabolism or the less the availability of oxygen or some other nutrients to a tissue, the greater the rate of formation of *vasodilator substances* in the tissue cells. The vasodilator substances then are believed to diffuse through the tissues to the precapillary sphincters, metarterioles, and arterioles to cause dilation. Some of the different vasodilator substances that have been suggested are *adenosine*, *carbon dioxide*, *adenosine phosphate compounds*, *histamine, potassium ions*, and *hydrogen ions*.

Oxygen Lack Theory for Local Blood Flow Control

Oxygen (and other nutrients as well) is required as one of the metabolic nutrients to cause vascular muscle contraction. Therefore, in the absence of adequate oxygen, it is reasonable to believe that the blood vessels simply would relax and therefore naturally dilate. Also, increased utilization of oxygen in the tissues as a result of increased metabolism theoretically could decrease the availability of oxygen to the smooth muscle fibers in the local blood vessels, and this, too, would cause local vasodilation.

Deficiency of other nutrients such as amino acids or fatty acids in the perfusing blood also causes local tissue vasodilation. In addition, vasodilation occurs in the vitamin deficiency berybery in which the patient has deficiencies of vitamin B substances *thiamine*,*niacin*,and *riboflavin*.

Autoregulation of Blood Flow When the Arterial Pressure Rises Above Normal

In any tissue of the body, an acute increase in arterial pressure causes immediate rise in blood flow. But, within less than a minute, the blood flow in most tissues returns almost to the normal level, even though the arterial pressure is kept elevated. This return of flow toward normal is called "*autoregulation* of blood flow."

This acute autoregulation mechanism is explained by (1) the metabolic theory and (2) the myogenic theory.

The *metabolic theory*: When the arterial pressure becomes too great, the excess flow provides too much oxygen and too many other nutrients to the tissues. These nutrients (especially oxygen) then cause the blood vessels to constrict and the flow to return nearly to normal despite the increased pressure.

The *myogenic theory*: This theory is based on the observation that sudden stretch of small blood vessels causes the smooth muscle of the vessel wall to contract for a few seconds. Therefore, it has been proposed that when high arterial pressure stretches the vessel, this in turn causes reactive vascular constriction that reduces blood flow nearly back to normal. Conversely, at low pressures, the degree of stretch of the vessel is less, so that the smooth muscle relaxes and allows increased flow.

Myogenic contraction is initiated by stretch-induced vascular depolarization, which then rapidly increases calcium ion entry from the extracellular fluid into the cells, causing them to contract.

Control of Tissue Blood Flow by Endothelial-Derived Relaxing Factor

The endothelial cells lining the blood vessels synthesize several substances that, when released, can affect the degree of relaxation or contraction of the arterial wall.

Nitric Oxide- A Vasodilator Released from Healthy Endothelial cell. It is a lipophilic gas that is released from endothelial cell by the activities of *nitric oxide synthase (NOS) enzymes* in response to a variety chemical and physical stimuli. NO has a half-life in the blood of only 6 seconds and act only in the local tissues where it is released. Rapid flow of blood through the arteries and arterioles causes *shear stress* on the endothelial cells because of viscous drag of the blood against the vascular walls. This stress contorts the endothelial cells in the direction of flow and causes significant increase in the release of nitric oxide. The nitric oxide then relaxes the blood vessels. The released NO increases the diameter of the larger upstream blood vessels whenever microvascular blood flow increases downstream.

NO synthesis and release from endothelial cells are also stimulated by some vasoconstrictors, such as angiotensin II, which bind to specific receptors on endothelia cells. The increased NO release protects against excessive vasoconstriction.

Long-Term Blood Flow Regulation

If a tissue becomes chronically overactive and therefore requires chronically increased quantities of oxygen and other nutrients, the arterioles and capillary vessels usually increase both in number and size within a few weeks to match the needs of the tissue-unless the circulatory system has become pathological or too old to respond.

Mechanism of Long-Term Blood Flow Regulation

The mechanism of long-term local blood flow regulation is principally to change the amount of vascularity of the tissues. For instance, if the metabolism in a given

tissue is increased for a prolonged period, vascularity increases; if the metabolism is decreased, vascularity decreases.

Humoral Control of the Circulation

Humoral control of the circulation means control by substances secreted or absorbed into the body fluids-such as hormones and ions.

Vasoconstrictor Agents

Norepinephrine and Epinephrine. When the sympathetic nervous system is stimulated in most or all parts of the body during stress or exercise, the sympathetic nerve endings in the individual tissues release norepinephrine, which excites the heart and contracts the veins and arterioles. In addition, the sympathetic nerves to the adrenal medullae cause these glands to secrete both norepinephrine and epinephrine into the blood. These hormones then circulate to all areas of the body and cause almost the same effects on the circulation as direct sympathetic stimulation, thus providing a dual system of control: (1) direct nerve stimulation and (2) indirect effects of norepinephrine and/or epinephrine in the circulating blood.

Angiotensin II. The real importance of angiotensin II is that it normally acts on many of the arterioles of the body at the same time to increase the *total peripheral resistance*, thereby increasing the arterial pressure. Thus, this hormone plays an integral role in the regulation of arterial pressure.

Vasopressin. *Vasopressin*, also called *antidiuretic hormone*, is even more powerful than angiotensin II as a vasoconstrictor, thus making it one of the body's most potent vascular constrictor substances.

Edothelin. This substance is present in the endothelial cells of all or most blood vessels. The usual stimulus for release is damage to the endothelium, such as that caused by crushing the tissues or injecting a traumatizing chemical into the blood

vessel. After severe blood vessel damage, release of local endothelin and subsequent vasoconstriction helps to prevent extensive bleeding from arteries as large as 5 millimeters in diameter that might have been torn open by crushing injury.

Vasodilator Agents

Bradykinin. Several substances called *kinins* cause powerful vasodilation when formed in the blood and tissue fluids of some organs. The kinins are small polypeptides that are split away by proteolytic enzymes from alpha2-globulins in the plasma or tissue fluids.

Bradykinin causes both powerful *arteriolar dilation* and *increased capillary permeability.* There is reason to believe that kinins play special roles in regulating blood flow and capillary leakage of fluids in inflamed tissues. It also is believed that bradykinin plays a normal role to help regulate blood flow in the skin as well as in the salivary and gastrointestinal glands.

Histamine. Histamine is released in essentially every tissue of the body if the tissue becomes damaged or inflamed or is the subject of an allergic reaction. Most of the histamine is derived from *mast cells* in the damaged tissues and from *basophils* in the blood.

Histamine has a powerful vasodilator effect on the arterioles and, like bradykinin, has the ability to increase greatly capillary porosity, allowing leakage of both fluid and plasma protein into the tissues. In many pathological conditions, the intense arteriolar dilation and increased capillary porosity produced by histamine cause tremendous quantities of fluid to leak out of the circulation into the tissues, inducing edema.

Vascular Control by Ion and Other Chemical Factors

Many different ions and other chemical factors can either dilate or constrict local blood vessels. Most of them have little function in *overall regulation* of the circulation, but some specific effects are:

1. An increase in *calcium ion* concentration causes *vasoconstriction*. This results from the general effect of calcium to stimulate smooth muscle contraction.
2. An increase in *potassium ion* concentration causes *vasodilation*. This results from the ability of potassium ions to inhibit smooth muscle contraction.
3. An increase in *magnesium* ion concentration causes *powerful vasodilation* because magnesium ions inhibit smooth muscle contraction.
4. An *increase in hydrogen ion* concentration (decrease in pH) causes dilation of the arterioles. Conversely, *slight decrease in hydrogen ion* concentration causes arteriolar constriction.
5. *Anions* that have significant effects on blood vessels are *acetate* and *citrate*, both of which cause mild degrees of vasodilation.

An *increase in carbon dioxide concentration* causes moderate vasodilation in most tissues, but marked vasodilation in the brain.

Circulation through Skeletal Muscle

During resting condition, blood flow to skeletal muscle is 4-7mL/100gm/min. During exercise, it increases to about 100ml/100gm/min.
The following factors regulating blood flow to skeletal muscle:
1. Mechanical factors
2. Chemical factors
3. Nervous factors

Mechanical factors: During contraction of the muscle, the blood vessels are compressed and the blood flow decreases. And during the relaxation of the muscle, the compression of the muscle is relieved and the blood flow increases. In several muscular exercise, the blood flow increases in between the muscular contraction

Chemical factors: the important chemical factors which regulate blood flow through the skeletal muscles are lack of oxygen, excess carbon dioxide, and increased hydrogen ion concentration. All these chemical increase the blood flow to muscle by causing vasodilation.

Nervous factors: the blood vessels of skeletal muscle are mostly innervated by sympathetic nerve fibers and, few parasympathetic nerve fibers are also seen. The special feature of sympathetic nerve fibers supplying the skeletal muscles is that this nerve fibers are vasodilators and not constrictors. Since sympathetic nerve fibers cause vasidilation of blood vessels in muscle by secreting acetylcholine, these fibers are called sympathetic cholinergic fibers.

Total Body Circulatory Readjustments During Exercise

Three major effects occur during exercise that are essential for the circulatory system to supply the tremendous blood flow required by the muscles. They are:
(1) mass discharge of the sympathetic nervous system throughout the body with consequent stimulatory effects on the entire circulation,
(2) increase in arterial pressure, and
(3) increase in cardiac output.

At the onset of exercise, signals are transmitted not only from the brain to the muscles to cause muscle contraction but also into the vasomotor center to initiate mass sympathetic discharge throughout the body. Simultaneously, the parasympathetic signals to the heart are reduced. Therefore, three major circulatory effects result.

First, *the heart is stimulated* to greatly increased heart rate and increased pumping strength as a result of the sympathetic drive to the heart plus release of the heart from normal parasympathetic inhibition.

Second, *most of the arterioles of the peripheral circulation are strongly contracted*, except for the arterioles in the active muscles, which are strongly vasodilated by the local vasodilator effects in the muscles as noted above. Thus, the heart is stimulated to supply the increased blood flow required by the muscles, while at the same time blood flow through most nonmuscular areas of the body is temporarily reduced, thereby temporarily “lending” their blood supply to the muscles. This accounts for as much as 2 L/min of extra blood flow to the

muscles. Two of the peripheral circulatory systems, the *coronary and cerebral systems*, *are spared this vasoconstrictor effect* because both these circulatory areas have poor vasoconstrictor innervation

Third, the muscle walls of the *veins and other capacitative areas of the circulation are contracted powerfully*, which greatly *increases the mean systemic filling pressure* leading to an increase in venous return.

These effects, working together, virtually always increase the arterial pressure during exercise. This increase can be as little as 20 mm Hg or as great as 80 mm Hg, depending on the conditions under which the exercise is performed. When a person performs exercise under tense conditions but uses only a few muscles, the sympathetic nervous response still occurs everywhere in the body. In the few active muscles, vasodilation occurs, but everywhere else in the body the effect is mainly vasoconstriction, often increasing the mean arterial pressure to as high as 170 mm Hg. Such a condition might occur in a person standing on a ladder and nailing with a hammer on the ceiling above. The tenseness of the situation is obvious.

Conversely, when a person performs massive whole-body exercise, such as running or swimming, the increase in arterial pressure is often only 20 to 40 mm Hg. This lack of a large increase in pressure results from the extreme vasodilation that occurs simultaneously in large masses of active muscle.