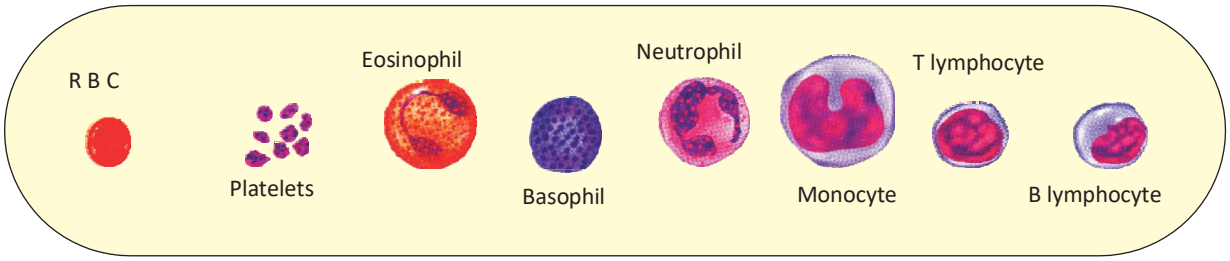
Body Fluids and Circulation:

Blood is the most commonly used body fluid by most of the higher organisms including humans for this purpose. Another body fluid, lymph, also helps in the transport of certain substances. In this chapter, you will learn about the composition and properties of blood and lymph (tissue fluid) and the mechanism of circulation of blood is also explained herein.

BLOOD: Blood is a special connective tissue consisting of a fluid matrix, plasma, and formed elements.

PLASMA: Plasma is a straw coloured, viscous fluid constituting nearly 55 per cent of the blood. 90-92 per cent of plasma is water and proteins contribute 6-8 per cent of it. Fibrinogen, globulins and albumins are the major proteins.

Blood Composition: Erythrocytes, leucocytes and platelets are collectively called formed elements (Figure 18.1) and they constitute nearly 45 per cent of the blood. Erythrocytes or red blood cells (RBC) are the most abundant of all the cells in blood. A healthy adult man has, on an average, 5 million to 5.5 millions of RBCs mm–3 of blood. RBCs are formed in the red bone marrow in the adults. RBCs are devoid of nucleus in most of the mammals and are biconcave in shape. They have a red coloured, iron containing complex protein called haemoglobin, hence the colour and name of these cells. A healthy individual has 12-16 gms of haemoglobin in every 100 ml of blood. These molecules play a significant role in transport of respiratory gases. RBCs have an average life span of 120 days after which they are destroyed in the spleen (graveyard of RBCs). Leucocytes are also known as white blood cells (WBC) as they are colourless due to the lack of haemoglobin. They are nucleated and are relatively lesser in number which averages 6000-8000 mm–3 of blood. Leucocytes are generally short lived. We have two main categories of WBCs –



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granulocytes and agranulocytes. Neutrophils, eosinophils and basophiles are different types of granulocytes, while lymphocytes and monocytes are the agranulocytes. Neutrophils are the most abundant cells (60-65 per cent) of the total WBCs and basophils are the least (0.5-1 per cent) among them. Neutrophils and monocytes (6-8 per cent) are phagocytic cells which destroy foreign organisms entering the body. Basophils secrete histamine, serotonin, heparin, etc., and are involved in inflammatory reactions. Eosinophils (2-3 per cent) resist infections and are also associated with allergic reactions. Lymphocytes (20-25 per cent) are of two major types – 'B' and 'T' forms. Both B and T lymphocytes are responsible for immune responses of the body. Platelets also called thrombocytes, are cell fragments produced from megakaryocytes (special cells in the bone marrow). Blood normally contains 1,500,00-3,500,00 platelets mm–3. Platelets can release a variety of substances most of which are involved in the coagulation or clotting of blood. A reduction in their number can lead to clotting disorders which will lead to excessive loss of blood from the body.

Blood Groups: As you know, blood of human beings differ in certain aspects though it appears to be similar. Various types of grouping of blood has been done. Two such groupings – the ABO and Rh – are widely used all over the world.

ABO grouping: ABO grouping is based on the presence or absence of two surface antigens (chemicals that can induce immune response) on the RBCs namely A and B. Similarly, the plasma of different individuals contain two natural antibodies (proteins produced in response to antigens). The distribution of antigens and antibodies in the four groups of blood, A, B, AB and O are given in Table 18.1. You probably know that during blood transfusion, any blood cannot be used; the blood of a donor has to be carefully matched with the blood of a recipient before any blood transfusion to avoid severe problems of clumping (destruction of RBC).

From the under mentioned table it is evident that group 'O' blood can be donated to persons with any other blood group and hence 'O' group individuals are called 'universal donors'. Persons with 'AB' group can accept blood from

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persons with AB as well as the other groups of blood. Therefore, such persons are called 'universal recipients'.

TABLE: Blood Groups and Donor Compatibility

Blood Group	Antigens on RBCs	Antibodies in Plasma	Donor's Group
A	**A**	**anti-B**	**A, O**
B	**B**	**anti-A**	**B,O**
AB	**AB**	**Nil**	**A,B,AB,O**
O	**Nil**	**anti-A, B**	**O**

Rh grouping: Another antigen, the Rh antigen similar to one present in Rhesus monkeys (hence Rh), is also observed on the surface of RBCs of majority (nearly 80 per cent) of humans. Such individuals are called Rh positive (Rh+ve) and those in whom this antigen is absent are called Rh negative (Rh-ve). An Rh-ve person, if exposed to Rh+ve blood, will form specific antibodies against the Rh antigens. Therefore, Rh group should also be matched before transfusions.

Erythroblastosis foetalis: A special case of Rh incompatibility (mismatching) has been observed between the Rh-ve blood of a pregnant mother with Rh+ve blood of the foetus. Rh antigens of the foetus do not get exposed to the Rh-ve blood of the mother in the first pregnancy as the two bloods are well separated by the placenta. However, during the delivery of the first child, there is a possibility of exposure of the maternal blood to small amounts of the Rh+ve blood from the foetus. In such cases, the mother starts preparing antibodies against Rh in her blood. In case of her subsequent pregnancies, the Rh antibodies from the mother (Rh-ve) can leak into the blood of the foetus (Rh+ve) and destroy the foetal RBCs. This could be fatal to the foetus or could cause severe anaemia and jaundice to the baby. This condition is called Erythroblastosis foetalis. This can be avoided by administering anti-Rh antibodies to the mother immediately after the delivery of the first child.

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Coagulation of Blood:

You know that when you cut your finger or hurt yourself, your wound does not continue to bleed for a long time; usually the blood stops flowing after sometime. Do you know why? Blood exhibits coagulation or clotting in response to an injury or trauma. This is a mechanism to prevent excessive loss of blood from the body. You would have observed a dark reddish brown scum formed at the site of a cut or an injury over a period of time. It is a clot or coagulam formed mainly of a network of threads called fibrins in which dead and damaged formed elements of blood are trapped. Fibrins are formed by the conversion of inactive fibrinogens in the plasma by the enzyme thrombin. Thrombins, in turn are formed from another inactive substance present in the plasma called prothrombin. An enzyme complex, thrombokinase, is required for the above reaction. This complex is formed by a series of linked enzymic reactions (cascade process) involving a number of factors present in the plasma in an inactive state. An injury or a trauma stimulates the platelets in the blood to release certain factors which activate the mechanism of coagulation. Certain factors released by the tissues at the site of injury also can initiate coagulation. Calcium ions play a very important role in clotting.

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LYMPH (TISSUE FLUID):

As the blood passes through the capillaries in tissues, some water along with many small water soluble substances move out into the spaces between the cells of tissues leaving the larger proteins and most of the formed elements in the blood vessels. This fluid released out is called the interstitial fluid or tissue fluid. It has the same mineral distribution as that in plasma. Exchange of nutrients, gases, etc., between the blood and the cells always occur through this fluid. An elaborate network of vessels called the lymphatic system collects this fluid and drains it back to the major veins. The fluid present in the lymphatic system is called the lymph. Lymph is a colourless fluid containing specialised lymphocytes which are responsible for the immune responses of the body. Lymph is also an important carrier for nutrients, hormones, etc. Fats are absorbed through lymph in the lacteals present in the intestinal villi.

CIRCULATORY PATHWAYS:

The circulatory patterns are of two types – open or closed. **Open circulatory system** is present in arthropods and molluscs in which blood pumped by the heart passes through large vessels into open spaces or body cavities called sinuses. Annelids and chordates have a **closed circulatory system** in which the blood pumped by the heart is always circulated through a closed network of blood vessels. This pattern is considered to be more advantageous as the flow of fluid can be more precisely regulated.

All vertebrates possess a muscular chambered heart. Fishes have a 2-chambered heart with an atrium and a ventricle. Amphibians and the reptiles (except crocodiles) have a 3-chambered heart with two atria and a single ventricle, whereas crocodiles, birds and mammals possess a 4-chambered heart with two atria and two ventricles. In fishes the heart pumps out deoxygenated blood which is oxygenated by the gills and supplied to the body parts from where deoxygenated blood is returned to the heart (single circulation). In amphibians and reptiles, the left atrium receives oxygenated blood from the gills/lungs/skin and the right atrium

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gets the deoxygenated blood from other body parts. However, they get mixed up in the single ventricle which pumps out mixed blood (incomplete double circulation). In birds and mammals, oxygenated and deoxygenated blood received by the left and right atria respectively passes on to the ventricles of the same sides. The ventricles pump it out without any mixing up, i.e., two separate circulatory pathways are present in these organisms, hence, these animals have double circulation. Let us study the human circulatory system.

Human Circulatory System:

Human circulatory system, also called the blood vascular system consists of a muscular chambered heart, a network of closed branching blood vessels and blood, the fluid which is circulated.

Heart, the mesodermally derived organ, is situated in the thoracic cavity, in between the two lungs, slightly tilted to the left. It has the size of a clenched fist. It is protected by a double walled membranous bag, **pericardium,** enclosing the pericardial fluid. Our heart has four chambers, two relatively small upper chambers called **atria** and two larger lower chambers called **ventricles**. A thin, muscular wall called the inter- atrial septum separates the right and the left atria, whereas a thick-walled, the inter-ventricular septum, separates the left and the right ventricles (Figure 18.2). The atrium and the ventricle of the same side are also separated by a thick fibrous tissue called the atrio-ventricular septum. However, each of these septa are provided with an opening through which the two chambers of the same side are connected. The opening between the right atrium and the right ventricle is guarded by a valve formed of three muscular flaps or cusps, the tricuspid valve, whereas a bicuspid or mitral valve guards the opening between the left atrium and the left ventricle. The openings of the right and the left ventricles into the

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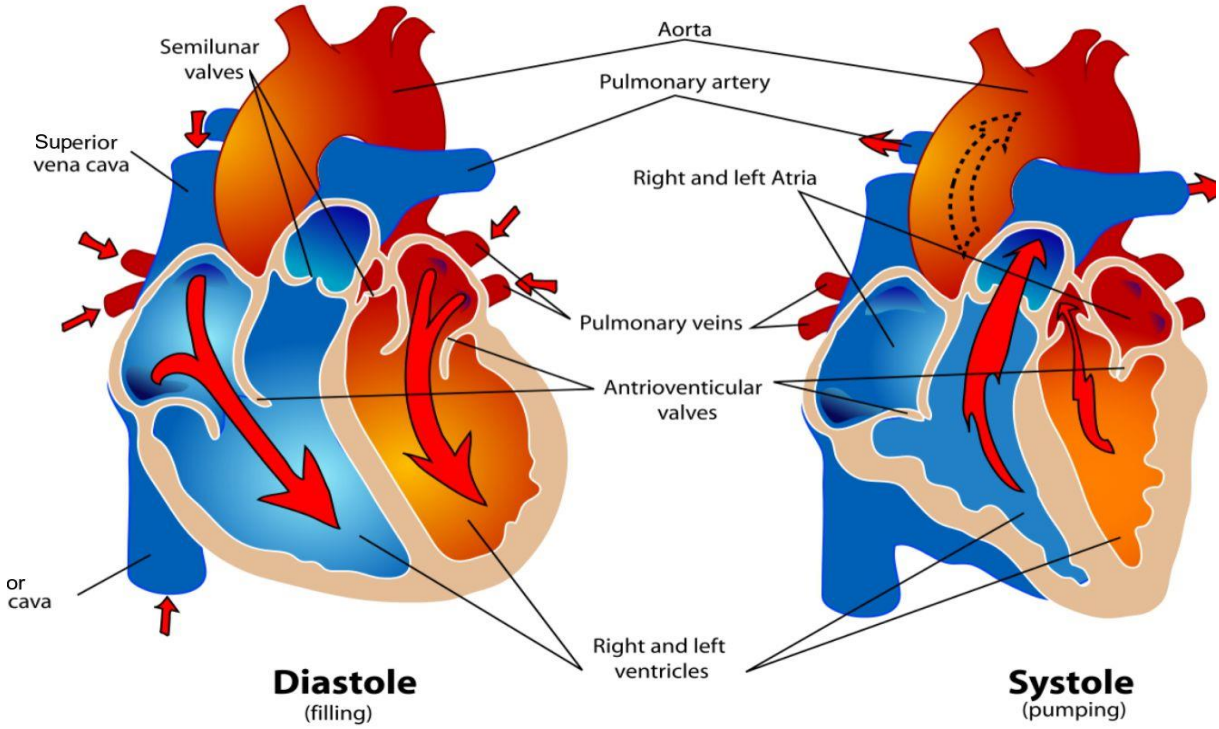

Pulmonary artery and the aorta respectively are provided with the semilunar valves. The valves in the heart allows the flow of blood only in one direction, i.e., from the atria to the ventricles and from the ventricles to the pulmonary artery or aorta. These valves prevent any backward flow.

The entire heart is made of cardiac muscles. The walls of ventricles are much thicker than that of the atria. A specialised cardiac musculature called the nodal tissue is also distributed in the heart (Figure 18.2). A patch of this tissue is present in the right upper corner of the right atrium called the **sino-atrial node** (SAN). Another mass of this tissue is seen in the lower left corner of the right atrium close to the atrio-ventricular septum called the **atrio-ventricular node** (AVN). A bundle of nodal fibres, atrio- ventricular bundle (AV bundle) continues from the AVN which passes through the atrio-ventricular septa to emerge on the top of the inter- ventricular septum and immediately divides into a right and left bundle. These branches give rise to minute fibres throughout the ventricular musculature of the respective sides and are called purkinje fibres. These fibres alongwith right and left bundles are known as bundle of HIS. The nodal

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musculature has the ability to generate action potentials without any external stimuli, i.e., it is autoexcitable. However, the number of action potentials that could be generated in a minute vary at different parts of the nodal system. The SAN can generate the maximum number of action potentials, i.e., 70-75 min^{-1}, and is responsible for initiating and maintaining the rhythmic contractile activity of the heart. Therefore, it is called the pacemaker. Our heart normally beats 70-75 times in a minute (average 72 beats min^{-1}).

Pericardium:

The pericardium is the sack that surrounds the heart. The tough outer surface of the pericardium is called the fibrous membrane. This is lined by a double inner membrane called the serous membrane that produces pericardial fluid to lubricate the surface of the heart. The part of the serous membrane attached to the fibrous membrane is called the parietal pericardium, while the part of the serous membrane attached to the heart is known as the visceral pericardium. The pericardium is present in order to lubricate its movement against other structures within the chest, to keep the heart's position stabilised within the chest, and to protect the heart from infection.

Coronary circulation:

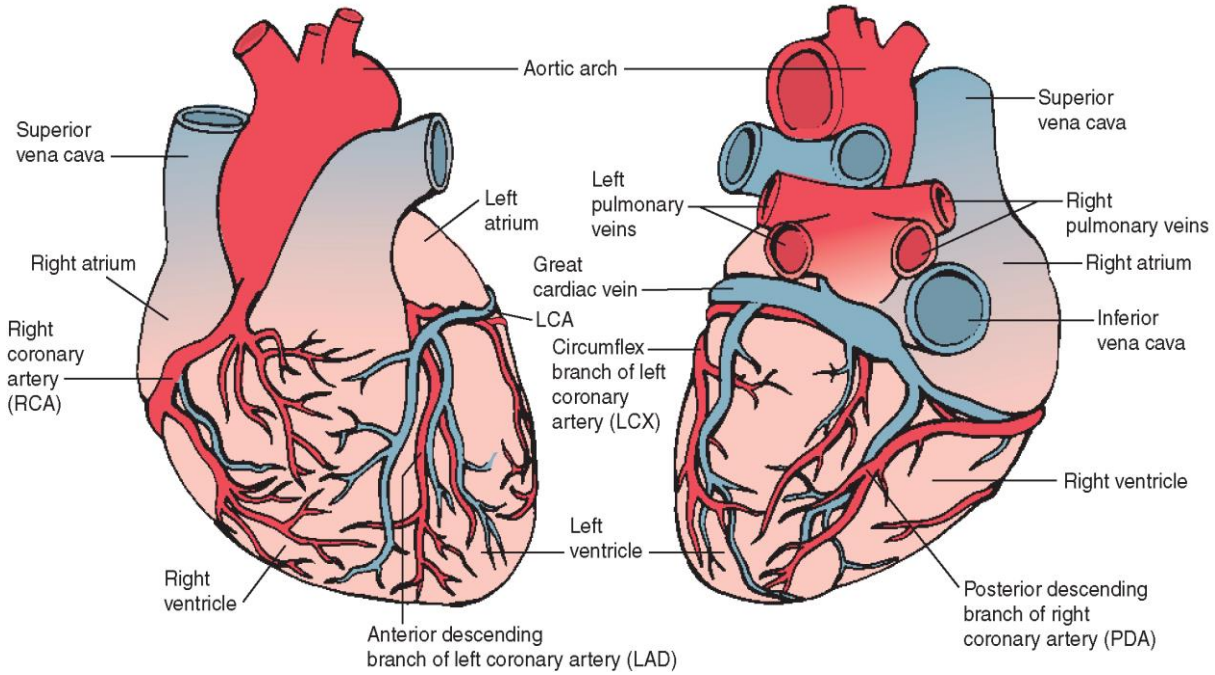

Figure: Arterial supply to the heart (red), with other areas labelled (blue).

Heart tissue, like all cells in the body, needs to be supplied with oxygen, nutrients and a way of removing metabolic wastes. This is achieved by the coronary circulation, which includes arteries, veins, and lymphatic vessels. Blood flow through the coronary vessels occurs in peaks and troughs relating to the heart muscle's relaxation or contraction.

Heart tissue receives blood from two arteries which arise just above the aortic valve. These are the left main coronary artery and the right coronary artery. The left main coronary artery splits shortly after leaving the aorta into two vessels, the left anterior descending and the left circumflex artery. The left anterior descending artery supplies heart tissue and the front, outer side, and the septum of the left ventricle. It does this by branching into smaller arteries—diagonal and septal branches. The left circumflex supplies the back and underneath of the left ventricle. The right coronary artery supplies the right atrium, right ventricle, and lower posterior sections of the left ventricle. The right coronary artery also supplies blood to the atrioventricular node (in about 90% of people) and the sinoatrial node (in about 60% of people). The right coronary artery runs in a groove at the back of the heart and the left anterior descending artery runs in a groove at the front. There is significant variation between people in the anatomy of the arteries that supply the heart [30] The arteries divide at their furtherst reaches into smaller branches that join together at the edges of each arterial distribution.

The coronary sinus is a large vein that drains into the right atrium, and receives most of the venous drainage of the heart. It receives blood from the great cardiac vein (receiving the left atrium and both ventricles), the posterior cardiac vein (draining the back of the left ventricle), the middle cardiac vein (draining the bottom of the left and right ventricles), and small cardiac veins. The anterior cardiac veins drain the front of the right ventricle and drain directly into the right atrium.

Small lymphatic networks called plexuses exist beneath each of the three layers of the heart. These networks collect into a main left and a main right trunk, which travel up the groove between the ventricles that exists on the heart's surface, receiving smaller vessels as they travel up. These vessels then travel

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into the atrioventricular groove, and receive a third vessel which drains the section of the left ventricle sitting on the diaphragm. The left vessel joins with this third vessel, and travels along the pulmonary artery and left atrium, ending in the inferior tracheobronchial node. The right vessel travels along the right atrium and the part of the right ventricle sitting on the diaphragm. It usually then travels in front of the ascending aorta and then ends in a brachio cephalic node.

Cardiac cycle:

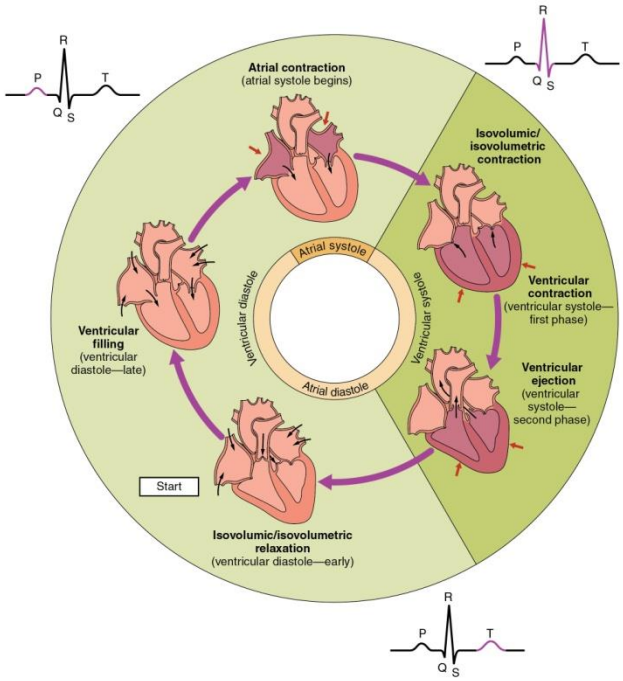


Figure: The cardiac cycle as correlated to the ECG

The cardiac cycle refers to the sequence of events in which the heart contracts and relaxes with every heartbeat.[9] The period of time during which the ventricles contract, forcing blood out into the aorta and main pulmonary artery, is known as systole, while the period during which the ventricles relax and refill with blood is known as diastole. The atria and ventricles work in concert, so in systole when the ventricles are contracting, the atria are relaxed and collecting blood. When the ventricles are relaxed in diastole, the atria contract to pump blood to the ventricles. This coordination ensures blood is pumped efficiently to the body.

At the beginning of the cardiac cycle, the ventricles are relaxing. As they do so,

they are filled by blood passing through the open mitral and tricuspid valves. After the ventricles have completed most of their filling, the atria contract, forcing further blood into the ventricles and priming the pump. Next, the ventricles start to contract. As the pressure rises within the cavities of the ventricles, the mitral and tricuspid valves are forced shut. As the pressure within the ventricles rises further, exceeding the pressure with the aorta and pulmonary arteries, the aortic and pulmonary valves open. Blood is ejected from the heart, causing the pressure within the ventricles to fall. Simultaneously, the atria refill as blood flows into the right atrium through the superior and inferior vena cavae, and into the left atrium through the pulmonary veins. Finally, when the pressure within the ventricles falls below the pressure within the aorta and pulmonary arteries, the aortic and pulmonary valves close. The ventricles start to relax, the mitral and tricuspid valves open, and the cycle begins again.

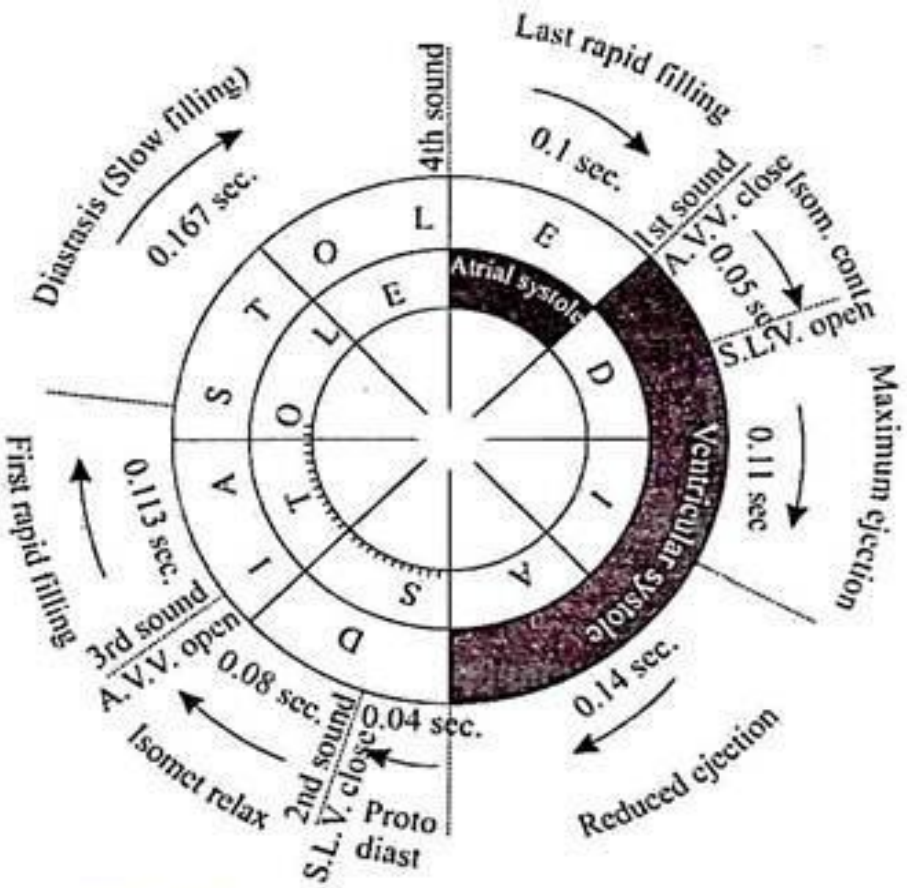
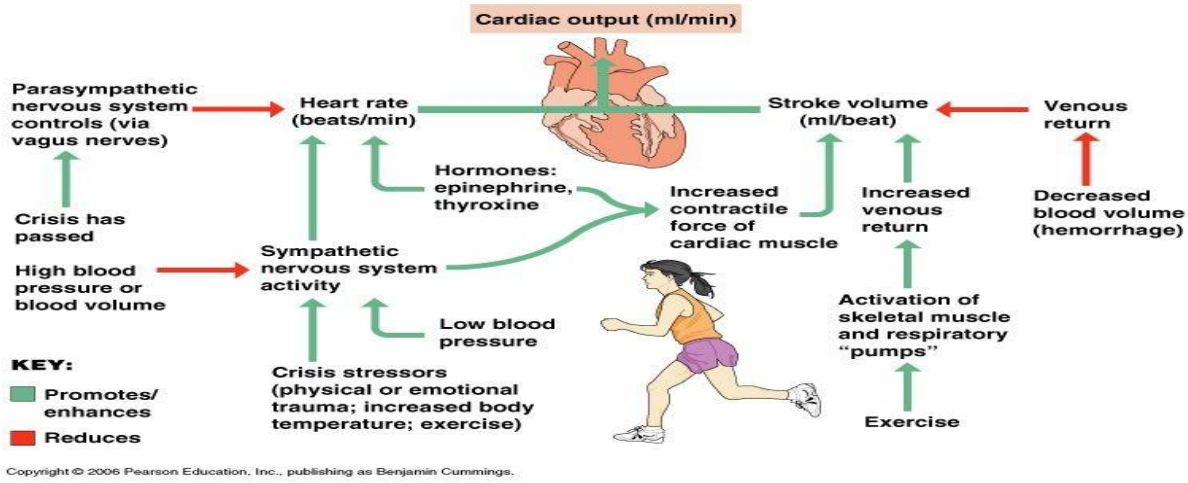


Fig. 7.43 Sequence of events during cardiac cycle.

Cardiac output



The Cardiac output (CO) is a measurement of the amount of blood pumped by each ventricle (stroke volume) in one minute. This is calculated by multiplying the stroke volume (SV) by the beats per minute of the heart rate (HR). So that: CO = SV x HR. The cardiac output is normalized to body size through body surface area and is called the cardiac index.

The average cardiac output, using an average stroke volume of about 70mL, is 5.25 L/min, with a normal range of 4.0–8.0 L/min. The stroke volume is normally measured using an echocardiogram and can be influenced by the size of the heart, physical and mental condition of the individual, sex, contractility, duration of contraction, preload and after load.

Preload refers to the filling pressure of the atria at the end of diastole, when the ventricles are at their fullest. A main factor is how long it takes the ventricles to fill: if the ventricles contract more frequently, then there is less time to fill and the preload will be less. Preload can also be affected by a person's blood volume. The force of each contraction of the heart muscle is proportional to the preload, described as the Frank-Starling mechanism. This states that the force of contraction is directly proportional to the initial length of muscle fiber, meaning a ventricle will contract more forcefully, the more it is stretched.

Afterload, or how much pressure the heart must generate to eject blood at systole, is influenced by vascular resistance. It can be influenced by narrowing

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of the heart valves (stenosis) or contraction or relaxation of the peripheral blood vessels.

The strength of heart muscle contractions controls the stroke volume. This can be influenced positively or negatively by agents termed inotropes.[40] These agents can be a result of changes within the body, or be given as drugs as part of treatment for a medical disorder, or as a form of life support, particularly in intensive care units. Inotropes that increase the force of contraction are "positive" inotropes, and include sympathetic agents such as adrenaline, noradrenaline and dopamine. "Negative" inotropes decrease the force of contraction and include calcium channel blockers.

Transmission of a cardiac action potential through the heart's conduction system

The normal rhythmical heart beat, called sinus rhythm, is established by the sinoatrial node, the heart's pacemaker. Here an electrical signal is created that travels through the heart, causing the heart muscle to contract.

The sinoatrial node is found in the upper part of the right atrium near to the junction with the superior vena cava. The electrical signal generated by the sinoatrial node travels through the right atrium in a radial way that is not completely understood. It travels to the left atrium via Bachmann's bundle, such that the muscles of the left and right atria contract together. The signal then travels to the atrioventricular node. This is found at the bottom of the right atrium in the atrioventricular septum—the boundary between the right atrium and the left ventricle. The septum is part of the cardiac skeleton, tissue within the heart that the electrical signal cannot pass through, which forces the signal to pass through the atrioventricular node only. The signal then travels along the bundle of His to left and right bundle branches through to the ventricles of the heart. In the ventricles the signal is carried by specialized tissue called the Purkinje fibers which then

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Heart rate:

Resting heart rate chart for men							
Age in Years	Heartbeats Per Minute						
	Athlete	Excellent	Good	Above Average	Average	Below Average	Poor
18-25	49-55	56-61	62-65	66-69	70-73	74-81	82+
26-35	49-54	55-61	62-65	66-70	71-74	75-81	82+
36-45	50-56	57-62	63-66	67-70	71-75	76-82	83+
46-55	50-57	58-63	64-67	68-71	72-76	77-83	84+
56-65	51-56	57-61	62-67	68-71	72-75	76-81	82+
65+	50-55	56-61	62-65	66-69	70-73	74-79	80+

The normal resting heart rate is called the sinus rhythm, created and sustained by the sinoatrial node, a group of pacemaking cells found in the wall of the right atrium. Cells in the sinoatrial node do this by creating an action potential. The cardiac action potential is created by the movement of specific electrolytes into and out of the pacemaker cells. The action potential then spreads to nearby cells.

When the sinoatrial cells are resting, they have a negative charge on their membranes. However a rapid influx of sodium ions causes the membrane's charge to become positive. This is called depolarisation and occurs spontaneously. Once the cell has a sufficiently high charge, the sodium channels close and calcium ions then begin to enter the cell, shortly after which potassium begins to leave it. All the ions travel through ion channels in the membrane of the sinoatrial cells. The potassium and calcium start to move out of and into the cell only once it has a sufficiently high charge, and so are called voltage-gated. Shortly after this, the calcium channels close and potassium channels open, allowing potassium to leave the cell. This causes the cell to have a negative resting charge and is called repolarization. When the membrane potential reaches approximately −60 mV, the potassium channels close and the process may begin again.

The ions move from areas where they are concentrated to where they are not. For this reason sodium moves into the cell from outside, and potassium moves

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from within the cell to outside the cell. Calcium also plays a critical role. Their influx through slow channels means that the sinoatrial cells have a prolonged "plateau" phase when they have a positive charge. A part of this is called the absolute refractory period. Calcium ions also combine with the regulatory protein troponin C in the troponin complex to enable contraction of the cardiac muscle, and separate from the protein to allow relaxation.

The adult resting heart rate ranges from 60 to 100 bpm. The resting heart rate of a newborn can be 129 beats per minute (bpm) and this gradually decreases until maturity. An athlete's heart rate can be lower than 60 bpm. During exercise the rate can be 150 bpm with maximum rates reaching from 200 to 220 bpm.

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