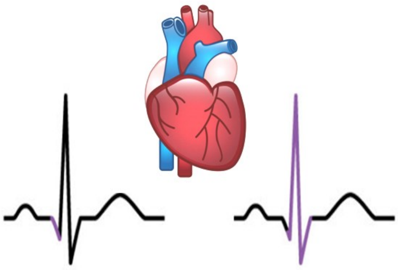


UNIT 3

CARDIAC PHYSIOLOGY

Structure

3.1 INTRODUCTION

In Unit 2, you have studied about the blood coagulation and the disorders of blood system. You know our body has a circulatory system comprising heart and blood vessels. Heart is a muscular organ that contracts rhythmically and autonomously pumping blood continuously through an extensive network of blood vessels (arteries, veins, capillaries) running throughout the body. The arteries carry blood away from the heart while veins deliver blood back to the heart. It is important to understand how does heart pump blood in the body.

Therefore, in this unit you will learn the structure and function of heart and its role in cardiac activity. The overview of blood vessels and blood circulatory pathways also discussed in this unit. The physiology of cardiac muscle contraction, excitation-contraction coupling, control of cardiac output and heart rate are also described in the unit. In next unit 4, you will study about the cardiovascular system (Blood vessels) and the heart related disorders in detail.

Expected Learning Outcomes

After studying this unit, you should be able to:

- discuss the structure and function of heart;
- explain the different role of heart chambers;
- define double circulation;
- explain the blood pressure, blood flow and resistance;
- discuss cardiac cycle and heart beat;
- explain the physiological role of calcium in cardiac muscle contraction; and
- describe cardiac output and its regulation.

3.2 HEART: STRUCTURE AND FUNCTION

Human circulatory system, also called the blood vascular system consists of a muscular chambered heart, a network of closed branching blood vessels – arteries, veins and capillaries, and the circulating fluid, blood. You have already studied about blood and its composition in unit 2.

Let us study about heart that is a crucial organ of cardiovascular system of the human body. Heart is a muscular organ that is located in the middle of chest between the lungs, behind the sternum (breastbone) and above the diaphragm (Fig. 3.1). The narrow lower end of the heart is slightly tilted towards the left, because of which it is believed that it is located on the left side of the chest. A normal adult heart is about the size of a fist and weights about 250-350 grams.

Watch youtube videos on HEART: structure and function

https://www.youtube.com/watch?v=rurD6E0t-F8

https://www.youtube.com/watch?v=A8L63GUaJaw

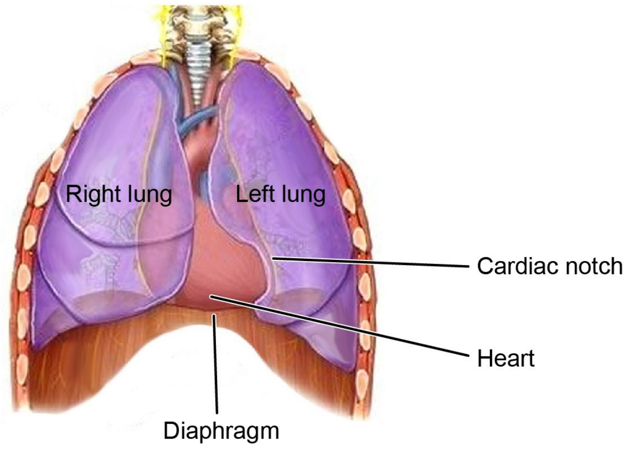


Fig. 3.1: Position of the human heart.

Heart has a thick muscular wall which consists of cardiac muscles cells. It is made up of three layers, called the **endocardium, myocardium, and**

pericardium (Fig. 3.2). The thickness of each layer varies in different part of the heart.

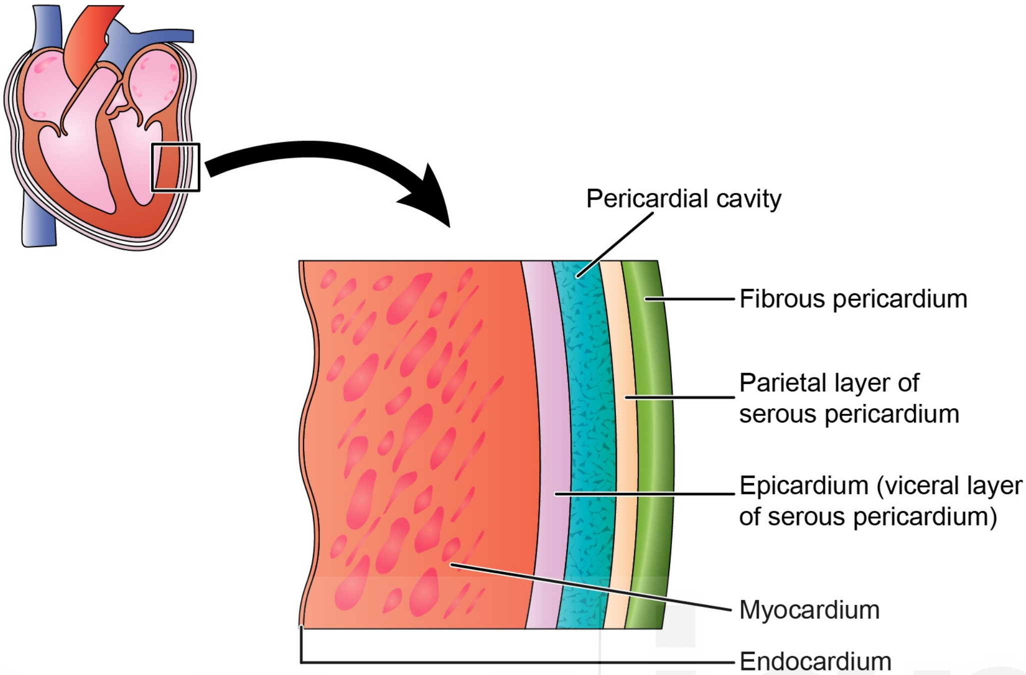


Fig. 3.2: Three layers of the heart wall - epicardium, myocardium and endocardium.

(a) Pericardium is the outermost and a double layer, made up an outer fibrous layer and inner serous layer. The serous layer is also double-layered, the outer parietal layer and internal visceral layer (epicardium). The serous layer contains a pericardial fluid between the two layers which protects the heart from mechanical injuries, such as shocks and jerks, and also reduces the friction due to the pumping action of the heart.

(b) Myocardium is the middle layer which consists of cardiac muscles which communicate through intercalated discs.

(c) The endocardium is the innermost layer which lines the heart chambers and valves.

You know that human body is made up of trillion of cells and each cell needs nutrients and oxygen for releasing energy required to perform functions adequately. Heart generates sufficient force to pump blood throughout the body. Blood carries the oxygen and nutrients to each cell of the organs enabling them to work properly. It also transports waste products (such as, carbon dioxide) from tissue to the respective organs for their elimination. Hence, heart is the vital organ for survival and proper functioning of the body.

3.2.1 Internal Structure of the Heart

Now let us discuss the internal structure of heart. The heart is divided into four chambers: two atria and two ventricles. The atria are upper chambers and the ventricles are the lower chambers. The atria are thin-walled and serve as the filling reservoirs, whereas ventricles are thick-walled and push the blood into the circulation. The thickness of these chambers varies due to difference in the amount of the myocardium tissues.

Heart pumps about 5 litres blood in a day in our body. Blood travels about 60,000 miles (96,560 kilometers) via a extensive network of blood vessels that connecting every cells of tissues and organs of the body.

Each longitudinal half of the heart, thus, consists of an auricle which lies above the ventricle. These two longitudinal halves are separated from each other by a **muscular partition or septum** to prevent the mixing of blood. The right half of the heart is filled with deoxygenated blood, whereas left half is filled with the oxygenated blood. The atrium and ventricle of each half communicate with each other through apertures for regular flow of blood. These apertures, called **atrioventricular apertures**, are **guarded by valves.** The right atrium and the right ventricle are connected by the **tricuspid valve** while left atrium and ventricle are connected by a bicuspid valve called the **mitral valve**. These valves serve as a gate at the chamber openings. They prevent backflow of blood to maintain the blood circulation in the right direction, *i.e.,* from atrium to the ventricles.

The atria receive blood from different organs of the body. The right atrium receives deoxygenated blood from different body organs *via* **superior and inferior vena cava** and the left atrium receives oxygenated blood from the lungs *via* **pulmonary vein**. Blood enters into the respective ventricles which pump blood out of heart. The right ventricle passes the deoxygenated blood to the lungs for oxygenation *via* **pulmonary artery**, while left ventricle pumps oxygenated blood to rest of the body parts through the systemic circulation *via* **aorta** (Fig. 3.3).

The openings of the ventricles into blood vessels are guarded by **semilunar valves** to regulate the flow of blood. **Pulmonary semilunar valves** are located at the opening of ventricles into pulmonary artery while **aortic semilunar valves** are located at the opening of ventricles into the aorta.

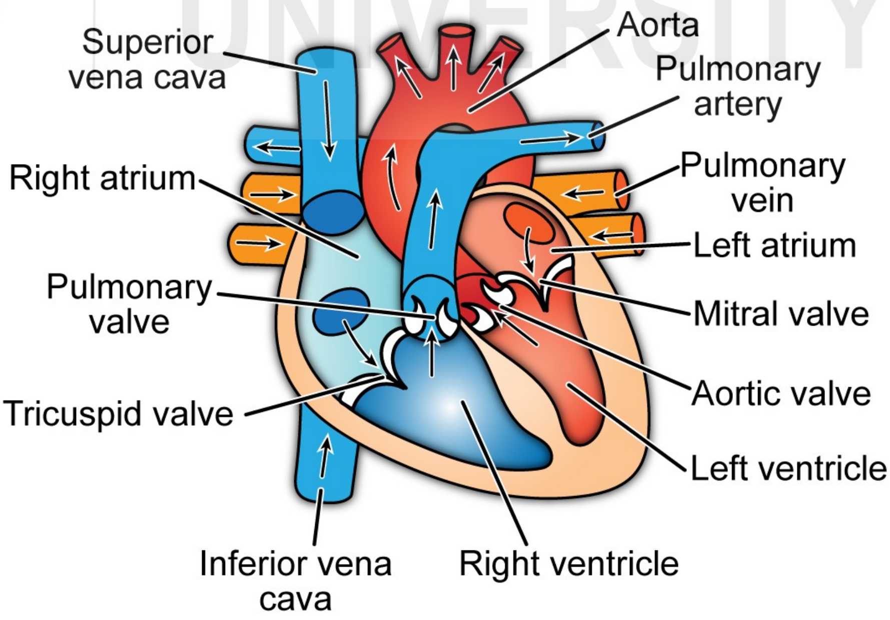


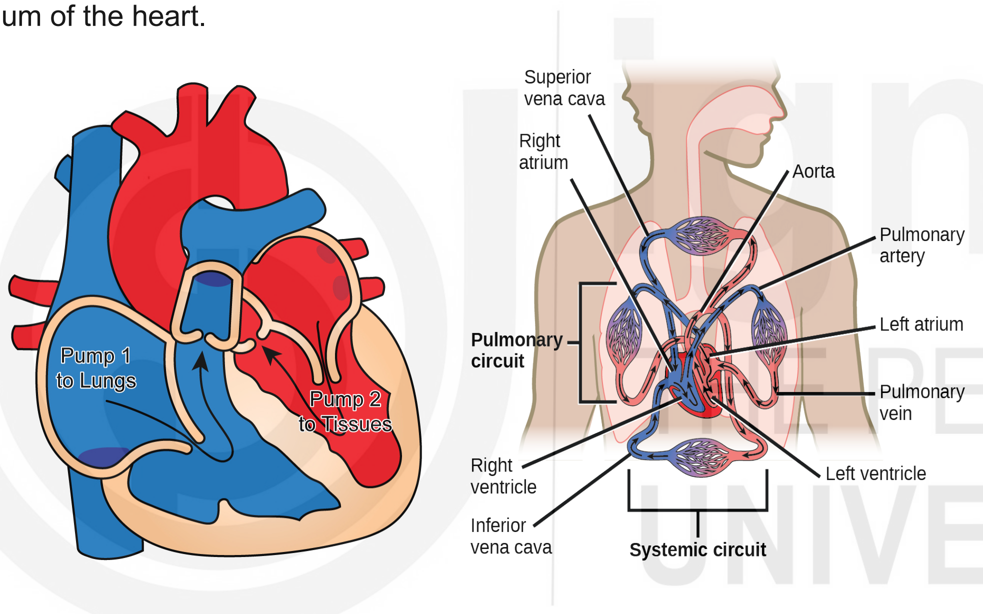
Fig. 3.3: Structure of a human heart Oxygen-poor blood shown in blue-purple color flows into the right chamber of the heart. The oxygen-rich blood, shown in red colour, is pumped out to the rest of the body.

3.2.2 Double Circulation

The mammalian heart, in fact, is a 'two-pumps-in-series' arrangement (Fig. 3.4). The right atrium and ventricle form the pump 1 (the right pump) and the left atrium and ventricle form the pump 2 (the left pump). Accordingly, our body has two circulatory systems that circulate blood back and forth throughout the body. Each of the two individual pumps circulate the blood into two different circuits (Fig. 3.5).

a) Pulmonary circuit- It is a short loop that connects heart to the lungs. The pulmonary artery transports oxygen-poor/deoxygenated blood from the right ventricle to the lungs where blood gets oxygenated and returns back to the left atrium of the heart *via* pulmonary vein.

b) *Systemic circuit*- The systemic circulation transports oxygen and nutrients-rich blood from heart to all parts of the body's tissue through aorta. From the tissues capillaries, blood pick up the carbon dioxide and waste products, and return back *via* veins (superior vena cava and inferior vena cava) to the right atrium of the heart.



(a) (b)

Fig. 3.4: a). The two pumps of the heart. One for receiving and pumping the oxygen-poor blood for oxygenation in the lungs (pump 1) via pulmonary circuit/ circulation; and the other for receiving and pumping the oxygen-rich blood from lungs to the body's parts (pump 2) via systemic circuit/ circulation. b). shows the double circulation (Image credit: OpenStax, CC BY 4.0)

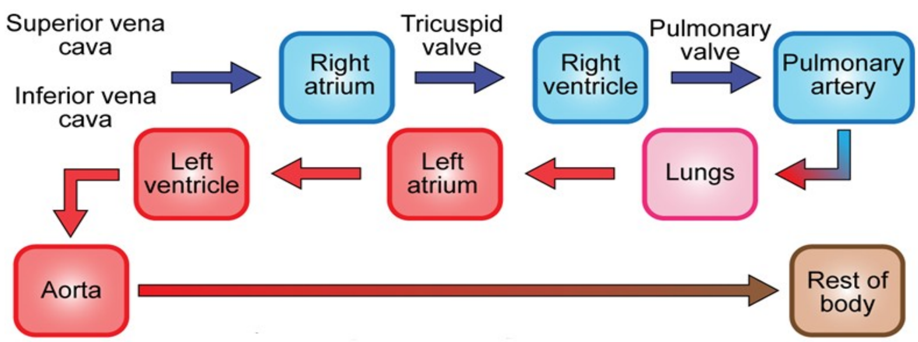


Fig. 3.5 Overview of blood flow pathway to the all parts of body from and to heart *via* systematic and pulmonary circulation.

A human heart, with an average rate of 75 contractions per minute, would contract approximately 108,000 times in one day, more than 39 million times in one year, and nearly 3 billion times during a 75-year lifespan.

Each of the major pumping chambers of the heart ejects approximately 70 mL blood per contraction in a resting adult.

- *This would be equal to 5.25 liters of fluid per minute and approximately 14,000 liters per day.*
- *Over one year, that would equal 10,000,000 liters or 2.6 million gallons of blood sent through roughly 60,000 miles of vessels.*

Function of the Heart

- To generate blood pressure in the arteries by contractions and relaxations of the heart's muscular chambers.
- Heart and blood vessels keep the nutrient & O_2-rich blood separate from the O_2-poor & metabolic waste-rich blood. The valves of heart and veins ensure the blood flow in one direction.
- With the help of chemoreceptors and pressure sensors, the heart and blood vessels regulate blood flow according to the needs of the body.

SAQ 1

Do as Directed:

(a) Fill in the blanks:

i) The right atrium receives deoxygenated blood from different body organs *via* ....*and* the left atrium receives oxygenated blood from the lungs *via*..

ii) The pulmonary artery transports .... from the right ventricle to the lungs.

iii) The systemic circulation transports .... from heart to all parts of the body's tissue through aorta.

iv) The right atrium and the right ventricle are connected by the ....

v) The left atrium and ventricle are connected by the ....

vi) The right atrium and ventricle form .... and the left atrium and ventricle form the ....

(b) Which one of the following sequences is correct in pulmonary circulation?

a) Right ventricle → Pulmonary artery → Lungs → Pulmonary vein → Left atrium

b) Left ventricle → Pulmonary vein → Body → Pulmonary artery → Right atrium

c) Left ventricle → Pulmonary artery → Lungs → Pulmonary vein → Right atrium

d) Right ventricle → Pulmonary vein → Lungs → Pulmonary artery → Left atrium

(c) Define double circulation.

(d) Enlist the layers of heart's wall.

3.3 BLOOD VESSELS

There are three kinds of blood vessels in human body—arteries, veins and capillaries (Fig. 3.6).

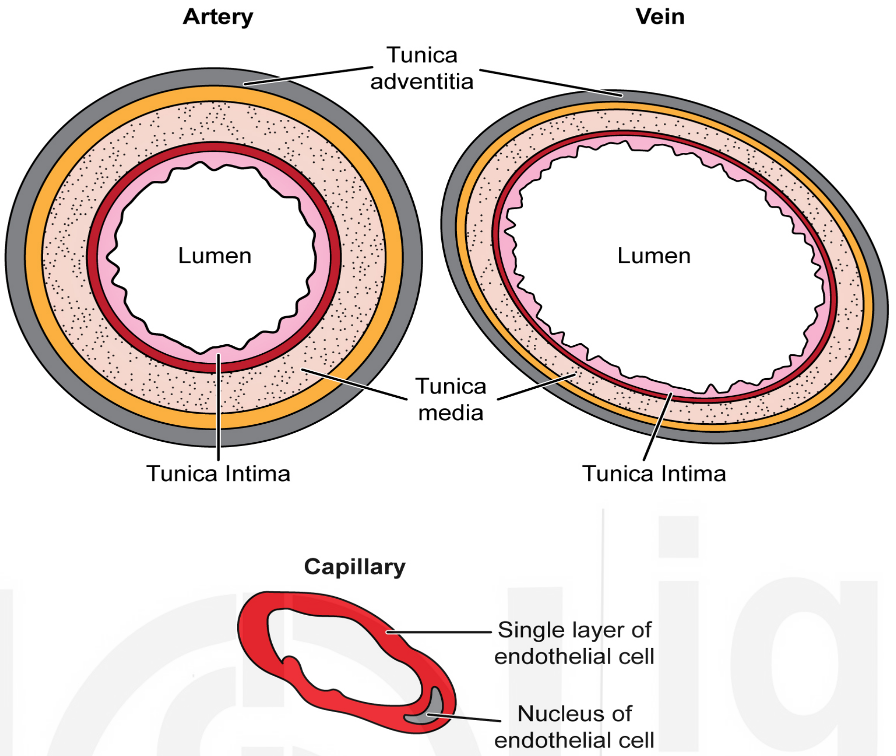


Fig. 3.6: Cross-section of an artery, vein and capillary.

3.3.1 Arteries

Arteries are blood vessels which normally carry oxygenated blood away from the heart to various organs of the body. These consist of an outer fibrous layer – Tunica adventitia; a thick elastic middle layer- Tunica media; and a smooth inner layer called Tunica intima or endothelium. The walls are thick and highly muscular with narrow lumen. The thick musculature provides elasticity and contractibility to the arteries. As a result, arteries can alter their diameter and regulate the amount of blood flow through them.

Arteries are situated deep in the skin and do not collapse when empty. In these, the blood is under high pressure and, therefore, flows very fast with jerks which can be felt as the pulse.

3.3.2 Veins

Veins are the blood vessels which normally carry the deoxygenated blood away from the tissues towards the heart. These also consist of three layers like arteries - Tunica adventitia; Tunica media; and Tunica intima. However, in contrast to the arteries, veins have thin and less muscular walls with a wide lumen. The pressure of blood in the veins is much lower as compared to the arteries. Therefore, in the veins blood flows slowly and without any jerks. Veins are situated superficially within the skin and are visible as bluish-green lines. These are provided with muscular flaps called valves which allow the blood to flow only in one direction, *i.e.*, towards the heart.

3.3.3 Capillaries

Capillaries are very narrow and thin tubes which connect the arteries and veins and form a network of vessels within the body. These are made up of a single layer of endothelium which is non-muscular. This layer is permeable to water and small-sized solutes, such as glucose and amino acids, and impermeable to proteins and large molecules. Small-sized solutes and respiratory gases are easily exchanged through the capillaries. Even WBCs can move out of the capillary wall by squeezing.

Capillaries are formed by repeated branching of smaller vessels called arterioles formed by branching of small arteries. The capillaries join to form the small vessels called venules, which then unite with each other to form veins.

SAQ 2

i) Differentiate structural difference between arteries and veins?

ii) Enlist the name of layers of blood vessels.

3.4 BLOOD PRESSURE

We are all familiar with the term " BP" that stands for blood pressure which is expressed as double number 120/80 mmHg. What does it mean? By this term we really mean only arterial blood pressure which is the pressure of force of blood flow in closed lumen of arteries. Blood pressure is the pressure of cardiac output and peripheral resistance. However, constant blood pressure is required for proper functioning of body.

Blood pressure (**BP**), a form of hydrostatic pressure, is a kind of pressure exerts on walls of blood vessels that originates as a result of pumping blood by the heart. The blood flows from an area of high hydrostatic pressure (in arteries) to area of low pressure (arterioles). That means, it is essentially the pressure difference that drives the blood in vessels. It is expressed in millimeter unit of mercury (mmHg).

An adult healthy human has the normal blood pressure 120/80 mmHg. The higher value, 120 mmHg, is the maximum pressure exerted during systole (ventricular contraction) when the heart contracts and pumps out blood. The lower value, 80 mmHg, is the minimum pressure exerted during diastole when the heart relaxes and refills with blood (ventricular relaxation). Therefore, blood pressure is expressed as double number: higher number (120 mmHg) for systolic blood pressure (SBP) and a lower (80 mmHg) for the diastolic blood pressure (DBP) (Fig.3.7).

The difference between the systolic and diastolic pressure is known as the **pulse pressure** (PP) which ranges amid 40 to 50 mmHg. The **mean blood pressure** (MBP) is an average pressure during whole cardiac cycle (Fig. 3.9). Its normal range, 95-100 mmHg, and the average, 96 mmHg, are the most important parameters for evaluation of blood flow efficiency in the body.

PP = SBP-DBP

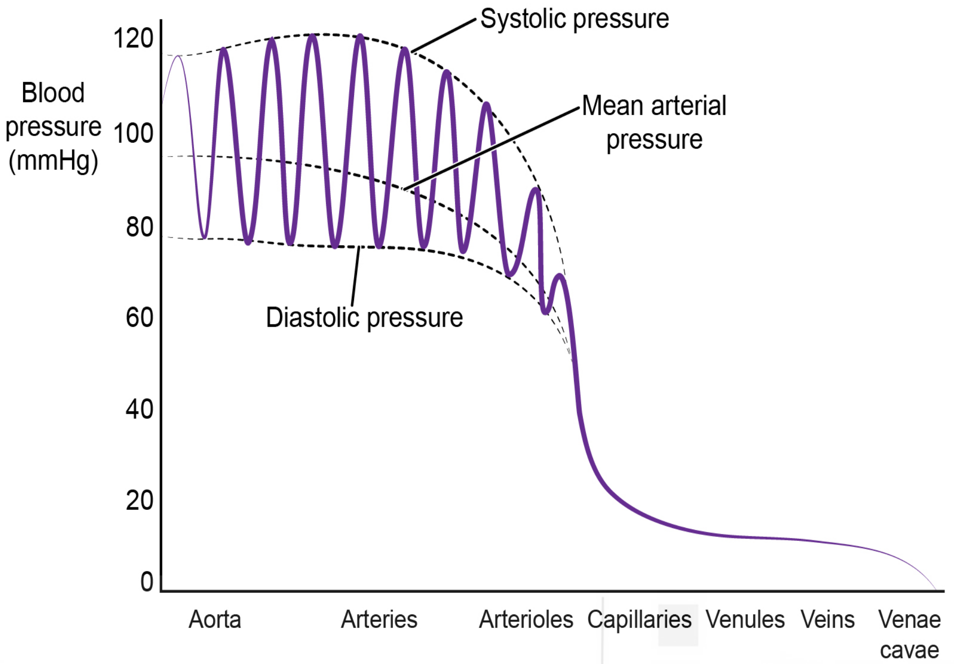


Fig. 3.7 Systolic and diastolic blood pressure in a normal human being.

The quantum of pressure exerted by blood (BP) is highest in the aorta and large systemic arteries. The blood pressure was measured for the first time in 1733 by an English priest Stephen Hales. In 1896, **an Italian physician Riva Rocci discovered sphygmomanometer** to measure BP in 'mmHg' (height of the mercury column in millimeters in a 'mercury manometer').

Sphygmomanometer

The blood pressure is usually measured in the brachial artery of the arm although it can be measured in capillaries, veins, and the vessels of the pulmonary circulation. However, the term 'blood pressure' without any specific descriptors typically refers to systemic arterial blood pressure- that is, the pressure of blood flowing in the arteries of the systemic circulation. As the distance from the heart increases, the pressure of blood in systemic vessels falls progressively.

3.4.1 Blood Flow and Resistance

The flow rate of blood in vessels is relatively constant which is necessary to maintain the normal blood pressure. Like all fluids, blood tends to move from a region of high pressure to the region of low pressure along the walls of the blood vessels. Blood flows in the same direction as the decreasing pressure gradient: arteries to capillaries to veins. A too-high flow can damage blood vessels and tissue, while too-low flow cannot deliver sufficient oxygen to each cell of tissues. In the arterial circulation system, as the resistant increases, blood pressure increases and consequently blood flow decreases.

Blood vessels create an opposite force, called **resistance**, when blood flows through them. In other words, resistance opposes the blood flow in the blood vessels and can be defined as a phenomenon of impediment or slowing down of blood flow. On the contrary, the ability of vessels to expand to accommodate increased fluid is called **compliance**. The greater is the compliance, greater will be the expansion ability to accommodate the pumped blood without increased resistance or blood pressure. Hence, it can be pertinently inferred that the **flow rate is directly proportional to the pressure difference between two points and inversely proportional to the resistance.**

There are several factors that affect the flow and pressure, such as blood vessel length & diameter, cardiac output, vascular compliance (vessel elasticity), peripheral resistance, viscosity of the blood, volume of the blood etc. The blood vessel diameter, length and blood viscosity are the main factors which offer resistance to the blood flow.

- The decrease in vessel diameter increases the resistance to blood flow which in turn raises the blood pressure. In other words, ‘under constant blood volume, larger the vessel diameter, lesser will be the pressure; on the other hand, smaller the diameter, more will be the pressure’.
- Likewise, longer the total vessel length, the greater will be the resistance, and the greater will be the blood pressure.
- Similarly, viscosity also affects peripheral resistance. Greater the viscosity greater will be the resistance as the fluid moves slowly, and greater pressure is required to pump the same volume of viscous fluid.
- Cardiac output (CO) is the measurement of flow of blood from the ventricles to the aorta, which is usually measured in liters per minute. It can be expressed as ‘heart rate (HR) times the stroke volume (SV – blood pumped out from the ventricle per heartbeat)’, i.e.,

  CO = HR x SV.

  Hence, any change in HR and/or SV affects cardiac output and, in turn, arterial pressure. This ultimately causes a proportionate change in blood flow to various tissues of the body.

SAQ 3

i) Fill in the blanks with appropriate words:

a) Unit of blood pressure is ....

b) Flow rate is directly .... to the pressure difference between two points and inversely proportional to the ....

c) Measurement of flow of blood from the ventricles to the aorta is called the...................

d) The ability of vessels to expand to accommodate increased fluid is called ....

3.5 PHYSIOLOGY OF THE CARDIAC MUSCLE & CONTRACTION

The heart is composed of three major types of cardiac muscle: atrial muscle, ventricular muscle, and specialized excitatory and conductive muscle fibers. Cardiac muscle cells found only in the heart are called cardiomyocytes that constitute the walls of the heart. Cardiomyocytes are responsible for pumping blood to the rest of the body. These cells have distinct characteristics which are given below.

- Cardiac muscle is striated, like skeletal muscle.
- It is made up of distinct **syncytial** cardiac muscle cells which are considerably shorter and have much smaller diameters than the skeletal muscle.
- Cardiac muscle cells are **branched** and interconnected. The sarcolemma of the branches of adjacent cells are strongly attached end-to-end by specialized junctions called '**intercalated discs'** to withstand the forces of contraction.
- Intercalated discs contain desmosomes, specialized linking proteoglycans, tight junctions, 'adhering junctions' into which myofibrils are attached, and 'gap junctions' that allow passage of ions to establish electrical connection between adjacent cells for synchronizing contraction (**Fig. 3.8**). Such types of special discs are not present in skeletal muscle cells.

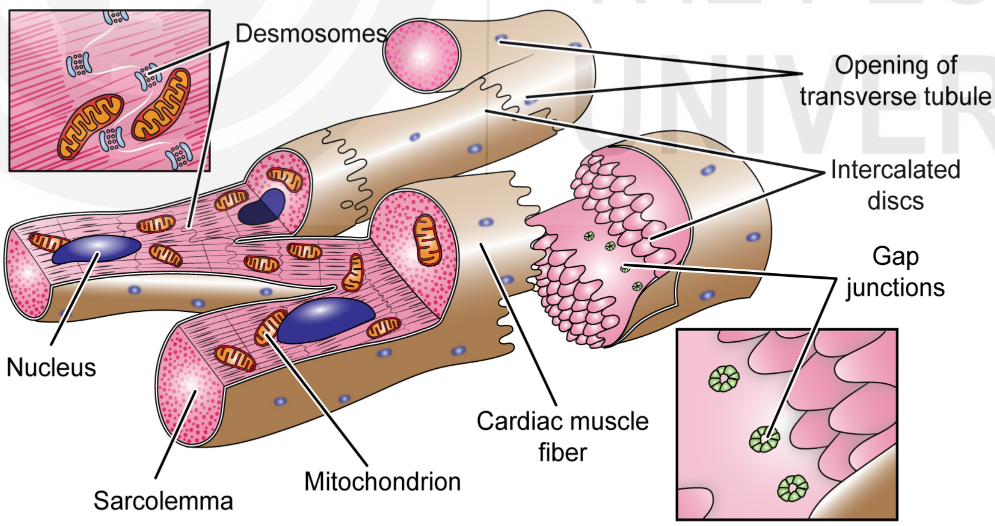


Fig. 3.8: Cardiac muscle fibers are connected to neighboring fibers by intercalated discs. [Image Source adapted fromTortora & Derrickson-Principles of Anatomy and Physiology, 12Ed].

- They are highly coordinated muscle cells that pump blood into the network of blood vessels. The atrial and ventricular muscles contract in a similar manner as those of skeletal muscle, however the duration of contraction is much longer with longer refractory period. This is provided by the entry of Ca^{++} ions into the sarcolemma of cardiac muscle cells.

- On the other hand, the excitatory conductive fibers contract very little because of their limited number of contractile fibrils. Instead, they exhibit exceptional **autorhythmicity**, providing an excitatory system that controls the rhythmical beating of the heart.

Let us understand the cardiac cycle and heart sounds.

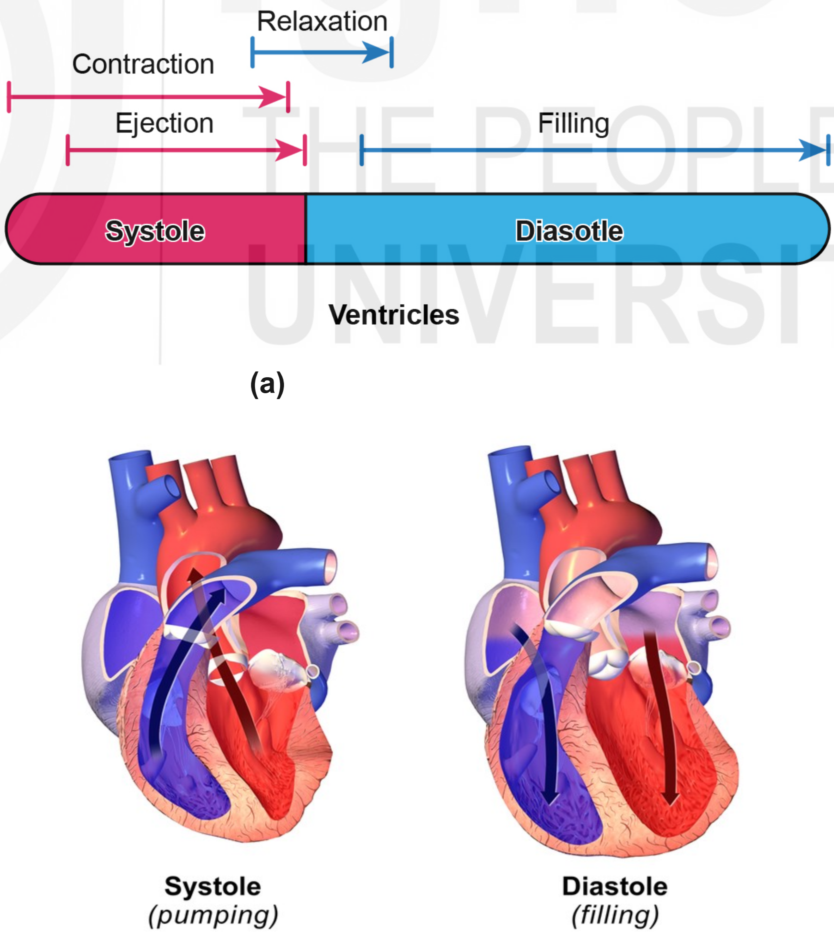
3.5.2 Cardiac cycle

You know that the cardiomyocytes play an important role in the contraction and relaxation of heart chambers sequentially in order to pump out blood from the heart and fill the chamber again. The time duration between the atrial contraction and the ventricular relaxation is known as the **cardiac cycle.** During cardiac cycle, atria and ventricle chambers work in coordinated manner to generate efficient force to pump blood out through and from the heart. In the process, electrical signals travel through the heart to pump blood to lungs and to rest of the body.

Cardiac cycle consists of two phases - Systole and diastole (Fig. 3.9a&b)

1. Systole: Systole is the pumping phase of the heart. It occurs when heart contracts to pump out the blood into the circulation.

2. Diastole: Diastole is filling phase of the blood into the heart when heart relax after contraction.



(b)

Fig. 3.9: Phases of cardiac cycle. (Image credit: Wikimedia.commons)

The cardiac cycle starts with the contraction of atrium and ends with ventricle relaxation. It consists of three basic steps.

a) **Atrial and Ventricular Diastole (Joint Diastole)** - Initially, all the four chambers are relaxed for a short period of time. This is called joint diastole. Blood continues to flow into the auricles through vena cava and the pulmonary veins; which then flows to the ventricles as the atrio-ventricular valves open. At this stage, semilunar valves are closed.

b) **Atrial Systole and Ventricular Diastole** - Both the atria contract simultaneously; the phase is called the atrial systole. The ventricle is still in the diastole state which increases the flow of blood into the ventricles by about 30%.

c) **Atrial Diastole and Ventricular Systole** - Now the ventricular muscles contract, ventricular systole and the atria undergo relaxation (diastole), coinciding with the ventricular systole. It increases the ventricular pressure causing the closure of tricuspid and bicuspid valves. As the ventricular pressure increases further, the semilunar valves guarding the pulmonary artery (right side) and the aorta (left side) are forced open, allowing the blood in the ventricles to flow through these vessels into the circulatory pathways.

The ventricles now relax again (ventricular diastole) and the ventricular pressure falls causing the closure of semilunar valves which prevents the backflow of blood into the ventricles.

The ventricular pressure declines further and the tricuspid and bicuspid valves are pushed open by the pressure in the atria exerted by the blood which was being emptied into them by the veins. The blood now once again moves freely to the ventricles. The ventricles and atria are now again in a relaxed (joint diastole) state.

Thus, cardiac cycle consists of three phases:

Phase I:Ventricular diastole and atrial diastole = 0.40 seconds.

Phase II: Atrial systole and ventricular diastole = 0.1 – 0.15 seconds

Phase III: Ventricular systole and atrial diastole = 0.30 seconds

One complete cycle constitutes one **heartbeat**, which lasts 0.8-0.85 seconds. Heart normally beats 72-75 times per minute in healthy body and its average limit of beat is about 100,000 times a day.

3.5.3 Heart Sounds

As the heart contracts and relaxes in a complete cardiac cycle, it produces two sounds: The first sound, the **lub** is generated by the closure of bicuspid and tricuspid valve and the second heart sound, the **dub** by the closure of semilunar valve.

The lub sound denotes the onset of ventricular systole while dub sound signifies the onset of ventricular diastole.

SAQ 4

Do as Directed:

a) What is Cardiac muscle?

b) Fill in the blanks:

i. Pumping phase of heart is called ....

ii. Filling phase of heart is called the ....

iii. Heart produces first sounds the............and second the .... during

iv. each heart beat.

v. One complete cardiac cycle constitutes............. which lasts ...seconds...................

vi. Heart normally beats ....per minute in healthy body.

3.6 CARDIAC CONDUCTION SYSTEM

The human heart beats continuously due to its own inherent and rhythmical electrical activity. The heart contraction process begins by the initiation of electrical signals in the specialized cells, called pacemaker or cardiomyocytes inside the heart (right atrium). The electrical potential trigger heart muscle cells (myocytes) to contract as a group. Hence, action potential is generated by the cardiac conduction system of the heart without any external stimulus. The cardiomyocytes contract in a repeated sequence to pump blood rhythmically and involuntarily in response to electrical impulses. Now let us know how heart muscles contract and relax during cardiac cycle.

Watch youtube videos by clicking on the following links:

1. Cardiac muscle excitation

https://www.youtube.com/watch?v=A8L63GUaJaw

2. Electrical conduction system https://www.youtube.com/watch?v=9oer9gflyfs

The constitutive elements of the '*cardiac conduction system*' include the sinoatrial/ sinoauricular (**SA**) node, the atrioventricular/auriculo-ventricular (**AV**) node, the atrioventricular bundle (**AV bundle/ bundle of His**), the left and right bundle branches and the Purkinje fibers (Fig. 3.10).

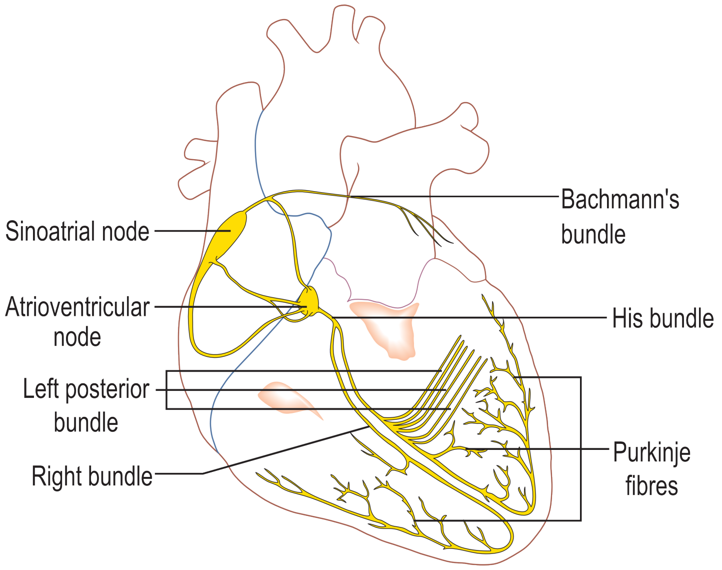


Fig. 3.10: Conduction system of the heart. (Source: Wikimedia commons).

These components have an inherent capacity to beat on their own, the property is known as ***autorhythmicity*** because they are self-excitable. During embryonic development, ~1% of the cardiac muscle fibers become autorhythmic fibers. This inherent and rhythmical activity is the driving force behind the heart's lifelong beat. These specialized fibers repeatedly generate action potentials that trigger heart's rhythmic contractions and relaxations.

These highly specialized fibers perform two crucial functions.

i) They act as a **pacemaker,** setting the rhythm of electrical excitation that causes contraction of the heart.

ii) They form the **cardiac conduction system,** a network of specialized cardiac muscle fibers that spread each cycle of cardiac excitation evenly throughout the heart so that the heart chambers contract in a coordinated and synchronous manner. This makes the heart an effective pump, more efficient than any other natural or man-made ones.

The functions of individual components of the conduction system are as follows.

- ✓ A patch of the excitable tissue is present in the **right upper corner of the right atrium**. It is called the **sinoatrial node**.
- ✓ **Sinoatrial (SA) node** normally generates the ***action potential***, i.e. the ***electrical impulse*** that initiates contraction. The SA node excites the right atrium and the action potential travels through ***Bachmann's bundle*** to excite left atrium.
- ✓ The action potential travels through the three internodal tracts in right atrial wall to the **atrioventricular (AV) node.**
- ✓ From the AV node, the impulse then travels through the **bundle of His** and down the two bundle branches (left & right) on either side of the **interventricular septum.**
- ✓ **Right bundle branch** depolarizes the right ventricle while **Left bundle branch** depolarizes the left ventricle and interventricular septum.
- ✓ Both bundle branches further branch out and terminate in millions of small fibers projecting throughout the myocardium called the **Purkinje fibers**.
- ✓ The action potential in the **His-Purkinje system** travel rapidly and evenly in such a way that papillary muscle contraction ***precedes*** that of the ventricles, thereby preventing regurgitation of blood flow through the bicuspid and tricuspid valves.
- ✓ There are several different channels in cardiac muscle cells for a given ion action potential; Na^+, K^+, Ca^{2+} and Cl^- ion channels. These ions cross the membrane through their respective specific ion channels/gates which are tightly regulated and operated (open/activated and close/inactivated) by various factors such as charge, concentration, ligands etc., hence called '***gated channels'***.

✓ The channels play very important role in maintaining the sarcolemma in a polarized state (resting state), or in generating and propagating the action potential.

3.7 EXCITATION-CONTRACTION COUPLING

Excitation-contraction coupling (ECC) is the process whereby an action potential stimulates a muscle cell to contract followed by subsequent contraction. This term was used by Alexander Sandow in 1952 while describing **the series of events occurring between the plasma membrane of muscle fibres** and Ca^{2+} release from the SR, which results in contraction.

In other words, it is a **bio-mechanical process** in which production of **bioelectricity** (an electrical action potential) leads to a **mechanical event** (contraction of cardiac muscle cells). This is achieved by converting a biochemical signal into mechanical energy *via* the action of **contractile muscle proteins**: actin and myosin. Calcium (Ca^{2+}) ion is the crucial mediator that couples electrical excitation to physical/mechanical contraction by moving in and out of the myocyte's contractile structures during each action potential.

3.7.1 Calcium-Induced Calcium Release (CICR)

The initial influx of Ca^{2+} into myocytes through Ca^{2+} channels during phase 2 of the action potential is insufficient to trigger contraction of myofibrils. This signal is amplified by the CICR mechanism, which triggers greater release of Ca^{2+} from the sarcoplasmic reticulum.

- The cell membrane of cardiomyocytes invaginates into the sarcoplasm forming a specialized system of **transverse tubules** called **T-tubules** that bring L-type Ca^{2+} channels into close contact with **ryanodine receptors**, specialized Ca^{2+} release receptors in the sarcoplasmic reticulum (SR).
- When Ca^{2+} enters the cells through Ca^{2+} channels and bind to the ryanodine receptors, the receptor proteins undergo conformation change and induce release of larger quantities of Ca^{2+} from abundant SR stores.
- The increased levels of cytosolic Ca^{2+} bind to troponin-tropomyosin complexes and induce myocyte contraction.

3.7.2 Contractile Cycle

Muscle contractile cycle requires ATP which first bind to the myosin protein. ATP gives energy to drive contractile cycle. The steps of contractile cycle are shown in the Fig. 3.11.

1. **Contractile cycle starts** when Ca^{2+} binds to the troponin C. This binding causes a displacement in tropomyosin and exposes an active **binding site** on actin.
2. When myosin interacts with the actin filament, ATP is hydrolysed by ATPase into ADP+Pi **and forms the cross-bridge** between myosin

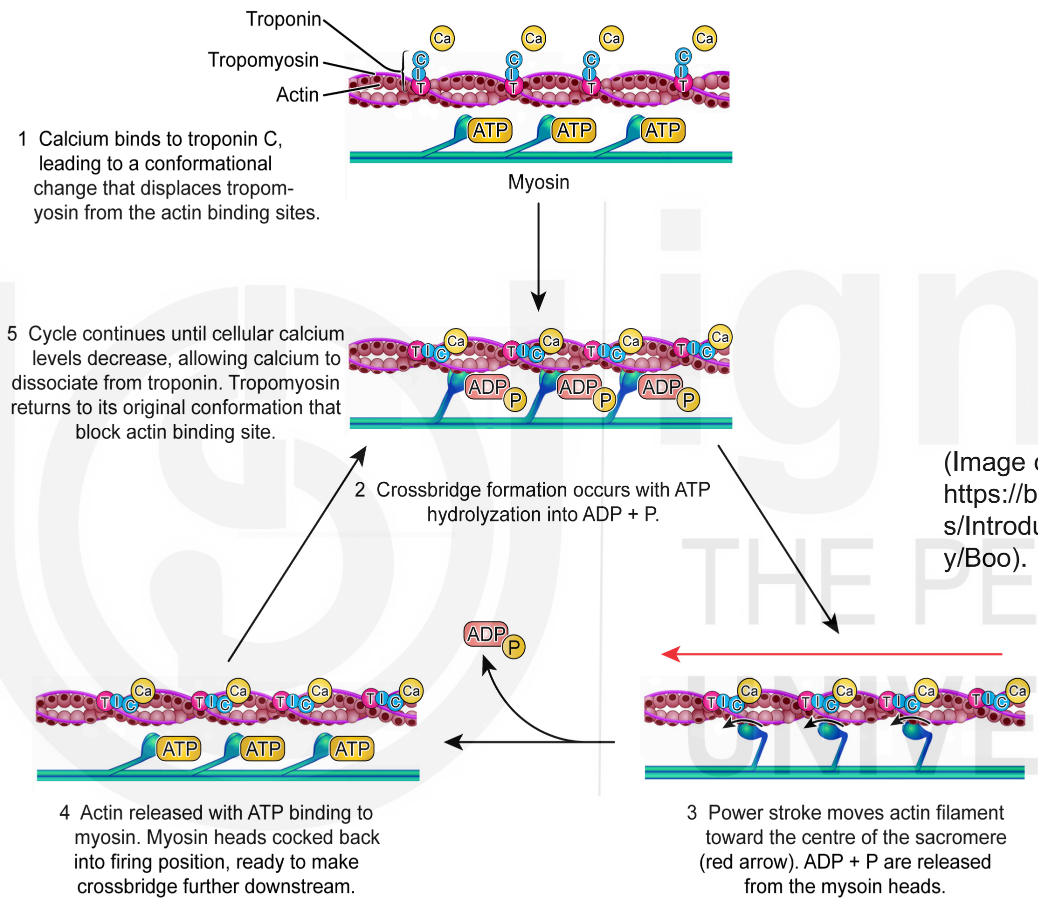
heads and actin filament. Hence, this is called cross-bridge muscles contraction cycle.

3. ATP hydrolysis gives a force to "bend" the myosin head which stimulates the release of ADP and Pi. Subsequently, myosin head binds to the actin. This interaction results in **power stroke** of muscle contraction. This can be represented as a chemical reaction given below.

Actin + Myosin + ATP → Actin-Myosin + ADP + Pi + Force (energy)

4. Released ATP again binds to the myosin head and cross-bridge forms between myosin and actin filaments.

The cycle undergo progressively itself as long as (i) the cytosolic Ca^{2+} concentration is sufficient and (ii) ATP is available.



(Image credit: https://bio.libretexts.org/Bookshelves/Introductory_and_General_Biology/Boo).

Fig. 3.11 Calcium-mediated cardiomyocytes contractile cycle

SAQ 5 **Fill in the blanks with correct words:**

i) The cell membrane of cardiomyocytes invaginates into the sarcoplasm forming a specialized system of transverse tubules is called ....

ii) Contractile cycle starts when .... binds to the troponin C.

iii) ATP is hydrolysed by .... into .... and forms the cross-bridge between myosin heads and actin filament.

iv) The term Excitation-contraction coupling is coined by ....

v) Actin + Myosin + ATP → ....

3.8 CONTROL OF CARDIAC OUTPUT

Cardiac output (CO) is the volume of blood ejected from the ventricles into major arterial trunks (left ventricle into *aortic trunk* & right ventricle into *pulmonary trunk*) per minute. It is a quantitative parameter of heart functioning. Each ventricle pumps out approximately 70 mL of blood per beat. This volume is called **Stroke Volume (SV)**.

Cardiac output equals the '***stroke volume (SV) times the heart rate (HR)***'.

CO (mL/min) = HR (beats/min) X SV (mL/beat)

Normal CO = 75 beats/min X 70 mL/beat **= 5.25 L/min**

This volume (**5.25 L**) is almost equivalent to your total blood volume, which is about 5 liters in a typical adult male. Thus, your entire blood volume flows through your pulmonary and systemic circulations each minute.

Cardiac output varies widely with the level of activity of the body. The normal values for cardiac output at rest and during activity depends on the following factor

- the basic level of body metabolism,
- exercise and age,
- body size of the individual.
- For *young*, *healthy men*, resting cardiac output averages about 5.6 L/min.
- For *women*, this value is about 4.9 L/min.

When one considers the factor of age as well; because with increasing age, body activity diminishes; the average cardiac output for the resting adult, in round numbers, is often stated to be almost exactly 5 L/min.

3.8.1 Regulation of Heart Rate

As you know by now that cardiac output depends on both HR and SV; adjustments in heart rate are important in the short-term control of cardiac output and blood pressure. The SA node initiates contraction and, if left undisturbed, would set a constant heart rate of about **100 beats/min**. However, tissues require different volumes of blood flow under different conditions. For example, during exercise, cardiac output rises to supply working tissues with increased amounts of oxygen and nutrients. Stroke volume may fall if the ventricular myocardium is damaged or if blood volume is reduced by bleeding. In these cases, homeostatic mechanisms maintain adequate cardiac output by increasing the heart rate and contractility.

Among the several factors that contribute to the regulation of heart rate, the most important are the autonomic nervous system and hormones released by the adrenal medulla (epinephrine and norepinephrine).

1. **Autonomic Regulation of Heart Rate**

   a) **Sympathetic** - **NOREPINEPHRINE** (NE) increases heart rate (maintains stroke volume which leads to increased cardiac output)

   b) **Parasympathetic** - **ACETYLCHOLINE** (ACh) decreases heart rate

   c) **Vagal tone** - parasympathetic inhibition of inherent rate of SA node, allowing normal HR

   d) **Baroreceptors** (pressure-sensing receptors which monitor the stretching of major arteries and veins caused by the pressure of the blood flowing through them) and

   e) **Chemoreceptors** (monitor chemical changes in the blood) watch changes in blood pressure and allow reflex activity with the autonomic nervous system

2. **Hormonal and Chemical Regulation of Heart Rate**

   a) **Epinephrine**- hormone released by adrenal medulla during stress; increases heart rate.

   b) **Thyroxine**- hormone released by thyroid; increases heart rate in large quantities; amplifies effect of epinephrine

   c) **Ca^{++}, K^+, and Na^+** levels are significant:

   - **Hyperkalemia**- increased K^+ level; KCl stops heart on lethal injection
   - **Hypokalemia**- lower K^+ levels; leads to abnormal heart rate rhythms
   - **Hypocalcemia**- depresses heart function
   - **Hypercalcemia**- increases contraction phase
   - **Hypernatremia**- high Na^+ concentration; can block Na^+ transport & muscle contraction

3. **Other Factors Affecting Heart Rate**

You are aware that normal heart rate in a fetus is 140 - 160 beats/minute; in a female 72 - 80 beats/minute and in a male it is 64 - 72 beats/minute. The factors which can affect heart rate are

(a) **Exercise** - lowers resting heart rate (40-60).

(b) **Heat** - increases heart rate significantly.

(c) **Cold** - decreases heart rate significantly.

(d) **Tachycardia** - **HIGHER** than normal resting heart rate (over 100); may lead to fibrillation.

(e) **Bradycardia- LOWER** than normal resting heart rate (below 60); is caused by parasympathetic drug side effects and physical conditioning. It is a sign of pathology in non-healthy patient.

SAQ 6

a) Choose the correct parentheses from the following:

i) K^+ level **(increases/decreases)** in hyperkalemia.

ii) **The (lower/higher)** K^+ level in hypokalemia causes abnormal heart rate rhythms.

iii) Hypernatremia- occurs due to increasing level of **(Na^+/K^+)** concentration;

iv) Tachycardia is condition of (**Higher/Lower)** than normal resting heart rate (over 100).

v) Bradycardia- is the symptoms of non-healthy people who have **(below/above)** heart rate 60.

vi) The average value for resting cardiac output is about **(5.6L/ 4.9L)** per min for women.

b) Define the cardiac output and strock volume.

3.9 SUMMARY

- The heart is a contractile muscular organ that pumps blood throughout the body. The heart, blood vessels, and blood are the key components of the cardiovascular system.
- Internally, the heart is divided into two auricles/atria and two muscular ventricles separated by four valves. Four valves in the heart keep blood flowing in the correct direction and prevent backflow.
- The heart has its own blood circulatory system. The **aorta** supplies oxygenated blood in the body and **vena cava** collects deoxygenated blood from the body.
- It has own conduction system, the sinoatrial (SA) node being its natural pacemaker. During the cardiac cycle, the chambers of the heart contract and relax, and blood flows from high-pressure to low-pressure areas
- There three major types of blood vessels are arteries, veins, and capillaries through which blood flow.
- Arteries carry blood away from the heart. Veins carry blood toward the heart. Capillaries connect the smallest arteries and veins and exchange substances between the blood and cells of the body.
- A single complete heartbeat is referred to as cardiac cycle that includes diastole, when the atria contract; and systole, when the ventricles contract.

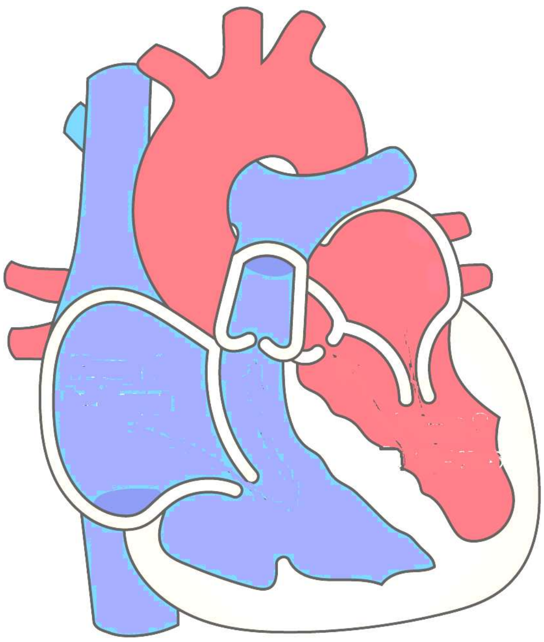
- EC coupling of cardiac muscle differs in significant ways from that of skeletal muscle. Most importantly, the amount of Ca^{2+} in the cytoplasm is never enough to activate all of the muscle protein. As a result, the force of contraction can vary with the amount of Ca^{2+} entering the cell. Several mechanisms may be involved in regulating Ca^{2+} entry during the action potential.

- As in skeletal muscle, Ca^{2+} is released from the *sarcoplasmic reticulum* (**SR**) by the action potential. However, the Ca^{2+} is not released directly by the depolarization accompanying the action potential. Instead, the Ca^{2+} entering the cell during the cardiac action potential triggers the release of Ca^{2+} from the SR. This is called **Ca^{2+}-induced Ca^{2+} release**.

- The autonomic nervous system and hormones released by the adrenal medulla (epinephrine and norepinephrine) are the major factors that control the heart rate.

3.9 TERMINAL QUESTIONS

1. Give the location and the function of heart.
2. discuss the structure of the heart.
3. Differentiate between systemic circuit and pulmonary circuit.
4. Discuss the structure of blood vessels
5. Discuss the cardiac cycle?
6. Explain the blood pressure and Resistance in blood flow.
7. Discus the cardiac conduction system?
8. Describe the contractile cycle.
9. Write a short note on regulation of heart rate.
10. Draw the diagram of heart with labeling its four chambers.



3.10 ANSWERS

Self Assessment Questions

1. (a)

   i. Superior and inferior vena cava and pulmonary vein.

   ii. oxygen-poor/deoxygenated blood .

   iii. oxygen and nutrients-rich blood

   iv. tricuspid valve.

   v. mitral valve.

   vi. the pump 1 (the right pump), pump 2 (the left pump).

(b) Right ventricle → Pulmonary artery → Lungs → Pulmonary vein → Left atrium

(c) Human heart has two types of blood circulation which pump blood back and forth throughout the body. Hence it is called double circulatory system. It has two ways: Pulmonary circuit (between the heart and lungs) and Systemic Circuit (between the heart and other organ system) through which the heart receive blood twice.

(d) Endocardium, myocardium, and pericardium

2. i)

	Arteries	**Veins**
General Characteristics	Arteries carry oxygenated blood from the heart to the rest of the body (except in the pulmonary artery)	They carry deoxygenated blood from different body parts back to the heart (except in the pulmonary vein)
Types of Arteries	Arteries are divided into *arterioles* and capillaries. In humans, the *aorta* is considered to be the largest artery, whereas the *arterioles* are the smallest. Arterioles supply blood to the capillary bed, where the actual gas exchange between cells and tissues occur.	The two largest veins are **Superior Vena Cava** (returning blood from tissues located above the heart) and **Inferior Vena Cava** (returning blood from tissues located below the heart) of which the **Inferior Vena Cava** is the larger and longer vein. **Venules** are smallest, serve as blood reservoirs of

		the body.
Wall of vessel	**Thick and strong walls**; composed of muscles, fibrous tissues, elastic fibers and endothelium. Composed of **three layers** namely *Tunica adventitia*, *Tunica media* and *Tunica intima*.	**Relatively thin walled**; composed mainly of fibrous tissues but less elastic fibers and muscles, inner most one is endothelium. Composed of the same **three layers** but of different thicknesses.
Diameter of lumen	Narrow lumen No valves	Wider lumen which contains numerous valves prevent backflow of blood.
Pressure needed	Blood flow at **high pressure**	Blood flow at **low pressure**

ii) Tunica adventitia; Tunica media; and Tunica intima.

3. (i)

a) mmHg

b) proportional

c) cardiac output

d) compliance

4. a) Cardiac muscle cells are the main cells that form the heart's wall. They are syncytial and involuntary cells that are responsible for the mechanical function of pumping blood throughout the rest of the body. They are considerably shorter and have much smaller diameters than the skeletal muscle.

b) i) Systole

ii) Diastole

iii) Lub, dup

iv) Heartbeat 0.8-0.85 seconds

v) 72-75 times

5. i) T-tubules

ii) Ca^{2+} binds to the troponin C

iii) ATPase into ADP+Pi and forms the cross-bridge.

iv) Alexander Sandow in 1952

v) Actin-Myosin + ADP + Pi + Force (energy)

6. a) increases

i) Lower K^+ level

ii) K^+ concentration;

iii) Higher than normal resting heart rate (over 100).

iv) below heart rate 60.

v) The average value 4.9L per min for women.

b) **Cardiac output (CO)** is the volume of blood released per minute by ventricles into major arterial trunks. It is a quantitative parameter of heart functioning.

Stroke Volume is volume of blood that come out from per beat of heart ventricles. Each ventricle pumps out approximately 70 mL of blood per beat. Cardiac output equals the '*stroke volume (SV) times the heart rate (HR)*'.

Terminal Questions

1. Refer to section 3.2
2. Refer to subsection 3.2.1
3. Refer to subsection 3.2.2
4. Refer to section 3.3
5. Refer to subsection 3.4.2
6. Refer to section 3.5
7. Refer to section 3.6
8. Refer to section 3.7.2
9. Refer to section 3.8
10. Refer to Fig. 3.3