UNIT 2 PHYSIOLOGY OF THE HEART

Structure

2.0 OBJECTIVES

After reading this unit, you should be able to:

- enumerate the various phase of cardiac cycle;
- enlist the determinants of cardiac out put and their effects; and
- give a description of contractile unit of sarcomere.

2.1 INTRODUCTION

The cardiovascular system controls the movement of blood through thousands of miles of capillaries so that every tissue in every part of the body is perfused. Essential nutrients are supplied and waste products are removed. The blood has to be kept fluid and the regional circulation has to be adjusted in relation to the needs of a tissue or organ at that time. For example skeletal muscle will need an increased blood flow during exercise. Hence numerous control mechanisms are necessary to supply essential nutrients to each cell of the body.

The heart acts as a pump that propels arterial blood through the aorta and receives the venous blood through the superior and inferior vena cava. The left ventricle is thicker as it has to pump blood at a higher pressure into the aorta. The right ventricle works at a lower pressure and pumps into the pulmonary artery.

The venous blood from the vena cavae passes into the right atrium and through the tricuspid valve into the right ventricle. From here during ventricular systole blood is pumped through the pulmonary valve into the pulmonary artery and the lungs where oxygenation takes place. The oxygenated blood is then returned to the left atrium through the four pulmonary veins. From the left atrium the blood passes through the mitral valve to the left ventricle during diastole and during ventricular systole through the aortic valve into the aorta.

The electrical impulse that initiates the heart beat originates in the sino atrial (SA) node. From here the impulse passes across both the atria to the atrio-ventricular node (AV node).There is a

physiological delay of the impulse in the AV node and there is also a limit to the number of impulses that can pass through. Thus if a large number of impulses come from the atria as in atrial fibrillation only a certain lesser number of impulses can go through to activate the ventricles. From the AV node the impulses pass through the Bundle of his to divide into the right and left bundle branches. The left bundle branch divides further into two fascicles–the anterior and posterior. The bundle branches end up as the Purkinje system. Conduction problems can occur at all levels. Thus you could have a sino atrial block, AV nodal block of varying degrees, right or left bundle branch block and fascicular block. These will be discussed in the sections on arrhythmias and ECG. The conduction system is shown in the diagram below:

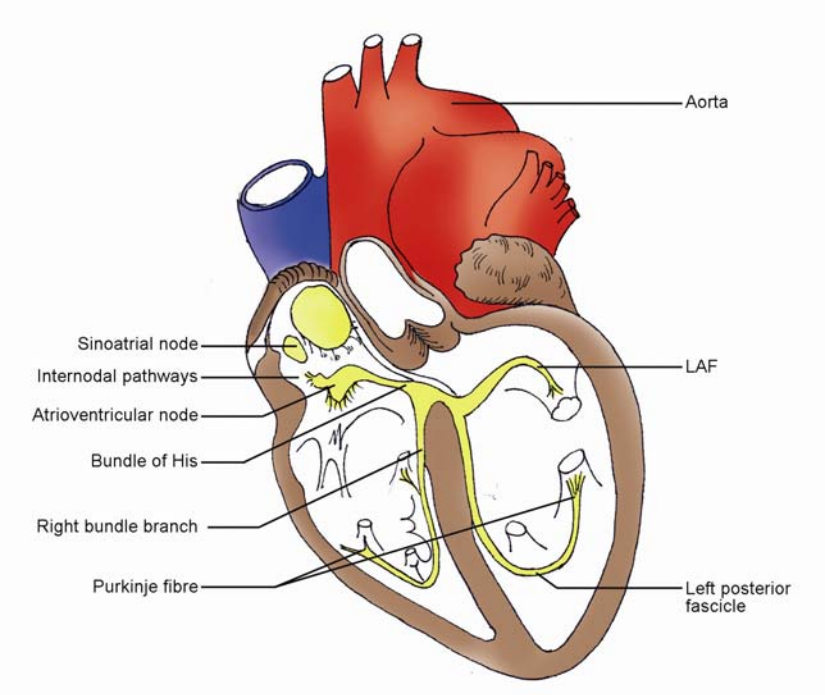

Fig. 2.1: Inrinsic conduction system of the heart

The function of the 4 heart valves is to prevent the blood from leaking back (regurgitation, incompetence) into the chamber just proximal to the valve during the corresponding part of the cardiac cycle. Thus the two semilunar valves aortic and pulmonary should prevent regurgitation into the left and right ventricle respectively during diastole. During systole the ventricle and corresponding great artery are in continuity as the valve is open. If these valves are stenosed (narrowed) the problem will be in systole when the ventricle has to get the blood through the valve. The two atrio-ventricular valves, the mitral and tricuspid have to prevent regurgitation into the left atrium and right atrium respectively during ventricular systole. If these valves are stenosed (narrowed) the problem will be in diastole when the atrium has to get the blood through the valve into the corresponding ventricle.

Check Your Progress 1

1) What is the function of the heart valves?

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2) Does the mitral valve remain open or closed during ventricular diastole?

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2.2 CARDIAC CYCLE

The term cardiac cycle means one pumping cycle which consists of contraction (systole) and relaxation (diastole) of both the atria and both ventricles. Both the atria contract at the same time and as they relax both the ventricles contract which gives a sequential pumping action to the heart. The atria remain relaxed during part of the ventricular relaxation (diastole) and then the cycle starts over again.

The pressure changes in the left ventricle, aorta and left atrium and the corresponding phase of the ECG, heart sounds and changes in the ventricular volume are shown in the figure below:

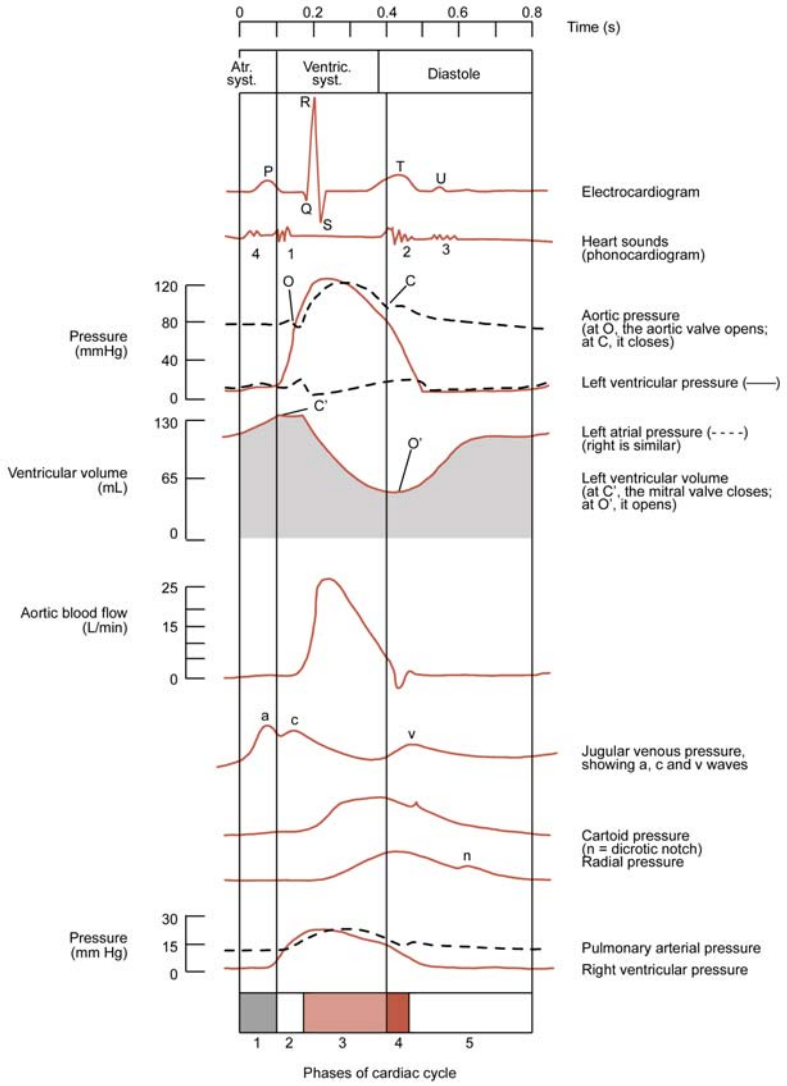

Fig. 2.2: Events of Cardiac Cycle

The phases of the cardiac cycle are:

1) **Atrial Systole**

This begins with the P-wave of the ECG. The atrio-ventricular valves are open and the ventricles are relaxed (diastole) and are filling with blood. The semilunar valves are closed and blood does not leak back from the aorta into the ventricles.

2) **Isovolumetric Contraction**

This term means that the internal volume of the ventricle is not changing. This phase starts with the R-wave on the ECG and the 1st heart sound. It is the brief initial phase of ventricular systole when the atrio-ventricular and semilunar valves are closed and the ventricular pressure rapidly builds up to open the semilunar valves.

3) **Ejection**

During the ejection phase of systole the semilunar valves are opened when the pressure gradient of the ventricles exceeds the pressure in the aorta and pulmonary artery. There is a phase of rapid ejection and a later phase of reduced ejection. The ventricular volume comes down and the T-wave on the ECG corresponds to the reduced ejection. During ejection the ventricular and great artery pressures equalize. At the end of ejection a quantity of blood remains in the ventricle and this is the residual or end systolic volume.

4) **Isovolumetric Relaxation**

This is the beginning of ventricular relaxation or diastole between the closure of the semilunar valves and opening of the atrio-ventricular valves. As the ventricular pressure falls after ejection there is a pressure gradient between the great arteries and ventricles and as these pressures cross the semilunar valves close. This corresponds to the 2nd heart sound. During isovolumetric relaxation the semilunar and atrio-ventricular valves are both closed. The volume of the ventricle remains the same and the ventricular pressure falls.

5) **Ventricular (Passive) Filling**

When the diastolic pressure in the ventricle falls below that in the corresponding atrium, the atrio-ventricular valves open and there is passive filling of the ventricules. There is at first a rapid inflow (which may be accompanied by the 3rd heart sound) followed by a slow inflow or diastasis when the ventricular pressure rises gradually. Towards the end of this phase the atrium contracts and there is an augmented flow of blood into the ventricule. The 4th heart sound when heard corresponds to atrial systole.

Phase 1: Atrial Contraction

Phase 2: Isovolumetric Contraction

Phase 3: Rapid Ejection

Phase 4: Reduced Ejection

Phase 5: Isovolumetric Relaxation

Phase 6**:** Rapid Filling

Phase 7**:** Reduced Filling

6) **Atrial Pressure Wave Form**

In the left atrium the three positive waves are the ‘a’, ‘c’, and ‘v’ waves and the troughs are ‘x’, ‘y’, and ‘z’.1

The ‘a’ is due to atrial contraction and is followed by the ‘z’ trough of atrial relaxation. The ‘c’ wave is due to upward movement of the mitral cusps and the ‘x’ descent due to the downward movement of the mitral valve ring with ventricular contraction. The ‘v’ wave is due to atrial filling during the latter part of ventricular systole with the mitral valve closed. The rising pressure ends when the mitral valve opens. The ‘y’ descent follows the flow into the ventricule in diastole.

From the opening of the mitral valve to its closure the atrial and ventricular pressures are nearly identical.

7) **Right Heart Pressures and Events**

Events on the right side of the heart mirror the changes on the left side but occur slightly later. So tricuspid valve closure follows mitral closure and pulmonary closure follows aortic valve closure. Inspiration increases the negative pressure in the thorax thus increasing the venous return to the right side which results in delayed pulmonary valve closure during inspiration. This explains the physiological widening of the splitting of the 2nd heart sound on inspiration.

Check Your Progress 2

1) Describe the five phases of the cardiac cycle.

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2) What is the ‘v’ wave in the left atrial pressure tracing due to?

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3) Why does the split of the 2nd heart sound widen during inspiration?

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2.3 CARDIAC OUTPUT AND ITS DETERMINATION

The cardiac output is the volume of blood pumped from the heart every minute. It is obtained by the volume pumped with each beat (stroke volume) multiplied by the heart rate. The cardiac output increases during exercise and falls in the common type of heart failure. The stroke volume depends in part on the amount of blood in the ventricule at the end of diastole. This determines the degree of stretch of the myocardial fibre. The greater the stretch (within limits) the stronger the force of contraction and the greater the stroke volume (Starlings law of the heart).

Control of the heart rate depends on the ratio of the sympathetic (increases) and parasympathetic (decreases) impulses to the sino atrial node which is the cardiac pacemaker. Receptors sensitive to pressure are located in the carotid sinus and the wall of the arch of the aorta.When the carotid sinus detects a sudden rise in arterial pressure, impulses pass from the carotid baroreceptors to the cardiac control centre in the medulla and impulses sent through the parasympathetic system reduce the heart rate. Similar effects result from the aortic baroreceptors as well. If the blood pressure drops the heart rate is reflexly increased. Various other reflexes from anger, fear, pain, temperature, etc. also increase the heart rate.

Blood Pressure

An adequate level of pressure is needed in the arteries to keep the blood flowing through the cardiovascular system. The chief determinant of arterial pressure is the volume of blood in the arteries and the important determinants of this are the cardiac output and the peripheral vascular resistance. The resistance offered by the arterioles accounts for almost half the total resistance in the systemic circulation. The muscle in the arterial wall allows them to constrict or dilate. When they constrict, the resistance increases and the blood pressure increases. The vasomotor centre in the medulla when stimulated sends impulses via the sympathetic to the smooth muscle in the arteries, arterioles and veins which results in their constriction.

Determinants of Vascular Tone

The vascular tone increases as the arterial size decreases. The tone at any time reflects the effects of excitory and inhibitory pathways. Neurotransmitters, physical forces like shear stress, intravascular pressure, metabolites and milleu of the surrounding tissue can all affect the vascular tone. Arterial segments where the endothelium is absent can also respond to stretch-the so-called intrinsic myogenic tone.

The endothelium is an important modulator of tone. It can produce, release, activate many vasoactive factors like NO (nitric oxide), prostacyclin and thromboxane. Cholinergic stimulation releases an Endothelium derived relaxation factor (EDRF) shown to be NO. Endothelial denudation abolishes the vasodilatory effect of acetylcholine.

There are chemoreceptors in the aortic and carotid bodies which sense a rise in PCO_2 (hypercapnia) and fall in O_2 saturation (hypoxia) and changes in pH. Appropriate stimuli are sent to the medullary centers. Vasomotor control is also exercised by higher centres in the cerebral cortex and hypothalamus which send impulses to the medullary centres. Local tissue mechanisms also affect local vasoconstriction and vasodilatation.

Venous Return

This is the amount of blood that is returned to the heart by the veins. This is influenced by various factors. Inspiration decreases the pressure in the central veins and thus increases the pressure gradient between the peripheral and central veins thus augmenting venous return. Skeletal muscle contraction also milks the venous flow towards the heart and the valves in the veins prevent gravitational return backwards. Significant veno dilatation can occur with conditions like sepsis and the use of certain drugs like nitrates. This can result in a serious fall in venous return. This can result in marked deterioration in conditions like right ventricular infarction and pericardial tamponade.

Preload

If other factors are unchanged the force of contraction depends on the degree of stretch of the myocardial fibres. In effect the preload is the ventricular end diastolic volume. It is influenced by the venous return, the compliance or distensibility of the ventricle and the atrial kick or atrial

component of ventricular filling. The atrial contribution is particularly important in hypertrophied non compliant ventricules.

Afterload

The afterload is the resistance imposed by the aortic valve, aorta and peipheral arterial resistance. The left ventricule has to develop sufficient tension to overcome the afterload. This becomes increasingly difficult with a failing heart. Afterload reduction is therefore one of the targets in heart failure therapy.

Check Your Progress 3

1) What are the factors in fluencing the venous return to the heart?

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2) Name two factors that influence myocardial contractility?

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2.4 THE FUNDAMENTAL CARDIAC UNIT

The fundamental contractile unit is the sarcomere. Each muscle cell apart from the nucleus, mitochondria and other structures contains parallel fibrils. Sarcomere is a subunit of the fibril. It consists of parallel actin and myosin filaments. The thin actin filaments are attached to its limiting membrane or the Z line and interdigitates with the thicker myosin filaments which are placed centrally. The myosin filaments have flexible heads which can come into contact with the actin filaments. The filaments are propelled past each other by the repeated making and breaking of cross bridges between the actin and myosin filaments. In the resting state when the calcium level is low the myosin binding sites on the actin filament are blocked by tropomyosin which is a regulatory protein. This prevents cross bridge formation. When there is activation and a rise in calcium, the myosin actin binding sites are exposed. The energy required for the cross bridge recycling is provided by adenosine tripshophate (ATP). The number of cross bridges depends on the available calcium molecules. The greater the number of bridges, the more forceful the resulting contraction. During systole there is a 50 fold increase in intracellular calcium concentration.

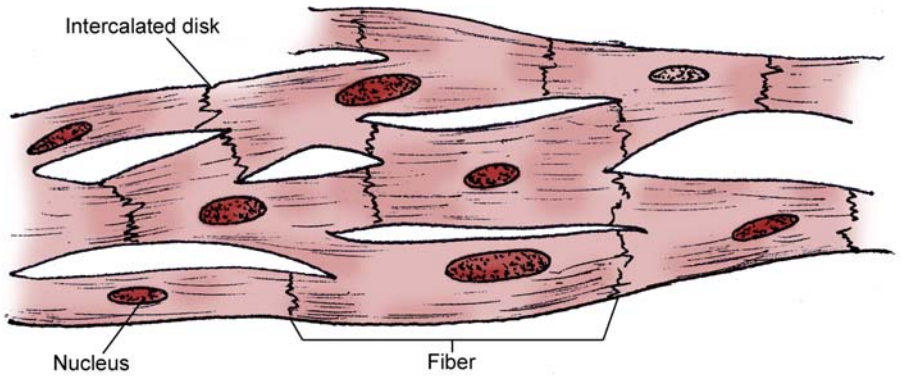

Fig. 2.3: Cardiac muscle

Myocardial Energetics

The oxidation of substrates like free fatty acids (FFA), glucose, lactate and ketone bodies results in the energy of Adenosine triphosphate (ATP) and Creatine phosphate (CP). The substrate used depends on several factors like its level in the blood, level of insulin and catecholamine level. In the resting, fasting state 70-80 per cent of the oxygen consumption can come from the oxidation of FFA. With high glucose levels and resulting high insulin levels the fuel shifts to glucose. Glucose is phosphorylated to glucose 6 phosphate. It is either synthesized to glycogen or enters glycolysis with pyruvate as the end product. Lactate is used as the major fuel when its level increases with severe exercise. Lactate may leave the myocardium or if acetylated to acetyl coenzyme A enters the tricarboxylic acid cycle. Catecholamines increase lipolysis and thus increase the FFA levels. Normally free fatty acids are the main substrate. In ischaemia the glycolytic pathway is stimulated. This cannot substitute for oxidative phosphorylation and inevitably ischaemia thus leads to a fall in ATP levels. This impairs myocardial function.

Contractility

Myocardial contractility is mostly dependent on the level of sympathetic nerve activity and is also increased by circulating catecholamines and inotropic drugs like dopamine and dobutamine. With increased contractility there is an increased oxygen demand which is out of proportion to the extra work performed. These factors become critical when there is a decrease in oxygen supply as with coronary artery disease.

2.5 LET US SUM UP

The heart is the muscular pump that pushes blood through the circulatory system. Each heartbeat can be felt as an arterial pulse. The heart valves when closed prevent the blood from leaking back into the heart. Understanding the cardiac cycle in reference to the opening and closing of the heart valves and genesis of the heart sounds is central to appreciating changes in valvular heart disease. The cardiac output is the volume of blood pumped out of the heart during each beat and is expressed as litres/minute. The pressure in the arteries, arterioles and veins is maintained by the vascular tone. This tone is adjusted through autonomic impulses from the vasomotor centre in the medulla. The centre is influenced by afferent impulses from many areas like the carotid body, aortic arch and chemoreceptors.

2.6 ANSWERS TO CHECK YOUR PROGRESS

Check Your Progress 1

1) Basically to prevent the backward flow of blood (leak) when the valve closes.

2) Open, to allow filling of the left ventricle.

Check Your Progress 2

1) Phase 1: Atrial Contraction

   Phase 2: Isovolumetric Contraction

   Phase 3: Rapid Ejection

Phase 4: Reduced Ejection

Phase 5: Isovolumetric Relaxation

Phase 6: Rapid Filling

Phase 7: Reduced Filling

2) Filling of the left atrium during ventricular systole (atrial diastole).

3) Inspiration increases the negative pressure in the thorax thus increasing the venous return to the right side which results in delayed pulmonary valve closure during inspiration. This explains the physiological widening of the splitting of the 2nd heart sound on inspiration.

Check Your Progress 3

1) Inspiration decreases the pressure in the central veins and thus increases the pressure gradient between the peripheral and central veins thus augmenting venous return. Skeletal muscle contraction also milks the venous flow towards the heart and the valves in the veins prevent gravitational return backwards.

2) Myocardial contractility is mostly dependent on the level of sympathetic nerve activity and is also increased by circulating catecholamines and inotropic drugs like dopamine and dobutamine.Contractility also increases with the fibre length.