CHAPTER - 00
BODY FLUIDS AND CIRCULATION

Every cell needs a regular supply of nutrients, O_2 etc to provide energy for growth and repair and constant removal of wastes like CO_2, NH_3, urea etc, to maintain homeostasis. In lower aquatic animals, these are carried out by diffusion, osmosis, active transport, cyclosis etc. In higher organisms, there is no direct supply of the useful materials into the cells or removal of waste from the body cells. So there is a need of an internal transport system.

All advanced animals, possess specific body fluids and its circulation for continuous supply of O_2, nutrients and other essential materials and a constant removal of CO_2 and other wastes. Our circulatory system circulates an extracellular fluid to the different parts of the body. Nutrients, waste products, respiratory gases, metabolic intermediates, informational molecules are transported through this circulating fluid.

In lower animals water from the surrounding medium used as circulating fluid $\rightarrow$ water circulatory system

Eg: Sponges - Water Canal System
Cnidarians - Gastro vascular system } Extra organismic circulation
Echinoderm - Water vascular system

Blood vascular system present in higher invertebrates like annelids, arthropods, molluscs, lower chordates and all vertebrates.

Two types of blood vascular system

1. **Open circulation**

   • found in arthropods, most molluscs, some annelids, hemichordates, urochordates

   • blood flows through open spaces and body cavities - sinuses

   • slow and less efficient circulation, cannot be regulated

   • direct exchange of materials between blood and cells

2. **Closed circulation**

   • found in most annelids, some molluscs(cephalopods) chordates.

   • blood flows through closed network of blood vessels

   • fast and more efficient circulation, can be regulated

   • exchange of materials occurs through tissue fluid

Human circulatory system

William Harvey - Father of circulation and modern physiology

Blood vascular system $\rightarrow$ Blood + Blood vessels + Heart

Lymphatic system $\rightarrow$ Lymph + Lymph vessels + Lymphoid tissues

Blood - Haematology

- specialised connective tissue - mesodermal origin
- fluid connective tissue have fluid matrix (plasma) and floating cells (blood corpuscles).
- adult body contains 5 - 6 litre, 55% plasma + 45% formed elements

Plasma - is a straw coloured/faint yellow coloured, slightly alkaline(7.4)viscous fluid contains mixtue of organic and irorganic constituent. It contains 90 - 92% H_2O, 6 - 8% plasma proteins, small amount of nutrients, nitrogenous wastes, respiratory gases, regulatory substances, electrolytes etc.

- plasma proteins - Albumin(osmotic balance), Globulins(defence) Fibrinogens and prothrombin(blood clotting).
- Clotting factors found in inactive form which are activated during coagulation process. Plasma without clotting factor is called **serum**
- nutrients like glucose, aminoacids. lipids, vitamins etc are always in transit in the body.
- nitrogenous wastes- urea, NH_3, uric acid, creatinine etc.
- regulatory substances- hormones, enzymes, vitamins, antibodies etc.
- dissolved mineral ions - Na^+, K^+, Ca^{++}, Mg^{++}, Cl-, HCO_3^-, PO_4^{3-} etc.

Formed elements/Blood corpuscles

RBC, WBC and platelets together constitute 45% of blood.

RBC - Erythrocytes

- most prevalent blood cells, formed from bone marrow precursor cell, erythroblast- erythropoiesis
- biconcave disc like with a diameter of 7 - 8 mm, 1 -2 mm thickness.
- devoid of nucleus/enucleated
- Hb content helps in gas transport, 270 - 280 million Hb/RBC
- carbonic anhydrase helps in CO_2 transport
- liver and spleen perform erythropoiesis during foetus stage.
- RBC count $\rightarrow$ 5 - 5.5 million/mm^3, life span - 120 days
- worn out RBCs are destroyed in liver and spleen(grave yard)
- Hb count $\rightarrow$ 12 - 16 gm/100ml, low Hb/RBC count leads to anaemia
- low RBC count $\rightarrow$ erythrocytopenia, high RBC count $\rightarrow$ polycythemia
- PCV (packed cell volume of blood) / Haematocrit value of blood $\rightarrow$ percentage volume of

RBC in blood - (40 - 45%)

WBC - Leucocytes

WBCs	Diagram	Nuclear shape	% of all WBCs	Functions
Neutrophils		Multilobed	60 -65%	phagocytosis, micropolicemen
Eosinophils		Bilobed	2-3%	allergic reactions resist infections
Basophils		S' shaped	0.5 - 1%	liberate histamine serotonin and heparin
Lymphocytes		Oval	20- 25%	produce antibodies, immunity
Monocytes		Kidney shaped	6-8%	phagocytosis - macrophages.

- most active and motile constituents of blood and lymph.
- colourless, nucleated, short lived, and defensive cells.
- wandering amoeboid cells, can change their shape and capable of squeeze out of blood capillaries by amoeboid movement, called diapedesis
- WBC count/TLC/Total Leucocyte Count $\rightarrow$ 6000 - 8000/mm^3.
- low WBC count $\rightarrow$ leucopenia, high WBC count $\rightarrow$ leucocytosis.

WBCs are broadly grouped into two categories

1. Granulocytes - Cells containing granules and polymorphic nucleus (PMNL) - Polymorpho Nuclear Leucocyte

a) Neutrophils $\rightarrow$ most abundant WBC(60 - 65%)

- chief phagocytic cells which destroy foreign organisms
- multilobed nucleus

b) Basophils $\rightarrow$ found in least proportion (0.5 - 1%)

- release histamine, serotonin and heparin
- involved in inflamatory reactions

- 2 - 3 lobed nucleus

c) Eosinophils → 2-3%, resist infections.

- produce anti-toxins against allergic conditions
- play role in parasitic infections, allergic and hyper sensitivity reactions etc
- bilobed nucleus

2. Agranulocytes

a) Monocytes → 6 - 8%, largest WBC,

- possess eccentric and bean shaped nucleus
- motile and phagocytic, engulf microbes and cellular debris
- can change into connective tissue macrophages

b) Lymphocytes → 20 - 25%, small cells with large round nucleus

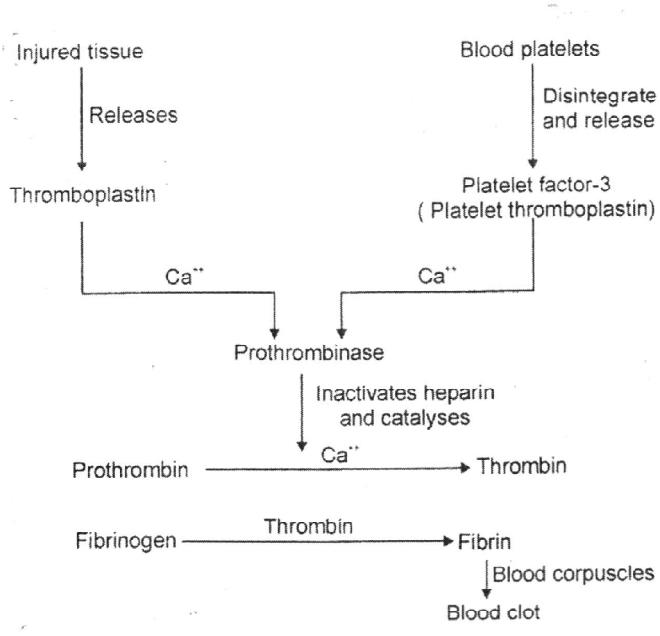
- produce serum globulins and play a key role in immunity.
- B - lymphocytes provide antibody mediated immunity - AMI
- T - lymphocytes provide cell mediated immunity - CMI

Thrombocytes/Platelets

- smallest blood cells, 2 - 3mm dm, life span about one week
- colourless, non-nucleated, irregular cells involved in clotting process.
- cytoplasmic fragments derived from megakaryocytes of bone marrow
- release platelet factors essential for blood coagulation.

Coagulation of Blood - Haemostasis

BLOOD COAGULATION



The mechanism which results in the sealing off a leaking or severed blood vessel to stop bleeding is called haemostasis. Inside an intact blood vessel, blood doesnot coagulate due to the presence of active anticoagulants like heparin, antithrombins etc. As soon as a blood vessel is ruptured, the injured area initiates the formation of a clot. Inactive procoagulants in the blood become active, overcome anticoagulants and cause blood coagulation.

• an injury stimulate platelet disintegration to release certain factors $\rightarrow$ intrinsic factors(platelet thromboplastin)

• injured tissue also release certain factors to initiate blood coagulation $\rightarrow$ extrinsic factors(Tissue thromboplastin).

• an enzyme complex called thrombokinase/prothrombinase is formed by a cascade process - a series of enzymatic reactions involving tissue factors, plasma factors and Ca^{++}

• prothrombinase inactivate anticoagulants and catalyse the conversion of inactive prothrombin into active thrombin

• thrombin convert inactive fibrinogen into active fibrin.

• fibrins form a network over the injury site which trap dead and damaged formed elements to form a dark reddish brown scum called clot/coagulum

Natural anticoagulants $\rightarrow$ Heparin, Antithrombin, Hirudin etc.

Anticoagulants used in blood banks

$\rightarrow$ EDTA - Ethylene Diamine Tetra Acetic acid

$\rightarrow$ CPD - Citrate Phosphate Dextrose

$\rightarrow$ ACD - Acid Citrate Dextrose

Blood groups

Blood grouping is a classification of blood based on the presence or absence of specific antigenic substances on the surface of RBC, Antigens are complex molecules such as proteins, glycoproteins, glyco lipids etc that are genetically unique to each individuals except identical twins. They occur on the surface of all cells and enable the body to distinguish its own cells from foreign matter. When the body detects an antigen of foreign origin, it activates an immune response.

More than 30 commonly occuring antigens and hundreds of other rare antigens are already identified on the surface of RBC. Most of the antigens are weak. Each of the antigens at times cause antigen- antibody reaction. Two particular types of antigens are much more likely than others to cause blood transfusion reactions. They are ABO grouping and Rh grouping.

ABO grouping

Blood Groups and Donor Compatibility				
Blood Group	**Antigen and RBCs**	**Antibodies in Plasma**	**Donor's Group (Can get blood from)**	**Recipient's Group (can give blood to)**
A	A	anti B	A, O	A, AB
B	B	anti A	B, O	B, AB
AB	A,B	None	A,B,AB, O	AB
O	None	anti A, B	O	A, B, AB, O

Karl Landsteiner $\rightarrow$ Father of blood gp - discovered A, B and O group.

AB blood group by Alfred Von Decastello and Adriano sturli

ABO grouping is based on two surface antigens/agglutinogens on the RBC(namely A and B) and two corresponding plasma antibodies(namely anti-A and anti-B)

A person may have neither of them or one of them or both of them. ABOblood type is controlled by a single gene(Isoagglutinogen gene) with 3 types of alleles - I^A, I^B and i. The gene located on the long arm of the 9th chromosome.

On the basis of nature of antigens and antibodies present, 4 types of blood in ABO grouping - A, B, AB, O

O group - Universal donor, AB group - Universal recipient

ABO incompatibility during blood transfusion

Blood transfusion means transfer of blood/blood products like packed RBC, plasma, platelets etc. When an incompatible blood is transfused, then reaction occurs between **donor's antigen** and **recipient antibody**, causing the clumbing of donor's blood inside the blood vessels of the recipent. It results in the blockage of blood vessels which may be fatal to the recipient.

Rh grouping

Rh antigen/Rhesus factor is an another antigenic protein present on the surface of RBC. Landsteiner and Alexander Wiener discoverd this antigen on the RBC of Rhesus monkey and many human beings. Nearly 80% of human have Rh factor on RBC, called Rh^+ and those who devoid of this antigen is Rh^- negative. Phenotypically, Rh^+ and Rh^-ve individuals are normal. The problem arises when an Rh^-ve prerson is exposed to Rh^+ve blood during blood transfusion or pregnancy

Rh incompatibility during blood transfusion

Normally human blood doesnot contain any antibody for Rh factor. So the first transfusion of Rh^+ blood into the person with Rh^- ve blood causes no harm. However, the recipient starts preparing antibodies(anti Rh factor) against Rh antigen. Any subsequent transfusion of Rh^+ve blood to the same patient will cause destruction of RBCs in recipient body.

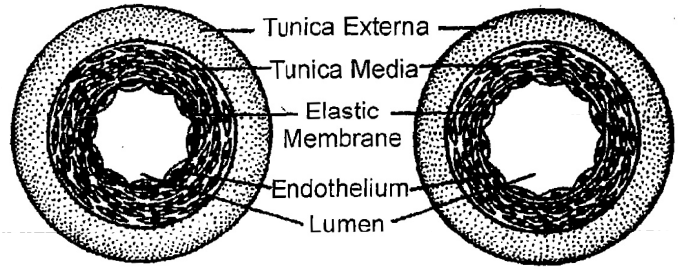
Rh incompatibility during pregnancy- Erythroblastosis foetalis

It is a special case of Rh incompatibility between Rh^-ve mother and her Rh^+ve foetus. Rh antigens of the foetus donot exposed to the maternal blood in the 1st pregnancy as the two bloods are well separated by placenta. At the time of delivery, there is a possibility of exposure of the maternal blood to small amount of foetus blood. In such cases, the mother starts preparing antibodies against Rh antigen. In case of her subsequent pregnancies, the Rh^- antibodies from the mother can leak into foetal blood and destroy the foetal RBC. This could be fatal to the foetus or could cause severe anaemia and jaundice. This can be avoided by administering anti- Rh antibodies to the mother immediately after the delivery of the first child / twenty eighth weeks of pregnancy.

Lymph/Tissue Fluid

- lymphatic system consist of lymph, lymph vessels, lymphoid tissues like lymphnodes, spleen, thymus etc.
- lymph is a colorless fluid present in the lymphatic system
- it is a transparent fluid derived from blood and other tissues, which accumulates in the interstitial space - interstitial fluid/tissue fluid
- it is similar to blood except RBC, large proteins etc.
- it contains water and watersoluble substances, lymphocytes, nutrients, gases, mineral ions, lesss proteins etc.
- an elaborate network of lymph capillaries and vessels collects this fluid and drains it back to major veins.
- lymph act as a middle man for the exchange of nutrients and gases
- it is an important carrier for nutrients, hormones, metabolic wastes etc.
- it helps in absorption of fat through lacteal present in villi.
- lymphocytes generated from lymph nodes responsible for immune response.

Blood vessels - Arteries, Veins and Capillaries $\rightarrow$ Angiology



- Basically wall of arteries and veins formed of 3 layers

1. **Tunica externa**- outermost layer, formed of collagen rich connective tissue.

2. **Tunica media**- middle layer formed of smooth circular muscle fibres and elastic fibrous connective tissue.

3. **Tunica interna** - innermost layer, formed of inner endothelium and outer layer of yellow fibrous tissue

Artery - is a blood vessel that carries blood away from the heart to the various parts of the body.

- carry oxygenated blood, except pulmonary artery
- wall is more thicker and elastic than veins
- deep seated vessels, without valves
- blood pressure is high and faster flow, narrow lumen compared to vein.

Vein - brings blood from the various parts of the body to the heart.

- carry deoxygenated blood, except pulmonary vein
- wall is thinner and less elastic
- superficially observed vessels, valves present to prevent backflow.
- blood pressure is low and slower flow, wide lumen compared to artery

Types of Circulation

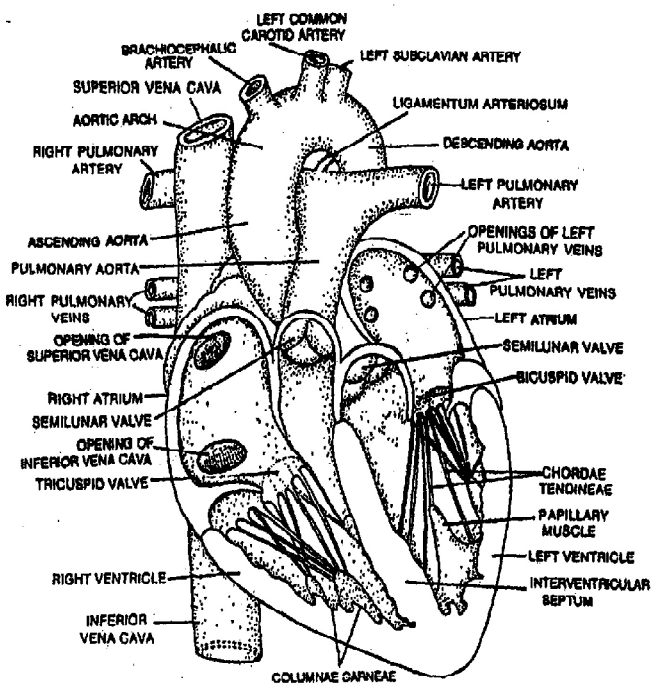
1. Single circulation - Found in fishes. They possess two chambared heart with an atrium and a ventricle. Heart pumps out only deoxygenated blood(venous heart), which is oxygenated by the gills and supplied to the body parts directly, from where deo_2 blood is returned to the heart.

2. Incomplete double circulation - Found in amphibians and reptiles, except crocodilians. They possess three chambered heart with two atria and a sigle ventricle. Left atrium receives oxygenated blood from the gills/lungs/skin and the right atrium receives deoxygenated blood from other body parts. However they get mixed up in the single ventricle which pumps out mixed blood.

In reptiles an incompletely partitioned ventricle is present.

3. Complete double Circulation- Found in aves, mammals and crocodiles. They possess tetralocular heart with two atria and two ventricle. Oxygenated and deoxygenated blood received by the left and right atria respectively passes on to the ventricles of the same sides. The ventricle pump it out without any mixing up.

Heart - Cardiology



Internal structure of human heart.

• muscular, contractile, automatic organ concerned with collection and pumping of blood- mesodermal origin.

• size - 12 cm × 9 cm, 250-300 gm wt, size of a clenched fist

• lies behind the sternum and between lungs in a space called mediastinum

• its conical apex slightly tilted towards left side.

• heart is protected by a double walled pericardium

• pericardial fluid protects heart from shake, shock and friction

• wall of heart consists of epicardium, myocardium and endocardium

• tetralocular heart with 2 thin walled atria and 2 thick walled ventricles. Left ventricular wall is thickest.

• heart chambers are separated by septa and valves.

• right and left atria are separated by inter atrial septum, bears an oval depression called fossa ovalis. It is the remnant of foramen ovale- an opening in the inter atrial septum of foetus. If foramen ovale is left open after birth- refers a hole in the heart - patent foramen ovale (PFO)

• right and left ventricles are separated by inter- ventricular septum

• atrio- ventricular septum separate atria and ventricles(AV septum) - thick fibrous tissue

• right auriculo- ventricular aperture is guarded by tricaspid valve.

• left AV aperture is guarded by bicuspid/mitral valve.

• the cusps of the valves are held in their position by fine elastic cords called **chordae tendinae** connected to **papillary muscles**.

• right atrium receives deoxygenated blood from **superior venacava**, **inferior venacava** and **coronory sinus**.

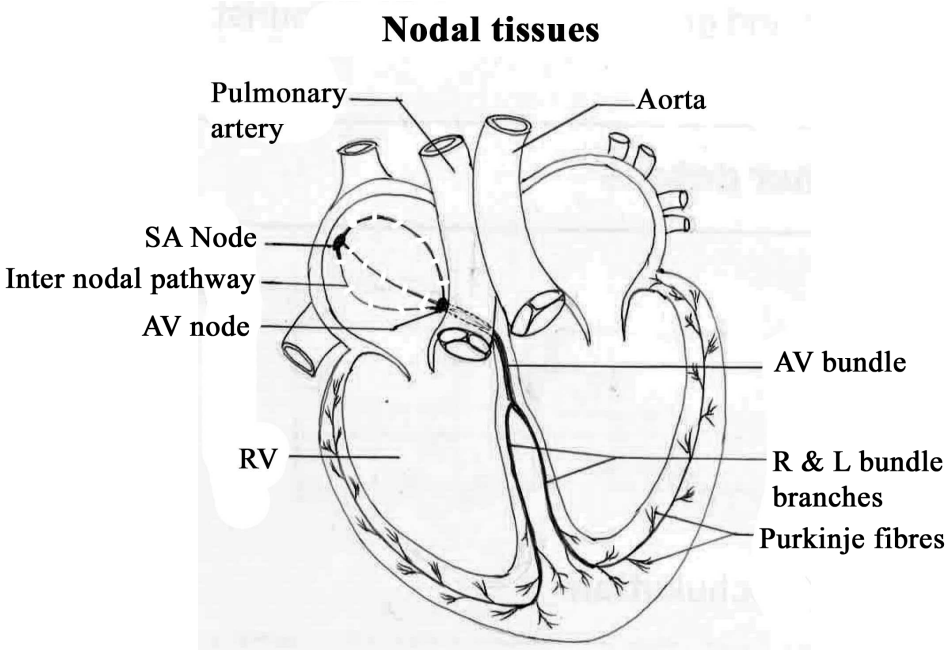
• left atrium receives oxygenated blood from two lungs through four **pulmonary veins**.

• right ventricle opens into pulmonary trunk, guarded by a pulmonary valve (semilunar).

• left ventricle opens into aorta, guarded by aortic valve (semilunar).

• aortic arch give rise to **brachio-cephalic artery**, **left common carotid** and **left subclavian** artery- supply blood towards shoulders, arms and head region. Brachio cepholic artery then give rise to **right common carotid** and **right subclavian artery**.

Nodal tissues



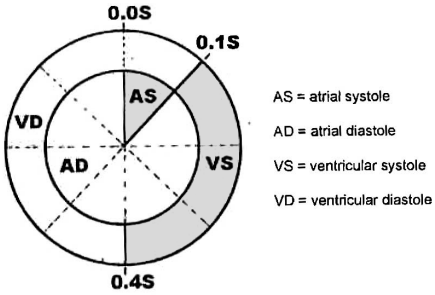
Human heart is **myogenic**, ie, cardiac impulse is generated and transmited by specialised cardiac musculature called nodal tissues. This specialised excitatory and conductive system consists of SA node, internodal pathways, AV node, AV bundle and purkinjee fibres.

Sino-atrial node situated on the right upper corner of right atrium near the opening of precava. It is called **pacemaker** because it functions as originator of cardiac impulse. **Atrio- ventricular node** lies in the lower left corner of right atrium, close to AV septum. It is called **pace setter**, as it generates impulse after being stimulated by SAN. Another bundle of nodal fibres called **AV bundle** arise from AVN which passes through AV septa to emerge on the top of the inter ventricular septum. AV bundle immediately divides into right and left bundle and then give rise to minute fibres throughout the ventricular musculature called **purkinjee fibres**. Among nodal tissues, SAN can generate maximum no: of action potentials (70 – 75/min)

Cardiac cycle

The sequence of events in the heart which is cyclically repeated during heart beat is called cardiac cycle. It consists of systole and diastole of both the atria and ventricles. Contraction phase is called systole and relaxation phase is called diastole. Average heart rate in human is 72 times/min. So the duration of single heart beat is 0.8sec. A single cardiac cycle involves events like. **Atrial Systole** (AS - 0.1 sec), **Atrial Diastole**(AD- 0.7sec), **Ventricular Systole**(VS - 0.3 sec), **Ventricular Diastole**(VD- 0.5sec) and **Joint Diastole**(JD- 0.4 sec).

Cardiac cycle



Joint diastole

• both atria and ventricles are in a relaxed state - 0.4 sec

• tricuspid and bicuspid valves remain open

• semilunar valves remain closed

• blood from the pulmonary veins and venacava flows into the Lt and Rt atria respectively.

• as the AV valves remain open, most of the blood (~70%) passively enters the ventricles from their respective atria

• rest of the blood is pumped into the ventricles by the contraction of atria.

Atrial systole - 0.1 sec

• SAN generated action potential spreads throughout atria cause atrial systole. As the atria contract, atrial blood empties into their respective ventricle and there by ventricular filling is completed.

• during atrial systole, blood flows into the atria stops, as the bases of venacava get closed by the contracting atrial wall.

• soon after systole, the atria enters into diastolic phase, for the next 0.7 sec- Atrial diastole

• atrial diastole coinciding with ventricular systole

Ventricular systole - 0.3 sec

Action potential conducted to the ventricular side by the AVN and bundle of His, from where the purkinje fibres transmits it throughout the ventricular musculature $\rightarrow$ **ventricular depolarisation**. Consequently ventricles contract and the pressure inside the ventricle increases, causing the closure of AV valves to prevent the backflow of blood into the atria. It produce the Ist heart sound/systolic sound called lub $\rightarrow$ low pitched and longer duration sound.

As the ventricular pressure increases further, the semilunar valves forced to open. Ventricular blood now forcefully pumped into the pulmonary trunk and aorta

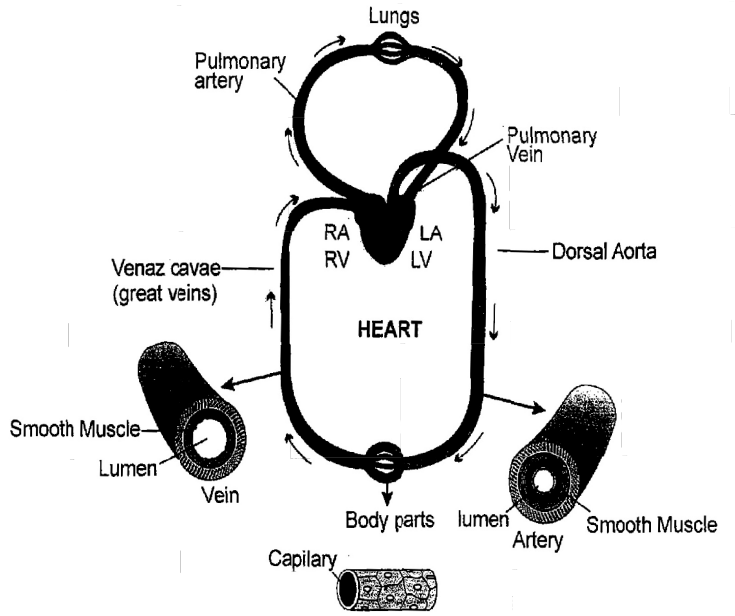
Ventricular diastole - 0.5sec

Ventricle now relax and the ventricular pressure falls due to ventricular repolarisation. It causes the closure of semilunar valves which prevent the backflow of blood into the ventricles. It produce the 2nd heart sound/dioastolic sound called dub → high pitched and shorter duration. As the ventricular pressure declines further, the tricuspid and bicuspid valves are pushed open by the pressure in the atria exerted by the blood. The atrial blood now once again moves freely to the ventricles.The ventricles and atria are now again in a joint diastole state, as earlier.

Amount of blood pumped out from each ventricle during ventricular systole is called **stroke volume**/beat volume - about 70ml/beat. Volume of blood pumped out by each ventricle per minute is called cardiac output/minute volume.

Cardiac output = stroke volume × heart rate, 70 × 72 = about 5 L

Double circulation-



Schematic plan of blood circulation in human

Blood flows through the human heart twice for completing a circuit / to supply once to the body. It involves a greater circulation called **systemic** and a lesser circulation called **pulmonary**.

1. Systemic circulation- The back and forth circulation of blood between heart and various body parts. It involves the flow of oxygenated blood from the left ventricle to all parts of the body through arterial system and deoxygenated blood from all parts of the body to the right atrium via venous system. Systemic circulation provides nutrients O_2 and other essential substances to the tissues and takes CO_2 and other harmful substances away for elimination.

2. Pulmonary Circulation - The back and forth circulation of blood betwen heart and lungs. The flow of deoxygenated blood from the right ventricle to the lungs through pulmonary artery and oxygenated blood from the lungs to left atrium via pulmonary veins. Pulmonary circulation meant for oxygenation of blood and removal of CO_2.

Coronary circulation- The to end fro circulation of blood between heart and heart muscles. The **right and left coronary arteries** arise from the base of ascending aorta supply oxygenated blood to the heart walls. **Coronary veins** brings deoxygenated blood to the **coronary sinus**, which in turn carries to right atrium.

Portal circulation - A vein first collect blood from capillary system of one organ and distributes the blood to some other organs by capillary system instead of sending it to the heart is called a portal vein. A portal vein and its branches collectively form a portal system.

1. Hepatic portal system, present in all vertebrates. A hepatic portal vein carries nutrient richblood from gut to liver.

2. Hypophyseal portal system, is a minor portal system found only in mammals. It enables the hormones of hypothalamus to reach adenohypophysis of pituitary.

Electrocardiogram- ECG

• graphical representation of the electrical actvity of the heart during a cardiac cycle. Electrocardio graph is the machine used to obtain electrocardiogram. Father of ECG- William Einthoven.

To obtain a standard ECG, a patient is connected to the machine with three electrical leads, one to each wrist and to the left ankle. For a detailed evaluation multiple leads are attached to the chest region are used.

A standard ECG has the following waves

P wave - is a small upward wave that indicates electrical excitation or depolarisation of atria which leads to atrial contraction.

QRS complex - is a complex of 3 waves (Q. R. S.), represents the depolarisation of ventricle which initiates ventricular contraction.

T wave - indicates ventricular repolarisation, means return of ventricles from excited to normal state. The end of the T-wave marks the end of systole.

Since normal ECG has a fixed wave pattern, any deviation from it indicates an abnormality or disease.Hence it is of a great clinical significance. By counting the number of QRS complexes that occur in a given time period, one can determine the rate of heart beat of an individual.

Regulation of cardiac activity

Human heart is myogenic, normal cardiac activities are autoregulated by specialised muscular tissue called nodal tissues. But the rate of heart beat is influenced by both neural as well as hormonal system.

A special neural centre(cardiac centre) in the medulla oblongata can moderate the cardiac functions through ANS. Sympathetic nerves can increase the rate of heart beat and cardiac output through the secretion of neurotransmitter(nor- adrenaline). Parasympathetic neural signals decrease the rate of heart beat and cardiac output by the release of Ach. Adrenal medulla accelerate heart beat and cardiac output by secreting adrenaline in response to emergency.

Disorders of circulatory system.

Hypertension and Hypotension

The pressure exerted by the flow of blood on the elastic walls of the arteries is called blood pressure. The instrument used to measure B.P is called sphygmomanometer. Bp is usually taken from left brachial artery of upper arm.

Systolic BP $\rightarrow$ pumping pressure, Diastolic BP - Resting pressure

Normal BP $\rightarrow \frac{120}{80}$ mmHg / 120 over 80.

Pulse pressure means pressure difference between systolic Bp and diastolic Bp = 40 mm Hg i.e., 120 - 80 = 40 mm Hg

Hypertension denotes high blood pressure, sustained rise in arterial Bp with systolic more than 140 and diastolic 90, ie $\frac{140}{90}$ or higher. Hypertension is called silent killer, leads to heart diseases and also affects vital organs like brain, kidney etc.

Hypotension means persistant low B P with systolic below 90 and diastolic below, 60, ie $\frac{90}{60}$ or below.

Coronary Artery Disease - CAD/Atherosclerosis

It is wall thickening and narrowing the lumen of medium and large arteries supplying blood to heart muscles. It can cause angina and heart attack. It is caused by deposits of calcium, fat, cholesterol, fibrous tissue etc within tunica interna and tunica media of arteries.

Angina pectoris - symptom of acute chest pain due to deficiency of O_2 in heart muscle - ischaemia. It may due to insufficient blood supply to its muscles due to obstruction of coronary arteries.

Heart attack / Myocardial infarction - damage or death of a part of the heart muscle due to inadequate blood supply/oxygen supply. It can cause cardiac arrest and death.

Cardiac Arrest - stoppage of heart beat and cause death

Heart Failure - also called congestive heart failure(CHF), because congestion of the lungs is one of the main symptom. It is a state of heart when it is not pumping enough blood to meet the needs of the body.